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- 5 Keep table formatting simple and consistent. A common error is to place a column of separate items into a single table cell, with each item separated by a hard return: instead each data item should have a table cell of its own. Sometimes tables are formatted with tabs instead of cells:

in this case, the key is to set the tab stops for the whole table so that one tab equals one column.

- 6 Image files should be sent as separate files. The same goes for Excel spreadsheets or charts. If you are embedding images in the file, it is probably best to do it at the end, after the text and references.
- 7 Be prepared to send the data used to generate graphs. Some publishers will use the data to regenerate the graphs according to their own style rules. In such a case, it helps if you send only the data that are actually shown in the graphs – not the spreadsheet with all of the data generated in the study.

What about PDF?

Send your Manuscript in a Word file. Don't send it as PDF or any other word processor format.

PDF files are not editable in the same way as word processor files. Some publishers will ask for, or even create, a pdf file of your manuscript for use during the peer review process, but a Word file will also be required for editing and production.

Tips for preparing images

Do not make electronic images too small. No effective way exists to increase the resolution of an image beyond its original size, and if an image is reduced in size and saved, picture data is permanently lost. Image files therefore have to be created and saved at high resolution. For a colour image that is to be printed as 4 X 4 in., the required size is $(4 \times 300) \times (4 \times 300) = 1200 \times 1200 = 1440\ 000$ dots. In many image formats (e.g. tagged image file format, or tiff), each dot will take eight bits (one byte) to store, so the image file will be 1.44 megabytes

Compression techniques can reduce the size of the image file. Zip compression is safe, because it uses an algorithm that packs the data tighter without throwing any of it away; In Compression during which files are saved in jpeg format, select the option for large file size (maximum picture quality).

Guidelines for Reviewers

Purpose of Peer Review

The purpose of peer review for *The Journal of the Egyptian Society of Cardio-Thoracic Surgery (JESCTS)* is twofold. One is to evaluate objectively the science of the submitted paper and the other is to provide a constructive critique indicating how the paper could be or could have been improved by the authors. Reviewers should respect the authors' efforts and avoid disparaging or unpleasant comments. Reviewers are not asked to copyedit papers, but should comment if language editing is needed.

Acceptance of a Manuscript for Review

Reviewers should accept assignments to review manuscripts that are within their sphere of expertise, which they plan to review within the 21 day deadline. Reviewers should decline assignments for which a conflict exists between the reviewer and authors or between the reviewer and commercial products that are integral to the content of the article.

Category of the Manuscript

The broad categories of papers for which peer review is undertaken are (1) original scientific articles; (2) new technology papers; (3) case reports, how to do it articles and images; and (4) review articles. The editor and/or associate editors review correspondence, invited commentaries, editorials, surgical heritage submissions and ethical and statistical papers.

General Requirements for Publication

The paper should conform to the format and restrictions for the category to which it belongs and be written in good, readable English. The paper should address an important or interesting subject and provide new and original information. Illustrative material should be well chosen and of good quality.

Original Scientific Article

Original scientific articles should provide new, reliable information that is relevant to the science and practice of cardiac and general thoracic surgery. The reviewer should assess the articles' interest to readers; strengths and weaknesses; originality; clarity of text, tables, illustrations and figure legends; presentation; analysis of results; credibility of results; importance of the findings; depth of scholarship; relationship of the results to the existing literature; and presence of marginally relevant or unnecessary archival material. Ethical issues, such as prior publication of all or part of the data; plagiarism; transgression of human or animal rights; or dishonesty should be noted, if detected.

Original scientific articles are usually one of three types: prospective, retrospective, or observational studies. For prospective studies the protocol of the study is planned

before data are collected. The most common form is the 'Prospective, randomized controlled trial', which is well suited for many experimental animal studies and some human trials. Retrospective studies use data recorded before the study protocol was designed. Most original scientific articles in clinical disciplines, particularly surgery, are retrospective, but modern statistical models are now available to analyze objectively retrospective data using a variety of statistical methods. Observational studies record observations of one or more groups of patients. These studies may record changes in various laboratory or biochemical tests in response to procedures or other therapy or determine the indications, efficacy and safety of a new procedure or laboratory or diagnostic test.

The following topics are offered to help guide the reviewer's assessment of an original scientific article. Not all topics are relevant to every article.

- 'Title' should reflect the content of the article and be concise and clear 'Abstract' should indicate the purpose of the study, subjects and methods used, most important results and the main conclusions supported by results.
- 'Introduction' should indicate the rationale and focus of the study and state the purpose or hypothesis.
- 'Methods' should present the design of the study, fully describe the number and subjects and exclusion and inclusion criteria; whether subjects were enrolled consecutively; methods used to gather data, including follow-up data; methods by which control and experimental groups were assembled; the primary outcome variable; secondary outcome variables; how outcome measurements were made and validated; the statistical design of the study; and the statistical methods used to analyze the study.
- 'Results' should concisely present the most important findings in text and relegate to tables data of lesser importance. Data should be reported as means or medians with appropriate indicators of variance and exact p values in tables and text. Figures should be well selected to highlight important findings and should not be used to present data of lesser significance. Survival and event curves should indicate specified confidence limits or subjects at risk. Regression diagrams should include the regression equations, regression coefficient and exact p value in the figure legend. Figure legends should adequately and clearly describe the important information illustrated.
- 'Comment' should not repeat results, but should point out the significance and conclusions of the new data, integrate the authors' new data with that in the prior literature, draw inferences and conclusions regarding the question or purpose addressed by the study and point out the limitations of the study. The 'Comment' section should not be a review of the literature.
- References should be properly cited, reasonably current, accurate, in proper format and selected. Important omissions should be noted.

New Technology

Articles describing new technology are necessarily descriptive and do not pose or test a hypothesis. These articles evaluate new devices, systems, machines, equipment, instruments, monitors, implantable material and similar technology designed for improving patient care and outcomes. The reviewer is asked to evaluate the efficacy, safety and indications of the new technology and the rigor, completeness and objectivity of the evaluation study.

Topics which the reviewer should consider include:

- Probable importance or usefulness of the technology.
- Problem or task that the technology addresses.
- Newness and innovation of the technology.
- How well the technology is described and illustrated.
- Protocol used for evaluation.
- Methods used to test the technology; and the results obtained.
- Reasons for selecting the methods of testing and evaluation.
- All studies used in the evaluation.
- Ease and difficulties in application including successes and failures.
- Advantages, complications and late adverse events of the new technology.
- Whether are included or should be included in the evaluation.

The conclusion section should summarize the indications, deficiencies and drawbacks. The article should have an objective, dispassionate tone and avoid the enthusiasm of an advertisement or endorsement.

The reviewer needs to inspect the 'Disclosure statement' after the text, before References. This statement should disclose the source of funds used for the evaluation study and whether or not the product was purchased, borrowed or donated by the manufacturer or inventor. Conflicts of interest statements for authors are managed by the editorial staff.

Case Reports, How to Do It, Images

Case reports describe interesting presentations of disease and innovative management of the patient's or patients' problem. *How to Do It* articles emphasize innovations in the operative

management of technical challenges and new ways of doing things. *Images*, which must fit on one printed page, are graphics of interesting presentations of disease within the chest.

Reviewers should evaluate the clarity and completeness of the case or procedure descriptions and the selection and quality of the illustrative material. Reviewers should also note whether or not the paper adheres to the format restrictions enumerated in "Information for Authors". The reference list should be selective rather than inclusive.

Review Article

Reviewers should assess the importance of the subject matter, need for the review and probable interest to readers. Reviews of very rare and unusual diseases are discouraged; subject matter should be sufficiently broad to have instructional and practical value for readers. Reviewers should note if authors have respected the format and restrictions of this category as stated in "Information for Authors".

The 'Introduction' should provide the rationale for reviewing the subject matter and provide the outlines of what is included and not included in the review. In the 'Methods' section reviewers should assess the methods used to search for articles, including search words and databases probed. The body of the review should be well organized with well chosen topical headings arranged in logical order. Within each topical heading the material should be presented in an integrated, comprehensive, objective manner. Statements should be referenced accurately. Reviewers should look for a "summing up" of the topical content before the author proceeds to the next topic. Reviewers should reject topical presentations consisting of "one sentence précis of referenced articles" arranged serially.

The review should provide a general overview of the subject matter assessing progress, pointing out deficiencies in present management and indicating opportunities and directions of future work. The reviewer should also assess the selection of references and note important absences or trivial inclusions.

Footnote.

This editor carefully reads all reviews and respects the time and effort that each reviewer has expended on behalf of the author and all readers. The reviewer remains anonymous; there is no reward beyond listing on the annual thank you list. The reviewer should direct his or her critique to the authors in the style and format that suits them best. The recommendation to the editor is made separately with or without additional comments.

Aortic root enlargement. How much is it safe and beneficial ?

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Background: enlargement of the aortic root during aortic valve replacement is a proposed technique in order to prevent the development of prosthesis-patient mismatch (PPM), however it is still an unproven technique. In order to evaluate the benefits and risks of aortic root enlargement in patients having a small aortic annulus undergoing aortic valve replacement, we examined the outcome of patients who underwent aortic valve replacement with or without adding aortic root enlargement.

The aim of our study was to evaluate the effect of adding aortic root enlargement to aortic valve replacement in patients who have a small aortic annulus in regards of increasing the perioperative risk and to determine the clinical benefit.

We collected the data of 50 patients having aortic stenosis with small aortic root and underwent isolated aortic valve replacement using a single type of aortic valve prosthesis (St Jude bileaflet mechanical aortic valve prosthesis) at our institution from Feb 2009 to Dec 2012, thirty five patients underwent AVR alone whereas the remaining fifteen patients underwent AVR concomitant with an aortic root enlargement procedure .

There was a statistically significant difference between both groups in CPB time, aortic cross clamp time. There was a statistically significant difference between both groups in terms of implanted valve size, iEOA (index Effective Orifice Area), peak and mean postoperative transvalvular pressure gradients. In the follow up 6 months after the operation there was no statistically significant difference between both groups in terms of improved NYHA functional class or improved EF, however there was a statistically significant improvement in the transvalvular pressure gradient , LV mass regression. Conclusion; aortic root enlargement is an invaluable technique in management of patients with small aortic root and can be added to AVR without significant increase in early morbidity and mortality to avoid severe PPM.

Advanced symptomatic aortic valve disease is treated by aortic valve replacement, aiming to relieve symptoms and increase life expectancy. Most surgeons intend to insert the largest possible prosthesis in order to reduce postoperative transvalvular pressure gradient and promote left ventricular mass regression(1).

On the other side, implanting a valve that is too small in relation to the body surface area results in the so called patient-prosthesis mismatch (PPM) which results in multiple potential deleterious sequelae(2-8).

Patient prosthesis mismatch (PPM) first described by Rahimtoola in 1978, and was defined as a condition in which the “effective prosthetic valve area, after insertion into the patient, is less than of a normal valve(9). Subsequently, Pibarot and Dumesnil defined (PPM) as a prosthetic valve effective orifice area (EOA) index to body surface area (BSA) of 0.85 cm²/m² or less(5).

Patients who develop (PPM) after aortic valve replacement are more subjected to less symptomatic improvement, lower post operative regression of the left ventricular mass(10-12) with a poor early and late post operative survival rate(13-14).

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Patients having a small aortic root, especially those who have a large body surface area are at increased risk of developing (PPM) in the post operative period. In order to minimize the possibility of post-operative development of (PPM) several techniques have been developed to enlarge the small aortic root, including the Nicks(15),Konno(16), and Manouguian (17) techniques.

The purpose of this study was to evaluate the effect of adding aortic root enlargement to aortic valve replacement in patients who have a small aortic annulus in regards of increasing the perioperative risk and to determine the clinical benefit.

Materials and method

The clinical data of 50 patients who had a predominant aortic stenosis with small aortic root who underwent isolated aortic valve replacement using a single type of aortic valve prostheses (St Jude bileaflet mechanical aortic valve prosthesis) at our institution, from February 2009 to December 2012 were prospectively analyzed. Patients are considered as having small aortic root when indexed EOA of the implanted valve (iEOA) was estimated to be $0.85\text{cm}^2/\text{m}^2$ or less of the body surface area (BSA). An aortic root enlargement was undertaken when it was not possible to implant at least a valve prosthesis 19mm after doing a thorough debridement of the aortic annulus. That means that without doing an additional ARE =Aortic Root Enlargement procedure these patients would have received a prosthetic valve that will result in making the calculated iEOA $0.85\text{cm}^2/\text{m}^2$ or less resulting in PPM.

Exclusion criteria of our patients were those having concomitant CABG, other valve surgical procedures, emergency surgery, infective endocarditis and redo operations.

Method of estimating the indexed effective orifice area

By dividing the In-vitro EOA of the implanted valve- as supplied by the manufacturer- by the patient's body surface area in order to get the iEOA. The prosthesis that we used in all patients included in our study was (St Jude bileaflet mechanical aortic valve prosthesis). PPM was considered when the iEOA was $0.85\text{cm}^2/\text{m}^2$ or less of the body surface area.

Method of estimating the left ventricular mass index(LVMI)

All patients were subjected to M-mode, two dimensional and Doppler transthoracic echocardiogram before and after AVR. The following measures were recorded, left ventricular internal diameter(LVID), interventricular septal thickness (IVST), posterior wall thickness(PWT), all these data were used to estimate the(LVMI) which is expressed in g/m^2 using the following formula described by the American Society of Echocardiography⁽¹⁸⁾ :

$$1.04[(LVID+PWT+IVST)^3-LVID]^3 \times 0.8 + 0.6, 1.04$$

is the specific gravity of the myocardium and 0.8 is the correction factor.

The LVMI was considered to be increased if it was at least $149\text{g}/\text{m}^2$ in men and at least $122\text{g}/\text{m}^2$ in women.

Operative technique

All patients were operated under standard cardiopulmonary bypass (GPB) with moderate hypothermia. Myocardial protection was carried out with hyperkalemic cold blood cardioplegia injected every 30 min into the coronary ostia directly besides the topical cooling. However, Retrograde cardioplegia through the coronary sinus was not routinely employed. Through an oblique aortotomy, the diseased valve was excised and the annulus was sized. Standard AVR with valve prosthesis was done using pledgeted 2-0 ethibond sutures. If, however, it was not possible to place even a 19-mm valve, root enlargement was undertaken based upon the technique of Nicks et al or Manouguian and Seybold-Epting . When the goal was to obtain an increase in aortic annular diameter of one valve size, the procedure given by Nicks et al. was performed. However, if more than one-size enlargement was needed, the procedure suggested by Manouguian and Seybold-Epting was used. With Nicks enlargement, the aortotomy was extended into the commissure between non coronary and left coronary sinuses. The incision was stopped 3-5 mm below the annulus. For a Manouguian procedure, aortotomy incision was extended into the noncoronary sinus and through the annulus, 10-15 mm below the annulus (onto the anterior leaflet of the mitral valve). A patch of autologous pericardium was sutured to the defect using a 4-0 polypropylene suture, starting at the lower most portion of the incision up to 2.0 cm above the plane of the annulus. The annulus was resized and the appropriate valve was chosen, corresponding to the size that passed comfortably through the annulus. Horizontal mattress pledgeted sutures were placed circumferentially around the native annulus with the pledgets on the aortic side or the ventricular side depending on the surgeon preference using 2-0 ethibond sutures. In the region of the patch, sutures were placed in the plane of the annulus with the pledgets located on the outer aspect of the patch.

Follow-up

All patients were subjected to post discharge follow up. Thorough history, clinical examination and echocardiographic study were undertaken to obtain New York Heart.

Association (NYHA) functional class, postoperative mean and peak transvalvular gradient, LVMI. Mortality data were also recorded.



Statistical analysis

Continuous data were presented as mean \pm SD, whereas nominal (categorical) data are presented as frequencies and percentages. Associations among nominal variables were compared by X^2 (Chi-square) test or Fisher's exact test as appropriate. Continuous variables were compared by two-tailed unpaired Student's *t*-test. A *P* value less than 0.05 was considered statistically significant.

Results

The preoperative characteristics of both groups of patients (AVR alone and combined AVR+ARE) are presented in the table 1. There was no significant difference between both groups in the preoperative data regarding the age, sex, body surface area, NYHA functional status, the percentage of preoperative atrial fibrillation, peak and mean transvalvular pressure gradients, EF, and co-morbidity like DM, COPD, hypertension, and impaired renal function.

Variables	AVR (n= 35)	AVR +ARE ARE (n = 15)	P value
No. of patients	35 (70%)	15 (30%)	–
Age (years)	37.7 \pm 13.7	35.3 \pm 11.2	0.521
Female	22 (63%)	8 (53%)	0.9
BSA (m ²)	1.65 \pm 0.12	1.63 \pm 0.14	0.591
NYHA class (mean)	3 \pm 0.42	3 \pm 0.41	0.684
NYHA IV	4 (11%)	2 (13%)	1.23
Atrial fibrillation	11 (31%)	5 (33%)	0.65
Peak transvalvular gradient (mmHg)	85 \pm 25.7	90 \pm 23.3	0.13
Mean transvalvular gradient (mmHg)	55 \pm 17.1	53 \pm 22.3	0.863
LVEF (%)	52 \pm 17	54 \pm 18	0.821
Comorbid conditions			
Diabetes	4 (11%)	5 (10.63%)	1.3
Hypertension	3 (8%)		0.84
COPD	10 (28%)	2 (13%)	0.79
Sr Creat > 1.5 (mg/dl)	1(2%)	1 (6%)	0.81

Table 1. Preoperative characteristics of both groups.

However, there was a statistically significant difference between both groups in CPB time and aortic cross clamp time that was significantly longer in the group of combined AVR+ARE, as the aortic root enlargement added an extra time of about 30 minutes to the time of aortic valve replacement alone.

There was a statistically significant difference between both groups in term of the implanted valve size. In the AVR alone patients the most commonly used valve was 19 (30 patients representing 86%), (5 patients received size 21 representing 14%

using the simple tilting technique without adding any other operative procedure) whereas in the 2nd group who received combined AVR+ARE the most commonly implanted valve size was 21(9 patients representing 60%) and (the remaining 6 patients who represent 40% received an aortic valve size 23).

There was a statistically significant difference between both groups in the indexed effective orifice area iEOA (in the AVR group the mean iEOA 0.73 cm²/m² as compared to the 2nd group AVR+ARE the mean iEOA 0.90 cm²/m²) which means that all

Variables	AVR (n=35)	AVR + ARE (n=15)	P value
Total CPB time (min)	67.9±11.6	110.6±15.9	<0.001
Aortic cross clamp time (min)	39.3 ±13.8	84.7 ± 8.3	<0.001
prosthetic valve size (mean ± SD)	19.39 ±0.8	20.79 ±2.33	<0.001
19 mm	30 (86%)	-----	
21 mm	5 (14%)	9 (60%)	
23 mm	-	6 (40%)	
iEOA (cm ² /m ²)	0.74 ±0.08	0.89 ±0.06	<0.001
iEOA <0.65 cm ² /m ²	3 (8%)	-	-

ARE, aortic root enlargement; AVR, aortic valve replacement; CPB, cardiopulmonary bypass; iEOA, indexed effective orifice area.

Table 2. Operative outcome in both groups

The postoperative outcome in the two groups is represented in table 3.

Variables	AVR (n = 35)	AVR+ARE (n = 15)	P value
Time to extubation (h)	20 ±42	40± 52	0.325
Reoperation for bleeding	3 (8%)	2(13%)	0.542
Postop renal impairment	3 (8%)	1 (6%)	0.824
Postop respiratory dysfunction	2 (5%)	1 (6%)	0.713
ICU stay (days)	2.3 ±3.8	3.6 ±4.2	0.761
Hospital stay (days)	8 ± 9	11± 9.4	0.433
In-hospital mortality	2 (5%)	1 (6%)	0.907
NYHA class	1.24 ±0.42	1.22 ±0.16	0.512
LVEF (%)	56.2 ± 16.6	58.3 ±15.8	0.237
Peak gradient (mmHg)	28.3 ± 7.53	16.5 ±9.22	<0.001
Mean gradient (mmHg)	17.1 ± 3.2	11 ± 2.6	<0.001

ARE, aortic root enlargement; AVR, aortic valve replacement; ICU, intensive care unit; LVEF, left-ventricular ejection fraction; NYHA, New York Heart Association.

Table 3. Postoperative outcome in the two compared groups.

Variables	AVR {n= 35}	AVR + ARE (n = 15)	P value
NYHA class	1.26 ±0.18	1.18 ±0.36	0.749
Peak gradient (mmHg)	26.2 ±5.67	13.5 ±6.24	<0.001
Mean gradient (mmHg)	15.1 ±7.23	11.4 ±3.21	<0.001
LVEF (%)	56.4 ±10.65	57.8± 11.21	0.521
LVMI (g/m2)	160.1 ±23.44	126.3 ±37.42	0.003
LVMI regression	-18.5 ±36.4	-39.3 ±32.1	<0.001

ARE, aortic root enlargement; AVR, aortic valve replacement; LVEF, left-ventricular ejection fraction; LVMI, left-ventricular mass index; NYHA, New York Heart Association.

Table 4. Postoperative outcome after 6 months in both groups.

patients who underwent AVR alone will have some degree of PPM= Patient Prosthesis Mismatch whereas no PPM in the group who received AVR+ARE which can be explained by the larger size aortic valve prosthesis that was implanted in these patients. Three patients (8%) from the AVR group developed postoperative severe PPM with iEOA less than 0.65cm²/m².

There were two mortalities in the AVR group compared to only one mortality in the AVR+ARE group. The mortality in the AVR group was attributed to postoperative respiratory dysfunction in 1 patient and another patient due to postoperative renal impairment who required repeated renal dialysis, while in the group of combined AVR+ARE there was only one mortality caused by respiratory failure with prolonged mechanical ventilation following reoperation for bleeding. There was no statistically significant difference between both groups in the immediate postoperative period in the incidence of reoperation for bleeding, postoperative renal impairment, postoperative respiratory dysfunction, ICU or hospital stay, NYHA functional class, EF. However there was a statistically significant difference between both groups in terms of peak and mean postoperative transvalvular pressure gradients with peak and mean gradients in the AVR group (28.3 ± 7.53 and 17.1 ± 3.2) respectively as compared to peak and mean gradients in the AVR+ARE group (16.5 ±9.22 and 11 ± 2.6) respectively and P value was <0.001.

The patients were subjected to postoperative follow up 6 months after operation; The data were collected and summarized in table 4.

In the follow up 6 months after the operation there was no statistically significant difference between both groups in terms of improved NYHA functional class or improved EF. However there was a statistically significant improvement in the transvalvular pressure gradient between both groups in the peak gradient (26.2 ±5.67 vs 13.5 ±6.24) in AVR and AVR+ARE respectively as well as in the mean gradient(15.1 ±7.23 vs 11.4 ±3.21) in AVR and AVR+ARE respectively, as well as significant LV mass regression (-18.5 ±36.4 vs -39.3 ±32.1) between AVR and AVR+ARE groups respectively.

Discussion

The surgical management of small aortic root during AVR has been discussed in literature for a long time, supra-annular implantation of the aortic valve prosthesis was initially applied to solve the problem of small aortic root allowing the implantation of a larger valve⁽¹⁹⁾. Other options to solve this surgical problem were insertion of a homograft, stentless bioprosthesis. However they were significantly associated with an increased morbidity and mortality. The first attempt to enlarge the aortic annulus was performed by Nicks and colleagues in 1970⁽¹⁵⁾, later on by Manouguian and Seybold-Epting⁽¹⁷⁾.

There remains an unproved perception that these procedures result in an increase in the risk of morbidity and mortality without having a significant beneficial clinical value. The purpose of our study was to evaluate whether adding ARE to AVR in the indicated patients increases the perioperative risk and its clinical benefits.

In this group of patients with a small aortic root it was found that although the addition of ARE procedure to AVR increases the aortic cross-clamp time and the total CPB time by an average of 30 min, it was not associated with any significant increase in perioperative morbidity and mortality. Peterson *et al.*⁽²⁰⁾ in their recent study have found operative mortality for aortic annular patch enlargement to be 3%, Castro *et al.*⁽²¹⁾, in a similar study on 114 patients, performed selective ARE in patients at risk for PPM, the 30 day mortality in their study was 0.9%. In our study the in hospital mortality rates were similar in either group (1 (6%) in AVR + ARE group vs. 2 (5%) in AVR-alone group; P = 0.907).

Our study documented the hemodynamic benefit of the ARE in patients having small aortic roots undergoing AVR procedures enabling the insertion of larger size prosthetic valves (size 21 in 60% of the patients and size 23 in

40% of the patients who underwent combined AVR+ARE vs insertion of size 19 in 86% and size 21 in 14% of the patients who underwent AVR alone).

Many old and recent ARE experience reports have shown that ARE procedures are well tolerated^[22-24]. There are, however, some others^(25,26) who have found no late adverse outcome following AVR in patients having a small aortic root who received mismatched valves. In 1997, Sommers and David⁽²⁷⁾ published a negative experience with ARE procedure in a retrospective study of 530 patients who underwent AVR with Hancock II prosthesis. They concluded that with similar long-term outcome with increased early morbidity and mortality there will be no significant clinical advantage in routine use of ARE at the time of AVR.

In our study we demonstrated that adding the ARE procedure to the AVR resulted in avoidance of the occurrence of PPM whether this PPM will or will not result in a late adverse outcome, we have also demonstrated that patients who were subjected to ARE in combination of AVR showed a significant decrease in peak and mean postoperative transvalvular pressure gradients as well as a significant LV mass regression.

Conclusion

We can conclude that the ARE procedure is an invaluable technique in management of patients with small aortic root and can be used without significantly increasing early morbidity and mortality in patients with small aortic root in which AVR using a small prosthesis would lead to severe PPM.

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Myocardial Revascularization Using the Radial Artery: Midterm Results

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Background. The high incidence of late obstruction of venous bypass graft combined with the proven advantage of arterial revascularization stimulated a search for alternative conduit for CABG. The use of radial artery (RA), condemned as a bypass graft more than 30 years ago, has been revived with encouraging early and midterm results.

Patients & Methods. Between January 2005 and December 2007, 50 consecutive patients with coronary artery disease underwent primary isolated CABG using the RA as one of the bypass conduits. Patients were followed-up during their hospital stay as well as for a minimum of 2 years thereafter. All RA grafts were used as composite grafts with the LIMA.

Results: 157 distal anastomoses were constructed (3.14 anastomosis/patient), 70 of these (44.5%) were done using RA grafts. Only one of the study patient died (2%) early after surgery, 1 patient (2%) developed early postoperative MI and 2 patients (4%) showed evidence of postoperative ischaemia, but none in an area revascularized by a RA graft. Temporary parasthesia developed in 18 patients (36%) with no incidence of ischaemic or functional complications in the hand. Patient survival was 95% at 2.6 years. Symptom-directed coronary imaging was available for 14.3%. RA angiographic patency was 100% with none of the radial artery evaluated showing significant narrowing.

Conclusion: The radial artery can be used safely to achieve total arterial revascularization with encouraging early and Midterm results. Its use does not appear to increase complexity and morbidity associated with CABG.

KEYWORDS: CABG – Radial Artery

The radial artery (RA) was first introduced into clinical practice by **Carpentier** and associates in 1973. However, 2 years later **Carpentier** abandoned its use because of severe diffuse narrowing that occurred in 35% of the grafts, a patency rate that was judged to be unacceptable.¹

Acar and colleagues reinvestigated the use of the RA in CABG after the unexpected finding that some of the RA grafts that were thought to be occluded in the early series of **Carpentier** were patent and functioning 15 years later. The improved results of RA grafts obtained during this new era were attributed to the use of Calcium channel blocking agents and other vasodilator drugs used that prevent perioperative spasm of the graft as well as to a modified surgical technique avoiding skeletonization and excessive dilatation of the graft.² These reports led many other groups to reassess the role of this conduit in coronary artery bypass procedures.

The RA has rapidly gained popularity due to encouraging early and mid-to-long term results. It is being used as a conduit of choice over the right internal mammary artery (RIMA) by many surgeons because of the absence of additional risk regarding sternal wound infection.³

In this study, we attempt to review the current knowledge regarding the use of RA grafts as a coronary bypass conduit as well as to evaluate the safety and efficacy of this graft in CABG surgery on midterm basis.

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Patients and Methods

Between January 2005 and December 2007, 50 patients with coronary artery disease underwent coronary artery bypass grafting (CABG) surgery using a radial artery graft as one of the bypass conduit in the department of Cardiothoracic Surgery, Faculty of Medicine, Cairo University.

In all patients, LAD was bypassed using LIMA while RA was used as the other bypass conduits. Revascularization was completed using GSV graft, if needed. A written informed consent was obtained from each patient before surgery.

General exclusion criteria include

- Patients above the age of 65 years.
- Emergency CABG.
- Patients undergoing concomitant valve procedure, LV procedure or another vascular/general surgical procedure.

Specific contraindications to the use of RA include

- Previous trauma to the forearm.
- Presence of A-V fistula for the purpose of hemodialysis.
- Radial dependent hand circulation as evidenced by positive Allen's test or dynamic Doppler evaluation.
- Raynaud's disease or scleroderma.
- Patients with known subclavian artery disease.
- Patients with chronic renal failure (serum creatinine >2 mg%) in whom future A-V fistula may be required.

III. Preoperative Assessment

All patients were subjected to complete history taking, clinical examination, full laboratory investigations, plain chest X-ray, ECG, Plain chest x-ray, echocardiography, coronary angiography, myocardial perfusion scintigraphy (if needed) and duplex scanning of the carotid arteries, lower limbs as well as the radial arteries. Adequacy of ulnar collateral circulation of the hand is assessed also by a modified Allen's test.

Operative Management

In all the patients routine anesthetic techniques were used. All arterial and peripheral intravenous lines were placed in the dominant hand.

Surgical technique

All patients underwent operation through a standard median sternotomy incision, myocardial revascularization was performed on cardiopulmonary bypass. Myocardial protection was achieved by intermittent warm, blood antegrade cardioplegia.

All distal anastomoses were constructed first on cross clamp, then a "hot-shot" dose of warm blood was usually given into the aortic root before release of the cross-clamp. All proximal anastomoses were constructed after application of a side occlusion clamp on the ascending aorta on a beating heart. All radial artery grafts were proximally anastomosed to the LIMA in an attempt to make maximal use of the length of the RA graft as well as to increase the incidence of arterial revascularization. The RA was anastomosed to LIMA in an end-to-side manner on cross-clamp after construction of distal RA anastomosis using 8/0 polypropylene running stitches, usually at the site of entry of the LIMA in to the pericardial sac, in a T- or Y-configuration. LIMA was uniformly used to bypass LAD in all patients.

RA was uniformly grafted to the largest, most important coronary artery apart from the LAD either the circumflex territory or the RCA territory. All distal RA anastomoses were constructed on coronary arteries with critical stenosis (>90%) and good distal run-off, in order to minimize the effect of competitive native flow. Distal anastomoses were constructed using 7/0 polypropylene running stitches except if coronary arteries are too thin where 8/0 polypropylene stitches were used. In some cases, sequential RA grafting was used, preference was for parallel anastomoses, if possible. Otherwise, diamond shaped (cross) anastomoses was used. If additional grafts were needed, saphenous vein was used to complete the revascularization.

Harvesting of the radial artery

The radial artery was always harvested from the non-dominant hand. RA harvesting was carried out concomitantly with harvesting of other conduits. The non-dominant upper extremity is prepared and draped on an arm board abducted to about 70° from torso. A pulse oxymeter probe is attached to the index of the side from which radial artery is to be harvested.

Preparation of the radial artery

A 24-gauge plastic cannula is inserted into the proximal end of the radial artery and the artery is gently held with fingers. No ties are necessary. Clean verapamil-nitroglycerine (VG) solution is injected through the cannula to flush (not distend) the artery with the other end freely open. The radial artery is left immersed for about 15 minutes to allow full relaxation. The VG solution used consists of: 300 ml of Ringer's solution, verapamil hydrochloride 5 mg, nitroglycerine 2.5 mg, heparin 500 U, NaHCO₃ 0.2 ml. The fascia overlying the RA graft is not opened except at the points of anastomoses. The distal end is usually used for coronary anastomosis.

Pharmacologic management

Before skin incision; continuous low-dose verapamil infusion was started to prevent RA spasm (0.5 mg/hr; 5 mg of verapamil in 100 ml 5% dextrose in water, intravenously at a rate of 10 ml/hr). In addition, intravenous nitroglycerine is initiated

at a dose of 0.5-4 $\mu\text{g}/\text{Kg}/\text{min}$ and kept for 24 hours postoperatively. Verapamil infusion is kept until patient is able to take oral medications, where oral verapamil, 120 mg in 3 divided doses is given.

Operative data and parameters

A record was made of ischemic time, bypass time, total operative time, radial artery harvest time, revascularization technique including (number and distribution of proximal and distal anastomoses and type of conduit for each coronary territory), weaning from CBP, ECG, inotropics, use of IAP, arrhythmias (following weaning from CBP), occurrence of any surgical problem requiring reinstatement of CPB.

Postoperative assessment

Patients of the study were followed up for the duration of their hospital stay and for a period of 2 years thereafter.

EARLY IN-HOSPITAL FOLLOW-UP

The following data were recorded: Period of mechanical ventilation, inotropic support, peak value of total creatinine kinase (CK) and myocardial band creatinine kinase (CK-MB), use of intra-aortic balloon pump (IABP) support, incidence of major complications (low cardiac output syndrome, postoperative ischaemia, postoperative myocardial infarction, graft spasm: defined as new temporary ischaemic ECG changes not associated with elevated cardiac enzymes and localized to ECG leads corresponding to myocardial territory supplied by the accused graft, re-exploration for bleeding and the need for blood transfusion, renal impairment requiring dialysis, chest infection and RA harvest site complications (including acute hand ischaemia, compartment syndromes functional hand impairment, cutaneous parasthesias, hematoma/seroma, forearm and hand swelling and wound infection. Duration of ICU stay, duration of hospital stay and mortality were also recorded.

SUBSEQUENT FOLLOW-UP

Patients were followed up after hospital discharge for a minimum of 2 years postoperatively. The following data are obtained; Cardiac adverse events (Myocardial infarction, recurrent angina, clinically significant arrhythmias, hospitalization for cardiac cause, coronary re-intervention). Patients with recurrent symptoms of myocardial ischemia are evaluated with necessary investigations, including: resting/stress ECG, Radionuclide imaging or CT/conventional coronary angiography. Culprit myocardial territory requiring re-intervention, whether supplied by a radial artery graft or a non-radial artery graft, is noted. On review of follow-up angiography, a radial artery graft is considered occluded if it has >50% stenosis or angiographic string sign. Mortality, event-free survival, forearm and hand complications: including subjective hand function, subjective hand weakness, parasthesias or sensory loss were also recorded.

Statistical analysis

All patients' data were tabulated and processed using SPSS V10.0 (SPSS Inc., Chicago, IL). Quantitative variables were expressed using mean, standard deviation and percentages.

Results

A total of 50 patients undergoing isolated primary coronary artery bypass grafting in the Department of Cardiothoracic Surgery, Faculty of Medicine, Cairo University were enrolled in this study. Preoperative clinical, cardiologic characteristics as well as coronary risk factors and co-morbidities are shown in Table (1).

▪ No. of patients	50
▪ Clinical characteristics:	
- Age (years)	52.57.3 \pm years (40-65 years)
- Female	10 (20%)
▪ Coronary risk factors:	
- Hypertension	10 (20%)
- Diabetes	30 (60%)
- Hyperlipidemia	38 (76%)
- Smoking	40 (80%)
- Obesity	20 (40%)
- Family history	6 (12%)
▪ Co-morbidity:	
- CVD	3 (6%)
- PVD	4 (8%)
- COPD	6 (12%)
▪ Cardiac profile:	
- Previous MI	30 (60%)
- EF:	
* >50%	38 (76%)
* <50%	12 (24%)
- CCS:	
* I	5 (10%)
* II	10 (20%)
* III	30 (60%)
* IV	5 (10%)
▪ Angiographic profile:	
- 2- vessel disease	14 (28%)
- 3- vessel disease	29 (58%)
- Lt main disease	7 (14%)
- Previous angioplasty	12 (25%)

Table 1. Preoperative patient characteristics

OPERATIVE RESULTS

A summary of operative data as well as grafting patterns of the study patients is listed in Table (2, 3&4).

▪ Total operative time (minutes)	319.0 ± 76.9
▪ Total bypass time (minutes)	102.2 ± 29.5
▪ Total aortic cross-clamp time (minutes)	67.8 ± 21.4
▪ RA harvest time (minutes)	35.0 ± 2.8

Table 2. Operative data

▪ Total No. of distal anastomosis	157
▪ No. of distal anastomosis per patient	3.14 (2-5)
▪ Total No. of LIMA anastomoses	50/157 (31.8%)
▪ Total No. of arterial anastomoses	120/157 (76.3%)
▪ No. of patients with total arterial revascularization	15/50 (30%)
▪ Total No. of GSV graft distal anastomoses	37/157 (23.7%)

Table 3. Grafting patterns in the study group

▪ Total No. of distal RA anastomoses	70/157 (44.5%)
▪ No. of separate RA grafts	32/50 (64%)
▪ No. of sequential RA grafts	18/50 (36%)
- 2 sequential anastomoses	16/50 (32%)
- 3 sequential anastomoses	2/50 (4%)
▪ Target site of the RA grafts:	
- Left anterior descending artery	0/70 (0%)
- Diagonal branches	14/70 (20%)
- Obtuse marginal branches	36/70 (51.4%)
- Posterior descending artery	13/70 (18.5%)
- Posterolateral artery	2/70 (2.8%)
- Ramus	5/70 (7.1%)

Table 4. Patterns of RA grafting in study patients

The RA was used as separate graft in 64% of study patients, while in the remaining portion, sequential RA grafting was adapted. The commonest sequential grafting patterns were: LIMA-RA-OM₁-OM₂; LIMA-RA-D-OM and LIMA-RA-OM-PDA.

EARLY POST OPERATIVE RESULTS

The following results were noted as seen in table (5).

▪ ICU stay (hours)	75 ± 9.1 hours
▪ Hospital stay (days)	11 ± 2.4 days
▪ Mechanical ventilation (hours)	8.5 ± 1.2 hours
▪ Inotropic support (dose of adrenaline)	0.03 ± 0.045 µg/Kg/min
▪ IABP support	2 (4%)
▪ Mean CK-MB level (IU/L)	13.2 ± 11.6 IU/L
▪ Postoperative MI	1 (2%)
▪ Postoperative ischaemia	2 (4%)
▪ Re-exploration for bleeding	2 (4%)
▪ Transfusion requirements:	
- Packed RBCs (units)	4.3 ± 1.8 units
- Fresh frozen plasma (units)	8.5 ± 4.9 units
- Platelets (units)	6.6 ± 1.7 units
▪ RA harvest site complications:	
- Hand ischaemia	-
- Paresthesias	18 (36%)
- Hand swelling	10 (20%)
- Hematoma	1 (2%)
- Forearm wound infection	-
- Functional impairment	-
▪ Sternal wound infection	2 (4%)
▪ Acute renal failure	1 (2%)
▪ Cerebrovascular accident	-

Table 5. Postoperative results

Evidence of myocardial ischaemia was seen in 2 patients (4%) as evidenced by ST-segment or T-wave changes. In all these cases, these changes were reversed by IV infusion of nitroglycerine and no elevation of cardiac enzymes was recorded. No evidence of myocardial ischaemia or infarction developed in a territory revascularized by a radial artery graft.

There was no episode of hand ischaemia following RA harvesting. Pulse oxymetric values and waveforms of both operated and non-operated forearms were comparable. 18 patients (36%) in our series developed paresthesias and numbness, mostly affecting the thenar area as well as the dorsum of the thumb and the first 3 fingers. Moreover, about 5 of these patients (10%) had a subjective sensory loss. In the majority of these patients, these sensory manifestations subsided spontaneously. Only three patients (6%) were discharged with some degree of sensory alteration in their hand. No patient complained of any motor loss or impairment of hand function. Hand swelling developed in 10 patients (20%) that resolved spontaneously before discharge except in 3 patients.

One patient of the study group died during the follow-up period, constituting a 2% mortality rate. This was a 53-year-old male patient who was markedly obese, diabetic, hypertensive with Ejection Fraction of 48%. He had critical stenosis of 4 major coronary arteries. He received LIMA-LAD, LIMA-RA-OM₁-OM₂ and SV-PDA grafting. Following weaning from CPB, patient needed high inotropic support (0.15 µg/Kg/min adrenaline) along with an intra-aortic balloon pump support to maintain the hemodynamics. Postoperative ECG along with results of serum cardiac enzymes documented the development of an inferior myocardial infarction. Patient could not be weaned from inotropic or intra-aortic balloon support and died on the 5th postoperative day because of refractory heart failure. However, no evidence of myocardial ischaemia developed in areas revascularized by RA graft.

LATE POST OPERATIVE RESULTS

Complete follow-up data were available for 42 patients (84%). Patients were followed up for an average of 2.5±0.4 years postoperatively.

Recurrence of angina: 9.5% of surviving patients had recurrence of their symptoms during the follow-up period. In one case, where myocardial perfusion imaging showed evidence of ischemia, PCI to a stenosed vein graft was undertaken. The remaining 3 cases, coronary imaging did not show any evidence of significant graft disease and symptoms were managed medically.

MI: Two patients (4.7%) developed documented STEMI. One patient died while the other received standard treatment. Post MI coronary angiography revealed patent arterial (LIMA/RA) grafts and venous grafts with a totally occluded posterolateral branch of RCA, which was diffusely diseased and deemed to be non-graftable in the pre-operative angiogram

Arrhythmias: Two patients (4.7%) were diagnosed with atrial fibrillation by the treating cardiologist 4 & 6 months after the surgery. It was not immediately clear when the onset of the atrial fibrillation was. One patient was successfully converted to sinus rhythm using amiodarone therapy and the other required prolonged anticoagulation

Coronary re-intervention (PCI or CABG): none of the patients in the study required re-operative CABG. None of the radial artery grafts required repeat coronary interventions. On the other hand, one patient (2.3%) required Balloon angioplasty and stenting of a stenosed vein graft to the RCA. Patient was symptomatic and myocardial perfusion imaging revealed evidence of reversible ischemia.

Congestive heart failure: none of the study patients developed congestive heart failure during the study follow-up period and all of the surviving patients were in NYHA class I or II

Hospitalization from a cardiac cause: 21.4% of study population required hospitalization for cardiac causes that included: Atrial fibrillation (4.7%), chest pain (12%) and valve surgery (4.7%).

Mid-term Survival

At an average of 2.6 years after surgery, patient survival was 95.2% (2/42). Two patients died late postoperatively, one due to documented STEMI 17.5 months after surgery. The cause of the other death is not determined. Overall actuarial survival of the study population is 93% (3/43).

Angiographic Patency

Seven patients (14.3%) had post-operative conventional or CT coronary angiography. In five of these patients, the indications for these studies were: chest pain, positive exercise test for ischemia, scintigraphy or stress echocardiogram suggesting myocardial ischemia, while in the other two patients, coronary imaging was part of pre-operative work-up for valve surgery. Angiographic evaluation was done 20 months, 27 months, 27.5 months, 29 months, 30 months, 32.7 months, and 33 months from surgery in each of the 7 restudied patients respectively. All RA grafts were perfectly patent with no evidence of anastomotic narrowing or string sign. No angiographic evidence of stenosis or flow limitation observed of either LIMA or RA in cases where RA grafts were used in a composite manner off the LIMA. In 1 patient, significant focal narrowing in the body of a vein graft to the RCA territory was found and was successfully managed percutaneously.

Forearm and hand Complications

At the end of the follow-up period, none of the study patient reported any subjective hand weakness or functional grip disability. Out of the three patients with early sensory derangement, only one (2.1%) has prolonged symptoms that finally disappeared after 15 months from surgery. None of the patients had reported permanent sensory loss or alteration. There was no incidence of remote forearm harvest site infection or excessive scar formation.

Discussion

From the technical point of view, the RA represents an excellent conduit for coronary bypass. It is an arterial graft that is used to the systemic blood pressure. Its diameter, slightly greater than the IMA, corresponds perfectly to the diameter of most coronary arteries. The quality of its wall (thick and resistant) offers good handling conditions for coronary and aortic anastomosis. Finally, its length, usually more than 20 cm, allows it to reach virtually all target vessels on the surface of the heart.

A major point of concern regarding the use of RA as a bypass conduit is the prevalence of preexisting disease in this vessel. In our series, none of the harvested radial artery grafts was grossly calcified or atherosclerosed. The routine preoperative use of duplex scanning to assess the quality of RA may have helped to identify diseased RA and to have them excluded from being used as a bypass conduit.

Our anti spasm protocol consisted of bathing and spraying the RA during harvesting with VG solution. Moreover, before skin incision, a continuous IV infusion of verapamil continued in the ICU. IV verapamil is replaced by oral verapamil 40 mg TDS once the patient is able to take oral medications. Oral verapamil is continued for at least 6 months postoperatively.

Based on the above mentioned protocol, along with the emphasis on meticulous harvesting technique, we have had no case of RA graft spasm in this series. No incidence of RA graft spasm (as evidenced by new reversible ECG changes in a myocardial territory supplied by RA graft) developed in this series. Moreover, on restudied angiograms after an average of 2.6 years from surgery, no angiographic string signs were encountered in our series.

The mean patient age in our study group was 52.5 ± 7.3 years, around 10 years younger than the mean age reported by others^{4,6}. The lower mean values for patients' age in our study may be explained by the sedentary life style and bad dietary habits along with smoking that are prevalent in our eastern countries. Moreover, the lower age limit attracted more surgeons to use arterial grafts, including the RA, in younger patients who are expected to show more long-term benefits.

We had a mean operative time of 319 ± 76.9 minutes. Our operative time is somewhat longer than that cited by **Possati et al. (1998)**⁷ who reported 225 ± 2.2 minutes and **Anyanwu et al. (2001)**⁸ who reported 212 ± 1.9 minutes. The longer mean operative time may be attributed to difference in learning curve subsequently acquired. It was our choice, in accordance with other groups, to place the RA grafts only on critically stenosed vessels with more than 90% occlusion. Cumulative experience has shown that RA grafts occlusion rate as well as the angiographic string sign rises if RA was placed on a moderately stenosed vessel.^{5,6}

Although RA harvest site complications were relatively common in our series, as it is the case in most others, these complications were simple, self-limiting. Overall incidence of harvest site complication was 40% (20/50). The commonest form was altered forearm and hand sensations (parasthesias, numbness or sensory loss) affecting 18 patients (36%). Other forms included hand swelling in 10 patients (20%) and forearm hematoma occurred in one patient (2%). **Moon et al. (2004)**⁹ reported a 49% incidence of hand complaints following RA harvesting, **Meharwal et al. (2001)**¹⁰, reported an incidence of 28% of hand numbness and parasthesia. **Saeed and co-workers**¹¹ reported a 67% incidence of altered hand sensation following RA harvesting. Several investigators pointed out that forearm wound has a considerably lower incidence of complications especially wound infection, than leg wound and causes much less interference with patient's ambulation. Many patients expressed preference for their forearm wound over their leg wound.

Contradictory evidence in literature exists regarding the potential role of RIMA in CABG. Some authors suggest that bilateral, compared with single, IMA grafting is associated with increased survival and fewer ischemic cardiac events.¹²

On the other hand, many surgeons mark their preference to RA grafts over RIMA grafts due to additional risk of sternal wound infection (especially in diabetic and obese patients), and because no difference exists in perioperative and midterm cardiac morbidity and mortality rates between RA and RIMA bypasses.³

Such conflicting results concerning the role of RA and RIMA deserved some focus from researchers recently. **Buxton and colleagues (2005)**¹³ have recently questioned the presumed superiority of the RA over RIMA. They confirmed that patency of LIMA and RIMA grafts are not significantly different; they also suggested that patency of LIMA and RIMA is superior to those of RA and GSV grafts which are themselves not statistically different in patency rates. These findings suggest that RIMA has been underutilized and that wider use of RIMA may help improve long-term results of CABG. **Munertto et al. (2003)**¹⁴, compared clinical and angiographic results of total arterial revascularization with composite grafts and conventional coronary surgery. Angiography at a mean of 12 ± 4 months showed a significant lower GSV graft patency rate (89%) compared with RA (99%) and suggested that the use of composite LIMA-RA Y-grafts may improve clinical and angiographic results. In our study, none of the restudied patients has a compromised LIMA or RA graft flow when the RA was used as LIMA-RA composite graft.

Conclusion

The ideal mode of using available conduits for CABG surgeries has not been settled. The choice of the ideal graft for each patient is a highly selective process according to the specific needs for each patient. This high selectivity must be based on many factors of evaluation including the biological characteristics of the graft, the proper matching between the size of the coronary vessels and the selected graft, the technical consideration for implanting the graft selected, the proper anti-spasm protocol and most importantly, suitability of the selected graft to the general condition of each patient. Choosing the proper conduit to be grafted lowers the incidence of postoperative mortality and limits other morbidity complications.

In the current study, we attempted to evaluate the role of the radial artery in CABG surgery and to evaluate whether the use of RA grafts in CABG is associated with higher morbidity/mortality on midterm basis.

Based on our results, which came in accordance with others, the use of radial artery grafts in CABG appears to be safe, reproducible and does not increase operative or midterm morbidity and mortality associated with CABG.

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Study the Role of the doubly committed subaortic VSD Patch closure as an independent risk factor in maintaining the balance of the aortic root structure and function and preventing the progression of AR in patient with VSD –AR syndrome

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Background: However, There was a controversy regarding the accurate timing for small subaortic doubly committed VSD closure, the early closure of it has been suggested to be effective in preventing the onset of AR as the lack of infundibular septal support for the aortic annulus and left to right shunting during the early systole flow creating a venturi effect which leads to displacement of the aortic valve cusp towards the right ventricle which ended by aortic valve cusp prolapse and aortic insufficiency. [1]

There was no standard surgical technique for outlet VSD closure. Various surgical techniques for VSD closure were described. Patch closure technique is considered to be the most reliable and definitive surgical procedure for preventing residual VSD and displacement of the aortic annulus. Running Direct VSD closure technique is safe, easy and can maintain the aortic cusp in its normal position but it is believed that the orientation of the VSD boundaries and relation to the aortic cusp was difficult so that the aortic valve cusp will be in risk of injury as well as there was a risk of downward pulling the aortic cusp towards the septum with disruption of the commissural support which may exhibit or aggravate AR which may in need for further aortic valve repair or replacement. [4]

The aim of the work is to study the short and intermediate clinical outcome of doubly committed subaortic VSD surgical closure techniques and their effect in maintaining the balance of the aortic root structure and function and preventing the progression of AR in patient with VSD –AR syndrome.

Materials and methods: Between May 2008 and October 2012, our non-randomized study included 90 patients with small subarterial doubly committed VSD who had been operated on at Ain Shams University Hospital and fulfilled inclusion criteria which include that all patients had running suture and patch closure of doubly committed subarterial VSD with diameter > 4mm. They were divided according to the technical type of intervention into two groups, Group A patch closure [45 patients] and Group B running suture patch closure [45 patients]. The degree of AR progression postoperatively was assessed by echocardiography every 6 months for 2 years.

Results: The repetition of postoperative clinical and echographic evaluation criteria for the degree of progression of AR every 6 months for 2 years postoperatively in both groups show that however there are 25 patients (56%) of Group A who had no preoperative AR, there are 35 patients (78%) who show no AR postoperatively and the remaining 10 patients (22%) had postoperative mild AR which remained unchanged and no patients had an increased AR. On the other hand there are 30 patients (67%) of Group B who had no preoperative AR, 25 patients (56%) of Group B show no AR postoperatively. 5 patients developed new postoperative AR with overall 20 patients (44%) of Group B who had postoperative AR, which was remained unchanged in 12 patients (26%) and increased in 8 patients (18%) who needed another operation for repair or replacement for aortic valve.

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Conclusion: We can concluded that the patch closure of the doubly committed subaortic VSD was safe and reliable surgical technique in keeping the balance of the aortic valve without any dysmorphic changes of the aortic root structure and function and preventing the progression of AR.

KEYWORDS: Cardiac defects, Infundibular ventricular septal defect, aortic regurgitation.

The lack of infundibular septal support for the aortic annulus and left to right shunting during the early systolic flow creating a venturi effect which leads to displacement of the aortic valve cusp towards the right ventricle which ended by aortic valve cusp prolapse and aortic insufficiency. [1]

However The early closure of VSD has been suggested to be effective in preventing the onset of AR, There was no standard surgical technique for outlet VSD closure. Various surgical technique for VSD closure was described, patch closure consider to be the most reliable and definitive surgical procedure for preventing residual VSD and displacement of the aortic annulus.

Small patch technique with the inner diameter less than that of VSD by 1–2 mm had no residual VSD or progression of AR, mild AR disappeared, and no change in the aortic or pulmonary annulus.[7]

Figure of eight patch for VSD-AR syndrome was suggested to support and elevate the sinus of valsalva. The upper half of it should matched the ventricular junctional zone, the intermediated part of it should be shorter than the distance between the adjacent two Right Coronary commissures, and its the lower part should matched the size of VSD.[3]

However running Direct VSD closure is safe, easy and can maintain the aortic cusp in its normal position, it believed that the orientation of the VSD boundaries and relation to the aortic cusp was difficult so that the aortic valve cusp will be in risk of injury as well as there was a risk of downward pulling of the aortic cusp towards the septum with disruption of the commissural support which may exhibit or aggravate AR which may be in need for further aortic valve repair or replacement.[4]

In relation to aortic valve there are different types of VSD including: perimembranous VSD and conal VSD with its multiple demanation (infundibular VSD, doubly committed VSD, subarterial VSD).within the conal septum there are different subtypes of VSD,our present study interested in a large circular or small crescentic VSD between the two commissures of Right Coronary cusp underneath part or whole of Right Coronary aortic cusp .the large circular VSD presented early in neonatal period with large left to right shunting result in heart failure and failure to thrive which indicating early surgical intervention to stop shunting, the occurrence of AR is infrequent in this type in comparison to a small perimembranous subaortic VSD. The crescent shape of a small subaortic VSD is a result of lacking fusion of the right sinus of valsalva to the crest of the septum, this type of defect appear to be associated

with an anomaly of the right sinus of valsalva where transition from sinus tissue to valve tissue is higher than normal. The deformation of the right coronary cusp and aortic regurgitation continues to progress during the life of the patient and it seems to be constant above 30 years of age..[8]

We all agree that the ventury effect plays an important role in limitation of the shunting through this defect so This defect never generates a large shunting, but lack of attachment of the right sinus of valsalva to the septum allows the right coronary cusp to be pushed into the defect by the diastolic pressure this increase the stress over the free edge and reduce the coaptation, once the height of right cusp is reduced a vicious cycle initiated and the aortic regurgitation was worsen which become significantly when thickening and retraction of the aortic cusp free edge occur.[9]

The left ventricular outflow tract (LVOT) consists of a fibromuscular structure its posterior wall was formed by the subaortic curtain and anterior leaflet of the mitral valve and its anterior wall was formed by the muscular and membranous septa. The anterior and posterior walls joined by the right and left fibrous trigones which maintain the dynamic behaviour of the LVOT. [5,6]

It has been agreed that The aortic root components including the crown shaped annulus, leaflets, commissures, subcommissural trigones,sinuses of valsalva and sinotubular junnection change in size and shape during the cardiac cycle.[7]

The closure of the perimembranous and subarterial VSDs with or without aortic valve repair is indicated when more than trivial AI is identified. [10 &11]

However, there is only a minimal chance for spontaneous closure of a subarterial VSD. All subarterial VSDs < 5 mm should be closed regardless of the presence of aortic valve prolapse to prevent the development of aortic regurge AR. Early closure of small infundibular VSD rather than delayed intervention achieved perfect result as the delayed intervention had been never correct the irreversible damage aortic valve[12]

The aim of our work is to Study of the short and intermediated clinical outcome of doubly committed subaortic VSD surgical closure techniques and their effect in maintaining the balance of the aortic root structure and function and preventing the progression of AR in patient with VSD –AR syndrome.

Material and Methods

In the period between May 2008 and October 2012, our non randomized study which included 90 patients had small subarterial doubly committed VSD < 5mm who had been operated on ain shams university hospital and fullfield the inclusion criteeria. Our Inclusion criteria include all patients had running suture and patch closure of doubly committed sub arterial VSD with diameter < 5 mm to permit the observation and removal of the prolapse right coronary sinus of valsalvas through the defect at the time of intervention and all of them

had an echo follow up ever 6 months for a period of 2 year to examine the degree of progression or regression of their AR. Then they are divided according to the type of intervention into two groups:

Group A patch closure (PC) [45 patients]

Group B running suture closure (RC) [45 patients]

Surgical technique:

In all patients Standard median sternotomy, cardio-pulmonary bypass establishment with direct aortobicaval annulation, moderate hypothermia 28°C, aortic cross clamping, myocardial preservation with antegrade blood Cardioplegia, tapping of caval cannula, right atriotomy and atrial trans-septal vent. The site of doubly committed VSD was confirmed to be underneath the right coronary cusp.

All patients in group A had VSD gortex patch closure. the size and shape of the patch depending on the size and shape of VSD, in all of our patients in this group two to three 5-0 polypropylene with Teflon pledget were inserted to the patch and a continuous sutures was done then sutured to each other.

All patients in Group B had VSD closure with interrupted running sutures on Teflon pledget with 5-0 polypropylene. At the end cardioplegic solution was infused into the ascending aorta to exclude aortic valve injury.

Results

Statistical analysis was done using SPSS version 13. The distribution of the variables among patient groups was analyzed by Chi-Square test, Fisher's exact test or χ^2 -test as indicated. Postoperative echocardiographic measurements were subtracted from the preoperative values and the means of the differences were calculated and compared. Means were compared with the unpaired or paired Student's test, as indicated. P values less than 0.05 indicated a statistically significant.

	Group A	Group B	ALL patients	P. VALUE
Patient No	45	45	90	NS
Female	4	3	7	NS
Age	3±1.8	3 ± 1.2	3 ± 1.5	NS
EF	65± 5	63 ± 4	64 ± 6	NS
VSD size	4± 0.3	4 ± 0.8	4± 0.5	NS
AR	20	15	35	NS

Table 1. The perioperative demographic variables

In group A 45 patients had patch closure, In group B 45 patients had direct closure, VSD: ventricular septal defect, AR aortic regurgitation, EF: ejection fraction.

The Demographic, preoperative clinical and echocardiographic criteria were compared between both groups in Table 1. Group A included 45 patients had subaortic VSD patch closure compared to group B included 45 patients had subaortic VSD direct closure. The selected variables between both groups was statistically non-significant.

	Group A	Group B
BYPASS TIME	25±9 min	10±3 min
Cross clamp	20±5 min	15±3 min

Table 2. Operative variables:

The selected operative values shows no statistical significant difference between both groups.

Postoperative mortality and mortality:

There was no postoperative mortality

no Infection, pericardial effusion 3 in group B and 1 in group A improved

with diuresis. No arrhythmia.

No residual VSD

	Preoperative AR		Postoperative AR			
	no AR	AR	no AR	Unchanged AR	Increased AR	
Group A	25 56%	20 44%	35 78%	10 22%	0 0	45 100%
Group B	30 67%	15 33%	25 56%	12 26%	8 18%	45 100%

Table 3. Postoperative evaluation of AR status in both groups

The repetition of postoperative echographic evaluation criteria for the degree of progression of AR every 6 months for of 2 year IN BOTH group shows that from 25 patients (56%) of group A had no preoperative AR, 35 patients 78% shows no AR postoperatively and the remaining 10 patients 22% had postoperative mild AR which was remained unchanged, no patients had an increased AR in a comparison with 30 patients (67%) of group B had no preoperative AR, 25 patients 56% of group B shows no AR postoperatively. 5 patients developed new postoperative AR with overall 20 patients had postoperative AR. The remaining 20 patients 44% had postoperative AR, which was remained unchanged in 12 patients 26% and increased in 8 patients 18% who needed another operation for repair or replacement for aortic valve.

Discussion

However the early closure of the doubly committed subaortic small VSD prevent the ventricle effect of left to right shunting which result in displacement and prolapse of the aortic cusp towards the right ventricular cavity that ends in AR, there are no standard surgical technique in dealing with that type of interventricular septal defect. [13]

VSD patch closure technique has been admitted as the most effective surgical technique in prevention of residual defect and aortic annular disruption.[14]

We studied the clinical and echocardiographic follow up outcome of 45 patients had patch closure of the their subaortic VSD, 20patients 44% of 45 patients had preoperative AR improved postoperatively to result in 30 patients 78% out of 45 patients had no AR postoperatively and the remaining 10 patients 22% had been remained unchanged mild AR withno one had an aggressive AR progression.

However the direct subaortic VSD closure technique was succeeded as a surgical technique in minimizing the degree of AR by returning the protruded cusp to its normal position, it fail in preventing of its progression.[16]

The direct closure technique was consider as the most safe and easy surgical technique that acualy improve the aortic cusp coaptation.

We studied 45 patients had direct closure, 8 patients 8% claim aggrevated AR and waiting for next step aortic intervention weather repair or replacement. The rest 37 patient had suceeful outcome,25 patients 56% had no AR and 12 patients 26% had unchanged mild AR.

Although Direct VSD closure could maintain the aortic cusp in its normal position but it fail to maintain the normal structure of the LVOTand aortic root. Moreover, it was easily injured or deformed the aortic cusp due to difficult orientation of the boundaries between the rim of VSD and aortic cusp or annulus.

Direct closure carry the rik of pulling down effect over the septum which ends by deformation of the aortic annulus and loss of the commissural support that aggrevated the degree of AR postoperatively. [16]

We can concludes that patch closure of the doubly committed subaortic VSD was safe and reliable surgical technique in keeping the balance of the aortic valve without any dysmorphism of the aortic root structure and function and preventing the progression of AR.

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Surgical management of left sided infective endocarditis: Predictors of morbidity and mortality in 214 patients

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Background: left sided infective endocarditis is a diagnostic and therapeutic challenge that requires surgical intervention to improve outcome. We audit in this report causes and predictors of morbidity and mortality in 215 patients operated on the past 10 years.

Methods: Retrospective data of 215 consecutive surgically managed patients with left sided infective endocarditis was analyzed. All patients were operated upon at Cairo university Hospitals between 2002 and 2012. Demographic, clinical, microbiological, echocardiographic data and surgical procedure obtained during hospitalization was used as variables for potential predictors of morbidity and mortality.

Results: In this study, there were 133 males and 81 females with a mean age of 34 ± 11 . Mitral valve was the most affected 43.9 %, followed by aortic valve in 32.2 %, double valve in 16.3 % and congenital defects in 7.4 %. The most common indication in this study was severe valve lesion in 51.8 % followed by congestive heart failure in 50.9 %. Culture negative endocarditis was present in 37.3 %. Staphylococcus aureus was the commonest organism cultured in 18.2 % of patients. The in-hospital mortality was 10.3% while the overall mortality was 13 % along a follow up period extending from 6 – 62 months. The predictors of mortality in this study were female gender, congestive heart failure, septic shock, systemic embolism, fungal endocarditis and mechanical ventilation more than 24 hours.

Conclusion: The prognosis of patients with septic shock and fungal endocarditis remains dismal, however early intervention in patients with IE while under medical treatment before development of CHF and / or systemic embolisation may improve outcome.

KEY WORD: Infective endocarditis, surgery in left side infective endocarditis

Infective endocarditis [IE] is an endovascular microbial infection of cardiovascular structures or of intracardiac foreign body facing the blood stream [1]. Surgery for IE is potentially lifesaving [2], and is required in up to 30 % of cases during acute infection and in 20 – 40 % during convalescence [3]. The indications of surgery in IE includes, hemodynamic decompensation due to acute valve regurgitation, persistent fever and bacteremia despite appropriate antibiotic treatment, development of abscess or fistulae caused by local spread of infection, large vegetations, recurrent emboli and prosthetic valve endocarditis particularly when associated with Staph. aureus infection [1,4,5].

The timing of operation is still a matter of debate. Surgical intervention is optimally performed before severe hemodynamic disability or spread of infection to perivalvular tissue [6].

With increase demands for surgery in patients with IE the identification of preoperative variables would predict patients at highest risk for morbidity and mortality. We thus audit in this report the surgical outcome of 215 patients operated for left sided IE to optimize timing and management of these patients aiming to improve outcome.

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Codex : o3/04/1301

Methods

This retrospective report studied the data of 215 consecutive patients admitted to Cairo University Hospitals between 2002 and 2012 and underwent surgery for left sided IE. For all patients who were discharged were contacted by direct phone calls and frequent visits to the outpatient clinic of the cardiology department.

We analyzed the clinical data (patient demography, duration of illness, IV drug abusers, time before referral and complications), microbiological data (causative organism and culture positive or negative) identification was obtained from blood culture serological testing and examination of surgical specimen, echocardiographic data (valve affected, cardiac complications, LV function and pericardial effusion), Surgical data (procedure, ICU stay, hospital stay), clinical outcome (early and late mortality, recurrence, late embolization, CNS complications, reoperation) and quality of life (neurological deficit and NYHA functional class).

Statistical Analysis

SPSS version 20 was used for data analysis. Mean and standard deviation were estimates of quantitative data. When appropriate parametric and non-parametric t-test (Mann Whitney test) were used for comparison of means of two independent groups. Chi-square / Fischer exact were tests of proportion independence. Logistic regression analysis was used to depict variables that contribute independently to the event of mortality among our patients. OR odd ratio and 95 % CI confidence interval showed the likelihood of mortality in the presence of specific predictor. Statistical significance was established at $p \leq 0.05$.

Results

In this retrospective study, 214 patients with left sided IE were operated upon. There were 133 males (62.1 %) and 81 females (37.8 %) with a mean age of 34 ± 11 year ranging from 7 – 69 years. Patients with known heart disease comprised 155 patients (72.4 %). However, underlying heart disease was present in 173 patients (80.8 %), 41 patients (19.1 %) had IE on normal heart. Clinical characteristics of patients are shown in table [1].

The indications of surgery in this group of patients was due to cardiac complications and include, severe valve lesions in 111 patients (51.8 %), congestive heart failure in 109 patients (50.9 %), large vegetations in 76 patients (35.5 %), uncontrolled infection in 72 patients (33.6 %), prosthetic endocarditis in 54 patients (25.2 %), Aortic root abscess in 39 patients (18.2 %), recurrent emboli in 25 patients (11.6 %).

The mitral valve was the most affected in 94 patients (43.9%), of these patients 72 had native mitral valve and 22 had mitral prosthetic valves, followed by aortic valve in 69

patients (32.2%), of these patients 49 had native aortic valve and 20 had prosthetic valve. Both valves were affected in 35 patients (16.3%), of these patients 23 patients were native and 12 patients had prosthetic valve endocarditis. Sixteen patients (7.4 %) had IE on congenital heart defects, including 9 patients with VSD, 6 patients with subaortic membrane and one patient with PDA.

Variables	No. of patients and %
Age	34 ± 11
Sex	133 males : 81 females
Underlying heart disease	
Rheumatic heart disease	87 (40.4%).
Prosthetic valve endocarditis	54 (25.2%)
Normal heart	41 (19.1%)
Congenital	16 (7.4%)
Floppy valve	10 (4.6%)
Degenerative	4 (1.8%)
HOCM	2 (0.9%)
Complications related to IE	
Congestive heart failure	109 (50.9%)
Embolization	122 (57%)
CNS emboli	21 (9.8%)
Splenic infarcts	17 (7.9%)
Intracranial haemorrhage	15 (7%)
Dialysis	9 (4.2%)
Mycotic aneurysm	6 (2.8%)
Splenic abscess	5 (2.3%)
Mean of symptoms duration before surgery	56.6 ± 91

Table 1. Clinical characteristics

Blood culture was only positive in 98 patients (45.7 %), The organism was identified by blood / tissue culture or serology in 134 patients (62.6 %). The most common organism was staphylococci, followed by streptococci. The organism could not be identified by blood / tissue culture or serology in 80 patients (37.3 %). Table 2 shows the identified organisms.

Surgical management was done for all patients in this study, mitral valve surgery was performed in 94 patients (43.9%) where 55 patients (25.7 %) underwent prosthetic valve replacement and 17 patients (7.9 %) underwent repair for native valve endocarditis and 22 patients (10.2 %) underwent redo valve replacement prosthetic valve IE. Aortic valve replacement was done in 69 patients (32.2 %) where 20 patients (9.3 %) underwent redo replacement for prosthetic valve EI and 12 patients (5.6 %) underwent Bentall procedure. Double valve replacement was done in 35 patients (16.3 %) where 12 patients

(5.6 %) underwent redo replacement. In 16 patients (7.4 %) congenital heart defect was repaired, with VSD patch closure in 9 patients (4.2 %), excision of subaortic membrane in 6 patients (2.8 %) and one patient with PDA ligation.

Organisms	No. of patients (214)
Staph aureus (blood / tissue culture)	39 (18.2 %).
Strept viridians (blood culture)	19 (8.8 %).
Fungal (blood culture / tissue / serology)	18 (8.4 %).
Gram –ve organisms (blood culture)	15 (7 %).
Bartonella (serology)	15 (7 %).
Brucella (blood culture)	14 (6.5 %).
Enterococci (blood / tissue culture).	14 (6.5 %).
Culture negative	80 (37.3 %).

Table 2. Microbiological characteristics

The mean follow up interval ranged from 6 months to 62 months with a mean of 42.2 ± 11.2 months. The in hospital mortality was 22 patients (10.3 %) and post discharge mortality was 6 patients (2.8 %), with a total mortality in this study of 28 patients (13 %). Table 3 shows causes of early mortality and table 4 shows causes and timing of late mortality.

In this study 214 patient were operated upon, 28 patients (13 %) died through the whole study period and 45 patients (21%) were lost for follow up.

In this study and after excluding the mortality and those lost for follow up, 141 patients remained to evaluate their quality of life that was reduced in 10/141 patients (7 %). Seven patients had dyspnea NYHA class III-IV, 2 patients had chronic lower limb ischemia and 1 patient suffered permanent neurological disability. In this study 6/214 patient (2.8 %) had relapse 2 of them died due to uncontrolled sepsis and congestive heart failure, while 4 patients were re-operated.

Causes of death	In-hospital mortality (n=22)
Congestive heart failure	9 (40.9 %)
Undetermined	4 (18.1 %)
Septic shock	2 (9 %)
Failure to wean from bypass	2 (9 %)
Chest infection	2 (9 %)
Intracranial hemorrhage	2 (9 %)
Post operative bleeding	1 (4.5 %)

Table 3. Causes early mortality.

Cause of death	Late mortality (n=6)	
	No. of patient	Time of death (months)
Congestive heart failure	1(16.6 %)	1
Undetermined	2 (33.3 %)	19 and 22
Intracranial hemorrhage	1(16.6 %)	15
Relapse of IE	2 (33.3 %)	9 and 11

Table 4. Causes and timing of late death

Clinical variables	Univariate analysis p. value	Multivariate analysis OR (95% CI), p. value
Age	0.53	
Female gender	0.037	5.72 (1.6 – 20.3), 0.007
Days before admissions	0.08	
IV drug users	0.38	
Microorganisms		
Staph Aureus	0.53	
Strept viridians	0.98	
Fungal	0.04	
Gram –ve organisms	0.48	
Culture negative	1.00	
Complications		
CHF	<0.001	3.71 (1 – 13.1), 0.042
Septic shock	0.02	
Cardiogenic shock	0.08	
Systemic emboli	0.04	
CNS emboli	0.36	
Pericardial effusion	0.11	
Pathological data		
Mitral valve IE	0.54	
Aortic valve IE	0.53	
Double valve IE	0.34	
Native valve IE	1.00	
Prosthetic valve IE	1.00	
Aortic root abscess/fistula	0.95	
Paravalvular leak or dehescence	0.79	
Rupture chordea	1.00	
Valve perforation	0.87	
Operative data		
Redo surgery	0.17	
Valve replacement	1.00	
Valve repair	0.53	
Cross clamp time (min)	0.04	
Perfusion time (min)	0.05	
Postoperative data		
Ventilation >24 hours	< 0.001	
ICU stay > 2 days	0.45	
Postoperative bleeding	0.29	
Reoperation for relapse	0.35	

Table 5. Uni and multivariate analysis of predictors of mortality.

Cardiovascular

In this study we analyzed the predictors of mortality after dividing patients into 141 patients in the survival group and 28 patients in the mortality group. Predictors of mortality were female gender, congestive heart failure, septic shock, systemic embolism, fungal endocarditis and ventilation > 24 hours. In the multivariate analysis, female gender and congestive heart failure were the significant predictors of mortality. Table 5, shows uni and multivariate analysis for predictors of mortality.

Discussion

Despite antibiotics and surgical therapy IE remains a disease with high mortality. Identification of predictors of mortality is a desirable goal to determine patient group who need early aggressive medical therapy and surgical intervention.

The incidence of in-hospital mortality in this study was 10.3 % and the overall mortality was 13 %, the overall reported mortality incidence in previous studies ranged from 6 – 25 % [7, 8]. However the mortality in countries like Tunisia, India and Turkey which share our patient characteristics as the rheumatic cardiac affection and the young age group were 19%, 21 % and 25 % respectively [9, 10, 11].

The late mortality in this study was 6 patients (2.8 %) along a follow up period that extended from 6 – 62 months with a mean of 42.2 months. Less data are available in the literature regarding long term outcome for patients with infective endocarditis, however it was estimated in most series that the survival rate is approximately 70 % [8]. Our long term low mortality could be explained by close follow up of our patients in one hand, but also we lost 21 % about 45 patients in the follow up which might have an impact in the long term results.

The univariate analysis of mortality predictors in this study were female gender, CHF, fungal endocarditis, septic shock, systemic emboli and postoperative ventilation > 24 hours, however in multivariable analysis, the most powerful predictor of mortality was female gender, followed by CHF.

The impact of gender on the outcome of infective endocarditis has not been adequately studied, however few studies have shown that female gender was associated with higher mortality than male gender and the Euro SCORE as a prognostic factor consider female sex a high risk among its variables. Many studies tried to explain gender difference and they incriminated that women receive treatment following clinical guideline less frequently and less aggressively than men. Mitral valvulopathy is more common in women and usually IE results from pre- or existing co-morbidities that are common in women such as renal failure, diabetes and immunosuppression [12, 13, 14].

Congestive heart failure is a recognized contributing factor in the mortality of infective endocarditis as shown in many studies. It was shown that CHF was an independently predictive of in-hospital and 1 year mortality in left sided IE

[15, 16]. As many as (50.9 %) of our patients were referred to us with congestive heart, most of developed failure while under medical treatment. Early surgical intervention would have been beneficial in this sub group of patients, since the prognosis of severe valve affection without heart failure is better than patients with CHF.

Septic shock was found as independent risk factor for mortality in this study. In contrast to CHF, septic shock represents uncontrolled systemic and disseminated infection. This unfavorable clinical status cannot be resolved by a local cardiac intervention and may explain why septic shock is associated with a high mortality rate. Other studies demonstrate our findings [6]. Fungal endocarditis was a significant risk factor for mortality in this study and was shown in other studies to carry a near 100 % mortality with medical and 50 % with combined medical and surgical intervention [17].

Embolic events were also found as independent risk factor for mortality in this study, this finding agrees with other studies [12].

Ventilation more than 24 hours was found an independent factor for mortality in our study. However in other studies patients whose ventilation after cardiac surgery is unexpectedly prolonged are prone to a larger number of complications and higher mortality [18].

There were several limitations in this study, first we could not detect micro-organism specific mortality prediction, and this could be explained by the high percentage (37.3 %) of culture negative patients due to prior use of antibiotics before referral to our hospital. Second as much as 21 % of our patients were lost for follow-up and this might affect our long term results. This was due to inadequate / wrong / unreachable contact information. Third in sub analysis group we did not have sufficient patient numbers to have adequate power to demonstrate difference between IE affecting different individual valves. Never the less we could conclude that more meticulous and aggressive strategy, including early surgery is needed for patients with IE in female gender and patients presenting with CHF or under treatment before they develop CHF. Patients presenting with septic shock and systemic embolization could be an indication for aggressive treatment, and again early surgery for those who are at high risk embolization could prevent such events.

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High Pre-operative Myocardial Ischemia Biomarkers as Predictors of Post-operative Mortality after CABG surgery: Tertiary Center Experience

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Objectives: To evaluate the predictivity of preoperative serum myocardial ischemia biomarkers for postoperative (PO) mortality in patients undergoing coronary artery bypass grafting (CABG) surgery.

Patients & Methods: The study included 300 patients with mean age of 62.2±4.2 years. Patients were evaluated for preoperative risk factors and donated fasting blood samples for ELISA estimation of preoperative serum levels of creatinine (sCr), cardiac troponin T (cTnT) and cTnI and Creatine Kinase-myoband (CK-MB) Isoenzyme. Intraoperative and PO complications were determined. The 30-day PO mortality rate and total mortality rate at the end of follow-up period were determined.

Results: All surgeries were conducted successfully without intraoperative mortalities or complications. One patient died during the 1st 30-days after surgery, 11 patients died during a mean follow-up period of 22 month for a follow-up mortality rate of 3.7% and a total mortality rate of 4%. Non-survivors were significantly (p<0.05) older, had increased frequency of associated co-morbidities and significantly higher serum levels of CK-MB, cTnT and cTnI. Concerning operative data, non-survivors consumed significantly longer theater time with significantly longer aortic clamping and CPB times. The ROC curve analysis defined old age, high preoperative cTnT serum levels, number of diseased vessels, high preoperative cTnI serum levels high preoperative CK-MB serum level, preoperative low left ventricle ejection fraction (LVEF), high preoperative serum creatinine and intraoperative aortic clamping time were specific predictors for PO mortality in descending significance. Regression analysis defined high preoperative serum cTnT and CK-MB and old age the most significant specific predictors of PO mortality.

Conclusion: Old age, multiple diseased vessels and low left ventricular ejection fraction in conjunction with high preoperative serum levels of myocardial ischemia biomarkers could predict PO mortality after CABG surgery. However, high preoperative troponin levels were significantly superior predictor for PO mortality than CK-MB.

KEYWORDS: Troponins, CK-MB, Preoperative levels, Postoperative mortality, CABG

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Coronary artery bypass grafting (CABG) is an established treatment for patients with ischemic heart disease. Although the number of older, sicker and high-risk patients undergoing CABG has been increasing, the mortality rates of this procedure have declined significantly over the last decade. The Society of Thoracic Surgeons database has documented that 87% of patients undergoing CABG can expect to survive without a major morbid event. However, up to 36% of patients undergoing cardiac surgery require prolonged intensive care unit (ICU) stay. Prolonged ICU stay not only results in higher mortality rates, but also raises enormous clinical and financial issues. The costs of CABG are determined by the costs of the operation itself, and the length of hospital and ICU stay ⁽¹⁻³⁾.

Although CABG is of considerable benefit for those in need for revascularization, it may nonetheless be associated with significant perioperative and postoperative

myocardial damage and necrosis, which may occur in varying degrees. Multiple mechanisms have been proposed to explain the finding of myocardial injury after CABG: intraoperative injury may result from cardiac manipulation, inadequate myocardial protection, and intraoperative defibrillation; in addition, postoperative myocardial injury may be associated with acute loss of bypass grafts⁽⁴⁾.

Regardless of the multiple modes of injury that may occur around the time of CABG, cardiomyocyte necrosis may be detected through measurement of cardiac enzymes such as creatine kinase or of more specific markers such as cardiac specific troponin (cTn). Depending on the assay used, these markers may be detectable in essentially all patients undergoing CABG^(5,6).

Multiple studies tried to evaluate preoperative predictors for postoperative cardiac events; **De Cocker et al.**⁽⁷⁾ identified twelve independent preoperative risk factors for a prolonged ICU stay following cardiac surgery and constructed a proportional hazards model that can predict whether a patient will have a prolonged ICU stay or not. **Krzych et al.**⁽⁸⁾ found preoperative assessment of B-type natriuretic peptide level in CABG patients could be a valuable diagnostic method for predicting several postoperative complications, especially pulmonary outcomes and requirement for hemodynamic support, and it correlated with the length of ICU stay and hospital stay. **De Lorenzo et al.**⁽⁹⁾ found elevated C-reactive protein (CRP) was more frequently found in patients who died after CABG than in those who survived and documented that an improvement to mortality risk prediction following CABG may be offered by the preoperative analysis of CRP.

The current prospective comparative study aimed to evaluate the predictivity of preoperative serum myocardial ischemia biomarkers for postoperative mortality in patients undergoing CABG surgery.

Patients and Methods

The current prospective study was conducted at Cardiovascular Surgery Department, KSA (kingdom of Saudi Arabia), KFMC (King Fahad Medical City), PSHC (Prince Salman Heart Center), since September 2010 till September 2011. After approval of the study protocol by the Local Ethical Committee and obtaining fully informed written patients' consent; all patients assigned for isolated elective coronary revascularization surgery with cardiopulmonary bypass (CPB) were enrolled in the study.

Exclusion criteria included the presence of preoperative heart failure, severe valvular disease requiring surgical repair before cardiac surgery, dialysis, inflammatory conditions manifested as markedly elevated baseline (preoperative) CRP (>10 mg/l) or leucocytosis (>10 × 10⁹/L), and intake of corticosteroids or immunosuppressant drugs. Patients had acute endocarditis, acute coronary syndrome within 10 days before

the procedure, stenosis of an internal carotid artery >70% and previous cerebrovascular accident were also excluded from the study.

Patients were evaluated for preoperative risk factors including age, gender, body mass index, previous myocardial infarction (MI) indicated by the presence of Q wave positive MI within the last 3 months, previous invasive coronary procedure; either percutaneous transluminal coronary angioplasty and/or intracoronary stent implantation, left main coronary artery stenosis of ≥50%, left ventricular ejection fraction (LVEF) of ≤30%, congestive heart failure, cerebrovascular disease indicated by ≥50% stenosis of carotid artery system, peripheral artery disease indicated by ≥50% stenosis of peripheral artery system, preoperative serum creatinine level >1.2 mg/dl, smoking (current smoker, Ex-smoker, non-smoker), hypertension, diabetes mellitus, chronic obstructive pulmonary disease and the number of diseased coronary arteries to be revascularized as indicated by coronary angiography.

Intraoperative data including left internal mammary artery usage, cardiopulmonary bypass and aortic cross-clamping times as well as the number of grafts were analyzed. Analysis of postoperative need for inotropic usage (the use of any inotropic agent other than dopamine at renal dose), blood transfusion (to maintain the hematocrit level ≥30%), prolonged mechanical ventilation (not weaning the patient from mechanical ventilation within the first 24 h after operation), re-intubation (need of repeat mechanical ventilation after weaning once), chest re-exploration, new-onset arrhythmia (onset of new arrhythmia requiring use of an anti-arrhythmic agent), cerebrovascular event (any neurological dysfunction except for delirium), postoperative renal dysfunction (serum creatinine level >1.20 mg/dl), fever (sublingual temperature >37.8°C or rectal temperature >38.2°C after the second postoperative day) or gastrointestinal complications (paralytic or mechanical ileus, gastrointestinal hemorrhage).

Preoperative blood samples (5ml) were collected under complete aseptic conditions at time of induction of anesthesia and was put in clean dry tube, allowed to clot and then serum was separated in clean dry Eppendorf tube till be assayed for estimation serum levels of creatinine (sCr)⁽¹⁰⁾, cardiac troponin I (cTnI)⁽¹¹⁾, cardiac troponin T (cTnT)⁽¹²⁾ and Creatine Kinase-myoband (CK-MB) Isoenzyme⁽¹³⁾ using an ELISA kit from Pelikine™ Inc., Concord, USA.

Outcome

The primary outcome was the determination of 30-day postoperative mortality rate and total mortality rate at the end of follow-up period. The study was extended to provide a minimum follow-up period of 6 months for the last case operated upon. The secondary outcome to verify the predictability of preoperative serum levels of the examined laboratory parameters and determined clinical and operative and postoperative data for short-term and follow-up mortality.

Statistical analysis

Obtained data were presented as mean±SD, ranges, numbers and ratios. Results were analyzed using Wilcoxon; ranked test for unrelated data (Z-test) and Chi-square test (X² test). Sensitivity & specificity of estimated parameters as predictors for postoperative mortality were evaluated using the receiver operating characteristic (ROC) curve analysis judged by the area under the curve (AUC) compared versus the null hypothesis that AUC=0.05. Regression analysis (Stepwise method) was used for stratification of studied parameters as predictors for postoperative mortality after CABG. Statistical analysis was conducted using the SPSS (Version 15, 2006) for Windows statistical package. P value <0.05 was considered statistically significant.

Results

The study included 300 patients; 205 males and 95 females with mean age of 62.2±4.2; range: 56-68 years. Fifty patients were morbidly obese (BMI>35 kg/m²), 185 patients were obese (BMI>30-35 kg/m²) and only 65 patients were overweight (BMI<30 kg/m²). All patients had associated medical co-morbidities with a mean associated co-morbidities of 1.8±0.8; range: 1-3; however, the majority of patients were either dyslipidemic and/or hypertensives. 9 patients had previous CABG and 21 patients had previous MI. Only 50 patients (16.7%) were previously non-smokers, 207 patients (69%) were ex-smokers and 43 patients (14.3%) were still smokers. Mean LVEF was 54.6±6.5%; range: 38-66% with the majority of patients had LVEF in range of 50-60%, (Table 1).

Data		Findings		
Age (years)	Strata	<60	108 (36%)	57±1.3 (56-59)
		60-65	113 (37.7%)	63.2±1.3 (61-65)
		>65	79 (26.3%)	66.8±0.7 (66-68)
Gender	Total	300 (100%)	62.2±4.2 (56-68)	
	Males	205 (68.3%)		
	Females	95 (31.7%)		
Body weight data	Weight		91.1±8.5 (78-109)	
	Height		165.3±3.8 (159-172)	
	BMI		33.4±3.2 (28.7-41.8)	
Smoking	Current		43 (14.3%)	
	Ex-smokers		207 (69%)	
	Non		50 (16.7%)	
Previous history of	Myocardial infarction	Yes	21 (7%)	
		No	279 (93%)	
	CABG	Yes	9 (3%)	
		No	291 (97%)	
	Cerebrovascular disease	Yes	15 (5%)	
		No	285 (95%)	
Associated co-morbidities	Diabetes mellitus		130 (43.3%)	
	Hypertension		160 (53.3%)	
	Renal dysfunction		20 (6.6%)	
	PVD		15 (5%)	
	Dyslipidemia		245 (81.7%)	
	Mean co-morbidities		1.75±0.8 (1-3)	
Left ventricular ejection fraction (%)	<50		50 (16.7%)	43.7±4.1 (38-49)
	50-55		115 (38.3%)	53.8±1.3 (50-55)
	>55-60		80 (26.7%)	58±1.5 (56-60)
	>60		55 (18.3%)	63.3±1.5 (61-66)
	Mean EF (%)		54.6±6.5 (38-66)	

Data are presented as mean±SD & numbers; ranges & percentages; BMI: body mass index; CABG: Coronary artery bypass grafting

Table 1. Patients' enrolment data

Cardiovascular

All surgeries were conducted successfully without intraoperative mortalities or complications. Only one patient died during the 1st 30-days after surgery for a 30-day mortality rate of 0.3 %. Throughout a mean follow-up period of 22±6.6; range: 6-32 months, 11 patients died for a follow-up mortality rate of 3.7% and a total mortality rate of 4%.

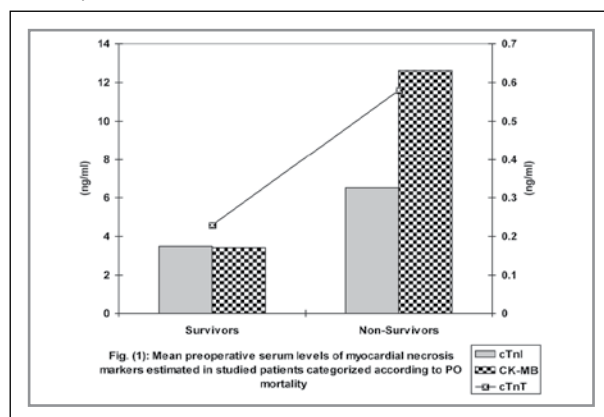
Analysis of patients' data showed that non-survivors were significantly (p<0.05) older and had increased frequency

of associated co-morbidities. As regards preoperative investigations, non-survivors had significantly (p<0.05) higher serum levels of CK-MB, cTnT and cTnI, (Fig. 1). Concerning operative data, non-survivors consumed significantly (p<0.05) longer theater time with significantly (p<0.05) longer aortic clamping and CPB times. Mean postoperative events was non-significantly (p>0.05) higher in non-survivors compared to survivors despite significantly (p<0.05) higher need for additional inotropics than dopamine at renal dose, (Table 2).

		Survivors (n=288)	Non-survivors (n=12)
Enrollment data	Age (years)	61.4±4.1 (56-68)	65.3±3.4 (56-68)*
	Gender; M:F	196:92	9:3
	BMI	32.9±2.9 (29-41.8)	35.4±3.8 (28.7-40.3)
	Current: EX: Non smokers	40:202:46	3:5:4
	Associated co-morbidities	1.6±0.7 (1-3)	2.3±0.8 (1-3)*
Data of preoperative investigations	Ejection fraction	58.1±5.3 (49-66)	53.7±6.6 (38-64)
	Number of grafted vessels	1.6±0.6 (1-3)	2.2±1 (1-3)
	Serum creatinine (mg/dl)	0.98±0.25 (0.4-1.4)	1.12±0.17 (0.8-1.5)
	Serum CK-MB (ng/ml)	3.43±2.26 (1.62-12.9)	12.63±13.5 (2.32-43.8)*
	Serum cTnT (ng/ml)	0.23±0.37 (0.003-1.32)	0.58±0.36 (0.05-1.17)*
Operative data	Serum cTnI (ng/ml)	3.51±2.75 (0.36-13.87)	6.54±2.62 (3.06-11.23)*
	Aortic clamping time	60.4±12.6 (45-85)	73.6±13.4 (50-90)*
	CPB time	90±13.8 (75-120)	100±16 (75-125)*
	Total operative time	203.5±25.2 (150-250)	230±21.4 (190-260)*
Postoperative events	Usage of additional inotropics	20 (6.9%)	3 (25%)*
	Blood transfusion	90 (31.3%)	5 (41.7%)
	Prolonged MV	17 (5.9%)	2 (16.7%)
	Re-intubation	10 (3.5%)	1 (8.3%)
	Fever	15 (5.3%)	1 (8.3%)
	GIT complications	21 (7.3%)	2 (16.7%)
	Increased sCr level	11 (3.8%)	1 (8.3%)

Data are presented as mean±SD & numbers; ranges & percentages; CK-MB: Creatine Kinase-myoband; cTnT: cardiac troponin T; cTnI: cardiac troponin I; BMI: body mass index; CPB: Cardiopulmonary bypass; MV: mechanical ventilation; GIT: gastrointestinal tract; sCr: serum creatinine

Table 2. Patients' enrolment data

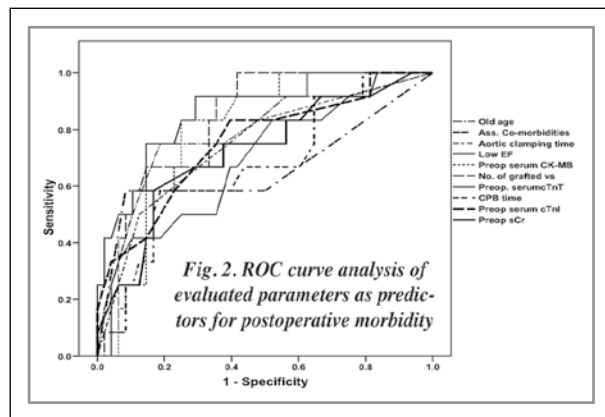


The ROC curve analysis of preoperative patients' data and preoperative investigation and intraoperative data as predictor for PO mortality defined old age and high preoperative cTnT serum levels as the highly significant (p<0.001, respectively) specific predictors for PO mortality. Number of diseased vessels and high preoperative cTnI serum levels were the following significant (p=0.002) specific predictors for PO mortality and followed by high preoperative CK-MB serum level (p=0.007). Preoperative low LVEF (p=0.041), high preoperative serum creatinine (p=0.041) and intraoperative aortic clamping time (p=0.018) were specific predictors for PO mortality, however, the significance is less than the other parameters. On contrary, the multiplicity of associated co-morbidities and CPB times were non-significant (p>0.05) specific predictors for PO mortality, (Table 3, Fig. 2).

Parameter	AUC	Std error	p	CI	
				Upper	Lower
Old age	0.831	0.056	<0.001	0.722	0.940
Number of diseased vessels	0.789	0.080	=0.002	0.633	0.946
Multiplicity of associated co-morbidities	0.663	0.108	=0.082	0.633	0.946
Ejection fraction	0.692	0.085	=0.041	0.524	0.859
CPB time	0.674	0.087	=0.065	0.502	0.946
Aortic clamping time	0.745	0.082	=0.018	0.555	0.888
High preoperative serum cTnT	0.863	0.058	<0.001	0.750	0.976
High preoperative serum cTnI	0.795	0.060	=0.002	0.678	0.912
High preoperative serum CK-MB	0.754	0.081	=0.007	0.595	0.913
High preoperative serum creatinine	0.721	0.085	=0.041	0.524	0.845

AUC: Area under curve; Std error: Standard error; CI: confidence interval; CPB: cardiopulmonary bypass; cTnT: cardiac troponin T; cTnI: cardiac troponin I; CK-MB: creatine kinase-myoband

Table 3. ROC curve analysis of preoperative laboratory parameters and clinical data and operative data as predictors for postoperative mortality



Verification of the estimated parameters as significant specific predictors for PO mortality using Regression analysis defined high preoperative serum cTnT as the most significant specific predictor in 7 analytic models, old age was the 2nd most significant specific predictor in 6 models, high preoperative serum CK-MB was the 3rd most significant specific predictor in 5 models, number of diseased vessels in 4 models, high preoperative serum creatinine in 3 models, prolonged aortic clamping time in 2 models and multiplicity of associated co-morbidities in one model, (Table 4).

		β	T	p
Model 1	Age	0.388	4.519	<0.001
	Number of occluded vessels	0.450	5.814	<0.001
	Aortic clamping time	0.229	2.703	=0.009
	Multiplicity of associated co-morbidities	0.211	2.727	=0.009
	High preoperative serum cTnT	0.240	2.754	=0.008
	High preoperative serum creatinine	0.224	2.761	=0.008
	High preoperative serum CK-MB	0.220	2.378	=0.021
Model 2	High preoperative serum cTnT	0.473	5.806	<0.001
	Age	0.462	5.370	<0.001
	High preoperative serum CK-MB	0.303	3.400	=0.001
	Number of occluded vessels	0.196	2.34	0.020
Model 3	Aortic clamping time	0.172	2.064	0.044
	High preoperative serum creatinine	0.171	1.778	0.081
	High preoperative serum cTnT	0.486	5.529	<0.001
	Age	0.458	5.479	<0.001
	High preoperative serum CK-MB	0.286	3.135	=0.003
	Number of occluded vessels	0.243	2.638	=0.011
	High preoperative serum creatinine	0.186	2.212	=0.031

		β	T	p
Model 4	High preoperative serum cTnT	0.534	6.060	<0.001
	Age	0.461	5.330	<0.001
	High preoperative serum CK-MB	0.310	3.311	=0.001
	Number of occluded vessels	0.270	2.857	=0.006
Model 5	High preoperative serum cTnT	0.477	5.236	<0.001
	Age	0.458	4.989	<0.001
	High preoperative serum CK-MB	0.435	4.802	=0.003
Model 6	High preoperative serum cTnT	0.499	4.802	<0.001
	Age	0.347	3.333	=0.002
Model 7	High preoperative serum cTnT	0.515	4.578	<0.001

β : Standardized coefficient; cTnT: cardiac troponin T; CK-MB: creatine kinase-myoband

Table 4. Regression analysis of preoperative laboratory parameters and clinical data and operative data as predictors for postoperative mortality

Discussion

The current study reported an overall PO mortality rate of 4% throughout a mean follow-up period of about 22 month with low 30-days mortality rate of about 0.3%. Evaluation of preoperative and intraoperative data as predictors for PO mortality revealed that multiple clinical, preoperative and operative data were specific predictors for PO mortality. Patients' age, multiplicity of associated co-morbidities and high preoperative serum creatinine were found to be significant predictor both by ROC curve and regression analyses.

These data coincided with that reported in literature where **Filizcan et al.**⁽¹⁴⁾ found age, preoperative cardiac troponin levels, and preoperative intra-aortic balloon counter-pulsation (IABP) use were predictive factors of in-hospital mortality of patients undergoing primary CABG for ST-elevated myocardial infarction (STEMI). **Chen et al.**⁽¹⁵⁾ also reported an in-hospital mortality rate of 4.31% and found abnormal preoperative C-reactive protein (CRP), abnormal troponin I, IABP, preoperative cardiac arrest and preoperative history of myocardial infarction were the risk factors for perioperative death. **Mejia et al.**⁽¹⁶⁾ reported that in multivariate analysis age >65 years, CPB >108 minutes, creatinine >2 mg/dl and systolic pulmonary pressure >60 mmHg were predictors of in-hospital mortality after CABG for acute MI.

Clinically, non-survivors were found to have low preoperative left ventricular ejection fraction (LVEF) and multiple occluded vessels; both parameters were found to be a significant predictor for PO mortality. In line with this finding, **Daneault et al.**⁽¹⁷⁾ found multi-vessel disease was associated with greater mortality in patients with preserved but not reduced LVEF and by multivariate analysis, LV dysfunction was the strongest predictor of 30-day and 3-year mortality.

Preoperative serum levels of CK-MB, cTnT and cTnI in non-survivors were significantly higher compared to survivors

and all of the three markers did well for the prediction of PO mortality, however, both ROC and regression analysis defined high preoperative serum levels of cTnT as the highly significant specific predictor, followed by serum cTnI levels and lastly serum CK-MB levels. These data go in hand with that previously reported for these three cardiac ischemia biomarkers estimated, either separately or in combination.

Gan et al.⁽¹⁸⁾ reported that the logistic regression revealed that preoperative CRP (>5.0 mg/L), elevated cTnI, emergent procedure and LVEF <40% were the independent PO mortality risk factors after CABG surgery. **Domanski et al.**⁽¹⁹⁾ also reported that among patients who had undergone CABG surgery, elevation of CK-MB or troponin levels within the first 24 hours was independently associated with increased intermediate- and long-term risk of mortality. **Søraas et al.**⁽²⁰⁾ found both peak CK-MB and peak cTnT independently predicted long-term mortality after CABG surgery when analyzed in separate multivariate Cox models, however, when analyzed simultaneously in the same Cox model, cTnT was a significant predictor and concluded that both CK-MB and cTnT are predictors of mortality after CABG surgery; however cTnT is a better predictor of long-term mortality after CABG surgery than CK-MB.

Sezai et al.⁽²¹⁾ in the setting of emergency CABG for acute MI, found the risk factors for early death were age \geq 80 years, shock, veno-arterial bypass, high CK-MB, non-use of a left internal thoracic artery graft and CPB time \geq 120 min. **Lim et al.**⁽²²⁾ evaluated serum levels of cTnI and CK-MB and inflammatory markers for prediction of post-CABG acute MI and found the peak cTnI at 24 hours and CK-MB significantly correlated with the amount of new late gadolinium enhancement, at 1 hour, cTnI, interleukin 6, and tumor necrosis factor- α were significantly elevated in patients with versus those without new late gadolinium enhancement, but ROC curve analysis showed cTnI was the most accurate at detecting new late gadolinium enhancement at 1 hour.

In support of the predictivity of preoperative myocardial necrosis markers for PO mortality, multiple studies of variant procedural interferences for coronary artery disease reported similar outcome. **Thielmann et al.**⁽²³⁾ reported that female sex, preoperative cTnI level, preoperative cardiogenic shock, and time to operation are major variables of mortality and morbidity results of CABG in STEMI. **Paparella et al.**⁽²⁴⁾ found preoperative cTnI values were significantly associated with a higher incidence of major postoperative complications including in-hospital mortality and perioperative myocardial damage was more pronounced in patients with preoperative cTnI exceeding 0.15 ng/ml which was found to be an independent predictor for 6-month mortality. **Koenig et al.**⁽²⁵⁾ found slightly increased cTnT concentrations in stable coronary heart disease patients are associated with several cardiovascular disorders and predict long-term events several weeks after an acute event or CABG. **Cockburn et al.**⁽²⁶⁾ found the use of troponin would have led to a fivefold increase in diagnosis of periprocedural MI in the British Bifurcation Coronary Study.

In support of the superiority of troponin over CK-MB for prediction of PO mortality, **Vranckx et al.**⁽²⁷⁾ assessed the differential implications of cardiac biomarker type on periprocedural myocardial infarction (PMI) reporting and found PMI was diagnosed in 9.8% of patients when cTn was used (CK-MB mass if cTn not available), and in 4.4% of patients when CK-MB mass was used (cTn if CK-MB mass not available).

It could be concluded that old age, multiple diseased vessels and low left ventricular ejection fraction in conjunction with high preoperative serum levels of myocardial ischemia biomarkers could predict PO mortality after CABG surgery. However, high preoperative troponin levels were significantly superior predictor for PO mortality than CK-MB.

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On-Pump Versus off-Pump Bypass Technique in Left Main Coronary Artery Disease: Does The Technique Affect Complete Revascularization?

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Objective: The aim of this multi-center study was to evaluate the validity, effectiveness, and safety of the off-pump versus the on-pump technique when used for myocardial revascularization in left main coronary artery disease; and also to investigate the accusation of under-revascularization that is traditionally directed to the off-pump procedure.

Methods: Between March, 2005 and April, 2009; 734 cases with left main disease (>50%) were subjected to coronary artery bypass grafting (CABG), 401 were operated upon using off-pump technique (54.6%) and 333 on-pump (45.3%). 170 patients with isolated left main disease fulfilling the inclusion criteria in each group were studied. The age range was 34-72 years old. with 112(65.8%) males in group A, and 118(69.4) males in B.

We classified them into two groups; group A (off-pump group), and group B(on-pump group). We excluded associated valve pathology or aneurysms. All patients of both groups had the same surgical exposure, we utilized the LITA, radial artery and the saphenous vein, the T or Y grafts were not performed in both groups, Demographic, operative and postoperative data were collected and analyzed.

Results: There was no intra-operative mortality in both groups, the hospital mortality was 0.58% in group A, and 1.17% in group B ($p=0.7$). The operative time was shorter in group A ($p=0.0481$), the total number of grafts was not significantly different in both groups (A= 4.12 ± 1.7 ; B= 4.08 ± 1.61 with $p= 0.87$). The ICU stay, hospital stay and duration of mechanical ventilation showed no significant difference ($p=0.18, 0.67$ and 0.45 respectively), the need for inotropic support was less in the off-pump group ($p=0.001$), post-operative morbidities and blood loss also showed statistically insignificant differences in favour of group A ($p=0.74$). Follow up of both groups showed no statistically significant difference regarding mortality or major morbidities related to revascularization.

The CABG operation is considered one of the oldest; yet still valid; procedures performed in the history of cardiac surgery. It was; and still; a landmark operation saving people's lives. The operation was first performed by Kolesov in the previous Soviet Union (Russia); in the early 1960 s (published in 1967), and it was popularized by Favaloro in the USA, and is still the leading heart operation performed today.^(1,2)

Significant left main coronary artery disease is diagnosed in 5% to 7% of patients undergoing coronary angiography.⁽³⁾ Compared to medical treatment; stenting of the left main is better (5 years mortality is 42% with medical treatment), yet the results of stenting are disappointing, because of the high rate of acute elastic recoil, abrupt vessel occlusion, and sudden closure and stenosis of stents due to thrombosis, leading to early mortality.^(4,5)

Despite major advantages offered by the bare metal stents(BMS), for the treatment of the ULMCA(unprotected left main coronary artery), still the mortality is high with an in-hospital mortality of 13.7% and 20.2% at 1 year; the result of surgery was much

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better with an overall in-hospital mortality of 2.3% and 11.3 % at one year^(5,6). The Cleveland Clinic Foundation(CCF) and consequently, the American College of Cardiology(ACC) / American Heart Association(AHA)/Society for Cardiovascular Angiography and Interventions guidelines(SCAI) discouraged PCI for the left main.⁽⁶⁾ According to the new guidelines of the CCF/AHA/SCAI for PCI; the surgical revascularization is still preferred; despite the availability of the DES(drug eluted stents) and the BMS.^(7,8)

There is no doubt of the superiority of the intervention; surgical or by PCI, over the medical treatment for the left main coronary artery disease. The debate is still between the advantages and long term results and safety of both the PCI and the surgical revascularization.^(9,10) However, we still have another sub-debate, between the off-pump and the on-pump revascularization for the critical left main coronary artery disease; yet it is not a matter of superiority comparing both; it is a matter of safer easy procedure; and validity of the technique.⁽¹¹⁾

Coronary artery bypass grafting was first launched without CPB in the 1960s by different proposals, the most popular of them, that technique proposed by Kolesov which was the first and the optimal OPCAB to be done using LITA to LAD⁽¹²⁾ Yet it came to surface again since more than two decades, now it accounts for 30% of the operated CABG patients. Many authors compared both; on-pump and off-pump CABG; not only in left main disease but also for the routine CABG procedures.^(13,14)

As critical left main disease should be optimally treated, by surgical re-vascularization.⁽¹⁵⁾, some patients and even some physicians may think that patients operated for CABG, using the OPCAB, might have less number of grafts, than the on-pump. Moreover, some studies might emphasize on this idea.⁽¹⁶⁾

Some authors may be convinced by the off-pump technique, but still convinced of the difficulty to do all targets, others may see it unsafe; Moreover; highly unsafe in left main disease, some authors even performed CABG for the left main on beating heart using CPB, taking the hazards and risks of the heart lung machine unnecessarily.⁽¹⁷⁾ Though the MEGA-ANALYSIS made by Cosgrove had classified the left main disease as not being an independent risk factor; yet still some surgeons had the concept that it is so risky to do it off- pump, even consider it as a mere risk factor by itself.⁽¹⁸⁾

Most reports stated the value of the OPCAB, in reducing early postoperative complications, and the equality of the late graft patency compared to the on-pump technique. ⁽¹⁹⁾. The average risk of on-pump CABG in low risk patients is 1%-2%; which is increased with increases of patients risks. Despite the new technologies reverting the CPB safer; still we have complications occurring with the pump, arrested heart

and lungs causing disturbed blood flow to the organs and the effect of activation of different immune reactions on the blood components.⁽²⁰⁾

There is no doubt that the abandoned tubing system, the normal pulsatile flow, the less heparin dose, and the less fluctuant systemic blood pressure in the OPCAB; make it safer with less complications than the on-pump.⁽²⁰⁾, the choice of the procedure should depend on the comfort level of the surgeon; because the two procedures seem equally effective; except in few situations.⁽²⁰⁾

All patients with left main coronary artery disease; in most reports were safely operated upon using off-pump technique; whatever the accompanying situation; emergency, unstable angina, bad LV function, or electrical instability of the myocardium, proving the conclusion that being left main, is no more an isolated risk factor.^(21,22)

Complete revascularization is feasible with same number of grafts, total arterial revascularization, use of bilateral ITAs ,the Y or T grafts and long patch anastomosis; all are feasible with the OPCAB, as in the on-pump even in left main coronary artery disease.⁽²³⁾

Patients and Methods

• Patient demography

Between March, 2005 and April, 2009, 734 patients of left main CAD (>50%), were candidates for CABG, 401 of them were operated upon using off-pump technique, and the other 333 were operated upon using on-pump technique. We randomly selected 170 patients of each group for the study; put them into two groups; group A the OPCAB patients; group B the on-pump patients; during our study we chose the isolated left main disease, with other exclusion criteria as follows:

• Exclusion criteria

We excluded any patient who had:

1. Associated valve disease.
2. Recent MI.
3. Recent stent to any coronary vessel.
4. Associated ventricular aneurysm.
5. Combined carotid artery disease requiring interference.
6. Redo cases for cardiac surgeries.

• Surgical techniques

The choice of off pump versus on pump was according to the surgeon's preference. In all patients of both groups, pedicled LIMA was harvested and grafted to LAD, the radial artery was harvested in 119 patients in group A(70%), and in 126 patients

in group B(74%) ,and used for good sized critically occluded left sided targets other than the LAD. The long saphenous vein was also harvested in 63 cases of group A and in 71 cases of group B, in such cases we had the right coronary artery or more than one target of the circumflex and Ramus and/or one or more than one diagonal branches to anastomose.

• OPCAB

Heparin (150U/kg) was given after the LIMA was harvested, it was safe to manipulate the heart to take a deep stitch in all cases without hemodynamic compromise. We started in all the cases with the LIMA to LAD. The dissection of the LAD was carried out easily in all the cases including 19 patients who had deep intra-myocardial LAD (11.1%).

In all cases of group A, the LAD was controlled proximally and sometimes distally with a sialistic (rubber) blunt needle stitch for better visualization. We did not use intracoronary shunts in any case, myocardial stabilizer and humidified carbon dioxide blower were standardly used in all cases.

After LIMA was anastomosed to the LAD. The OMs were then grafted using the radial or venous conduit; we performed separate and/or sequential techniques; according to the anatomy of each patients vessels; with the other OMs, ramus or diagonals, according to the state of targets. Our routine was the sequential; unless the second or third target was so small or so big; we grafted it separately with the vein or radial artery. The RCA or the PDA were the last to anastomose; the proximal anastomoses were then performed using a side biting vascular clamp.

• Pitfalls

The intra-myocardial LAD , even if very deep or just close the septum could be dissected and exposed safely without the need of CPB , and the controlling rubber stitch around the coronary could be taken ,sometimes there was a jet of blood from the ventricle which was controlled by just compression by a gauze for a minute or two as it only splits the ventricular muscle fibers and did not cut through, we were never pushed to control by sutures or obliged to convert to CPB because of this, the dissection of the intra-myocardial OMs or ramus even if so deep was not also a problem in OPCAB ,yet we had to dissect the muscle fibers little proximally to seat the graft well in its take off at the heel of the anastomosis, so as not to be angulated or kinked,the rubber stitch should take a bulk of the muscle fibers and not applied directly around the coronary.

• On-pump

In on-pump cases, after LIMA was harvested, we had aorto-common atrial cannulation and used intermittent antegrade warm blood cardioplegia. We started with the posterior and

lateral targets and finally the LIMA to LAD. Then after declamping,we performed the proximal anastomoses using a side biting clamp on a beating heart.

We assessed the flow in the grafts and graft patency by TTFM (Transit Time Flow Meter).Using intra-operative flow-probes to measure blood flow transit time to calculate volumetric flow and derived parameters such as resistance through the graft. We used the Medi-Stim Flow-meter System, intra-operatively, before and after protamine sulfate administration. The flow indicating good patent graft is $> 20\text{mL}/\text{min}$. yet there were some grafts of $< 20\text{mL}/\text{min}$. but patent and had no ECG changes. The flow curves and the mean values of flow were recorded; The transit time taking the mean flow, diastolic flow (%of time), and pulsatility index (PI).The time of the distal anastomosis, the time taken for conduit preparation, and the total operative time were registered. The number of sequential and separate grafts were registered, the graft flow, operative and postoperative data were registered and analyzed

The patients were followed-up after discharge in out patient department, by clinical evaluation, ECG,echocardiography, multi-slice C.T. coronary angiography or conventional coronary catheterization; which was performed for symptomatic patients.

Comparison of baseline characteristics of both groups and statistical analysis were done, results were expressed as mean \pm SD or absolute frequencies and proportions. Statistical significance was defined as p value < 0.05

Results

The demographic data in both groups showed no significant statistical difference in both groups (Table 1), and the preoperative EF% showed no significant difference ($p=0.43$ and 0.61), the associated diseases also revealed insignificance; diabetes, hypertension and dyslipidemia ($p=0.96$, 0.77 and 0.056 respectively),also the effect of smoking and the positive family history for ischemic heart diseases had no significant difference in both groups;($p=0.27$ and 0.382 respectively)

• Operative and postoperative data

The length of operation was significantly shorter in the OPCAB than the on- pump($p=0.0481$),the use of blood was more in group B than in A,($p=0.036$); the number of distal anastomoses in both groups showed no significant difference($p=0.87$),the blood loss in both groups showed insignificant difference($p=0.74$);there was no significant difference in the number of patients who required re-exploration for bleeding($p=0.82$),the use of inotropic support was less in A($p=0.001$);the use of IABP and duration of mechanical ventilation showed no significant difference in both A and B groups,($p=0.74$ and 0.45),the ICU stay and the hospital stay were not having statistical significance in both groups($p=0.18$ and 0.67)

	<i>Group A(n=170)off- pump.</i>	<i>Group B(n=170)on- pump.</i>	<i>p-value</i>	<i>SS</i>
<i>Age-mean/years</i>	59.73±14.2	58.91±10.5	0.41	SI
<i>Sex</i>	Males=112(65.8%)	Males=118(65.8%)	0.43	SI
<i>Diabetes</i>	N=89(52%)	N=91(53.5%)	0.96	SI
<i>Dyslipidemia</i>	N=94(55.2%)	N=92(54%)	0.056	SI
<i>Hypertension</i>	N=68(40%)	N=71(41.7%)	0.77	SI
<i>Smoking</i>	N=61(35.8%)	N=66(38.8%)	0.27	SI
<i>Family hist.</i>	N=46(27%)	N=45(26.4%)	0.382	SI
<i>Preop.EF%(mean)</i>	43.57±10.3	44.71±11	0.61	SI
<i>OR.durat/min.</i>	139.4±26.13	203.4±51.2	0.0481	S
<i>Inotropic supp</i>	0.317±0.19	0.82±0.28	0.001	S
<i>Drain/cc</i>	469.19±291.7	556.36±364.5	0.74	SI
<i>Bleeding(post-op)</i>	N=6(3.4%)	N=8(4.6%)	0.82	SI
<i>Vent./hours</i>	4.7±2.11	6.2±2.5	0.45	SI
<i>IABP</i>	N=3(1.76%)	N=3(1.76%)	0.74	SI
<i>AF</i>	N=16(9.41%)	N=21(12.35%)	0.29	SI

Table 1. Pre-and post-operative data (SS=statistical significance,S=statistically significant,SI=statistically insignificant)

	<i>Group A(n=170)off- pump.</i>	<i>Group B (n=170)on- pump.</i>	<i>p-value</i>	<i>SS</i>
<i>ICU stay/days</i>	2.19±0.93	2.7±1.1	0.18	SI
<i>Hospit.stay</i>	6.54±2.4	7.2±2.9	0.67	SI
<i>Blood tran.(pack)</i>	1.6±0.8	2.7±1.4	0.036	S
<i>No.grafts</i>	4.12±1.7	4.08±1.61	0.87	SI
<i>Stroke</i>	N=1(0.58%)	N=1(0.58%)	0.92	SI
<i>St.wo.infect</i>	N=3(1.76)	N=4(2.3%)	0.46	SI
<i>Stern.dehesc</i>	N=1(0.58%)	N=2(1.176%)	0.7	SI
<i>Chest infect</i>	N=2(1.17%)	N=7(4.11%)	0.057	SI
<i>GIT complications.</i>	N=3(1.17%)	N=3(1.17%)	0.64	SI
<i>Renal imp.</i>	N=2(1.17%)	N=9(5.3%)	0.032	S
<i>In-hosp.m</i>	N=1(0.58%)	N=2(1.17%)	0.7	SI
<i>Sequential</i>	N=97(57%)	N=91(53.5%)	0.39	SI
<i>Periop. MI</i>	N=2(1.17%)	N=4(2.3%)	0.51	SI
<i>RCA or PDA grafts</i>	N=123(72.35%)	N=119(70%)	0.617	SI
<i>Medi-stim flow.mL/min.</i>	53.61±23.9	52.7±21.6	0.68	SI
<i>Vent. Arrhy.</i>	N=4(2.35%)	N=4(2.35%)	0.91	SI

Table 2. Post operative results. (SS=statistical significance,S=statistically significant,SI=statistically insignificant)

	Group A	Group B	p-value	SS
2grafts	18 (10.5%)	20(11.76%)	0.74	SI
3 grafts	87(51.17%)	87(51.17%)	0.976	SI
4 grafts	43(25.29%)	40(23.52%)	0.83	SI
5grafts	22(12.94%)	23(13.52%)	0.92	SI
Coronary angiography.	32(18%)	28(16%)	0.86	SI
Post.op.isch.	17(10%)	16(9.4%)	0.73	SI

Table 3. Number of grafts and graft patency (SS=statistical significance, S=statistically significant, SI=statistically insignificant)

Apart from renal impairment, postoperative complications showed insignificant difference in both groups; including: The peri-operative MIs, the CVSs, the wound infections, chest infections, arrhythmias (ventricular or supra-ventricular), gastrointestinal complications (ileus-peptic ulcers-bleeding-mesenteric vascular occlusion); the in-hospital mortality also was not significantly different in both groups ($p=0.7$), the follow-up with the coronary angiography, echocardiography and ECG showed equal mid-term outcomes in both groups. Over 3 years of the start of the study; 32 patients of group A were subjected to coronary angiography (18%), 17 (10%) patients were symptomatic for ischemic chest pain and recent ECG changes, the others were submitted electively to coronary angiography; revealing patent grafts. In group B, 28 (16.4%) patients were submitted for coronary angiography over 3 years, 16 patients (9.4%) were positive for recent ischemic events, the p-value of graft patency was 0.71 and 0.9 for the postoperative graft occlusion shown by coronary angiography.

Discussion

The left main CAD is not uncommon; it constitutes 5%-10% of the cases submitted for coronary angiography; despite it is an emergency, yet it is not an independent risk factor.⁽¹⁸⁾ Left main disease is risky when associated with acute coronary syndrome and hence it is for emergency CABG⁽²⁶⁾. Compared to medical treatment; CABG, has better survival rate, the outcome of surgery is still better and safer than the most-up to date-drug illuted stent for the left main.⁽²⁷⁾ Yet, some may use the staged hybrid therapy in the treatment of high risk patients.⁽²⁸⁾

With the new technologies and advances in PCI techniques, some physicians may regard left main stent as a safe and better than the conventional CABG, yet it is still controversial and in need for more supporting evidences.⁽¹⁰⁾

The resurgence of OPCAB, almost 2 decades before; opened the door for almost 20%- 30% of cases in the USA to be operated by this technique. (National Society of Cardiothoracic Surgeons, Adult Cardiac Database Spring Report 2005).

As on-pump CABG is a time-honored procedure, various co-morbidities are encountered associating and complicating this technique i.e; neurological morbidities, peripheral vascular diseases, retinopathy, renal impairment, left ventricular dysfunction, atheromatous aorta, and old age; All may be barriers for surgery using the CPB; The off-pump solved this problem not for all; but for the left main CABG too.⁽¹⁶⁾

There are many reports about the efficiency and safety of the OPCAB for left main CAD, and even better outcomes than the on-pump, regarding all aspects of morbidity and even less mortality. We performed our cases; all of them; without intra-operative mortality, or pre-operative use of intra-aortic balloon; other authors had same results.⁽¹⁶⁾

In our study we had no differences in both groups regarding the demographic data of the patients as in most similar studies^(17,23,33), we had only statistical significance in the duration of operation which was less in the OPCAB, also we had less use of the inotropic support in the OPCAB, as in the study made by Lu and colleagues in 2005; yet we had no difference regarding the ICU and hospital stay, which they had; the OPCAB had less ICU and hospital stay in their study; with lower incidence of chest infection and strokes in the OPCAB; while we had an unnoticeable differences; which might be due to the advances in CPB machines and techniques, closing the gap between both techniques.⁽³⁰⁾ In a study made on 2011 by Ishamudin and his colleagues, they stated that, the OPCAB is effective and safe

as equal as the on-pump in left main disease with no difference in the number of grafts and less blood needed for transfusion, as we had in our study; while Selke and his colleague had an opinion that the OPCAB has less number of grafts and even unsafe exposing patients who were converted from OPCAB to CPB to morbidity and mortality; but our conversion rate was 7% and we had almost equal number of grafts in both study groups.⁽³³⁾

Murzi and colleagues collected the data of 2375 patients of left main disease operated over 13 years starting from 1996 to 2009; and revealed concomitant results regarding less postoperative complications; namely; mortality, stroke, renal dysfunction, pulmonary complications and infectious complications; in the OPCAB than the on-pump; though these results were the same as ours, yet it was only numerical with no statistically significant difference between both techniques. Their results regarding the total number of grafts were in favor of the on-pump (more numbers of grafts). Meaning; under-revascularization in OPCAB patients. This might be due to their early experience at the early cases, but in our study, the number of grafts was not affected by the technique, and total revascularization was accomplished in both groups equally. The late postoperative follow up in the series of Murzi was similar in both groups (at 1,5 and 10 years), our results were similar. Also they confirmed that CPB was an independent predictor of in-hospital mortality in left main disease subjected for CABG.⁽²⁹⁾

Despite the results of some reports for left main revascularization showed that in hospital mortality, operative deaths, postoperative complications were less in OPCAB than the on-pump, with equal late outcome, yet still the number operated by this technique is much less; this might be due to the slow and difficult learning curve of this procedure.⁽³⁰⁾ But in our study we had insignificant difference in this regards, indicating good advancement in both techniques.

Though some reports had less number of grafts in the OPCAB than the on-pump,⁽²³⁾ specifically in left main disease, yet others reported it was the same in both techniques. This controversy about the idea of incomplete revascularization in the OPCAB is not right. In the OPCAB all vessels; even the small or the far targets could be safely accessible and grafted⁽³¹⁾. In our study we concluded that the left main CAD, is not an independent risk factor, and there is no effect on the outcome of surgery; this was concomitant with the study of Cosgrove⁽¹⁸⁾ and the other proven risk models (Euro SCORE). In which the left main is not identified as an independent risk factor for mortality.⁽³²⁾

Conclusion

Our study revealed that the OPCAB is a safe and convenient technique in the treatment of the left main CAD. The conversion rate to CPB was 7%; with almost equal mortality and morbidity compared to on-pump technique, with less need for blood transfusion and inotropic support.

Moreover, under revascularization was not encountered as no significant statistical difference in the number of grafts between OPCAB and on-pump CABG; any coronary vessel; anterior, lateral or posterior; small targets; epicardial or intramyocardial vessels could be anastomosed in off-pump cases, provided that surgery and anesthesia teams are well trained and adequately experienced.

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Levosimendan vs. Intra-Aortic Balloon Pump In High-Risk Cardiac Surgery

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The aim of this work is to blot the feasibility of using levosimendan (a newly introduced drug in the Egyptian market) against intra-aortic balloon pump in high-risk cardiac patients (left ventricular ejection fraction <35%) operated under cardiopulmonary bypass. In 15 patients, we deployed intra-aortic balloon pump immediately prior to induction of anesthesia and in the other 15 cases, levosimendan infusion was started after induction of anesthesia with an initial bolus of 12 U_g/kg for 10 min, followed by 0.1 -0.2 mg/kg/min till the end of the infusion .Intra-operative and Postoperative data were analyzed. In the levosimendan group, cardiac index was higher after cardiopulmonary bypass, at the end of the operation, and in the immediate postoperative period compared to the control group (IAB). The level of troponin I in the levosimendan group was significantly lower after the operation. ICU stay was shorter in the levosimendan group. **Conclusion:** Infusion of levosimendan before the initiation of cardiopulmonary bypass in patients with ischemic cardiomyopathy led to superior hemodynamic parameters compared to patients in whom an Intra-aortic Balloon was inserted, further studies to be considered on a larger scale of patients.

Current cardiac surgery programmes are characterized by surgical candidates with older age, more number of preoperative co-morbidities, worse clinical conditions and more depressed left ventricular (LV) function, the so-called 'high-risk patients', as compared to past surgical series.(1)

Intra-aortic balloon pump (IABP) is the most widely used circulatory-assist device in high-risk patients undergoing cardiac surgery (2) One of the life-threatening complications in patients with low (<35%) left ventricular ejection fraction (LVEF) is the development of perioperative myocardial dysfunction, which may lead to multiple organ failure in the postoperative period, and increase the duration of hospitalization and mortality.(3,4) A multicenter study found that prophylactic use of intra-aortic balloon pump (IABP) improved outcomes in high-risk cardiac patients.(5) yet, others surgeons have been dissuaded from its wider prophylactic use by reported high IABP-related complication rates (6). Thus, disagreement about the prophylactic use of IABP and the optimal time of support still exists worldwide, and the need for IABP assistance is still considered to be the witness of a complication rather than a therapeutic tool.

Recent upsurge in referral of patients with high perioperative risk or compromised left ventricular function for cardiac surgery has lead to an increasing use of pharmacologic support in the form of vasodilator and inotropic therapy to achieve improvement of tissue perfusion in the perioperative period or to support weaning from cardiopulmonary bypass (CPB). Traditionally, catecholamines including dopamine, dobutamine, epinephrine, and isoproterenol have been used as inotropic support after cardiac surgery (7) Most of the currently available inotropic drugs enhance myocardial contractility by increasing concentrations of intracellular calcium, which leads to an increase in myocardial oxygen consumption (8)

Levosimendan is a new calcium-sensitizing agent that has been developed for the treatment of decompensated heart failure. This agent sensitizes troponin C to calcium in a manner that is dependent on calcium concentration, thereby increasing the effects of calcium on cardiac myofilaments during systole, and improving contraction at a

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low energy (9-10). Levosimendan also leads to vasodilatation through the opening of ATP-sensitive potassium channels (11). By these inotropic and vasodilatory actions, levosimendan increases cardiac output without increasing myocardial oxygen demand

Theoretically, levosimendan has several advantages over conventional inotropic agents. Unlike agents that act through adrenergic pathways, levosimendan does not cause diastolic calcium overload, which can impair myocardial relaxation (12). Furthermore, it does not increase myocardial oxygen requirements, and may improve myocardial perfusion as a result of vasodilatation (13). Long-term benefits could also result from levosimendan use, as the presence of a pharmacologically active metabolite with a long elimination half-life (75–80 h) could lead to persistent hemodynamic effects (14).

Therefore, the aim of this research was to study the effect of levosimendan on the hemodynamics of patients with ischemic cardiomyopathy undergoing Coronary artery bypass graft using the cardiopulmonary bypass, and to compare it to same category of patients in whom an Intra aortic balloon was inserted.

Patients and Methods

The ethical aspect of this research was accomplished as informed consent was obtained from each patient. From January 2011 to July 2012, we composed a study group of 30 consecutive patients with LVEF < 35%, who underwent elective coronary artery bypass grafting with or without additional procedures (mitral valve surgery, Left ventricular reconstruction) Unstable cases who underwent urgent operation, cases with acute MI within 3 months before surgery as well as cases with extensive peripheral vascular disease were excluded from the research avenue. Also patients with severe form of COPD, renal failure requiring hemodialysis, previous history of CVS, were also excluded from the study.

Preoperative Evaluation: A thorough history taking and physical examination was done, complete laboratory investigation, CXR, 2D and M mode echocardiography, myocardial viability study if needed.

In All patients a Swan-Ganz catheter was inserted through the right internal jugular vein to monitor the hemodynamics of the patient.

IABP group: Inside the OR just before induction of general anesthesia the IABP was inserted through the femoral artery (preferably the right side) using seldinger technique under local anesthesia and sedation, sheathless insertion was the preferred method. (Datascope Sensation, linear 7.5F, 40 mL; Datascope Corp, Fairfield, NJ). Heparin infusion was started in the ICU after confirming that there is no mediastinal bleeding, at a rate of 5u/kg/h to maintain ACT within 150 sec. The IABP was kept for at least 24 hours postoperatively, or should be kept till the patient's hemodynamics and parameters shows no clinical or laboratory findings of low cardiac output status.

Levosemendan group: Levosimendan (Symdax) was administered intravenously through a central venous line after induction of anaesthesia; hemodynamics were closely monitored. An initial loading dose of 12 µg/kg levosimendan for 10 min was administered, followed by a continuous infusion of 0.1 µg/kg/min levosimendan for the following 23 hours. On completion of the total 24-h dose, the infusion was turned off immediately (no tapering). All patients should receive a total dose of 12mg.

Median sternotomy incision was the preferred incision, standard cardiopulmonary bypass was initiated through aorto-right atrial cannulation in all cases after assuring that the ACT is above 480 sec. Left internal thoracic artery was almost always grafted to the left anterior descending artery, while saphenous veins was used to graft other targets the Warm intermittent blood – potassium cardioplegic arrest was used for myocardial protection, blood was transfused to patients with hemoglobin < 9.0g/dL. At the end of CPB, heparin was neutralized with protamine sulfate. Perioperative haemodynamic data were obtained for statistical analysis.

In the IABP group, epinephrine and/ or norepinephrine infusion were started if needed to keep the cardiac index above 2.0 l/min/m². In the Levosimendan group, norepinephrine is almost always used to avoid severe peripheral circulatory failure.

VARIABLE	IABP	LEVOSIMENDAN	P VALUE
No. of patients	15	15	NS
(Sex(male/female)	11/4	9/6	NS
Age	59.33±6.59	60.14±7.62	NS
NYHA class	2.5±0.89	2.46±0.91	NS
Euroscore	5.78±1.48	5.07±1.56	NS
(%) LV Ejection fraction	30.93±2.73	31.35±2.59	NS

IABP=intra-aortic balloon pump, NYHA=New York heart association

Table 1. Demographics and baseline characteristics of the research group

Plasma Troponin I and plasma creatine kinase-MB fraction were measured successively before and after surgery, and measurements collected for statistical analysis. Other intra operative data were collected (ischemic time, bypass time, grafts done and full hemodynamic study)

Statistical analysis was performed with an SPSS software v. 20. All data are expressed as mean and standard deviation. Categorical variables are expressed as number and percentage, A *p* value < 0.05 was considered statistically significant.

RESULTS

Surgical details are presented in table 2, showing no statistical significant difference regarding the ischemic time, cardiopulmonary bypass time, number of grafts or additional procedures done (LV reconstruction or mitral repair)

VARIABLE	IABP	LEVOSIMENDAN	P VALUE
Ischemic (time(min)	57.93±19.40	55.93±18.70	NS
Cardiopulmonary (bypass time(min)	79.2±24.26	80.26±20.85	NS
Number of grafts	3.53±0.91	3.46±1.28	NS
LV reconstruction	(7%) 1	(13.3%) 2	NS
Mitral valve repair	(20%) 3	(13.3%) 2	NS

IABP=intra-aortic balloon pump

Table 2. Operative details

Postoperative outcome and morbidity are shown in table 3, we had one mortality in each group and that was due to multiorgan failure from low cardiac output status, which was not corrected by the insertion of an intra-aortic balloon in the patient of the levosimendan group, nor the patient in the intra-aortic balloon group who suffered from low cardiac output status responded to the infusion of levosimendan. The total time of postoperative mechanical ventilation showed no statistically significant difference between the two groups. Two patients in the IABP group required re-exploration due to excessive mediastinal drainage within the first 12 hours, while one patient in the levosimendan group required re-exploration.

The total blood loss was significantly higher in the IABP group within the first 24 hours with a mean of 816 ml compared to 556 ml in the levosimendan group and that was most probably due to the initiation of continuous heparin infusion in the IABP group within 12 hours after the operation to avoid any ischemic accidents in the lower limbs.

The total ICU was 4.24±0.99 days in the IABP group while in the Levosimendan group it was 3.18±0.97 days, and that was statistically significant. Two patients in the IABP group and one in the Levosimendan group were complicated by acute renal failure postoperatively and required 2-3 sessions of hemodialysis, all the three patients recovered from this temporary renal shutdown and required no further treatment or dialysis. Four patients in the IABP group and 3 in the levosimendan group had postoperative atrial fibrillation or frequent atrial or ventricular ectopics, all of which responded to low dose loading with amiodarone to avoid any negative inotropic effect known for this drug. Three patients, two in the IABP group and one in the Levosimendan group had deep wound infection that require rewiring and advancement pectoral muscle flap.

Variable	IABP	LEVOSIMENDAN	P value
Mortality	1 (7%)	1(7%)	NS
Ventilation time (hrs)	9.93±3.95	10.16±3.33	NS
Total blood loss in 24 hours (ml)	816.6±319	556±161	S (<0.05)
Re-Exploration for bleeding	2(13.5%)	1(7%)	NS
Total ICU stay (days)	4.24±0.99	3.18±0.97	S(<0.05)
Postoperative Hemodialysis	2(13.5%)	1(7%)	NS
Post operative Arrhythmias	4(26%)	3 (20%)	NS
Postoperative mediastinitis	2(13.5%)	1(7%)	NS

NS=not significant, IABP=intra-aortic balloon pump

Table 3. Postoperative findings and outcome.

The most important finding after analyzing the hemodynamic parameter of the patients in the two groups was the significant difference in the cardiac index 2 and 6 hours postoperatively where it was 2.33±0.50 l/min/m² in the IABP group compared to 2.91±0.59 l/min/m² in the Levosimendan group 2 hours postoperatively, while at 6 hours it was 2.38±0.59 in the IABP and 2.96±0.69 l/min/m² in the levosimendan group. Also chronologically speaking, from 5min before CPB to the end of the operation, and 2h- 6h after CPB, systemic vascular resistance index decreased significantly in the levosimendan group.

PARAMETER	GROUP	BASELINE	5MIN BEFORE CPB	30MIN AFTER CPB	2H AFTER CPB	6H AFTER CPB	POD1
Heart rate (beats/min)	IABP	71.4±14.6	71.2±14.1	83.1±10.8	82.9±15.1	81.2±22.1	84.2±21.2
	LEVO	75.2±17.6	78.7±23.9	85.9±15.4	92.0±17.6	89.9±17.6	90.2±13.4
MAP (mmHg)	IABP	78.5±12.2	78.1±18.2	80.1±6.5	76.9±10.9	75.1±9.1	83.3±12.0
	LEVO	85.4±11.3	75.9±14.7	70.1±8.9*	74.8±12.1	70.1±11.0	77.9±9.1
PCWP (mmHg)	IABP	20.5±8.5	21.7±5.9	22.8±8.1	21.1±7.2	21.5±5.1	23.0±5.1
	LEVO	22.7±12.1	19.9±6.1	25.6±11.2	23.2±7.1	22.6±6.4	22.9±6.1
CVP (mmHg)	IABP	8.3±2.7	7.7±1.1	10.2±2.6	8.6±3.2	8.5±4.1	9.9±1.8
	LEVO	7.8±3.5	6.3±3.5	9.9±2.5	9.6±3.4	9.1±3.0	10.2±2.9
Cardiac index (l/min/m ²)	IABP	1.42±0.2	1.89±0.42	2.43±0.42	2.33±0.50	2.38±0.59	2.19±0.49
	LEVO	1.54±0.38	2.22±0.57	2.71±0.92	2.91±0.59*	2.96±0.69*	2.51±0.58
SVRI (dyne.s cm ⁻⁵ /m ²)	IABP	3498±844	3132±571	2471±539	2512±683	2378±849	2702±701
	LEVO	3692±966	2398±601*	1928±658*	2091±858*	1774±703*	2382±603

* = P value < 0.05, CPB = cardiopulmonary bypass, CVP = central venous pressure, IABP = intra-aortic balloon pump, Levo = levosimendan, MAP = mean arterial pressure, POD = postoperative day, PCWP = pulmonary capillary wedge pressure, SVRI = systemic vascular resistance index. CI = cardiac index.

Systemic arterial vascular resistance index was calculated according to standard formulas: SVRI = (MAP - CVP) / CI, CI = CO / BSA.

Table 4. Perioperative hemodynamic parameters

Marker	Group	baseline	6h postoperative	POD 1
cTnI (ng/ml)	IABP	0.02 ± 0.01	7.13 ± 5.75	4.1 ± 2.88
	LEVO	0.023 ± 0.01	2.33 ± 1.98*	3.99 ± 2.4
CK-MB(u/l)	IABP	18.9 ± 10.8	60.2 ± 24.3	87.4 ± 49.8
	LEVO	19.1 ± 14.0	69.4 ± 35.1	68.0 ± 23.4

* = P value < 0.05 between groups, CK-MB = creatine kinase MB-isoenzyme, cTnI = cardiac troponin I, IABP = intra-aortic balloon pump, Levo = levosimendan, POD = postoperative day.

Table 5. Markers of myocardial damage

The markers for myocardial damage; Cardiac troponin I and creatine kinase MB isoenzyme were compared in the two groups, and there was a significant drop in the cardiac troponin I in the levosimendan group 6 h postoperatively as shown in table 5.

The total postoperative hospital stay was less in the levosimendan group yet this was statistically insignificant, also the Ejection fraction before discharge from the hospital improved as compared to the preoperative EF but this was statistically insignificant.

	IABP	LEVOSI- MENDAN
Postoperative EF (%)	33.49±3.34	32.92±3.64
Total hospital stay (days)	10.27±3.31	9.19±2.24

Discussion

In the last decade, patients referred for cardiac surgery are different than before. The co morbidities and the risk score of the patients is getting higher. This is in part due to the patients preference not to perform cardiac surgery except as a last resort, and also due to the overconfidence of the cardiologist in inserting coronary stents in multivessel disease: left main disease: poor LV function: coronary anatomy which is unfavorable for PCI. So more patients are transferred to perform CABG in a stage of dilated ischemic cardiomyopathy.

Since cardiac transplantation is not available in our country, and since the new left ventricular assisted devices carries a huge economic burden that we might not be able to cope with, we were faced with the problem of having a patient with ischemic dilated cardiomyopathy, and the available treatment options are

limited. The Intra-Aortic balloon has been used a long time ago in our institutions with fair outcomes, the main drawback of using the intraaortic balloon is the high complication rate related to its insertion (vascular, ischemic, bleeding). A retrospective study by Lavana and colleagues (15) suggested starting IABP before surgery aiming at reduction of hospital mortality. Yet, the main disadvantages of IABP include the development of limb ischemia, injury of the femoral vessels, or bleeding (both local and mediastinal due to heparin administration, IABP insertion can also be risky or contraindicated in cases of extensive peripheral vascular disease. According to the Benchmark Registry, the IABP-associated complications rate is 7.0%. (16)

Levosimendan, a member of the Ca^{2+} -sensitizer drugs, meets most of the goals of treatment in Heart failure and also promotes cardioprotection (17). Levosimendan has been shown to exert a positive inotropic effect as a result of an increase in calcium sensitivity of the subunit C of troponin (18). Further, the anti-ischemic properties of levosimendan have been related to the vasodilating and preconditioning effects related to both the interaction with K_{ATP} channels and to nitric oxide (NO) production (19).

Rajek and colleagues (20) were the first to report the use of levosimendan in patients with congestive heart failure and a preoperative left ventricular ejection fraction of $19 \pm 5\%$ undergoing elective cardiac surgery. There was a dramatic increase in CO after 60 minutes of levosimendan infusion and it stayed higher than 5 L/min during the first postoperative day, while pulmonary capillary wedge pressure (PCWP) decreased. Heart rate, mean arterial pressure (MAP), and pulmonary arterial pressure did not change during levosimendan infusion. Several other publications (21, 22, 23) have confirmed these findings of Rajek and colleagues (20). In our study, the cardiac index was higher in the levosimendan group while the Systemic vascular resistance index was significantly lower in the Levosimendan group and this comes in favor with the previous studies concluding the potent inotropic and vasodilatory effect of Levosimendan.

Landoni and colleagues (24) in their recent meta-analysis showed a significant reduction of mortality with the use of levosimendan in high risk cardiac patients. The results of our research suggest starting levosimendan infusion after induction of anesthesia as a good alternative to IABP in high-risk cardiac patients.

In our study group, the levosimendan sub-group had a lower level of troponin I 6 h after the operation. Previous studies attributed the cardioprotective properties of levosimendan to facilitation of adenosine triphosphate-dependent potassium channel opening. (25–26)

Numerous uncontrolled case series have indicated that levosimendan results in increased CI and reduced pulmonary capillary wedge pressure (PCWP) when given alone or in

combination with catecholamines (27,28). When compared to placebo, levosimendan increased cardiac output at unaltered myocardial oxygen consumption and without increase in arrhythmias (29, 30). However, these placebo-controlled trials are not directly comparable to our study, which compares levosimendan infusion to intra-aortic balloon insertion in patients with preoperatively impaired left ventricular function.

All our patients had preoperatively impaired LV function and received levosimendan intra-operatively (after induction of anesthesia) as a prophylaxis against low cardiac output syndrome (LOS). Given the possible preconditioning properties of levosimendan, timing of administration could be an important issue when evaluating outcome. This issue has been addressed by several investigators. Tasouli et al. (31) have presented a study where 45 patients with LOS were randomised to receive levosimendan either in the OR or in the ICU. Haemodynamic responses were similar in the two groups, but the OR group had significantly shorter ICU and hospital stay.

Limitations of the study

The most important limitation of this study is the limited number of patients enrolled in the study, and the obvious limitations related to the multicentre data collection. The clinical evaluation and procedures were performed at different centers by different surgeons. Although the hemodynamic efficacy has been established in the perioperative period, levosimendan has been studied only as a short-term therapy.

Conclusion

The initial assessment indicates that Levosimendan could be an effective and well-tolerated agent for the treatment of patients undergoing coronary artery bypass graft with ischemic cardiomyopathy. The initial results show comparable results to intra-aortic balloon pump in this subset of patients with favorable outcomes. However these encouraging preliminary results with levosimendan in cardiac surgical patients need to be verified by larger, multicenter randomized controlled trials, evaluating the optimum dosage and duration of therapy, its combination with other inotropics, and its long term effects.

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THE OUTCOME OF SURGICAL MANAGEMENT OF STAB WOUNDS OF THE HEART: ANALYSIS OF 115 CASES

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Background: Eighty to ninety percent of stab wounds to the heart result in cardiac tamponade. In most cases, the etiology is penetration of the myocardium with hemorrhage into the pericardial sac.

Objectives: The aim of this work is to evaluate our results in the management of the patients with stab wounds of the heart to detect the outcome of these patients requiring an emergency thoracotomy.

Patients and methods: Preoperative and operative variables were reviewed for all patients treated for cardiac stab wounds at Zagazig Emergency Hospital as regard age, sex, anatomical site of injury, time since stab, clinical status of the patient, diagnostic procedure, site of thoracotomy and outcome of the patient

Results: This is a retrospective study of the last 10 years which included 115 patients presented by stabbed heart. There were 109 males and only 6 females and the age ranged from 15 to 65 years with the predominant age group between 20-30 years with mean age of 28.5 ± 5.8 years. The anatomical site of injury on the pericardium was on left side just to the left of the sternum in 32 cases, near the left parasternal line in 44 and near the left midclavicular line in 39. As regard time since stab, most of the patients were coming within the first hour of injury. The clinical status of the patients were stable in 35 patients with systolic blood pressure > 90 mmHg, unstable in 40 patients with SBP < 90 mmHg, and 16 patients were shocked and 24 patients arrested before thoracotomy. Emergency room thoracotomy was done in 28 patients and operative room thoracotomy was done in 87 patients. The commonest sites of stabbed heart were in the right ventricle followed by the left ventricle. Mortality occurred in 27 patients, nineteen of them were after ER thoracotomy and 8 of them were after OR thoracotomy. Morbidity occurred in 19 patients of 88 survivals. Prognostic factors of outcome of the patient's including clinical status, patients who needed cardiopulmonary resuscitation had mortality rate of 68.57% and patients needed ER thoracotomy had mortality rate of 67.86%.

Conclusion: All patients suspected of having cardiac stab wounds must be fully resuscitated and undergo emergency thoracotomy, as significant survival can be achieved and death is not always the outcome.

KEYWORDS: Stab, wound, heart

Trauma in general represents the third most common cause of death in the United States after neoplasia and cardiovascular disease, claiming more than 150,000 lives each year⁽¹⁾.

Cardiothoracic injury causes 25% of deaths immediately following trauma, and the majority of these fatalities involve either cardiac or great vessel injury⁽²⁾. In addition, between 25,000 and 30,000 Americans die from gunshot wounds each year, and 10% of these deaths are the direct result of stab wounds of the heart⁽³⁾.

Cardiac stab wounds are most commonly caused by knives, but wounds from items such as ice picks and screwdrivers are also frequently encountered⁽⁴⁾. The two most common clinical manifestations of stab wounds of the heart are hemorrhage and pericardial tamponade⁽⁵⁾.

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One effective technique is the use of subxiphoid pericardial windows, incisions made in the pericardium by a subxiphoid approach. This is commonly employed in cases of suspected occult penetrating cardiac trauma. An alternative approach is to utilize serial echocardiography⁽⁵⁾. Chest X-ray study, central venous pressure measurement, and pericardiocentesis lack the sensitivity and specificity to make useful screening tests⁽⁶⁾.

The induction of the patient represents a particularly critical time because of increased susceptibility to decompensation as positive pressure ventilation decreases blood return to the heart. A pericardial window may be created if the diagnosis of stab wounds is still uncertain and subxiphoid pericardiectomy has not been performed in the trauma bay. The approach to the heart is usually via either a median sternotomy or a left anterior thoracotomy. The former is considered the standard approach but may be more time consuming than the latter, which does not necessitate any special surgical instruments⁽⁷⁾.

Several factors including the patient's physiologic status on admission, presence of tamponade, mechanism of injury, type and number of cardiac chambers involved, injury severity score, and site of thoracotomy all have an effect on prognosis⁽⁸⁾.

The aim of this work is to evaluate our results in the management of the patients with stab wounds of the heart to detect the outcome of these patients requiring an emergency thoracotomy.

MATERIALS AND METHODS

The records of all patients undergoing an emergency thoracotomy for stab wounds of the heart from 2000 to 2010 in Zagazig Emergency Hospitals were reviewed. The hospital records were cross-checked with emergency room records to ensure that no patients were missed.

Data gathered included patient age, sex, site of injuries, physiologic status on admission, the investigations which were used, indication for thoracotomy, presence or absence of tamponade, timing and location of thoracotomy Emergency Room (ER) versus Operating Room (OR), and patient prognosis. Tamponade was considered to be present if it was described in the operative note, either by the explicit word "tamponade" or a "tense pericardium filled with blood".

This study included all patients with intrapericardial cardiac wounds who reached alive to the hospital. We excluded from this study, arrived dead patients or any stabbed patients either with superficial wound or with penetrating wounds not attacking the heart itself and its intrapericardial great vessel.

Clinical status of the patient before thoracotomy were detected and the patients were divided into stable patients when the Systolic Blood Pressure (SBP) was > 90 mmHg, unstable patients when the SBP was < 90 mmHg, shocked patients when SBP was < 40 mmHg and arrested patients when shocked then arrested before thoracotomy.

All patients had manifested at least one sign of life. Signs of life included a pulse, measurable blood pressure, or cardiac rhythm. The patients were met in a dedicated trauma resuscitation room where initial resuscitation efforts were undertaken aggressively for every patient. Patients were examined clinically and if stable, diagnosis was usually confirmed by chest X-ray and two-dimensional ultrasound, or preferably by echocardiogram, if it was immediately available. Patients who were in extremis with penetrating chest trauma and who lost their vital signs in transport or in the resuscitation room underwent Emergency Room Thoracotomy (ERT). Patients who survived ERT, and other patients in more stable conditions, were taken to the operating room for a definitive procedure. The whole operations were performed by trauma-trained cardiothoracic surgeons without cardiopulmonary bypass.

Efforts were made to perform all thoracotomies in the OR if possible. Cardiorrhaphy was made by Prolene, Silk, Nylon and Tickron sutures (figure 1).

Postoperatively, all patients were transported to ICU with monitoring of all vital signs and drainage by intercostal tubes to detect and manage any complication until discharge.

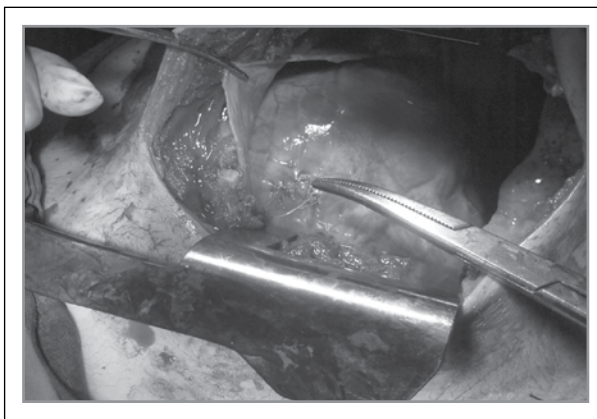


Fig 1. Thoracotomies were done in the OR if possible. Cardiorrhaphy was made by Prolene sutures.

RESULTS

This is a retrospective study of the last 10 years including 115 patients with stabbed heart.

There were 109 males (94.78%) and only 6 females (5.22%) and the age ranged from 15 to 65 years with the predominant age group between 20-30 years with average age of 28.5 ± 5.8 years. The anatomical site of injury on the pericardium was on left side just to the left of the sternum in 32 cases (27.83%), near the left parasternal line in 44 (38.26%) and near the left midclavicular line in 39 (33.91%).

As regard time since stab, most of the patients were coming in the first hour of injury (55 patients, 47.83%). The clinical status of the patients were stable in 35 patients (30.43%) (SBP > 90 mmHg), unstable in 40 patients (34.78%) (SBP < 90 mmHg), shocked in 16 patients (13.92%) and 24 patients were arrested before thoracotomy (20.87%) (Table1).

Clinical status of the patients before thoracotomy was detected. The number of the patients in different clinical status was described with other preoperative data.

Data	No	%
Age group		
15-20 years	20	17.39
20-30 years	44	38.26
30-40 years	25	21.74
40-50 years	16	13.91
50-60 years	10	8.7
60-65 years	3	2.61
Sex		
Male	109	94.78
Female	6	5.22
Anatomical site of wound		
Just to the left of the sternum	32	27.83
Near to the left parasternal line	44	38.26
Near to the left midclavicular line	39	33.91
Time since stab		
< one hour	55	47.83
1-2 hours	33	28.69
2-4 hours	14	12.17
4-6 hours	8	6.96
> 6 hours	5	4.35
Clinical status of patient before thoracotomy		
Stable	35	30.43
Unstable	40	34.78
Shocked	16	13.92
Arrested	24	20.87

Table (1): Preoperative data

Emergency room thoracotomy was done in 28 patients (24.35%), including left anterior, left anterior extended to right and left anterolateral thoracotomy. Operative room thoracotomy

was done in 87 patients (75.65%) including left anterolateral, left posterolateral and median sternotomy as shown in table (2).

The commonest site of stabbed heart were in the right ventricle (44 patients, 38.26%) followed by the left ventricle in 39 patients (33.91%), then left atrium and right atrium represent the least site of stab and there were associated stab in the chest wall, lung, diaphragm and abdomen as shown in table (2).

Cardiorrhaphy was made by Prolene 2/0 in 13 patients, 3/0 in 36 patients and 4/0 in 17 patients. Silk 3/0 was used in 8 patients while nylon 3/0 used in 11 patients and Tickron suture 2/0 used in 30 patients.

Data	No	%
ER thoracotomy (28 cases, 24.35%)		
Left anterior	11	9.57
left anterior extended to right	5	4.35
left anterolateral thoracotomy	12	10.43
OR thoracotomy (87 cases, 75.65%)		
Left anterolateral	41	35.65
Left posterolateral	33	28.7
Median sternotomy	13	11.3
Stabbed site (115 cases, 100%)		
Right ventricle	44	38.26
Left ventricle	39	33.91
Left atrium	13	11.3
Aorta	8	6.96
Pulmonary	6	5.22
Right atrium	5	4.35
Associated stabs (38 cases, 33.04%)		
Lung	35	One patient
Chest wall	24	may have
Diaphragm	17	> one
Abdomen	13	associated
		stabbed

Table 2. Operative data

Morbidity occurred in 19 patients of 88 survival (21.59%) including wound infection, cerebral insult, arrhythmia, myocardial infarction and empyema. Mortality was found in 27 patients (23.48%), while ER mortality was 19 (16.52%) whether intraoperative in 8 patients (6.96%) and postoperative in 11 patients (9.57%), and OR mortality was 8 (6.96%) whether 5 intraoperative (4.35%) and 3 postoperative (2.61%) as showed in table (3).

	No	%
Morbidity		
Cases	19	21.59
Survival	88	
Types of complications		
Wound infection	8	One patient may have
Cerebral insult	5	> one
Arrhythmia	6	complication
Myocardial infarction	3	
Empyema	6	
Mortality	27	23.48
ER mortality	19	16.52
<i>Intraoperative</i>	8	6.96
<i>Postoperative</i>	11	9.57
OR mortality	8	6.96
<i>Intraoperative</i>	5	4.35
<i>Postoperative</i>	3	2.61

Table 3. Morbidity and mortality

The clinical status of the patients were prognostic factors of outcome of the patients as patient who was shocked or arrested before thoracotomy has a mortality rate of 50% and 60% respectively. Also, patients having cardiopulmonary resuscitation CPR and those with ER thoracotomy has mortality rate of 68.57% and 67.86% respectively, but tamponade and associated injuries had only 33.33% and 34.55% mortality rate respectively as shown in table 4.

	Survivor		Non-survivor	
	No	%	No	%
Patients (n = 115)	88	76.52	27	23.48
Clinical status				
Stable (n = 35)	33	94.29	2	5.71
Unstable (n = 40)	37	92.5	3	7.5
Shocked (n = 16)	8	50	8	50
Arrested (n = 24)	10	41.67	14	58.33
CPR (n = 35)	11	31.43	24	68.57
Associated injuries (n = 55)	36	65.45	19	34.55
Tamponade (n = 66)	44	66.67	22	33.33
ER thoracotomy (n = 28)	9	32.14	19	67.86

Table 4. Prognostic factor of outcome

DISCUSSION

Over the last thirty years, the incidence of heart trauma has increased eight times. In most cases of penetrating heart injuries, the cause was stab wound in civilian conditions, but during the last couple of years, the number of heart lesions by fire arms have increased in our country, as well as worldwide⁽⁹⁾.

Most of heart penetrating injuries are caused by stabbing wounds, usually representing 60-70% of cases, while firearms wounds takes 30-40%⁽¹⁾.

If a patient arrives at a medical facility in a compensated state with intact vital signs, the chance for survival is substantially increased if well and quickly managed⁽¹⁰⁾.

This matches with our study as patients arrived rapidly within the first hour of stabbing and quickly managed and survived but with delay and loss of vital signs, the patients become unstable or shocked and their management becomes critical as matched with other investigator⁽¹¹⁾.

The victims of penetrating cardiac injuries are predominantly young males as usual regarding urban violence⁽⁸⁾. This matches with our study as the male represents 94.78% with age predominant between 20-30 years (mean age, 28.5 years).

There are three typical manifestations of penetrating cardiac injury: hemorrhage, pericardial tamponade, and the combination of both⁽¹⁰⁾. Hemorrhage may lead to shock while pericardial tamponade is classically associated with decreased blood pressure, increased central venous pressure, and distant heart sounds, together better known as Beck's triad⁽¹²⁾.

Due to the muscular nature of the ventricle, walls lacerations following stabs often seal temporarily, thus allowing time for transportation. This is in contrast to the thin atrial walls that seldomly seal without external force. Tamponade, usually considered to be a premonitory condition and uniformly lethal if untreated, had a lower than expected survival rate⁽¹³⁾.

Some patients presenting with penetrating cardiac injuries may be completely stable, and the diagnosis can be missed⁽¹⁴⁾. This matched with our study as clinical picture of our patients was stable in 35 patients (30.43%) with SBP > 90 mmHg.

In our study, none of the victims presented evidences of penetrating head injury, unconsciousness could be a consequence of their poor hemodynamic status. This matches with other study who expected that an interaction between blood pressure and consciousness level would almost certainly be included in the logistic model, since Glasgow Coma Scale (GCS) in penetrating cardiac trauma may suffer influence from the victim hemodynamic status⁽¹⁵⁾.

A noninvasive method including transthoracic echocardiography and computed tomography can be used successfully to diagnose penetrating cardiac injury⁽¹⁶⁾. Initial assessment in the trauma usually includes transthoracic two-

dimensional echocardiography which was found to have a greater than 90% accuracy, specificity, and sensitivity for the diagnosis of cardiac penetration⁽¹⁴⁾.

In selected cases and if the patient is compensated and hemodynamically stable, contrast-medium enhanced multiphasic computed tomography may be used to localize the site and extent of the injury as well as to exclude other relevant pathologies⁽¹⁶⁾.

Other strategies such as pericardiocentesis, electrocardiography and chest radiography are of limited value as they are associated with high rates of false results and non-specificity. Tamponade is defined sonographically as the presence of both Pericardial Effusion (PE) and diastolic collapse of the right ventricle⁽¹⁰⁾.

In our study, diagnosis was confirmed by cardiac ultrasound, and echocardiography used regularly in the acute stable (35 patients; 30.43%) and rapidly in 14 of unstable patients (34.78%) in our institution, and has been shown to be reliable, in the absence of haemothorax. Chest X-rays were used in stable patients and chest CT was used only in 13 patients of stable group. Pericardiocentesis is not used in our trauma unit in the acute setting for diagnosing cardiac trauma, as it has been shown to be unpractical, and this may explain why this was not performed as an initial diagnostic procedure or as initial treatment as explained by other investigators who stated that treatment by aspiration alone has been shown to be inadequate in the acute setting, as recurrent pericardial effusions may occur, requiring numerous aspirations⁽¹⁷⁾.

Emergency thoracotomy and repair of myocardial wounds are the only way of salvaging patients with penetrating cardiac wounds⁽¹⁸⁾. Resuscitative thoracotomy will enable the physician to arrest the source of haemorrhage, cross-clamp the aorta if necessary, and perform internal cardiac massage⁽¹⁹⁾.

It is essential that thoracotomy is performed extremely rapidly following loss of signs of life and further loss of blood should be controlled immediately. The site of the cardiac wound is significant, as wounds to the relatively thin right-ventricular wall are more often associated with pericardial tamponade, which is likely to be a major factor associated with survival in a stabbed heart⁽²⁰⁾.

The right ventricle is injured in about half of surviving patients; the left ventricle less often, and one of the atria is performed least often⁽²¹⁾. Similar distributions of injuries have been reported by other authors and can be attributed to the different exposure of the chambers with respect to the anterior chest wall⁽²²⁾.

In our study, the commonest site of stabbed heart were in the right ventricle (44 patients, 38.26%) followed by left ventricle in 39 patients (33.91%), then left atrium and right atrium represent the least site of stab.

The place of resuscitative thoracotomy for penetrating injuries is well established. The optimum site for surgery is the operating theatre, but it is clear that in some circumstances, there is no time to transport the patient to a theatre. Emergency room thoracotomy for patients with severe haemodynamic instability or those that have lost vital signs may then be required. The surgical approach to the heart is usually either a median sternotomy or a left thoracotomy. Emergency left thoracotomy was performed to rapidly access the thoracic cavity and to evaluate cardiac tamponade⁽²⁰⁾.

In our study, ER thoracotomy was done in 28 patients (24.35%), including left anterior, left extended anterior to right and left anterolateral thoracotomy. OR thoracotomy was done in 87 patients (75.65%) including left anterolateral, left posterolateral and median sternotomy.

Cardiorrhaphy is the procedure most often used for repair. Usually done by prolene or Dacron 2/0 and 3/0 in the ventricular wound and 3/0 and 4/0 in atrial wound, some of them on Teflon pledgett⁽¹⁴⁾. This matched with our study in which we used Prolene, Silk, Nylon and Tichron sutures. Patients surviving cardiorrhaphy must be monitored postoperatively for delayed sequelae that may require further evaluation⁽²⁰⁾.

Survivors of cardiac injuries should be observed closely postcardiorrhaphy for physical findings or symptoms suggesting need for further evaluation⁽²³⁾. In our results, all patients were transported to ICU with monitoring of all vital signs and drainage by intercostal tubes to detect and manage any complication until discharge. Complications not directly attributable to the injury itself but to subsequent organ hypoperfusion due to hemorrhagic shock and reduced cardiac output. this may include Systemic Inflammatory Response Syndrome (SIRS), cerebral hypoxia and organ failure. Reported mortality rates range from 10% to 70%, reflecting a variety of presentations, injury mechanisms and pre-hospital care capabilities⁽¹⁰⁾.

In our study, morbidity occurred in 19 patients of 88 survival (21.59%). The ER mortality was 9.57% (11 patients) postoperatively and 6.96% (8 patients) intraoperatively and OR mortality was 4.35% (5 patients) intraoperatively and 2.61% (3 patients) postoperatively. Also, Tyburski et al.⁽¹²⁾ reported a mortality rate of 47% and 42% respectively.

Several prognostic factors have been identified for survival and outcome in patients with penetrating cardiac trauma: status of the patients on presentation, location of injury i.e. right versus left ventricle, presence or absence of vital signs upon ER admission, absence of cardiac arrhythmia and pericardial tamponade limiting exsanguinations into the left hemithorax⁽²⁴⁾.

In our study, the clinical status of the patients was a prognostic factor of outcome of the patients as patient who was shocked or arrested before thoracotomy has a mortality rate of 50% and 60% respectively. Also, patients having Cardiopulmonary Resuscitation (CPR) and those with ER

thoracotomy has mortality rate of 68.57% and 67.86% respectively, but tamponade and associated injuries had only 33.33% and 34.55% mortality rates respectively.

Tyburski et al.⁽¹²⁾ concluded that the physiologic status of the patient at presentation, mechanism of injury, and presence of a tamponade were significant prognostic factors in his series of penetrating cardiac injuries.

CONCLUSION

Prompt and accurate diagnostics of cardiac stab wounds, immediate reanimation, fast transport and urgent surgical intervention by well coordinated team of experts, are relevant parameters for successful treatment of this highly lethal condition.

We recommended that all patients suspected of having cardiac stab wounds must be fully resuscitated and undergo thoracotomy, as significant survival can be achieved and death is not always the outcome.

Thoracotomy, whether done in the emergency room or the operating room, is necessary to completely assess the ultimate survivability of penetrating stab wounds to the heart as the clinical status of the patients, CPR and ER thoracotomy were a prognostic factors of outcome of the patients and associated with high mortality rate.

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Immediate and Mid-term CLINICAL AND Functional Outcome after Mitral Valve RepLACEMENT with Preservation of Annulopapillary Continuity

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Background: Mitral valve replacement (MVR) is known to cause deterioration in the left ventricle (LV) function, the major mechanism responsible being disruption of the annulo-papillary continuity, thus favoring preservation of the mitral subvalvular apparatus.

Objective: To assess the immediate and mid-term clinical outcome and functional changes in LV performance after MVR with preservation of annulopapillary continuity.

Patients and Methods: Fifty consecutive patients who underwent MVR were studied. All patients were suffering from rheumatic mitral valve disease and in all of them preservation of the annul papillary continuity was done using different techniques. The choice of the techniques depended on the nature of the subvalvular apparatus.

Results: The study included 28 females (56%) and 22 males (44%), with mean age was 29.06 ± 3.84 . The techniques of preservation were: Modified Khonsari technique in 30 patients (60%), the anterior leaflet was divided into 2 to 5 chordal segments in 14 patients (28%), and with artificial chordae were used in 6 patients (12%). All the valves used were of the mechanical type. Intraoperative TEE was done in 46 patients, and none of them had any observable left ventricular outflow tract obstruction (LVOTO). After 6 months postoperatively, LVEDD decreased significantly from 5.39 ± 0.809 to 4.91 ± 0.54 cm ($P=0.001$), and LVESD was significantly reduced from 3.636 ± 0.517 to 3.32 ± 0.57 cm ($P=0.03$). The EF improved from 59.34 ± 6.32 preoperatively to be 64.06 ± 5.60 at 3 months and 66.46 ± 5.98 at 6 months postoperatively ($P < 0.001$). The preoperative NYHA class was significantly improved at discharge, 3rd month, and 6th month postoperatively ($P < 0.001$).

Conclusion: The techniques of the preservation of annulopapillary continuity were safe and effective which improve left ventricular ejection fraction and result in reduction in both left ventricular systolic and diastolic diameters, with no fear of LVOTO or interference with prosthetic leaflets motion.

KEYWORDS: Mitral valve replacement, chordal preservation, subvalvular apparatus.

Cardiac function after mitral valve replacement (MVR) for chronic mitral regurgitation has been reported to be impaired owing to postoperative elevation of left ventricular (LV) afterload, and postoperative management of severe cases using conventional MVR is sometimes troublesome [1, 2].

Preservation of the mitral subvalvular apparatus prevents disruption of the annulo-papillary continuity and deterioration in the left ventricle function. However, it has been associated with the hazards of implantation of a smaller sized prosthesis causing patient prosthesis size mismatch and entrapment of the prosthetic valve [3]. Left ventricular outflow tract obstruction (LVOTO), longer operating time and greater technical complexities have also been the concerns [4, 5].

Variety of techniques of annulo-papillary preservation has been introduced. These differ primarily in the location where the anterior leaflet chordae are inserted in the

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mitral annulus. The tension of the preserved main anterior leaflet chordae may act on the posterior annulus (Feike's technique), the trigonal area (Miki's technique), on the anterior annulus (Khonsari's I and II technique), or on a point half-way between these locations (Hetzler's technique) [6].

Some studies have shown an insignificant difference between complete and partial preservation [7, 8], while others have shown a significant difference between the two [9, 10]. Yet there is a consensus over preservation of the mitral apparatus to be superior to complete resection [11]. Therefore the aim of this study was to evaluate effects of chordal preservation on left ventricular function and clinical outcomes on an immediate and midterm basis.

PATIENTS AND METHODS

Fifty consecutive patients who underwent MVR with complete preservation of the annulo-papillary continuity were included at the Cardiothoracic Surgery Department, Kasr El-Aini Hospital, Cairo University, in the period between April 2006 and May 2010. Informed consent was obtained from all patients before inclusion in the study. Patients with associated coronary heart disease requiring coronary artery bypass surgery; patients with associated other valvular disease necessitating other valves replacement; patients with infective endocarditis; and patients with redo heart surgery were excluded.

Preoperative evaluation

Preoperatively, patients were subjected to thorough history taking, complete clinical general and local cardiological examination, complete laboratory investigations, 12-leads ECG, plain chest x-ray, and M-mode, two dimensional and doppler echocardiography to estimate left ventricular enddiastolic diameter (EDD), left ventricular end-systolic diameter (ESD), fractional shortening (FS), ejection fraction (EF), and left ventricular wall motion.

Surgical technique

All patients were submitted to MVR through median sternotomy. Patients were operated by one of the following techniques according to the surgeon's decision modified Khonsari technique or replacement of the chordae tendineae with artificial chordate (Gore-Tex artificial chords). In modified Khonsari technique, semi-elliptical-shaped piece of tissue was excised from the annulus of the anterior leaflet, leaving a 5-10 mm long rim of leaflet whose free edge remained attached to the primary and secondary chordae tendineae. The strip was detached only from the annulus at the anterolateral commissures and reattached to the annulus beginning at the posteromedial commissures in a counterclockwise fashion with mattress sutures that was also used for the valve replacement.

When the leaflet was found to be thickened and calcified, it was divided into 2 to 5 chordal segments depending on the size of the valvular leaflet. Each segment then was trimmed into chordal buttons and reattached to the annulus in an anatomic fashion. When the chordal buttons appeared to be excessive and couldn't be excised, a tonsil clamp was used to hold it on the atrial side of the annulus when the valve sutures were tied. A 4-0 prolene sutures were used to attach markedly redundant leaflet tissue to the left atrial endocardium to prevent its extension over the sewing ring.

The posterior leaflet, when pliable, was retained completely, together with the attached chordae tendineae. Redundant leaflet tissue was folded up into the annulus by placing the valve sutures through the annulus and bringing them through the leading edge of the leaflet tissue. Incisions or small wedge resections of the leaflet were performed if the posterior leaflet was thickened and fibrotic to allow implantation of a larger valve.

Postoperative evaluation

Postoperatively, all patients were transferred to the intensive care unit (ICU), where monitoring of the hemodynamic parameters were ensured. Patients were followed up during hospital stay with physical examination, ECG, chest X-ray, and echocardiography. M-mode, two-dimensional and doppler echocardiography that were performed for all patients before discharge and 3 months and 6 months postoperatively. Either valve related or non-valve related complications were recorded. The Guidelines for Reporting Morbidity and Mortality After Cardiac Valvular Operations were used for definition of valve-related complications [12].

Statistical analysis

All statistical calculations were done using computer programs Microsoft Excel version 17 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows. Data were statistically described in terms of range, mean \pm standard deviation (\pm SD), frequencies (number of cases) and relative frequencies (percentages) when appropriate. Wilcoxon test of ranks was used to compare dependent echocardiographic data. A probability value (p value) less than 0.05 was considered statistically significant.

RESULTS

Preoperative clinical presentation and assessment are shown in (Table 1). The study included 28 females (56%) and 22 males (44%). The mean age was 29.06 ± 3.84 . The mean body surface area (BSA) was 1.6 ± 0.12 . Patients were classified according to New York Heart Association (NYHA) classification, 6 patients (12%) were in class II, and 44 patients (88%) were in class III. Three patients (6%) had a history of thrombo-

embolisation, 14 patients (28%) had AF, and 36 patients (72%) had sinus rhythm. The duration of symptoms was 3.5 ± 1.23 years. Preoperative echocardiography showed that subvalvular apparatus was mildly thickened and fused in 44 patients (88%), while in 6 patients (12%) it was markedly thickened, fused, and calcified. The mean LVESD was 3.636 ± 0.517 cm, the mean LVEDD was 5.39 ± 0.809 cm, the mean FS was 31.76 ± 5.69 , and the mean EF was 59.34 ± 6.32 .

The details of operative assessment are shown in (Table 2). The techniques of preservation were: Modified Khonsari technique in 30 patients (60%), the anterior leaflet was divided into 2 to 5 chordal segments in 14 patients (28%), and replacement of the chordate tendineae with artificial chordae was done in 6 patients (12%). All the valves used were of the mechanical type, 29 patients (58%) had a Carbomedics mitral prosthesis, 13 patients (26%) had Sorin, 6 patients (12%) had Medtronic, and 2 patients (4%) had Mira. Resumption of normal sinus rhythm was regained spontaneously in 23 patients (46%), after DC shock in 17 patients (34%), while 10 patients (20%) had persistent atrial fibrillation at termination of the CPB. Intraoperative TEE was done in 46 patients, and none of them had any observable LVOTO by retained native anterior mitral leaflet.

Postoperative complications are shown in (Figure 1). Re-exploration for bleeding in the early postoperative hours was needed in 4 patients (8%). New onset AF occurred in 6 patients (12%) postoperatively. Superficial wound infection occurred in 3 patients (6%) and responded well to antibiotic therapy and repeated dressing. Two patients (4%) had thromboembolism in the form of transient ischemic attack (< 24h). one patient (2%) suffered from vaginal bleeding due to excessive anticoagulation (INR was 4.3) which was controlled by plasma transfusion and modification of the Cumarin dose. One patient (2%) had right lower lobe collapse, which responded well to physiotherapy.

Comparisons of pre- and post-operative echocardiographic parameters are shown in (Table 3). The mean LVEDD decreased from 5.39 ± 0.80 preoperatively to 5.25 ± 0.63 at 7th day postoperatively, but the difference was not statistically significant ($P=0.72$). The mean LVEDD decreased significantly after 6 months postoperatively to be 4.91 ± 0.54 ($P=0.001$). The mean LVESD showed mild reduction from 3.63 ± 0.51 preoperatively to 3.63 ± 0.61 in the early postoperative period. The reduction was also mild after 3 months postoperatively 3.44 ± 0.58 ($P=0.36$), but at the 6th month postoperatively the mean LVESD was significantly reduced to 3.32 ± 0.57 ($P=0.03$). The EF was mildly improved from 59.34 ± 6.32 preoperatively to 60.4 ± 5.82 ($P=0.71$). The EF continued to improve significantly with time to be 64.06 ± 5.60 at 3 months and 66.46 ± 5.98 at 6 months postoperatively ($P < 0.001$). The FS was reduced slightly in the early and late postoperative periods. The mean difference in FS between the preoperative and at 7 days, 3 months, and 6 months postoperative was not significant ($P=0.999, 0.998, \text{ and } 1$ respectively).

The postoperative changes in NYHA class are shown in (Figure 2). The preoperative NYHA class was significantly improved at discharge, 3rd month, and 6th month postoperatively ($P < 0.001$). At discharge there were 2 patients (4%) with NYHA I, 42 patients (84%) with NYHA II, and 6 patients (12%) at NYHA III. At the 3rd month postoperative, there were 22 patients (44%) with NYHA I and 28 patients (56%) with NYHA II. At the 6th month postoperative there were 39 patients (78%) with NYHA I and 11 patients (22%) with NYHA II.

Variables	Study Group (N=50)
<i>Demographic Data:</i>	
Age (years), mean	29.06±3.84
Sex (M/F)	22/28
BSA	1.6±0.12
<i>NYHA class:</i>	
-NYHA-II	6 (12%)
-NYHA-III	44 (88%)
<i>Subvalvular Apparatus:</i>	
-Mildly thickened	44 (88%)
-Markedly thickened	6 (12%)
<i>Echocardiography Parameters:</i>	
LVESD (cm)	3.636±0.517
LVEDD (cm)	5.39±0.809
FS	31.76 ±5.69
EF	59.34±6.32

Table 1. Preoperative clinical presentation and assessment.

Variables	Study Group (N=50)
<i>Techniques of preservation:</i>	
- Modified Khonsari technique	30 (60%)
- Division of anterior leaflet	14 (28%)
- Replacement with artificial chordae	6 (12%)
<i>Types of mechanical valve:</i>	
- Carbomedics	29 (58%)
- Sorin	13 (26%)
- Medtronic	6 (12%)
- Mera	2 (4%)
<i>Resumption of normal sinus rhythm:</i>	
- Spontaneous	23 (46%)
- After DC shock	17 (34%)
- Persistent AF	10 (20%)

Table 2. Operative assessment.

Variables	Preoperative	7 days postoperative	3 months postoperative	6 months postoperative
LVEDD	5.39±0.80	5.25±0.63	5.06±0.54	4.91±0.54 *
LVESD	3.63±0.51	3.63±0.61	3.44±0.58	3.32±0.57 *
FS	31.76±5.69	31.60±13.75	31.44±9.59	31.74±9.27
EF	59.34±6.32	60.4±5.82	64.06±5.60 *	66.46±5.98 *

*: significant difference with preoperative value.

Table 3. Comparison of pre- and post-operative echocardiographic parameters.

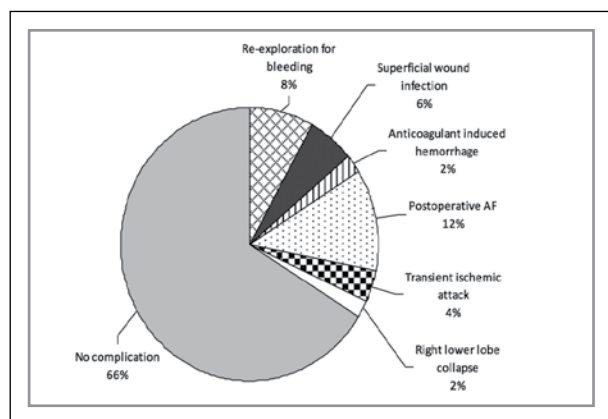


Fig 1. Postoperative complications.

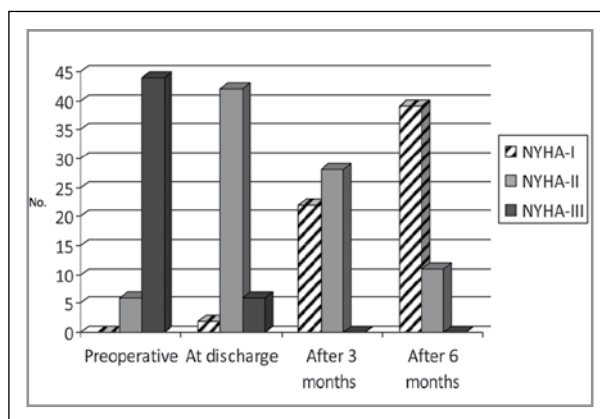


Fig 2. Postoperative changes in NYHA class.

DISCUSSION

It is hypothesised that improved LV systolic performance after subvalvular apparatus preservation is due to a reduction of LV afterload; chordal transection resulted in chamber dilatation and dykinesia at the sites of insertion of the severed papillary muscles [13].

In 1994, a randomised trial, showed that chordal preservation resulted in better LV function than those with no preservation, even after 7 years [14].

The superiority of chordal sparing over conventional MVR in terms of exercise capacity, LV systolic dimensions and ejection fraction was shown by Hannein et al., [7] and Rozich et al.,[15]; however, no significant differences were noted between those receiving posterior or bileaflet chordal preservation. Left ventricular ejection fraction (LVEF) usually falls after conventional MVR for chronic MR. The falls has been explained by the increased afterload produced by a competent mitral valve [16].

In the present study, the EF continued to improve significantly with time to be 64.06 ± 5.60 at 3 months and 66.46 ± 5.98 at 6 months postoperatively. Similarly, Straub et al., [17] reported that in the chordal preservation group the EF remained almost unchanged 7 days after operation (from 44.4 ± 14.0 % to 42.7±8.7%) and increased significantly to 54.2 ± 11.2 % 3 months postoperatively. Gaiotto et al., [18] performed MVR with preservation of the annulopapillary continuity in patients with end stage dilated cardiomyopathy. They reported an improvement in LVEF at the 3rd postoperative month.

A reduction in LVEDD has been found uniformly to correlate well with the level of clinical improvement after valve surgery [19]. In the present study, LVEDD and LVESD showed a significant reduction within 6 months of follow-up.

Similarly, Kayacioglu et al., [4] reported that the LVEDD and LVESD decrease in the preservation group and increased in the conventional group postoperatively but the changes were statistically insignificant. EF decrease slightly postoperative in patients with preserved chordae, however it decreased significantly in patients with conventional MVR. Gaiotto

et al., [18] reported a reduction in the LVEDD ($p = 0.038$) and LVESD ($p = 0.008$) in patients with end stage cardiomyopathy who underwent MVR with preservation of the annulopapillary continuity.

Chowdhury et al., [6] reported that the left ventricular end-systolic volume (LVESV) decreased slightly from the preoperative level in the total excision group in the immediate postoperative period. Although there was gradual improvement at 1 to 4 years of follow up, the improvement was not statistically significant.

In the present study, the annulo-papillary preservation results in a great improvement in functional class (NYHA) and postoperative AF than those undergoing conventional MVR, consistent with the above studies [6, 11].

In conclusion, total chordal preservation is possible in the majority of patients undergoing MVR for rheumatic heart disease. It improves left ventricular EF and result in reduction in both left ventricular systolic and diastolic diameters. The techniques total chordal preservation can be safely performed without effect on the choice of the prosthetic size or fear of left ventricular outflow tract obstruction or interference with prosthetic leaflets motion.

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Bilateral Internal Mammary Artery Grafting For Coronary Artery Bypass: Influence on The Early Morbidity and Mortality

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Objective: To evaluate the influence of using bilateral internal mammary artery (BIMA) grafting on the morbidity and mortality after coronary artery bypass grafting (CABG).

Patients and Methods: The study included 60 patients with multivessel coronary disease. Patients were submitted for either group A (N=30) underwent CABG using left internal mammary artery grafts (LIMA/RA/SVG), or group B (N=30) underwent CABG using skeletonized (LIMA and RIMA) ± (RA/SVG). All patients were followed postoperatively and during hospital stay.

Results: Baseline demographic, clinical characteristics and preoperative risk factors were similar in both groups. There were insignificant differences in mean number of vessels grafted and mean duration of surgery between both groups. The mean time for aortic cross clamping (ischemia) was significantly low in group A (66.6 versus 81.97 minutes in group B). No mortality was found in both groups during early postoperative or hospital stay. There was no difference between the groups mean period of ICU and hospital stay and incidence of operative and early postoperative complications, No deep sternal wound infection, mediastinitis, intractable arrhythmias, CVS accidents, prolonged mechanical ventilation occurred in either group.

Conclusion: Compared with single IMA grafting, BIMA grafting in appropriate selected patients provides proper myocardial revascularization without any increase in operative and early postoperative morbidity or mortality.

KEYWORDS: Coronary artery, grafting, internal mammary artery.

The internal mammary arteries (IMAs) are most frequently used arterial conduits in coronary artery bypass grafting (CABG) [1]. The standard operation of CABG uses a single left internal mammary artery (LIMA) to the LAD, and supplemental saphenous vein grafts (SVGs) to the other coronary vessels [2]. Vein graft failure leads to reduced survival, recurrent angina, late myocardial infarction, and the need for further intervention [3].

Bilateral internal mammary artery (BIMA) grafting can provide better event-free survival than single IMA grafting in selected patients [4]. Moreover, the skeletonized IMA harvesting technique maintained sternal blood flow and may decrease sternal complications [5].

This prospective comparative clinical study was carried out to compare the results of two matched groups of patients: in one group, CABG was performed using LIMA and in another group CABG was performed using BIMA. The results were evaluated in the early postoperative period and during hospital stay, to evaluate the influence of using BIMA grafting on the morbidity and mortality post CABG.

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PATIENTS AND METHODS

Patients

This study included 60 patients diagnosed as ischemic heart disease, and subsequently underwent surgical myocardial revascularization from June 2009 to May 2011. The inclusion criteria were: multivessel coronary disease and age below 65 years old. We excluded patients with left ventricular ejection fraction <30%, single vessel disease, emergency CABG, body mass index >30, chronic obstructive pulmonary disease, insulin dependent diabetes mellitus (IDDM), and Euroscore >7. Patients were submitted for either group as follows: group (A) includes 30 patients underwent CABG using left internal mammary artery grafts (LIMA/RA/SVG), or group (B) includes another 30 patients underwent CABG using skeletonized (LIMA and RIMA) ± (RA/SVG).

Preoperative preparation

Preoperative stage of preparation / assessment included standard steps in all patients which started by careful and thorough history taking and clinical examination taking into consideration the patient's age, sex, risk factors, 12-lead resting ECG) routine investigations (Labs, Plain chest X-rays; echocardiographic examination, coronary angiography, Doppler study for the carotid arteries, and the radial artery, in addition to the modified Allen's test. The preoperative EUROSCORE followed for predicting postoperative morbidity and mortality complications, as previously described [6].

Technique of IMA harvesting

The pedicle IMA was harvested as an en-bloc including the satellite veins and the surrounding adipose tissue, using metal clips and electrocautery. For prophylaxis of vasospasm, spraying of papaverine and intraluminal injection of milrinone were carried out.

Skeletonization of the IMA was performed using an ultrasonic scalpel. The fascia covering the IMA was opened first. The space between the satellite vein and the IMA was dissected using the ultrasonic scalpel. The removal of excessive tissue around the IMA and control of the side-branches were also carried out by the ultrasonic scalpel. Vasospasm prophylaxis protocols were same as pedicle graft.

Procedure of Cardiopulmonary Bypass

Cardiopulmonary bypass was carried out at normothermia in all cases. Intraoperative myocardial protection was achieved using antegrade intermittent warm blood cardioplegia starting with the initial dose of 300 ml/minute for 3 minutes containing 15 ml/Eq of Potassium chloride. All distal anastomoses were

constructed during one period of aortic cross clamping. Additional doses of cardioplegia were given after completion of each anastomotic point (200 ml/minute for 2 minutes containing 6 mEq of KCL. Venting of the heart was carried out through the same cardioplegia cannula double-line via the aortic root.

After all distal anastomoses were finished, and before removal of aortic cross clamping, all patients were given a hot shot of pure warm oxygenated blood at a rate of 300 ml/minute for 3 minutes (with no KCl added to it), via the cardioplegia line. Two grams of magnesium sulphate was given via the same line upon removal of the aortic cross clamp.

Data Collection

A record was made of the operative data and parameters that include: ischemic Time, cardiopulmonary bypass time, revascularization technique, number and distribution of proximal and distal anastomoses, and any need for IABCP support to aid the haemodynamic status.

All patients were followed postoperatively and during hospital stay. The collected results of CABG include: ICU stay, hospital stay, hospital mortality, and hospital Morbidities (MI, IABCP support, ATN, AF, Pneumothorax, Sternal dehiscence, mediastinitis, prolonged mechanical ventilation, intractable arrhythmias, CVS accidents, Chest tube drainage, blood transfusion, and reoperation for bleeding).

Statistical Analysis

All patients' data were tabulated and processed using SPSS 11 (SPSS, Inc., Chicago, IL). Quantitative variables were expressed using mean and standard deviation (SD), they were compared using t-student test. Qualitative variables were expressed as number and percent compared using Chi-square test or Fischer's exact test when appropriate. In all tests, P value considered significant when P<0.05.

RESULTS

Sixty patients were allocated into two equally-numbered. All of patients were male, had mean age of 56 ± 3.8 years in group A, and 55 ± 4.2 in group B, with insignificant difference. Acceptable degrees of preoperative risk factors were found with insignificant differences between both groups (Table 1). In group A, 14 (47%) patients were ex-cigarette smokers versus 18 patients in group B (60%). Systemic Hypertension was found in 22 of group A patients (73%); versus 18 in group B (60%). Diabetes Mellitus was present in 19 patients of group A (63%) vs 10 patients (33%) in group B. Preoperatively, blood sugar level was strictly well-controlled using IV insulin infusion in all patients. In group A, dyslipidemia was discovered in 3 patients

(10%) versus 9 of group B patients (30%). Blood cholesterol level was well-controlled (below 250 mg) using oral lipid-lowering drugs in all patients preoperatively.

Regarding the operative details (Table 2), the mean number of vessels grafted was 3.27 vs 3.6 grafts in group B ($p=0.28$). The mean duration of surgery was 103.17 minutes for group A patients; versus 115.90 minutes for group B patients ($p=0.19$). The mean time for aortic cross clamping (ischemia) was 66.6 minutes for group A cases; versus 81.97 minutes in group B cases, that was statistically significant ($p=0.004$).

Postoperative outcome results are shown in (Table 3). The mean period of ICU stay was 2.57 ± 1.30 days for group A cases; vs. 2.50 ± 1.59 days for group B cases ($p=0.860$), the mean hospital stay time was 8.9 ± 3.4 days for group A patients; vs. 7.8 ± 1.7 days for group B patients ($p=0.109$).

No mortality was found in both groups during early postoperative or hospital stay. ECG changes of new myocardial infarction (MI); elevated ST segment/pathological Q waves, were noticed in 1 of group A vs 2 cases of group B cases ($p=0.561$). The patients were discharged home safely on combined medications (anticoagulant-vasodilator-B-blocker). The mean period for postoperative mechanical ventilation (in hours) was 7.77 ± 2.90 hrs in group A vs 8.18 ± 2.68 hrs in group B ($p=0.565$). Atrial fibrillation (AF) occurred in 2 (6.7%) patients group A vs 2 (6.7%) patients in B ($p=1.000$). Acute tubular necrosis (ATN) occurred in 2 (6.7%) patients group A vs 2 (6.7%) patients in group B ($p=1.000$). Pneumothorax (PNX) occurred in 3 (10%) patients in group A and 5 (16.7%) patients in group B ($p=0.456$). Mean no of blood units transfused to group a patients was 3.4 units vs 2.6 units in group B ($p=0.193$) 2 patients were reopened for bleeding in both groups (6.7%) ($p=1.000$).

No deep sternal wound infection or mediastinitis occurred in either group. Also, intractable arrhythmias, CVS accidents, prolonged mechanical ventilation didn't occur in either group.

Variables	Group A (N=30)	Group B (N=30)	P-value
Age (years)	56 ± 3.8	55 ± 4.2	(NS)
Dyslipidemia	3 (10 %)	9 (30 %)	0.053 (NS)
Systemic Hypertension	22(73%)	18(60%)	0.27 (NS)
Ex-cigarette Smoking	14(47%)	18(60%)	0.30 (NS)
Diabetes Mellitus	13(43%)	10(33%)	0.42 (NS)

NS: non-significant difference.

Table 1. Preoperative data.

Variables	Group A (N=30)	Group B (N=30)	P-value
No. of vessels/ patient	3.27 ± 1.22	3.60 ± 1.18	0.28 (NS)
Crossclamp time (min.)	66.60 ± 18.8	81.97 ± 21	0.004 (S)
Bypass time (min.)	103.17 ± 40.7	115.90 ± 34.5	0.19 (NS)

NS: non-significant difference. S: significant difference. LAD: Left anterior descending artery.

Table 2. Operative Details.

Variables	Group A (N=30)	Group B (N=30)	P-value
ICU stay (hours)	2.57 ± 1.30	2.50 ± 1.59	0.86 (NS)
PO mechanical ventilation (hours)	7.77 ± 2.90	8.18 ± 2.68	0.56 (NS)
Hospital stay (days)	8.9 ± 3.4	7.8 ± 1.7	0.10 (NS)
MI	1 (3.3%)	2 (6.7%)	0.55(NS)
AF	2 (6.7%)	2 (6.7%)	1 (NS)
ATN	2 (6.7%)	2 (6.7%)	1 (NS)
Reopen	2 (6.7%)	2 (6.7%)	1 (NS)
PNX	3 (10%)	5 (16.7%)	0.45 (NS)
Blood transfusion units/patient	3.4 ± 2.8	2.6 ± 1.9	0.20 (NS)

NS: non-significant difference. MI: Myocardial infarction. PO: Postoperative. ICU: Intensive care unit. AF: Atrial fibrillation. ATN: Acute tubular necrosis. PNX: Pneumothorax.

Table 3. Post-Operative Outcome.

DISCUSSION

Coronary artery bypass grafting carries a higher operative mortality and less favorable long-term benefit. Bilateral internal mammary artery grafting (BIMA) has been shown to yield excellent perioperative and long-term results [7]. The current study shows that the use of BIMA grafts is safe and is not associated with increased early complications compared to the LIMA graft. Given the accelerated attrition of saphenous vein grafts on the one hand and the lesser use with BIMA grafts on the other, BIMA grafts have the potential benefit of longer patency [8].

No mortality was found in either LIMA or BIMA groups during early postoperative or hospital stay. The potential survival and event-free benefits of the use of BIMA grafts for CABG in literature remain controversial. Some studies showed that use of BIMA grafts results in better cardiac event-free survival than use of the left IMA graft only [4, 9], whereas others showed that the benefit was not significant [10, 11]. Increased operative mortality [12], and similar or decreased operative mortality have been reported [13]. However, the reports of favorable results for BIMA graft tend to have longer follow-up periods [14, 15].

In the presents study, an appropriate selection of patients might has a role in favorable postoperative outcome. We excluded patients with left ventricular ejection fraction <30%, single vessel disease, emergency CABG, body mass index >30, chronic obstructive pulmonary disease, insulin dependent diabetes mellitus (IDDM). Also, and to reduce high-risk mortality and complications in our study, all patients had a Euro-Score not more than 7, as it was stated that score points 6 plus means a high-risk of perioperative mortality [6].

Despite the relative complexity and the technical demand of the technique of BIMA revascularization, the cross clamp time and the total bypass times were increased in the BIMA group but with no statistical significance in relation to the LIMA group except for the ischemic (cross clamp) time. This can be explained by the number of distal anastomotic points fashioned in our study which was relatively more in BIMA group than those reported in LIMA group (mean= 3.2 in LIMA versus 3.7 in BIMA).

In our study, none of the patients had sternal wound infection. Our rate is similar to those reported by others like Barner et al. [16] who reported 0%; Bical et al. [17], who reported also 0%, and better than results of Kouchoukos et al. [18], Carrel et al. [19], Lev-Ran et al. [20], who reported an incidence of 6.9%, 4.8% and 1.9% respectively in their BIMA patients; our exclusion criteria & our choice of use of skeletonization in harvesting bilateral IMA grafts, has been successful in preserving the sternal blood supply.

In our study, number of blood units transfused to LIMA patients was 3.4 units versus 2.6 units in BIMA group with insignificant difference. Thus, the use of BIMA was not significantly associated with transfusion requirement. One possible explanation may be the fact that in the BIMA group the skeletonized technique was routinely used in the dissection of both internal mammary arteries, while in the LIMA group the entire pedicle was used. This factor is important because blood transfusions, particularly in patients undergoing CABG, increase the risk of infection [21] and prolong hospital stay [22].

In our study, the incidence of reoperation for bleeding was 6.7% in each groups which correlates with the studies of He et

al. [23] 5.6%, Lytle et al. [24] 6.2%, Dion et al. [25] 5.8% and Ashraf et al. [26] 4.6%, in the BIMA group.

Further support for BIMA comes from the analysis of the length of stay. A more prolonged ICU and hospital stay times were needed by the LIMA group as compared to the BIMA patients BIMA, with insignificant difference. Thus, BIMA did not prolong hospital stay; if anything there was a suggestion that BIMA may actually shorten it. Various analyses considering parameters that may reflect selection bias and confounding reached the same conclusion. Thus there is further evidence that even the immediate in-hospital cost of the procedure may be less than (or at least the same as) the cost of LIMA revascularization [27].

In conclusion, limited to the early postoperative and hospital stay follow-up, and compared to CABG (using LIMA/RA/SVG combination), BIMA ±RA/SVGS did not increase operative or early postoperative mortality and morbidity and provided proper myocardial revascularization.

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Prediction of Atrial Fibrillation After Open Heart Surgery

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Atrial fibrillation is still an unsolved complication after open heart surgery that needs an additional care and cost.

Aim and methodology: Pre, intra and post operative data of 200 patients (150 valvular and 50 CABG) were collected and statistically analyzed to study incidence, sequels and factors affecting occurrence of atrial fibrillation in patients undergoing open heart surgery

Results and conclusions: 53 patients had POAF with a percentage of 26.5%; the incidence of POAF was 22% after CABG and 28% after valvular surgery. POAF increased ICU & hospital length of stay. Old age, history of paroxysmal AF, low average post-op serum K level, prolonged p-wave duration and increase left atrial diameter were independent predictors of POAF. Patients with those factors should be the target of prophylactic therapy.

KEY WORDS (POAF, predictors)

Atrial fibrillation (AF) is the most common complication after open heart surgery; it has been shown to occur in about 30% to 50% of the patients undergoing cardiac surgery.(1) Its incidence after valvular surgery ranges from 38% to 64% exceeding that after coronary artery bypass surgery which ranges from 17% to 33%. (2)

Post-operative atrial fibrillation (POAF) has been sometimes associated with multiple predisposing factors such as (advanced age, left atrial enlargement, hypertension, diabetes, obesity, and left ventricular hypertrophy), operative and post-operative factors such as atrial ischemia and electrolyte imbalance. (3)

Complications of POAF include hemodynamic instability, cerebral stroke, and an increase in the length of hospital stay as well as in overall health care costs. The bleeding burden brought on by the requirement for anticoagulation should also not be neglected. POAF is often self-limiting and benign in its course. Beta-blockers, amiodarone and others have been used in the clinical setting with the aim of reducing the incidence of POAF in the cardiac surgical patient population. (4)

Studying the factors affecting occurrence of atrial fibrillation in patients undergoing open heart surgery may appropriately target high-risk patients for aggressive prophylactic treatment and spare low-risk patients from unnecessary treatment. (5)

Aim of the work

The objective is to study incidence, sequels and factors affecting occurrence of atrial fibrillation in patients undergoing open heart surgery.

Patients and Methods

This study was conducted on 200 patients who had open heart surgery in cardiothoracic surgery department, Tanta university hospital in the period from June 2006 to October 2009.

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Exclusion criteria included patients who were not in sinus rhythm before surgery, requirement for class I or III anti-arrhythmic drugs for at least one week before or in the early postoperative period, off-pump technique, redo and emergency surgery, patients who died intra or postoperatively due to causes not related to atrial fibrillation, and those with congenital heart disease were also excluded.

Various open heart surgeries were done for these patients; 150 valvular (84 mitral valve surgeries “79 replacements and 5 repairs”, 37 aortic valve replacements and 29 multiple valves surgeries “14 mitral + aortic, 13 mitral + tricuspid, and 2 mitral + aortic + tricuspid valves”) and 50 coronary artery bypass grafting (CABG) surgeries.

Pre operative demographic, clinical, laboratory, electrocardiographic and echocardiographic data were collected.

All procedures were performed using cardio-pulmonary bypass (CPB), Aortic cross clamping (ACC) time and cardiopulmonary bypass (CPB) time were recorded by minutes in every case. Patients were monitored by continuous ECG during a minimum period of 48 hours postoperatively. Subsequently, the monitoring was by repeated daily observations by nurses and physicians, at least every 8 hours. An ECG was immediately performed when the patient had irregularity of pulse, palpitation, chest distress or other symptoms related to possible AF, and when needed, restarting of continuous ECG monitoring was done.

Post-operative atrial fibrillation (POAF) definition included arrhythmia successfully treated as well as those persistent at discharge. AF was defined as an irregularly irregular rhythm with a fluctuating baseline and no discernable P waves. The arrhythmia, as defined by physician assessment, was on the basis of a telemetry strip or from a 12-lead electrocardiogram recording. AF definition was limited to recorded information and for the period of hospitalization.

Post-op mechanical ventilation time (hours), ICU length of stay (days), hospital length of stay (days), the amount of blood transfusion (units) and post-op use of vasopressors were recorded in every case.

In patients with POAF; time of occurrence of AF, its duration and incidence of stroke or mortality were recorded till hospital discharge.

Statistical analysis

The collected data were organized, tabulated and statistically analyzed using SPSS software statistical computer package version 13. For qualitative data, comparison between two or more than two groups; Chi-square test (X²) was used. For quantitative data, the range, mean and standard deviation

were calculated. For comparison between means of two groups; student's t-test was used. For comparison between more than two means, the F value of analysis of variance (ANOVA) was calculated. Multivariate linear regression analysis was done to predict the occurrence of POAF based on a set of predictive factors (independent variables), a p-value of less than 0.05 was considered statistically significant.

Results

(1) Frequency of POAF

From 200 patients; 53 patients had POAF with a percentage of 26.5%; the incidence of POAF was 22% after CABG and 28% after valvular surgery.

(2) Patients' demographic & clinical data

Age of overall patients ranged from 16 to 75 years, with mean value equals (39.8 ± 14.5 years), 114 (57%) were males, 9 (4.5%) had history of paroxysmal AF, 20 (10%) had chronic lung disease, 49 (24.5%) had hypertension, 15 (7.5%) had prior myocardial infarction (MI), 40 (20%) were diabetics, 56 (28%) were using pre-operative B-blockers.

(3) Demographic & clinical data and POAF

Age and history of paroxysmal AF were highly significant higher in POAF patients than those without AF in both CABG and valvular groups, while **chronic lung disease and DM** were significantly higher among POAF patients in CABG group and were higher among POAF patients in valvular group but with no significant difference from those without AF. **Gender, history of hypertension, MI and pre-op B-blockers use** were not significantly related to occurrence of POAF in both CABG and valvular groups as shown in Table (1).

(4) Patients' laboratory data

Average post-op serum potassium (K) level of overall patients ranged from 3 : 5.5 mmol/L with mean value equals (4.13 ± 0.5 mmol/L), **pre-op white blood cells (WBC) count** of overall patients ranged from 2500: 18200 /mm³ with mean value equals (5979 ± 2194/mm³), **and post-op WBC count** of overall patients ranged from 4000 : 26000 /mm³ with mean value equals (9022 ± 2873/mm³).

(5) Laboratory data and POAF

Average post-op serum potassium (K) level was highly significant lower in POAF patients than those without AF in both CABG and valvular groups, while **pre-op and post-op WBC count** were not significantly related to occurrence of POAF in both CABG and valvular groups as shown in Table (2).

Variables	Patients who had open heart surgery (n=200)							
	CABG group (n=50)				valvular group (n=150)			
	With AF (n=11)		Without AF (n=39)		With AF (n=42)		Without AF (n=108)	
	n	%	n	%	n	%	n	%
Age (Years):								
Range	42-75		37-72		16-65		16-64	
Mean ± SD	63.45 ± 9.04		54.02 ± 7.18		40.95 ± 12.33		31.80 ± 10.61	
t-test	3.631*				4.531*			
P	0.001*				0.0001*			
Gender:								
Males	9	81.8	34	87.2	19	45.2	52	48.1
Females	2	18.2	5	12.8	23	54.8	56	51.9
X ²	0.205				0.103			
P	0.651				0.856			
History of paroxysmal AF:								
Yes	3	27.3	0	0	6	14.3	0	0
No	8	72.7	39	100	36	85.7	108	100
X ²	11.315*				16.071*			
P	0.001*				0.0001*			
Chronic lung disease								
	5	45.5	3	7.7	6	14.3	6	5.6
X ²	9.103*				3.131			
P	0.003*				0.077			
Hypertension								
	7	63.6	21	53.8	8	19.0	13	12.0
X ²	0.334				1.234			
P	0.563				0.267			
Myocardial infarction								
	5	45.5	10	25.6	0	0	0	0
X ²	1.604				-			
P	0.205				-			
DM								
	8	72.7	14	35.9	7	16.7	11	10.2
X ²	4.723*				1.203			
P	0.030*				0.273			
B-blockers preop use:								
Yes	7	63.6	34	87.2	5	11.9	10	9.3
No	4	36.4	5	12.8	37	88.1	98	90.7
X ²	3.222				0.235			
P	0.073				0.628			

*Significant or P<0.05

Table 1. Distribution of patients who had open heart surgery with and without POAF regarding their demographic & clinical data.

Variables	Patients who had open heart surgery (n=200)			
	CABG group (n=50)		Valvular group (n=150)	
	With AF (n=11)	No AF (n=39)	With AF (n=42)	No AF (n=108)
	Range Mean ± SD	Range Mean ± SD	Range Mean ± SD	Range Mean ± SD
Average post-op serum K level (mmol/L)	3.0-4.2 3.51 ± 0.42	3.2-5.5 4.28 ± 0.5	3.1-4.8 3.94 ± 0.56	3.0-5.0 4.21 ± 0.42
t-test	4.625*		3.178*	
P	0.0001*		0.002*	
Pre-op WBC count /mm³	3500-9800 5981.82±2172.01	3000-11000 6060.54±2114.94	2500-18200 6128.57±2828.97	2800-13000 5890.74±1958.38
t-test	0.110		0.585	
P	0.913		0.559	
Post-op peak WBC count /mm³	6500-17000 8338.67± 2065.11	5000-19000 9379.29±3187.14	4000-16000 8762.32±2776.94	4000-26000 9076.54±2892.81
t-test	1.17		0.61	
P	0.262		0.541	

*Significant or P<0.05

Table 2. Distribution of patients who had open heart surgery with and without POAF regarding their laboratory data.

Variables	Patients who had open heart surgery (n=200)			
	CABG group (n=50)		Valvular group (n=150)	
	With AF (n=11)	No AF (n=39%)	With AF (n=42)	No AF (n=108)
	Range Mean ± SD	Range Mean ± SD	Range Mean ± SD	Range Mean ± SD
Heart rate (b/min)	60-95 74.73 ± 10.99	48-90 71.67 ± 9.86	60-110 82.71 ± 11.34	55-110 79.17 ± 12.10
t-test	0.887		1.640	
P	0.380		0.103	
P-R interval(msec)	130-188 162.09 ± 15.69	125-210 159.67 ± 21.41	150-210 172.62 ± 15.47	140-210 167.22 ± 11.40
t-test	0.349		2.344*	
P	0.729		0.020*	
P wave duration (msec)	100-136 120.18 ± 12.14	97-130 110.72 ± 8.31	105-140 123.76 ± 9.58	95-138 120.92 ± 9.60
t-test	3.000*		1.625	
P	0.004*		0.106	

*Significant or P<0.05

Table 3. Distribution of patients who had open heart surgery with and without POAF regarding their pre-op electrocardiographic data.

(6) Patients’ pre-op electrocardiographic data:

Pre-op heart rate of overall patients ranged from 48:110 beat/minute with mean value equals $(78.2 \pm 12 \text{ b/m})$, **P-R interval** of overall patients ranged from 125:210 millisecond with mean value equals $(166.6 \pm 15.4 \text{ msec})$, and **P wave duration** of overall patients ranged from 95:140 millisecond with mean value equals $(119.5 \pm 10.4 \text{ msec})$.

(7) Pre-op electrocardiographic data and POAF:

P-R interval was significantly prolonged in POAF patients than those without AF in valvular group but not in CABG group, in contrast to **P wave duration** which was significantly prolonged in POAF patients than those without AF in CABG group but not in valvular group. **Pre-op heart rate** was not significantly related to occurrence of POAF in both CABG and valvular groups as shown in Table (3).

(8) Patients’ pre-op echocardiographic data:

Left atrial diameter of overall patients ranged from 28:60 mm with mean value equals $(44.9 \pm 7.4 \text{ mm})$, and **Left ventricular ejection fraction (LVEF%)** of overall patients ranged from 42 : 80 % with mean value equals $(62.2 \pm 7.2 \%)$.

(9) Pre-op echocardiographic data and POAF:

Left atrial diameter was highly significant higher in POAF patients than those without AF in both CABG and valvular groups, while **LVEF%** was significantly lower in POAF patients than those without AF in CABG group but not in valvular group as shown in Table (4).

(10) Patient’ surgical, myocardial protection and post-op data:

Aortic cross clamp (ACC) time of overall patients ranged from 30:140 minutes with mean value equals $(67.2 \pm 23.7 \text{ min})$, **CPB time** of overall patients ranged from 45:180 minutes with mean value equals $(93.4 \pm 29.7 \text{ min})$, **post-op mechanical ventilation time** of overall patients ranged from 4:40 hours with mean value equals $(9.5 \pm 4.2 \text{ h})$, **amount of blood transfusion** was more than 2 units in 63 (31.5%) patients, and **post-op use of vasopressors** in 57 (28.5%) patients.

(11) Surgical, myocardial protection and post-op data and POAF:

ACC time, CPB time and post-op mechanical ventilation time were highly significant higher in POAF patients than those without AF in both CABG and valvular groups, while **amount of blood transfusion and post-op use of vasopressors** were not significantly related to AF in both CABG and valvular groups as shown in Table (5).

Variables	Patients who had open heart surgery (n=200)			
	CABG group (n=50)		Valvular group (n=150)	
	With AF (n=11)	No AF (n=39)	With AF (n=42)	No AF (n=108)
	Range	Range	Range	Range
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Left atrial diameter (mm)	34-57 45.73 ± 7.35	28-45 36.49 ± 3.77	43-60 50.26 ± 4.01	30-60 45.70 ± 6.85
t-test	5.706*		4.047*	
P	0.0001*		0.0001*	
LVEF%	42-57 48.64 ± 5.48	42-77 63.56 ± 7.00	50-79 63.43 ± 6.37	44-80 62.56 ± 6.31
t-test	6.512*		0.751	
P	0.0001*		0.454	

*Significant or $P < 0.05$

Table 4. Distribution of patients who had open heart surgery with and without POAF regarding their pre-op echocardiographic data.

Cardiovascular

Variables	Patients who had open heart surgery (n=200)							
	CABG group (n=50)				Valvular group (n=150)			
	With AF (n=11)		No AF (n=39)		With AF (n=42)		No AF (n=108)	
	Range	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD
ACC time (min)	60-130		40-120		30-130		35-140	
	97 ± 23.09		75.26 ± 21.73		70.02 ± 26.01		60.17 ± 20.15	
t-test					2.892*		2.471*	
P					0.006*		0.015*	
CPB time(min)	80-180		60-170		45-170		45-180	
	135.91 ± 33.08		103.97 ± 25.68		94.81 ± 31.88		84.63 ± 24.76	
t-test					3.416*		2.079*	
P					0.001*		0.039*	
post-op mechanical ventilation time (h)	8-40		5-16		4-24		4-22	
	16.0 ± 9.63		8.41 ± 2.78		10.57 ± 4.31		8.75 ± 2.92	
t-test					4.407*		2.976*	
P					0.0001*		0.003*	
> 2 units blood transfusion	With AF (n=11)		No AF (n=39)		With AF (n=42)		No AF (n=108)	
	n	%	n	%	n	%	n	%
	6	54.55	16	41.03	12	28.57	29	26.85
X ²					0.636		0.045	
P					0.425		0.832	
post-op use of vasopressors	5		18		9		25	
	45.45		46.15		21.43		23.15	
X ²					0.002		0.051	
P					0.967		0.821	

*Significant or P<0.05

Table 5. Distribution of patients who had open heart surgery with and without POAF regarding their surgical and myocardial protection and post-op data.

(12) Demographic, clinical, laboratory, electrocardiographic, echocardiographic, surgical, myocardial protection and post-op predictors of POAF in CABG and valvular patients:

Multivariate regression analysis of demographic, clinical, laboratory, electrocardiographic, echocardiographic, surgical, myocardial protection and post-op variables revealed **old age, history of paroxysmal AF, low average post-op serum K level, prolonged p-wave duration and increase left atrial diameter** as independent predictors of POAF among CABG and valvular patients as shown in Table (6).

(13) Occurrence and sequels of POAF:

The mean time to develop POAF was 2.25 ± 0.83 day after surgery (54.72% on the second post-operative day); the time of occurrence of AF was clustered around the first 4 postoperative days, with 96.2% of the patients developing AF

during those days and only 3.8% developing AF after the fourth postoperative day as shown in Fig (1).

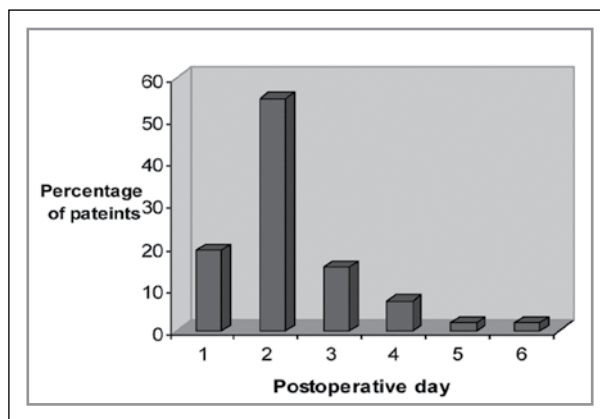


Fig 1. Time to develop POAF.

Variables	CABG and valvular patients (n=200)		
	Standardized B coefficients	t	P
Demographic and clinical data:			
Age	0.237	2.703*	0.008*
Gender	0.028	0.425	0.671
History of paroxysmal AF	0.253	4.087*	0.0001*
Chronic lung disease	0.004	0.052	0.958
Hypertension	0.009	0.120	0.905
Myocardial infarction	0.079	1.177	0.241
DM	0.038	0.570	0.570
B blockers pre-op use	0.018	0.207	0.836
Laboratory data:			
Average post-op serum K level	0.224	3.679*	0.0001*
Pre-op WBC count	0.048	0.791	0.430
Post-op peak WBC count	0.040	0.684	0.590
Electrocardiographic data			
Heart rate	0.107	1.791	0.075
P-R interval	0.051	0.787	0.432
P wave duration	0.203	2.111*	0.036*
Echocardiographic data			
LT atrial diameter	0.454	4.435*	0.0001*
LVEF%	0.039	0.654	0.514
Surgical, myocardial protection and post-op data data:			
ACC time	0.184	0.810	0.419
CPB time	0.046	0.200	0.842
post-op mechanical ventilation time	0.118	1.758	0.081
> 2 units blood transfusion	0.008	0.058	0.837
post-op use of vasopressors	0.026	0.384	0.583

B= Regression Coefficient *Significant or P<0.05

Table 6. Demographic, clinical, laboratory, electrocardiographic, echocardiographic, surgical, myocardial protection and post-op data as predictors of POAF among CABG and valvular patients.

Cerebral stroke occurred in 2 patients; one in CABG group and one in valvular group and they were both in non AF patients. No **mortality related to POAF** occurred in both CABG and valvular groups.

(14) Patients' Intensive care unit (ICU) & hospital length of stay:

Intensive care unit (ICU) length of stay of overall patients ranged from 2:8 days with mean value equals (3.1 ± 1.4) and hospital length of stay of overall patients ranged from 5:18 days with mean value equals (9.4 ± 2.8)

(15) ICU & hospital length of stay and POAF:

ICU length of stay and hospital length of stay were highly significant prolonged in POAF patients than those without AF in both CABG and valvular groups as shown in Table (7)

Discussion

The low **incidence of POAF** (26.5%) in our study may be referred to the relatively younger age (mean=39.8 years) of our patients; 56.1 years in CABG group and 34.4 years in valvular group, also our study only investigated POAF that occurred during hospitalization. So, we might have underestimated the incidence of POAF that may have occurred after discharge.

Variables	Patients who had open heart surgery (n=200)			
	CABG patients (n=50)		valvular patients (n=150)	
	With AF (n=11)	No AF (n=39%)	With AF (n=42)	No AF (n=108)
	Range Mean ± SD	Range Mean ± SD	Range Mean ± SD	Range Mean ± SD
ICU length of stay (day)	3-8 5.27 ± 1.49	2-5 2.87 ± 0.92	2-8 4.59 ± 1.29	2-6 2.43 ± 0.75
t-test	6.598*		12.740*	
P	0.0001*		0.0001*	
Hospital length of stay (day)	6-18 11.91 ± 3.59	6-15 9.23 ± 2.09	7-16 11.88 ± 2.42	5-15 8.24 ± 2.33
t-test	3.160*		8.504*	
P	0.003*		0.0001*	

*Significant or P<0.05

Table 7. Distribution of patients who had open heart surgery with and without POAF regarding their ICU length of stay and hospital length of stay.

In our study; age was found highly significant predictor of POAF (p value < 0.001) in both valvular and CABG groups and in both univariate and multivariate analysis, this is consistent with almost all studies that identified age as the most significant predictor of POAF. (6,7)

Many studies have excluded patients with a history of paroxysmal AF because they are expected to be at greater risk for developing the POAF as they have an underlying pathologic substrate for the development of AF. In several studies preoperative history of paroxysmal AF was an independent predictor for POAF. (8,9)

In our study; these patients were included and history of AF was found to be a highly significant predictor of POAF in both univariate and multivariate analysis (p value < 0.001).

In our study; low post-operative average serum potassium level (K) was found to be a highly significant predictor of POAF. This is in agreement with (Auer J et al., 2004) in their study on analyzed data of 253 patients undergoing cardiac surgery. They found the rate of postoperative AF in patients with serum potassium levels of 3.9 mmol/L or less, compared with those with serum potassium levels of 4.4 mmol/L or greater were 50.7% and 32.9%, respectively (p < 0.05), and they add POAF to cardiovascular diseases that may be adversely influenced by low serum potassium concentrations. (10)

PR interval was found highly significant predictor of POAF in the study of (Amar D et al., 2004) where PR interval was 170 ± 29 msec in POAF group and 164 ± 26 msec in non AF group (p value < 0.001), while **in our study;** it was significant only in valvular group and not in CABG group. (11)

Prolonged P wave duration, indicating intra-atrial conduction delay, was found highly significant predictor of POAF in the study of (Shen T et al., 2007) where prolonged P wave duration ≥ 120 msec was found in 26/103 (26%) patients with POAF and only in 31/209 (15%) patients without AF (p value < 0.05) (9). while **in our study;** prolonged P wave duration ≥ 120 msec was found in 37/53 (70%) patients with POAF and only in 77/147 (52%) patients without AF, this increase in patients with prolonged P wave duration in our study may be explained by the higher percentage of mitral lesions in our study while their study was on CABG patients.

In our study; Prolonged P wave duration in standard ECG was found a significant predictor of POAF only in CABG group 6/39 (15.4%) in non AF patients and 6/11 (55%) in POAF patients but not in valvular group. Prolonged P wave duration was significant predictor of POAF in multivariate analysis (p value = 0.036).

Left atrial diameter was found highly significant in prediction of POAF in the study of (Shen T et al., 2007) on 312

CABG patients; 103/33.01% patients developed post-CABG AF, (41%) had left atrial enlargement (≥ 40 mm) in post-CABG AF group and only (23%) in post-CABG non AF group (9), this is consistent with **our study** where (64%) had left atrial enlargement in post-CABG AF group and only (26%) in post-CABG non AF group.

While left atrial diameter was found insignificant in the study of (Guler N et al., 2007) on 83 CABG patients; 27 (32.5%) patients developed post-CABG AF, and there was no significant difference as regard left atrial diameter in POAF and non AF groups (39.1 vs 36.1 mm, respectively; p value = 0.55) (12), this is inconsistent with **our study** where patients with POAF had a significantly larger mean left atrial diameter compared with patients without POAF in both CABG (45.7 vs 36.5 mm, respectively; p value < 0.001) and valvular groups (50.3 vs 45.7 mm, respectively; p value < 0.001) and in both univariate and multivariate analysis.

ACC time has been proposed as a main underlying factor to develop POAF by some authors as (Ahlsson AJ et al., 2007) who found that the mean ACC time was 65 minutes in non AF 342 patients and 79 minutes in POAF 182 patients (p value < 0.001) (6), which was rejected by others as (Mariscalco G et al., 2006) who found that the mean ACC time was 55 minutes in non AF 48 patients and 56 minutes in POAF 22 patients (p value < 0.88). (13)

In **our study**; ACC time was highly significant increased in POAF patients than those without AF in both CABG and valvular groups in univariate but not multivariate analysis.

(Sinno H. et al., 2003) explained this effect of ACC time on the incidence of POAF by demonstrating that atrial ischemia creates a substrate for maintaining POAF by slowing the conduction, thus favouring re-entry phenomena (14).

Prolonged CPB time has been found as a predisposing factor to POAF by some authors as (Gasparovic H et al., 2010) in their study on 215 CABG patients where 55 (26%) patients had POAF and the mean time of CPB time was 85 minutes in non AF group and 93 minutes in POAF group (p value = 0.05), their explanation was the increase in inflammation and oxidative stress (4), which was rejected by others as (Ramlawi B et al., 2007) as CPB time was less in POAF group (74.8 min) than non AF group (76.6 min); p value = 0.05. (15)

CPB time in **our study** was significantly higher in POAF patients than those without AF in both CABG and valvular groups in univariate but not multivariate analysis.

In **our 53 POAF cases**; The mean time to develop POAF was 2.25 ± 0.83 days (54.72% on the second post-operative day), 11 patients were discharged from hospital with POAF and the mean duration of POAF in the residual 42 patients was 2.14 ± 1.24 days.

This is consistent with (Shen T et al., 2007) who found that

the incidence of POAF was 103/312 equals 33%, and 77.9% of POAF attacks occurred on the 1st:3rd post-operative days (9), and with the study of (Gasparovic H et al., 2010) on 215 CABG patients where POAF occurred in 55 (26%) patients and the mean time to develop AF was 2.9 ± 2.1 days and the mean duration of AF was 15.3 ± 12.1 h. (4)

In **our 200 patients** during the period of hospitalization; 2 attacks of cerebral stroke occurred with an incidence of 1% (one in CABG group and one in valvular group and they were both in non AF patients). This is consistent with (Gasparovic H et al., 2010) where only one patient in non AF group (160 patients) had transient ischemic attacks and no central nervous system manifestations occurred in POAF group (55 patients) (4), and against (Villareal RP et al., 2004) who found that frequency of stroke was significantly higher in POAF group (5.2% of 994 patients) in comparison to (1.7% of 5481 patients) in non AF group; our explanation is the great number of patients in their retrospective study which may give more accurate results about this rare complication. (16)

In **our study**; ICU length of stay was highly significant prolonged in POAF patients than those without AF in CABG group (5.3 ± 1.5 vs 2.9 ± 0.9 days) and in valvular group (4.6 ± 1.3 vs 2.4 ± 0.8 days), this is consistent with (Mariscalco G and Engstrom KG, 2008) where POAF prolonged ICU length of stay from 1.1 ± 1.8 days in non AF group to 2.2 ± 4.2 days in POAF group (17), While (Salaria V et al., 2005) found in their study on 131 patients where POAF occurred in 30 patients that the mean ICU length of stay was 5 days in POAF group and 4 days in non AF group which was statically insignificant. (18)

In **our study**; hospital length of stay was highly significant prolonged in POAF patients than those without AF in CABG group (11.9 ± 3.6 vs 9.2 ± 2.1 days) and in valvular group (11.9 ± 2.4 vs 8.2 ± 2.3 days) this is consistent with most studies; for example (Mathew JP et al., 2004) found, in their multi center study on 4657 patients undergoing CABG surgery at 70 centers located within 17 countries, that POAF prolonged hospital length of stay from 8.5 days in non AF group to 10.5 days in POAF group. (19)

Summary & Conclusion

Patients who are at increased risk for developing postoperative atrial fibrillation are those with old age, history of paroxysmal AF, low average post-op serum K level, prolonged p-wave duration, increase left atrial diameter. Those patients should be the target of prophylactic therapy.

Acknowledgment

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Risk Stratified Outcome of Congenital Heart Surgery In Assiut University Pediatric Cardiothoracic Surgery Unit

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 Esam Abd Allah;
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There are several risk scoring systems have been introduced into the field of congenital cardiac surgery in the last decade. Those include the risk adjustment for congenital heart surgery (RACHS-1) system, Aristotle basic complexity score (ABC score) and recently, the STS-EACTS mortality score and categories. **Objectives:** We applied the 3 classification tools to the Assiut University pediatric cardiac surgery unit patients to test our results in comparison to other centers. Besides the direct outcome comparison, we looked for correlations between the risk category and both the mortality and morbidity and also the risk factors for different outcomes in our center.

Methodology: a retrospective descriptive study including All pediatric patients (ages ranging from 0 to 16 years old, excluding preterm babies) who underwent cardiac surgery in Assiut University pediatric cardiac surgery unit between January 2010 and December 2012. Demographic data was reviewed for: age at the first presentation at the hospital, gender, age at the onset of symptom presentation, presence of genetic syndrome, and diagnosis of congenital heart disease. The preoperative and intraoperative data included type of operation, cardiopulmonary bypass time (CPB time), and aortic cross clamp time (AoX time). The postoperative data included outcomes like in-hospital morbidities and mortalities, which were categorized by the RACHS-1 method, ABC level, and STS-EACTS mortality categories [1, 2, and 3].

Results: During the 36-month study period, a total of 443 congenital cardiac surgical procedures were performed. The majority of procedures were open-heart surgery (71.3%; n = 316). The most frequent open heart procedures were atrial septal defect closure (18.9%, n = 84), tetralogy of Fallot repair (16.3%, n = 72), followed by ventricular septal defect closure (11.5%, n = 51). Average cardiopulmonary bypass time and average aortic cross clamp time were 76.05 ± 40.45 and 49.3 ± 29.9 minutes, respectively. Most of the procedures were stratified into the RACHS-1 levels of 1 and 2 (46 % and 41.5 %, respectively), ABC levels of 1 and 2 (44 % and 31.8 %, respectively), and STS-EACTS mortality categories of 1 and 2 (49.9 % and 37 %, respectively). Overall, the mean Aristotle basic complexity score was 5.44 ± 2.18 . The mean STS-EACTS mortality score was 0.447 ± 0.443 . Postoperative in-hospital mortality was 5.6%, with increasing mortality rates at the higher levels of the RACHS-1 and the ABC. The mean ABC score was 5.44 ± 2.18 , which represents a complexity between ABC levels 1 and 2. Likewise, the mean STS-EACTS mortality score was 0.447 ± 0.443 which again placed our complexity of procedures into categories 1 – 2. These scores imply a procedural-based level of complexity in the institute, which would be useful information for a longitudinal study. The most common events were cardiac arrhythmia events, which required medical intervention, temporary pacing or electrical cardioversion (28%), and postoperative pyrexia & chest infections (12%). Multivariate analysis identified cardiopulmonary bypass time, cross clamp time, RACHS-1 category, ABC levels, STS-EACTS mortality categories as risk factors for prolonged postoperative hospital stay (P – values < 0.05).

Conclusions: The RACHS-1, ABC, and STS-EACTS mortality scoring systems are useful tools for assessing mortality discharge in a medium volume cardiac center in Egypt. The overall postoperative in-hospital mortality rate was found to be 5.6

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%. The important risk factors for postoperative mortality were younger age, smaller weight, higher RACHS-1 levels, higher ABC levels, higher STS-EACTS mortality categories, longer bypass time, and longer cross clamp time. The most common complications were serious cardiac arrhythmias and postoperative fever.

As a result of the growing frustration of pediatric cardiac surgeons over the fact that their surgical performance was being evaluated based on hospital mortality without regard for the complexity of the operations performed, several risk adjusted scoring systems have been developed to assess the surgical performance in the field of pediatric cardiac surgery [1, 2, 3]. In contrast to adult cardiac surgery, measuring the performance of surgical outcome in the field of pediatric cardiac surgery has been difficult because of the relative low number and heterogeneity of patients and the diversity of operations [4–6]. Developed in 2002, the risk adjustment for congenital heart surgery (RACHS-1) method can be used to stratify individual patients into six categories, based on type of surgery and age at operation, for predicting hospital mortality [1, 7–10]. In 2004, another well-known tool is the Aristotle basic complexity score (ABC score) which allocates the complexity scores on the basis of the primary procedure (ranging from 1.5–15) and complexity levels (1–4) [2, 5, 11]. In 2009, the newest model, developed from the empirical based analysis from the European Association for Cardiothoracic Surgery (EACTS) congenital heart surgery database and the Society of Thoracic Surgeons (STS) congenital heart Surgery database, is the STS-EACTS mortality score and categories [3]. A large, recent study of 77,294 registered procedures showed a high degree of discrimination for predicting mortality, using these three tools and c statistic (0.74–0.78) [12]. *{For the details of the 3 risk scores and their categories, see the associated appendixes 1, 2, 3, at the end of this paper}.*

We applied the 3 classification tools to the Assiut University pediatric cardiac surgery unit patients to test our results in comparison to other centers. Besides the direct outcome comparison, we looked for correlations between the risk category and both the mortality and morbidity and also the risk factors for different outcomes in our center.

Methodology

1. Data Source

The present study was designed as a retrospective descriptive study and approved by the Assiut Faculty of medicine Review Board and Ethics Committee. All pediatric patients (ages ranging from 0 to 16 years old, excluding preterm babies) who underwent cardiac surgery in Assiut University pediatric cardiac surgery unit between January 2010 and December 2012 were identified using the Assiut University pediatric cardiac

surgery unit database. Demographic data was reviewed for: age at the first presentation at the hospital, gender, age at the onset of symptom presentation, presence of genetic syndrome, and diagnosis of congenital heart disease. The preoperative and intraoperative data included type of operation, cardiopulmonary bypass time (CPB time), and aortic cross clamp time (AoX time). The postoperative data included outcomes like in-hospital morbidities and mortalities, which were categorized by the RACHS-1 method, ABC level, and STS-EACTS mortality categories [1, 2, and 3]. Retrospective variables were identified, and a statistical analysis was performed on the effects of preoperative and intraoperative factors on surgical outcomes.

2. Study Variables

Postoperative death before hospital discharge was used as the main outcome variable. For secondary outcome variables, postoperative morbidities were considered. These included cardiac arrest, reoperation, postoperative reintubation, low cardiac output, acute renal failure requiring peritoneal dialysis, pyrexia (>38 degrees Celsius), pleural effusion, and serious cardiac arrhythmia such as complete AV block, junctional ectopic tachycardia, supraventricular tachycardia, atrial ectopic tachycardia, ventricular tachycardia, and ventricular fibrillation requiring medical or electrical cardioversion.

3. Data Analysis

Patients' baseline characteristics and potential confounders were summarized using descriptive statistics (showing the percentage, median, and range). The ROC curve was examined for validation of the RACHS-1 level, ABC level, and STS-EACTS mortality categories. Associations between potential risk factors and poor outcomes were assessed with univariate analysis. Continuous variables were assessed with a Mann-Whitney U test, and the categorical variables were evaluated by a Fisher's exact test or a chi-square test. Multivariate analysis was performed with forward stepwise logistic regression, combined for each outcome. A P value < .05 was considered to be statistically significant.

Statistical analysis was performed with SPSS 16.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Demographic Data

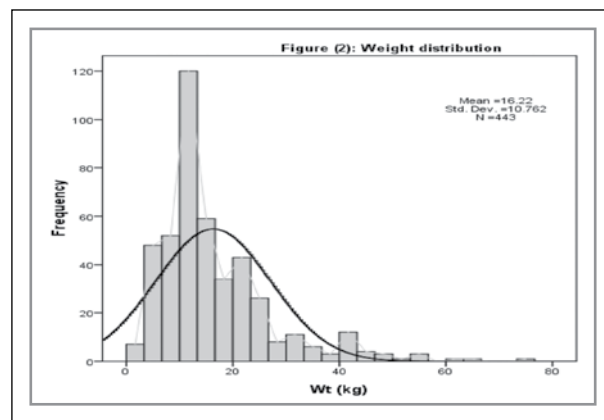
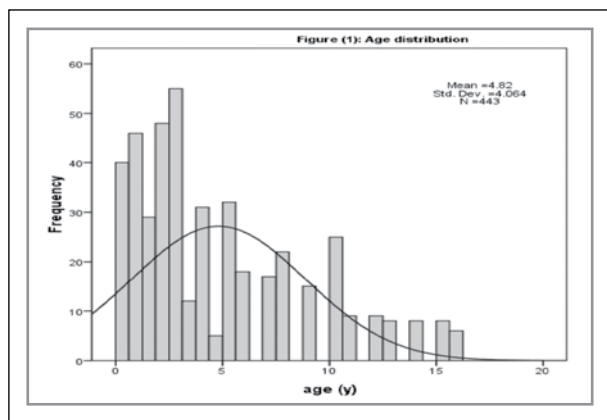
During the 36-month study period, a total of 443 congenital cardiac surgical procedures were performed on patients at Assiut University pediatric cardiac surgery unit their ages < 16 years old & excluding preterm babies. Demographic data of these patients are shown in Table 1.

Characteristics	n (%) or mean ± SD (range)
Sex:	
• Male	208 (47%)
• Female	104 (45.2) 235 (53%)
Age at surgery (years):	
• <30 days;	4 (0.9%)
• 31 days to 1 year;	74 (16.7%)
• ≥1 year;	365 (82.4%)
Weight at time of surgery:	16.2 ± 10.8 (3 – 74)
Definite genetic syndrome:	
• Down syndrome	3 (0.6%)

Surgical Procedures

The majority of procedures were open-heart surgery (71.3%; n = 316). The most frequent open heart procedures were atrial septal defect closure (18.9%, n = 84), tetralogy of Fallot repair (16.3%, n = 72), followed by ventricular septal defect closure (11.5%, n = 51) (see Table 2). Average cardiopulmonary bypass time and average aortic cross clamp time were 76.05 ± 40.45 and 49.3 ± 29.9 minutes, respectively. Most of the procedures were stratified into the RACHS-1 levels of 1 and 2 (46 % and 41.5 %, respectively), ABC levels of 1 and 2 (44 % and 31.8%, respectively), and STS-EACTS mortality categories of 1 and 2 (49.9 % and 37 %, respectively). Overall, the mean Aristotle basic complexity score was 5.44 ± 2.18. The mean STS-EACTS mortality score was 0.447 ± 0.443 (see Table 3).

Table 1. Patients' baseline characteristics in the present study (n = 443).



Procedure	Number	%	Mortality (n, %)
PDA closure	87	19.6%	0
ASD closure:	84	18.9%	0
• Direct closure	13	2.9%	
• With pericardial patch	71	16%	
Tetralogy of Fallot repair:	72	16.3%	4/72 (5.5%)
• With trans-annular patch	33	7.4%	1/33 (3%)
• Without trans-annular patch	31	7%	2/31 (6.4%)
• TOF absent PV repair	2	0.4%	0
• With shunt takedown	4	0.9%	1/4 (25%)
• RV decompression without VSD closure	2	0.4%	0
VSD closure:	51	11.5%	1/51 (1.9%)
• Direct closure	14	3.1%	0/14
• With patch	37	8.3%	1/37
Coarctation repair:	21	4.7%	2/21 (9.5%)
• Resection with end-to-end	4	0.9%	0
• Extended resection with end-to-end	9	2%	0
• Subclavian flab aortoplasty	8	1.8%	2

Table 2. Surgical procedures in this study (n:443)

Cardiovascular

<u>Procedure</u>	<u>Number</u>	<u>%</u>	<u>Mortality (n, %)</u>
<i>SAM resection + trans-aortic septal myectomy</i>	16	3.6%	0
<i>Modified B-T shunt</i>	14	3.1%	6/14 (42.8%)
<i>AVSD repair:</i>	12	2.7%	2/12 (16.6%)
· <i>Partial</i>	8	1.8%	1
· <i>transitional</i>	2	0.4%	1
· <i>complete</i>	2	0.4%	0
<i>Double chamber RV repair</i>	12	2.7%	0
<i>Partial anomalous pulmonary venous return repair</i>	11	2.5%	0
<i>Bidirectional Glenn (BCPC)</i>	8	1.8%	1/8 (12.5%)
<i>Mitral valve replacement</i>	7	1.6%	0
<i>Aortic valve repair</i>	6	1.3%	0
<i>Atrial septectomy</i>	5	1.1%	0
<i>ASO:</i>	5	1.1%	2/5 (40%)
· <i>Simple</i>	3	0.7%	1/3
· <i>With VSD closure</i>	1	0.2%	0
· <i>With PS resection</i>	1	0.2%	1
<i>PS: Pulmonary valvotomy + trans annular patch</i>	3	0.7%	1/3 (33%)
<i>Pulmonary artery banding</i>	3	0.7%	0
<i>Double valve replacement</i>	3	0.7%	0
<i>Pulmonary conduit re-operation</i>	2	0.4%	0
<i>Mitral valve repair</i>	2	0.4%	0
<i>Completion Fontan (TCPC)</i>	2	0.4%	1/2 (50%)
<i>PA-VSD; Pericardial patch augmentation of central & branch Pas + shunt or RVOT trans-annular patch.</i>	2	0.4%	0
<i>Truncus arteriosus repair</i>	2	0.4%	0
<i>Septation of common atrium with bilateral SVC & unroofed CS + AML cleft closure</i>	2	0.4%	0
<i>Central aorto-pulmonary shunt</i>	2	0.4%	2/2 (100%)
<i>Aortic valve replacement with root enlargement</i>	1	0.2%	0
<i>Re-implantation of scimitar vein into LA</i>	1	0.2%	0
<i>PV replacement with bioprosthesis</i>	1	0.2%	0
<i>Ross procedure</i>	1	0.2%	1/1 (100%)
<i>Supra-valvar AS: 2-sinus repair by pericardial pantaloons patch</i>	1	0.2%	0
<i>Rastilli repair: D-TGA, VSD, PS</i>	1	0.2%	1/1 (100%)
<i>Ebstein's tricuspid valve repair</i>	1	0.2%	0
<i>TAPVR repair + bilateral BDG</i>	1	0.2%	1/1 (100%)
<i>Resection of intracardiac tumour</i>	1	0.2%	0
Total	443		25 (5.6%)

Table 2. Surgical procedures in this study (n:443)

RACHS-1 levels	No. %	ABC levels	No. %	ABC scores [2]	Mean ABC score ± SD	STS-EACTS mortality categories	No. %	STS-EACTS mortality scores [3]	Mean STS-EACTS score ± SD
I	204 (46%)	1	195 (44%)	1.5 – 5.9	3.2 ± 0.5	1	221 (49.8%)	0.1 – 0.3	0.18 ± 0.07
II	184 (41.5%)	2	141 (31.8%)	6 – 7.9	6.4 ± 0.5	2	164 (37.2%)	0.4 – 0.7	0.45 ± 0.08
III	45 (10%)	3	98 (22%)	8 – 9.9	8.1 ± 0.3	3	16 (3.6%)	0.8 – 1.2	0.83 ± 0.1
IV	10 (2.5%)	4	9 (2.2%)	10 – 15	10.4 ± 0.48	4 & 5	42 (9.4%)	1.3 – 5	1.65 ± 0.38
Total	443		443		5.44 ± 2.18		443		0.447 ± 0.443

Table 3. Distribution of cases along the different RACH-1 risk categories, ABC complexity levels, and STS-EACTS mortality categories

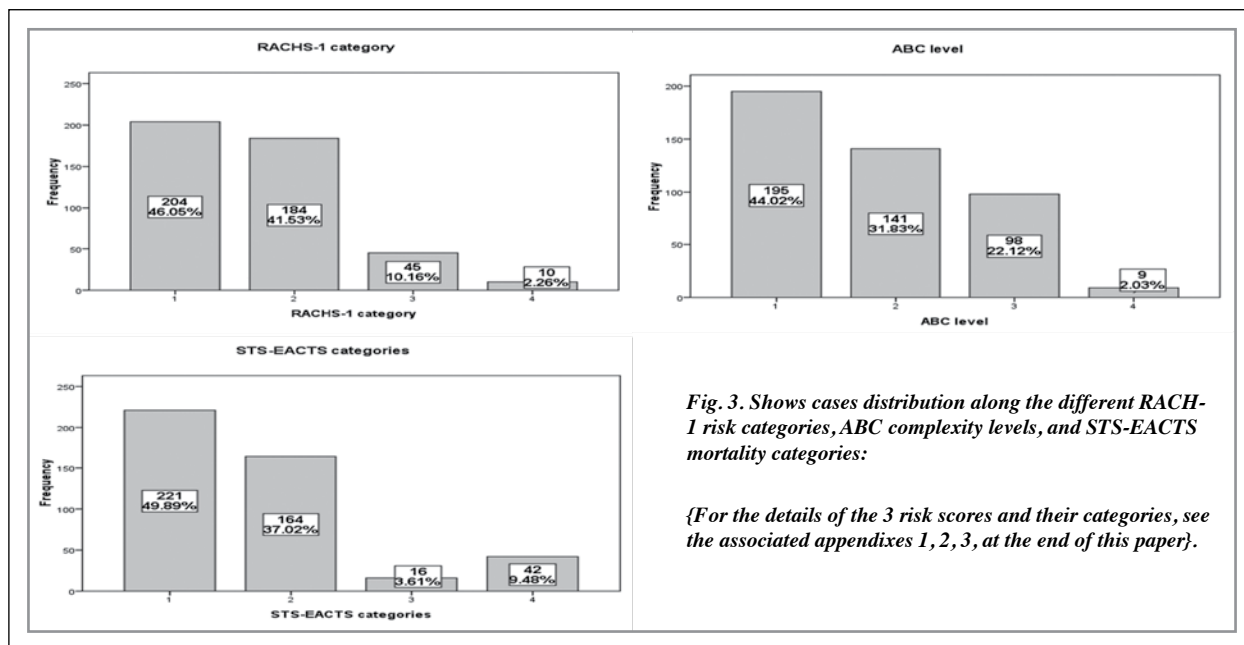


Fig. 3. Shows cases distribution along the different RACH-1 risk categories, ABC complexity levels, and STS-EACTS mortality categories:

{For the details of the 3 risk scores and their categories, see the associated appendixes 1, 2, 3, at the end of this paper}.

Mortality.

Overall in-hospital postoperative mortality in the present study was 5.6 % (25 of 443).

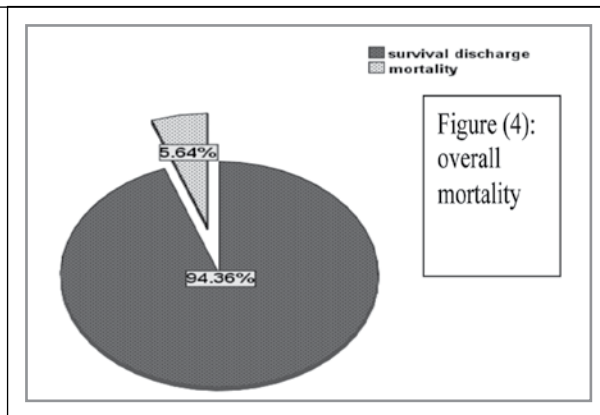


Fig 4. Overall mortality

<u>Variables</u>	<u>Alive discharge</u> n (%); Total: 418 (94.4%)	<u>Mortality discharge</u> n (%); Total 25 (5.6%)	<u>P – value</u>
<i>Age: median (range)</i>	3.5 ys (0 – 16)	2 ys (0 – 13)	0.006 [§]
<i>Weight : median (range)</i>	13.5 kg (3 – 74)	9 kg (3 – 30)	0.007 [§]
RACHS-1 category:			< 0.001 [§]
• 1	202/204 (99%)	2/204 (1%)	
• 2	173/184 (94%)	10/184 (5.4 %)	
• 3	35/45 (77.8%)	10/45 (22.2%)	
• 4	7/10 (70%)	3/10 (30%)	
• 5 & 6	0	0	
ABC levels:			< 0.001 [§]
• 1	193/195 (99%)	2/195 (1%)	
• 2	128/141 (90.8%)	13/141(9.2%)	
• 3	91/98 (92.9%)	6/98 (6.1%)	
• 4	5/9 (55.6%)	4/9 (44.4%)	
STS-EACTS mortality categories:			< 0.001 [§]
• 1			
• 2	216/221 (97.7%)	4/221 (1.8 %)	
• 3	156/164 (95.1%)	8/164 (4.9%)	
• 4	12/16 (75%)	4/16 (25%)	
• 5	33/42 (78.6%)	9/42 (21.4%)	
	0	0	
<i>Cross clamp time (median)</i>	50 min (0 – 125)	72.5 min (0 – 155)	< 0.001 [§]
<i>CPB time (median)</i>	70 min (15 – 190)	100 min (25 – 200)	0.01 [§]

[§]: Correlation is significant at 0.01 (2-tailed)

Table 4. Correlation between different variables in this study and the mortality: by Pearson Correlation test

Figure (5) Illustrates the mortality using the RACHS-1 system, with the mortality increasing significantly between level 2 and levels 3 and 4 (P value < .05). Figure 6 shows the mortality, based on the ABC level; with the highest percentage of mortality at ABC level 4 (44.4%). Mortality rate and the STS-EACTS Mortality categories are also shown in Figure 7. For this method, the highest proportion of mortality cases was in category 3 (25%).

Using the **ROC curve** statistical method, we tested our mortality results against the 3 risk scoring systems to measure the sensitivity and specificity of these risk scores, and hence detect the method with the best predictability for the mortality in our cases. The area under the ROC curve was measured for each risk scoring system. Larger values of the test result variable(s) indicate stronger evidence for a positive actual state (better matching). RACHS-1 risk categories system provided the best results with area under the curve of 0.791, followed by STS-EACTS mortality categories system with area under the curve of 0.758, and the least predictability was by the ABC complexity levels system with an area under the curve of 0.708. See Figure 8 and the underlying table.

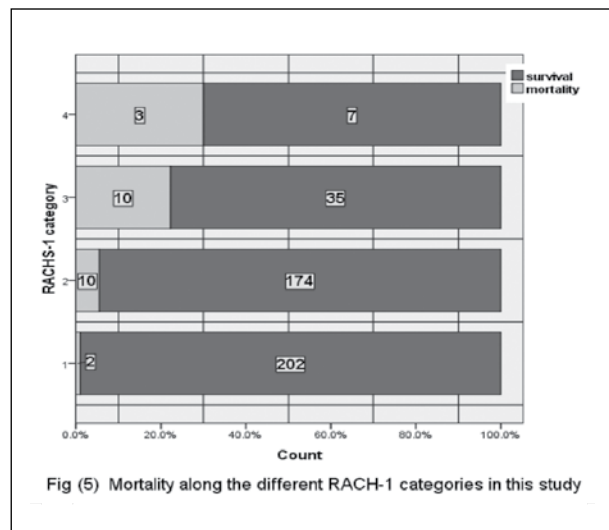


Fig (5) Mortality along the different RACHS-1 categories in this study

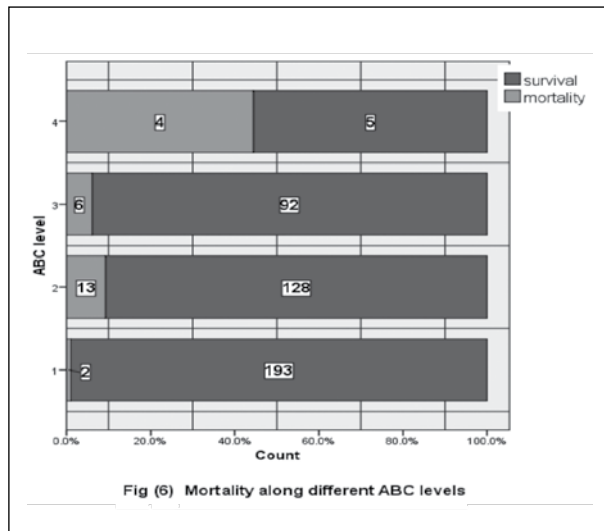


Fig (6) Mortality along different ABC levels

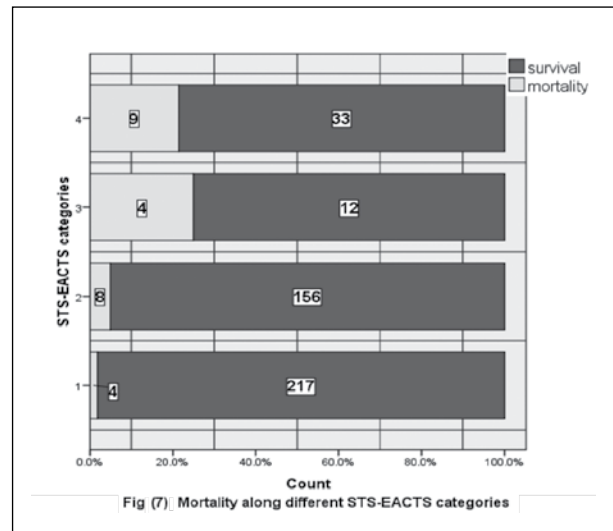


Fig (7) Mortality along different STS-EACTS categories

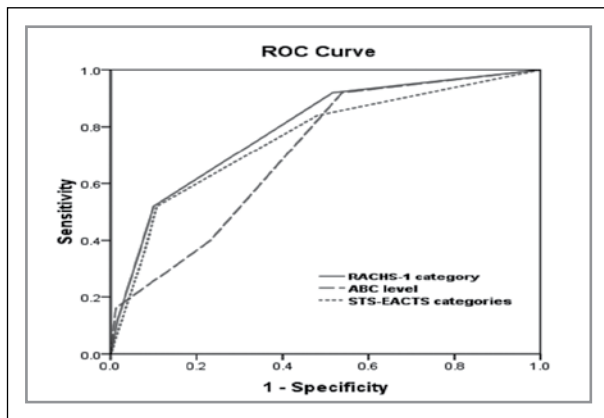


Fig 8.

Area Under the Curve

Test Result Variable(s)	Area	Std. Error ^a	Asymptotic Sig. ^b	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
RACHS-1 category	.791	.046	.000	.701	.881
STS-EACTS categories	.758	.053	.000	.655	.862
ABC level	.708	.047	.000	.617	.799

No.	age	Wt kg	Diagnosis	Surgery	Death at PO day	RACHS-1 category	cause
1	4 m	5	Coarctation of aorta	Subclavian flab aortoplasty	3	I	Pneumonia, MRSA
2	6 y	20	Tetralogy of Fallot	Total correction	2	II	Uncontrolled Arrhythmia (JET)
3*	2 m	3	D-TGA small ASD	M B-T shunt + pulmonary artery banding + atrial septectomy	2	III	Low cardiac output + bleeding
4*	2 m	3	D-TGA, VSD, ASD	M B-T shunt + pulmonary artery banding	4	III	Low cardiac output
5*	1 m	3	D-TGA, ASD	M B-T shunt + pulmonary artery banding	4	III	Low cardiac output
6*	50 d	5	D-TGA, PS	ASO + resection of sub PS	1	IV	Low cardiac output
7	2 y	11	Transitional AVSD, PH	Total correction	1	II	Pulmonary hypertensive crisis

Cardiovascular

8	2 y	11	Small VSD, severe PS (PG 115 mmgh)	VSD direct closure + pulmonary valvotomy + transannular patch	2	II	Uncontrolled Arrhythmia (V. tach)
9	9 m	7	Coarctation of aorta	Subclavian flab aortoplasty	1	I	Low cardiac output
10	13 y	30	Rheumatic AS	ROSS procedure	1	III	Bleeding
11	8 y	30	Down S, tetralogy of Fallot, small branch Pas, S/P: modified B-T shunt (non functioning)	Central Aorto-Pulmonary shunt	1	III	Low cardiac output
12	4 y	15	Mitral atresia, DORV, D-TGA, severe PS. S/P: left bidirectional Gleen	Completion Fontan (TCPC)	3	III	Pneumonia, MRSA
13	5 m	5.5	Hypoplastic LV, DORV, D-TGA, severe PS	Bidirectional Gleen	7	II	Diffuse Cerebral infarction
14	40 d	4	D-TGA.	ASO	3	IV	Low cardiac output
15	4 m	5.5	tetralogy of Fallot, small branch Pas,	Modified B-T shunt	3	III	Low cardiac output
16	8 m	7	tetralogy of Fallot, small branch Pas,	Modified B-T shunt	4	III	Low cardiac output
17	6 m	5	tetralogy of Fallot, small branch Pas,	Emergency central aorto-pulmonary shunt after recovery from cardiac arrest during cyanotic spell.	3	III	Low cardiac output
18	7 m	6	Single ventricle, bilateral SVC, TAPVC	Total correction of TAPVC + bilateral bidirectional Gleen	5	II	Chest infection, pulmonary hypertension
19	3.5 y	11	D-TGA, VSD, PS	Rastilli repair using conduit made of CoreMatrix	4	IV	Low cardiac output
20	9 y	18	tetralogy of Fallot, S/P: left modified B-T shunt through thoractomy	Shunt takedown, total correction of TOF	1	II	Coagulopathy, bleeding
21	1.5 y	8	DORV (Fallot type), small branch Pas,	Modified B-T shunt	3	III	Low cardiac output
22	2.8 y	9	Partial AVSD, severe PH	Repair of Partial AVSD	1	II	Pulmonary hypertensive crisis
23	2 y	9	Tetralogy of Fallot	Total correction	1	II	Low cardiac output
24	4 y	15	Tetralogy of Fallot	Total correction	1	II	Uncontrolled Arrhythmia (JET)
25	2.5y	9	VSD, severe PH	VSD patch closure	1	II	Pulmonary hypertensive crisis

Table 5. Summary of discharge mortality cases

Complications and Length of Stay.

Table 6 shows the major postoperative complications and morbidities occurring in our cases. The most common events were cardiac arrhythmia events, which required medical intervention, temporary pacing or electrical cardioversion (28%), and postoperative pyrexia & chest infections (12%).

See table (7) for detailed postoperative complications.

Multivariate analysis identified cardiopulmonary bypass time, cross clamp time, RACHS-1 category, ABC levels, STS-EACTS mortality categories as risk factors for prolonged postoperative hospital stay (P – values < 0.05).

Variables	No. (%)
1 Serious cardiac arrhythmia: (total events)	124 (28 %)
- Junctional ectopic tachycardia	37 (8.4 %)
- Autonomic ectopic tachycardia	21 (4.7 %)
- Supra-ventricular tachycardia 2 (0.8)	41 (9.2 %)
- Ventricular tachycardia 3 (2.3)	12 (2.7 %)
- Ventricular fibrillation 1 (0.4)	4 (0.9 %)
- Sinus bradycardia 1 (1.3)	9 (2 %)
- Complete heart block requiring permanent pacemaker	0
2 Postoperative pyrexia, chest infections	54 (12.2 %)
3 Bleeding, cardiac tamponade, and unstable hemodynamic requiring reoperation	21 (4.7 %)
4 Required reintubation	16 (3.6 %)
5 Pleural effusion and chylothorax	13 (2.9 %)
6 Pneumothorax (needed more ICT)	6 (1.35 %)
7 Neurological deficit	4 (0.9 %)
8 Wound infection and mediastinitis	2 (0.45 %)
9 Renal failure required peritoneal dialysis	1 (0.27%)
Total	241 (54.5 %)

Table 6. Major postoperative complications and morbidities

Discussion

In recent years, the attitude towards quality of health care and the cost of congenital heart surgery has received much attention from the public and is the subject of government coverage scrutiny. The RACHS-1 method was established to analyze the impact of case mix on pediatric cardiac surgical outcomes by Jenkins et al. [1, 7]. In 2006, the STS and EACTS also incorporated the RACHS-1 into their databases [13, 14]. Many institutes in Europe and North America reported use of the RACHS-1 with comparisons of inter-institutional performance [5, 6, 8, 12]. Some authors also validated RACHS-1 stratification for use with a subset of pediatric cardiac surgeries, by considering the area under the ROC curve (0.75–0.86) [8, 10]. Meanwhile, Lacour-Gayet et al. [2, 11] introduced the Aristotle basic complexity score (ABC score) to predict surgical mortality. The complexity tool allocates a

basic score (range from 1.5 to 5) and a level (range from 1 to 4) for each operation. Subsequently, the authors developed the Aristotle Comprehensive complexity score for a more complex stratification, based on procedure-dependent factors such as anatomical factors, age at procedure, and patient-adjusted factors such as extracardiac factors and general factors [2, 11]. The novel method has been accepted for use in several studies, with its validity (by c statistic) at 0.74 to 0.8 [3, 11, 12]. The most recent complexity stratification tool, published in 2009, is the STS-EACTS congenital heart surgery mortality score. It uses additional factors such as age, weight, and peri-operative LOS and was shown to have a high validity (by c statistic) of 0.816 [2, 12]. These stratification tools are helpful methods for analyzing the case mix in pediatric cardiac surgeries.

To date, few reports have mentioned any evaluation of pediatric cardiac outcomes from developing countries [14, 15, 16]. V´elez and colleagues from Colombia, indicated that patients

with RACHS-1 levels 1 to 4 had mortality rates of 0.7%, 7.2%, 20.7%, and 33.8%, respectively [14]. In study from a tertiary center in Thailand about one year of pediatric cardiac surgery work, Chodchanok and associates found a postoperative in-hospital mortality of 6.1%, with increasing mortality rates at the higher levels of the RACHS-1 and the ABC. Their mean ABC score was 7.1 ± 1.9 , which represents a complexity between ABC levels 2 and 3. Likewise, the mean STS-EACTS mortality score placed their complexity of procedures into categories 2-3 [15]. Also, in Guatemala, a study demonstrated improvement in congenital heart surgery (from 1997 to 2004) using the RACHS-1 stratification [16].

In the present study, postoperative in-hospital mortality was 5.6%, with increasing mortality rates at the higher levels of the RACHS-1 and the ABC. Nevertheless, no patients were at RACHS-1 levels 5 and 6. The mean ABC score was 5.44 ± 2.18 , which represents a complexity between ABC levels 1 and 2. Likewise, the mean STS-EACTS mortality score was 0.447 ± 0.443 which again placed our complexity of procedures into categories 1 – 2. These scores imply a procedural-based level of complexity in the institute, which would be useful information for a longitudinal study.

Overall, the present study shows that three scoring systems can be applied to a medium volume hospital. The areas under the ROC curves for the RACHS-1 and STS-EACTS systems, for predicting in-hospital mortality, are impressive, 0.79 and 0.75, respectively. These values are close to the results from other studies [3, 6, 8, 10, 13]. Interestingly, the mortality rate distributed by the ABC risk categories looks a bit different from those of the RACHS-1 or STS-EACTS systems. In the ABC complexity categories, the highest mortality percentage was found at mortality level 4 (44%), followed by level 2 (9%), and then level 3 (6%). As a possible explanation, some of the procedures that are classified in the ABC complexity category 3, such as total correction of tetralogy of Fallot, have been performed commonly in our center with a low mortality rate in all its variants (5.5%); see table (2). On the other hand, the systemic to pulmonary artery shunt, which is categorized in the ABC category 2, shows a high mortality rate (42.8%). For a small sample size, the proportion of mortality is skewed considerably toward the ABC categories 4 and 2. As a result, the area under the ROC curve for the ABC system was 0.7 (the least predictability of the 3 systems).

By comparing our results to those of the largest database from the STS and EACTS congenital registry [3, 12], the performance at our center has a higher mortality, especially for higher STS-EACTS categories. Jacobs and colleagues in his 2009 study of 58,506 operations at 73 centers revealed an overall discharge mortality as follows: in Category 1= 0.55% (0% to 1.0%), Category 2 = 1.7% (1.0% to 2.2%), Category 3 = 2.6% (1.1% to 4.4%), Category 4 = 8.0% (6.3% to 11.1%), and Category 5 = 18.4% (13.9% to 27.9%) [12]. On the other hand, our series revealed mortality rates of 1.8%, 4.9%, 25%,

and 21.4% for categories 1 – 4 respectively with no operations in category 5. Accordingly, the performance of congenital heart surgery at our center needs to be improved to achieve a standard of quality matching the STS-EACTS results.

Using Pearson Correlation test, we found that the younger age, the smaller weight the higher RACHS-1 levels, higher ABC levels, higher STS-EACTS mortality categories, longer bypass time, and longer cross clamp time were significantly associated with increased mortality. The bypass times and aortic cross clamp time significantly affect the mortality since they generally reflect the difficulty of procedures and the complexity of diseases.

For operations done more than twice, reviewing every death case, we found that modified B-T shunt and arterial switch operations have the highest risk of surgery (mortality discharge of 42% and 40%, respectively). The causes of death included postoperative low cardiac output, and cardiac arrhythmias, both of which failed to be managed properly in ICU. That reveals the importance of increasing our experience in the management of such cases in the postoperative ICU. Also, limited availability of some drugs as milirinone (phosphodiesterase inhibitor, a potent ino-dilator) and dual chamber pacing devices pay important role in those deaths.

In the present study, the most common complications were postoperative serious arrhythmias (28%), followed by postoperative fever and chest infections (12%). In comparison to others, Chodchanok and associates in their series from Thailand reported postoperative fever (43%), and bleeding tamponade, causing unstable hemodynamics requiring reoperation (9.6%) to be their most common postoperative complications. Other morbidities appeared to be similar to those reported by other authors [14, 15, 16].

Limitations

- (1) The patient population in the present study was rather small. The sample size was adequate for estimating only a two-sided 95% confidence interval (alpha level of 0.05) for a prevalence of mortality of $15 \pm 5\%$. After categorizing patients into the risk models, the statistical power was reduced though some variables showed a strong association with the mortality discharge.
- (2) Since this was a retrospective study, selection bias is inevitable. Some variables, such as noncardiac anomalies, genetic syndromes diagnosed by characteristics, and socioeconomic status could not be traced.
- (3) This is the first time that the RACHS-1 classification and ABC scoring system has been applied to our population. The experts and pediatric cardiologists of our institutions have to scrutinize and explore the raw data before interpretation.

- (4) In the present study, the exclusion criteria was limited by age (between 0–18 years of age), which could skew the results. We excluded preterm, which represents a high-risk group in the ABC and STS-EACTS scoring systems, to reduce conflicts from mortality due to unrelated factors. In addition, adolescents (>18 years old), who had been admitted to adult care units, were excluded by the unique infrastructure of the hospital. Since this is a preliminary report, to provide an initial measurement of the surgical performance at the institute, we intend to adjust the criteria in the next longitudinal study.
- (5) An aggregated database over a longer time may suggest trends that can be used to improve the subsets. Moreover, the inter-institutional case-mix will reveal overall outcomes for nation-wide improvements in quality of care for these patients.

Conclusions

The RACHS-1, ABC, and STS-EACTS mortality scoring systems are useful tools for assessing mortality discharge in a medium volume cardiac center in Egypt. The overall postoperative in-hospital mortality rate was found to be 5.6%. The important risk factors for postoperative mortality were younger age, smaller weight, higher RACHS-1 levels, higher ABC levels, higher STS-EACTS mortality categories, longer bypass time, and longer cross clamp time. The most common complications were serious cardiac arrhythmias and postoperative fever.

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Carotid Artery Disease and CABG, What to do? Tertiary Center's 5 Years Experience

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Background and Aim of the work: Stroke has been one of the most feared of the peri-operative complication of cardiac surgery especially with significant carotid stenosis > 70% .

In this research we described our experience in treating patients who presented to our institution with co-existing coronary and carotid artery disease ,to determine whether significant asymptomatic carotid artery stenosis can be safely ignored in patients going for CABG ? and is duplex ultrasonography is enough in screening patients going for CABG or we can go further ?

Patients and Methods: Retrospective chart review of 156 patients with asymptomatic high grade carotid artery stenosis > 70% undergoing CABG (+/-valve surgery) during about 5-years period (January 2008- November 2012). Those patients are divided into two groups:

Group A (CABG + CEA): 35 patients had prophylactic CEA (either staged or combined) along with CABG + valve surgery. Group B (CABG): 121 patients had only CABG +/-valve surgery without prophylactic CEA. The data of the two groups were collected and analyzed. Carotid duplex US done for all patients going for CABG .

MRI/MRA or CTA brain angiography was done for patients who have bilateral significant carotid artery stenosis (as proved by carotid ultrasonography).

Results: Demographic data in both groups was almost the same. No significant difference in the incidence of stroke rate in both groups (6% in group A and 2% in group B). CABG with bilateral carotid artery disease with good communication between anterior and posterior intracranial circulation as proved by MRA/MRI brain or CTA brain has the same result of unilateral significant carotid artery disease.

Conclusion: Staged carotid endarterectomy approach is good and safe alternate for patients with concomitant symptomatic carotid stenosis.

Prophylactic CEA is unnecessary in asymptomatic patients however more patients should be enrolled to confirm this observation.

In bilateral carotid artery disease: CTA brain or MRA/MRI brain should be considered to evaluate communication between anterior and posterior intracranial circulation.

KEYWORDS: Stroke, carotid stenosis, CABG, stroke.

Abbreviation: CAD = coronary artery disease, CABG = coronary artery bypass grafting, CEA = carotid endarterectomy, US = ultrasonography, MRI/MRA = magnetic resonance imaging/magnetic resonance angiogram, CTA brain = computerized tomography Angiography.

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The incidence of coexisting coronary artery disease and carotid artery disease is 2-14% and 8% of patients going for CABG have significant carotid stenosis^(1,2).

Stroke is one of the most dangerous major complication in cardiac surgery and it is known that significant carotid stenosis (more than 50%-80%) is a strong predictor for perioperative stroke up to 10%, and when carotid artery stenosis more than 80% the risk of perioperative stroke can reach up to 19%^(2,3).

The risk of stroke after CABG was about 2.2% in asymptomatic patients with carotid stenosis less than 50% and remained unchanged since 1970 till nowadays and according to literatures in patients with prior stroke or TIA (transient ischemic attack) it jumps to 8.5%⁽¹⁺³⁾.

In the other hand 50% of stroke victims don't have significant carotid disease⁽⁴⁾.

Current guidelines stated (class IIa, level of evidence C) that carotid end arterectomy is recommended before CABG or concomitant to CABG in patients with symptomatic carotid stenosis or asymptomatic but have unilateral or bilateral carotid stenosis more than 80 %^(3,4).

Carotid duplex ultrasonography screening is highly recommended for patients going for CABG specially elective cases older than 65 years of age, left main coronary artery

lesion, history of peripheral vascular disease, smokers, history of previous TIA or stroke or carotid bruit by auscultation (class: I a, level of evidence :C)^(3,4).

Most of stroke cases occur after initial uneventful recovery from surgery, and it is known that median time of stroke onset is 2 days after on-pump CABG and 4 days after off-pump CABG^(3,4).

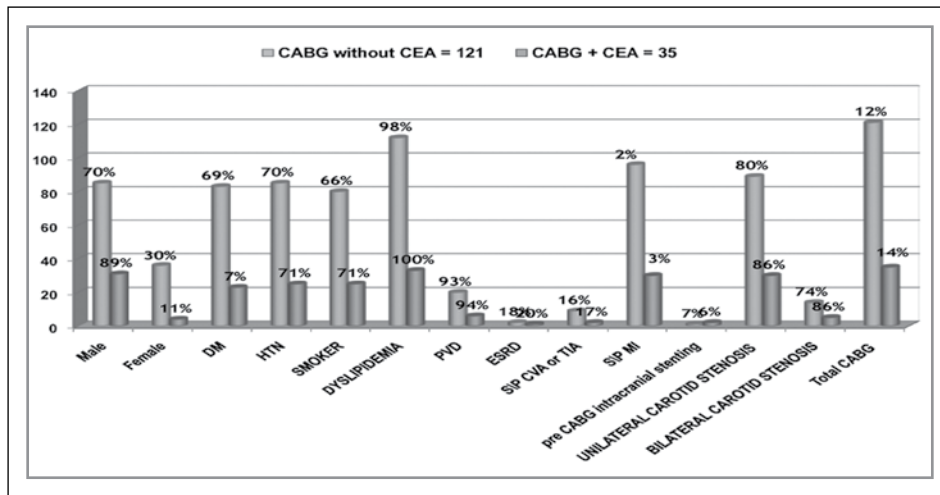
There is no consensus regarding the potential benefit of CEA for asymptomatic disease prior to CABG. Most of the data are controversial. Hines et al in a retrospective analysis did not find any increased risk of stroke from prophylactic CEA or combined CEA+CABG. The authors concluded that patients with 80-99% carotid stenosis undergoing CEA prior to or in conjunction with CABG have a decreased incidence of postoperative stroke. In a prospective study by Bilfinger et al, the risk of post-operative stroke was higher in patients undergoing combined CABG/CEA compared to CABG alone⁽⁵⁻⁷⁾.

Patients and Methods

This is retrospective chart review and prospective observation was conducted at Cardiovascular Surgery Department, Prince Salman Heart Center (PSHC), King Fahad Medical City (KFMC), Riyadh, Saudi Arabia; of 156 patients with asymptomatic high grade coronary artery stenosis more than 70% undergoing CABG (+/- valve surgery in some cases).

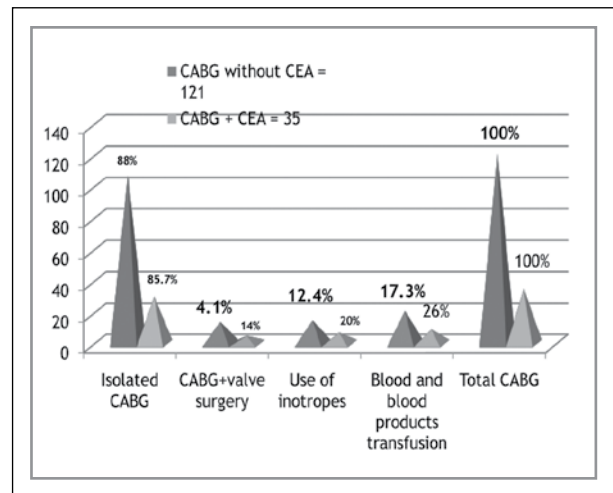
Pre-operative variables: (table 1)

	CABG+CEA=35 PATIENTS	CABG alone 121 PATIENTS	P VALUE
Age	66.4+/- 11	69.5+/- 12	NS
Sex	4 F+ 31 M	85 M+36 F	NS
DM(diabetes mellitus)	23(80.5%)	83(68.59%)	NS
HTN(hypertension)	25(71.42%)	85(70.2%)	NS
Smoker	25(71.4%)	80(77.1)	NS
Dyslipidemia	33(94.28%)	112(92.5%)	NS
PVD(peripheral vascular disease)	6(17.14%)	20(24.2%)	NS
ESRD(end stage renal disease)	1(2.8%)	2(1.65%)	NS
SVP CVA (cerebrovascular accident)or TIA(transient ischemic attack)	2(5.7%)	9(7.43%)	NS
SVP recent MI(myocardial infarction)	30(85.71%)	96(79.33%)	NS
Unilateral carotid artery stenosis	30(85.71%)	89(73.55%)	NS
Bilateral carotid artery stenosis	5(14.28%)	14(11.57)	NS
Pre CABG intracranial intervention	2(5.7%)	1(0.83%)	NS
CTA brain	5(14.28%)	11(9.09%)	NS
MRA\MRI brain	2(5.7%)	2(1.65%)	NS



Operative variables: (table 2)

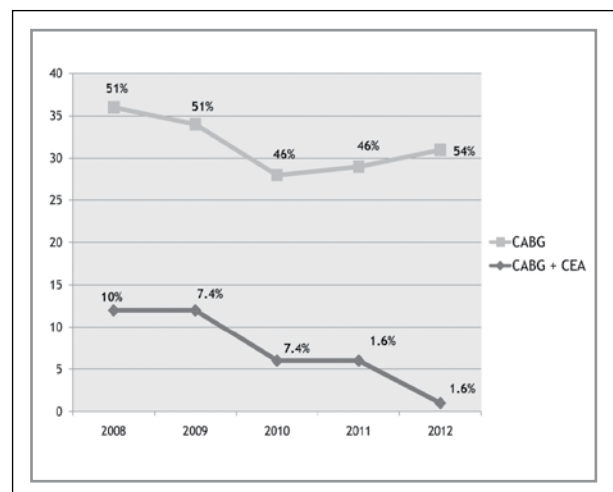
	CABG+CEA 35 patients	CABG ALONE 121 patients	P value
Isolated CABG	30(85.7%)	107(88.4%)	ns
CABG+valve surgery	5(14.3)	14(11.6%)	ns
Mean No of grafts	3.2	3.5	ns
TBPT(total bypass time)	120+/- 40	118+/-35	ns
AXCT(aortic cross clamp time)	55+/- 30	65+/-38	ns
Need for inotropes	7(20%)	15(12.3%)	ns
Blood and blood products transfusion	9(25.7%)	21(17.3%)	ns



Number of cases per year in both groups: table 3

	2008	2009	2010	2011	2012
CABG+CEA	12	12	6	4	1
CABG	24	22	22	23	30

Notice the trend of decreasing number of CEA cases by time in this schedule



Cardiovascular

Post-operative variables: (table 4)

	CABG+CEA (35 CAESS)	CABG (121 CASES)	P VALUE
Total deaths	3(8.5%)	3(2.5%)	ns
Stroke related deaths	1(2.8%)	0%	
Disabling stroke:	2(5.7%)	2(1.6%)	ns
-Carotid related	1(ipsilateral hemisphere stroke)	1(1.1%)	
-Non carotid related	1(contra lateral hemisphere stroke)	1(1.1%)	
Ventilator time(hours)	20+/- 12	18+/- 13	ns
ICU stay(days)	7days+/- 5.5	5+/- 3.3	ns
Total hospital stay(days)	13 days+/- 11	10+/- 6	ns
Reopened for bleeding	3(8.5%)	7(5.7%)	ns
Low cardiac output syndrome	2(5.7%)	5(4.1%)	ns
Respiratory complications	2(5.7%)	2(1.6%)	ns
Multi-organ failure(MOF)	1(2.8%)	2(1.6%)	ns
IAB	1(2.8%)	2(1.6%)	ns
Acute renal failure	1(2.8%)	1(1.1%)	
Myocardial ischemia	3(8.5%)	5(4.1%)	

Total number of deaths and stroke in both groups:

	CABG+CEA	CABG with- out CEA	Total
Deaths /stroke	5(14.28%)	4(3.3%)	9
no death ,no stroke	30	117	147
Total	35	121	156

P value =0.17(ns), odd ratio =3.1(ns), C.I.=0.6-17.3(ns)

Operations were performed during about 5 years period (January 2008- November 2012).

Carotid duplex ultrasound done for all CABG patients ,and MRIMRA brain (magnetic resonance imaging\magnetic resonance angiogram) or CTA brain (computerized tomography Angiography) were done for all patients with bilateral significant carotid artery disease as requested by vascular surgeon or intervention radiologist fig (1) and (2).

156 patients divided into 2 groups:

Group A (CABG +CEA):35 patients had prophylactic CEA (either staged or combined) along with CABG (+/-valve surgery).

Group B (CABG without CEA):121 Patients had only CABG+/- valve surgery without prophylactic CEA:

All patients data were analyzed including preoperative variables, intra-operative variables and post-operative outcome.

All patients in both groups were screened for carotid artery lesion by using duplex ultrasonography, but in 19 cases with bilateral significant internal carotid artery stenosis we did for them CTA brain +/- MRIMRA brain as recommended by the neurology team or vascular team or intervention radiologist, and 3 of these cases required intracranial vascular stenting before CABG due to a significant intracranial vascular lesion to minimize risk of stroke post CABG.

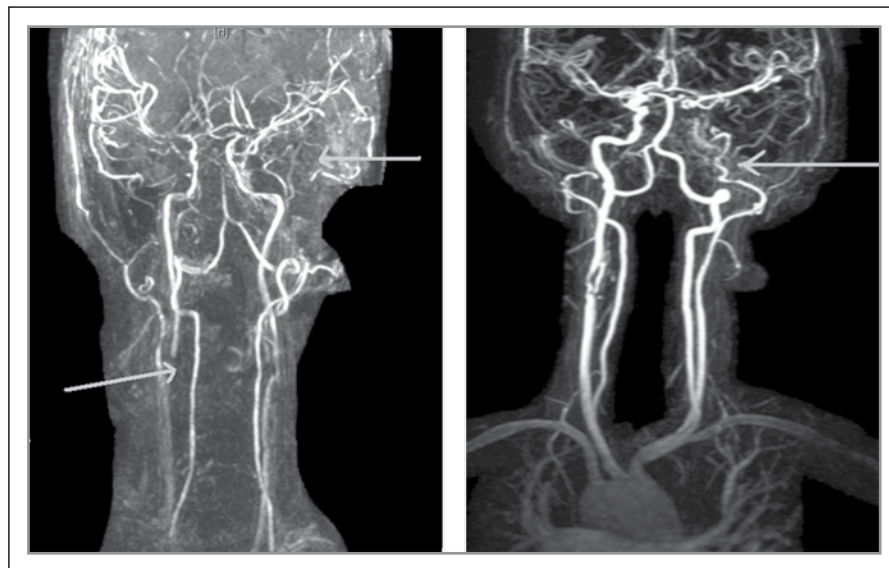


Fig 1. The MR angiography shows attenuated caliber of the left internal carotid artery with two areas of short segment stenosis, one at the upper cervical segment and the other one is seen at the supraclenoid segment. Both MCAs show irregularity throughout their courses likely due to atherosclerotic disease involvement. Diffuse mild irregularity of both PCAs is also noted, right more than left. The A1 segment of the left anterior cerebral artery is severely stenosed and the A2 segment of the left anterior cerebral artery is supplied from the other side through the anterior communicating artery. The right posterior communicating artery is occluded. The left posterior communicating artery is hypoplastic.

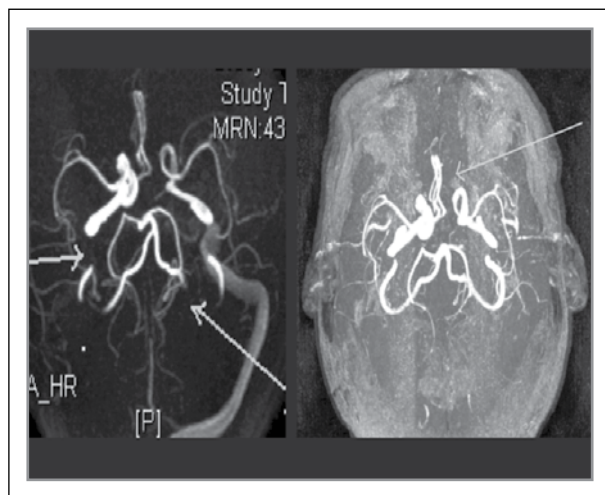


Fig 2. Significant atherosclerotic disease of the intracranial arteries affecting both anterior and posterior circulation.

Discussion

Most of the studies confirmed the poor prognostic results of having significant carotid artery disease with CABG and this poor outcome persists even with carotid revascularization before or with CABG with elevated stroke and mortality rate^(4,5).

In our study, 3 patients died in group A (8.5%) and 3 patients died in group B (2.5%) with p value is not significant (due to relatively small number of study group).

The deaths in group A was as following;

1st case was 70 years old female who was diabetic on insulin, with renal impairment, with past history of CVA with 80%LICA (left internal carotid artery)stenosis and 70%RICA(right internal carotid artery) stenosis, and post recent anterior STEMI, LM lesion with severe triple vessel disease, EF=50% ,her Euroscore II was 8.5 .She died 72 days post operative(CABGX 4 +CEA) due to multiorgan failure(MOF) (long ventilation time , pneumonia, sepsis , acute renal failure required dialysis ,high liver enzymes..), in spite of all these morbidities her post operative CT brain showed no new evidence of CVA.

2nd case was 80 years old male with severe right internal carotid artery stenosis 90% and mild left internal carotid artery lesion , ischemic cardiomyopathy with EF 35% , recent anterior STEMI ,DM ,DLP, severe LM lesion with severe double vessel disease, moderate renal impairment and his Euroscore II was 12.9% ,he died 5 days post combined surgery (CABG x3 +CEA)after big stroke in the contralateral side hemisphere and craniotomy was done +insersion of intraventricular shunt to relieve high intracranial tension and severe brain edema.

3rd case was 65 years old female, diabetic on insulin, hypertensive and dyslipidemic , obese ,BMI above 35 with history of recurrent TIA ,and carotid duplex ultrasound showed severe bilateral internal carotid artery disease ,she presented with unstable angina and her coronary angiography showed critical LM lesion with severe triple vessel disease ,

And her echo showed MRWMA(multiple regional wall motion abnormalities) +severe MR, EF 30%, RV(right ventricle) mild dysfunction , with diastolic dysfunction grade 2; Euroscore IIwas 15.9% . Emergency CABG X4 +mitral repair +CEA done for her but she didn't survive the surgery and died one month post operative with low cardiac output syndrome then MOF.

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In group B there were 3 mortalities (2.5%):

1ST case: 73 years old female presented by recent inferolateral STEMI, will known to be diabetic ,hypertensive ,and here echo showed severe diastolic dysfunction and EF 50% , RV moderate dysfunction with moderate tricuspid regurge, her coronary angiography showed severe triple vessel disease and her Euroscore II was 6%. CABG X4 done for her and she was extubated 2 days post operative ,She got acute renal failure and died 22 days post CABG .

2nd case was 66 years old male transferred from periphery hospital as a case of anterior STEMI thrombolysed for further work up , ECHO showed EF 55% ,moderate diastolic dysfunction and no valve lesion ,and his coronary angiography showed severe triple vessel disease, his Euroscore was 2%. CABG X4 done for him but he died after 24 hours post operative due to massive unexplained medical bleeding.

3rd case was 75 years old lady presented with recent anterolateral STEMI, with un-protected LM severe lesion in angiography and CABG X 3 done for her but she died 3 days post operative due to low cardiac output syndrome and cardiogenic shock due to extensive post operative myocardial infarction.

In our study the total post operative strokes was 5 cases ;3(2.5%) in group A and 2(1.6%) in group B, also in a study done by Robert and Jonson on 203 patients the stroke rate was 6.9% in CABG+CEA and 4.6% in CABG alone group with insignificant p value(0.579) and they concluded that the combined procedure did not yield a more favorable variance of observed CVAs from expected CVAs⁽¹²⁾.

In a study done by Byrne etal on 758 patients CABG+CEA done for them ,the overall mortality was 3.1% and 7 disabling strokes occurred in this series(0.9%) with combined stroke and mortality in 4.3%of cases in contrary to our study where the death related stroke was 1 case only (2.8%)⁽¹³⁾.

In a multicenter study done by Douglas etal on 1563 patients underwent isolated CEA and 109 patient underwent CEA\CABG ,they found that the risk of complications was higher in 2nd group with risk of stroke 5.5% compared to 1st group which was 1.2%(p=0.001), and death was 0.3% in 1st group vs 5.5% in 2nd group(p=0.001) , and return to operating room was 1.2% vs 7.6%(p=0.001)⁽¹⁴⁾.

In a systematic review of outcome in patients with staged carotid artery stenting and CABG ,done by Luis and his co-workers they found that the presence of CAS(coronary artery stenosis) is an independent risk of stroke after CABG and carotid stenosis itself is associated with a significant increase in CABG mortality and stroke⁽⁵⁾.

In a research done by Brow etal ;they suggested that carefully planned management of concomitant coronary and carotid disease can achieve better results with no major complication in reverse staged (CABG then CEA) or prior

staged group (CEA then CABG) with mortality 2.7% and no strokes versus the combined group (CEA\CABG)with mortality 4.3% and stroke 8.6% (p=0.001)⁽¹⁵⁾.

In study done by Raja etal on 6152 patient underwent CEA before or after CABG(STAGED procedure) versus 16639 patients who under both procedures CEA+CABG(SYNC approach) they concluded that no difference in mortality or stroke between staged or combined approach ,in spite staged procedure were associated with a higher hospital charges and greater risk of all complications including neurological complications⁽¹⁶⁾.

All studies recommended carotid ultrasonography as screening cheap modality for patients going for CABG ,but we added in our study the value and the need for CTA brain or MRA\MRI brain in some special cases and it had changed our strategy in management for some cases as we had to do intracranial intervention by stenting of intracranial vessels in 3 cases before CABG by help of intervention radiologist and neurologist consultant (fig 1,2).

In our study we concluded that:

Carotid duplex ultrasonography sometimes is not enough to evaluate carotid artery lesion specially in bilateral carotid artery stenosis with suspicion of intracranial artery lesions, in such cases CTA brain or MRI\MRA brain is highly recommended to asses intracranial vasculature and communications and if we still need intervention from the vascular surgeon or radiology interventionist or neurologist ;specially in cases with poor intracranial vascular communication or stenosis prior to CABG and for more precise perioperative neurological risk stratification.

Prophylactic CEA in asymptomatic patients undergoing CABG is unnecessary, however more patients should be enrolled to confirm this observation, also combined CEA\CABG can be performed in patients having diffuse intracranial vasculopathy to improve the inflow circulation to the brain.

Also we concluded that staged CEA approach is good alternative and safe for patients with symptomatic carotid disease.

Gender plays an important role in outcome of CABG surgery and female sex is important independent risk factor for post-operative morbidities and mortalities after CABG surgery (4/6 deaths were females in our study=66.7% of all mortalities).

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Regain Interest in Semi-continuous Sutures in Prosthetic Valve Replacement

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Background and aim of the study The continuous suture technique has numerous advantages as a simple, quick, and effective method for valve replacement⁽⁵⁾. The semi-continuous suture technique is a modification of the continuous technique aiming to avoid its technical disadvantages. This method combines advantages of the continuous and interrupted suture techniques⁽⁶⁾. In this study we evaluated the semi-continuous suture technique in patients undergoing prosthetic valve replacement, comparing it with the conventional interrupted suture technique.

Patients and methods 131 patients with valvular lesions were included in the study, underwent valve replacement. Patients were divided into two groups according to the suture technique used in valve replacement. Group I (conventional interrupted suture technique), 76 patients, there were 43 males and 33 females, mean age 36.6 years. 18 patients underwent isolated aortic valve replacement (AVR), 36 underwent isolated mitral valve replacement (MVR), and 22 patients underwent double valve replacement (DVR), and group II (semi-continuous suture technique), 55 patients, there were 27 males and 28 females, mean age 36.9 years. 15 patients underwent isolated AVR, 24 underwent isolated MVR, and 16 patients underwent DVR.

Results Statistical analysis showed that the aortic cross clamp time, cardiopulmonary bypass time, and operation time, were significantly decreased in group II than in group I, And the implanted valve size was significantly larger in group II. 2 patients in group I developed paravalvular leakage, and one patient in group II. There is no late postoperative leakage in both groups. 3 cases of late endocarditis in group I, and one case in group II. Valve thrombosis occurred in 5 patients in group I, and in 4 patients in group II.

Conclusion: The semi-continuous suture technique is suitable for all types of prosthetic valve replacement, especially those of rheumatic origin, and with small left atrium and small aortic annulus. It is simple, with short period of valve implantation, associated with few postoperative complications, and especially suitable for patients in developing countries.

There are two methods of continuous and interrupted suturing of prosthetic valve implantation. Although it has been reported that the rate of periprosthetic leakage in the continuous method is high following the operation^(1,2), it is supposed that this high rate of leakage is not common in rheumatic valve disease, because the annulus in these patients is usually thick and fibrotic^(3,4).

The continuous suture technique has numerous advantages as a simple, quick, and effective method for aortic valve replacement (AVR), specially from the viewpoints of less thrombogenic materials around the prosthesis and lower risk of infection because a pledget is not used. However the continuous suture method is technically difficult. In particular when tangling the sutures or tearing of tissue due to excessive tension occurs, adverse complications such as paravalvular leakage may develop⁽⁵⁾.

The semi-continuous suture technique is a modification of the continuous technique aiming to avoid the above technical disadvantages. It is an over-and-over semicontinuous suture with the valve prosthesis held above the native annulus. The

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prosthesis is secured with a “hoistlike” lowering technique. This method combines advantages of the continuous and interrupted suture techniques⁽⁶⁾.

In developing countries where most patients present late for surgery and are usually in a decompensated state, good surgical technique, decrease ischemic time, and duration of cardiopulmonary bypass can play a vital role in improving the outcome. To this end, a continuous suture technique was developed for valve replacement⁽⁷⁾.

In this study we evaluated the semi-continuous suture technique in patients undergoing prosthetic valve replacement, comparing it with the conventional interrupted suture technique.

Patients and Methods

We conducted this prospective study between January 2007 and December 2009, at Sohag university hospital in Egypt. A total of 131 patients with valvular lesions (112 rheumatic, 10 degenerative, and 9 congenital) underwent valve replacement (33 aortic, 60 mitral, and 38 double valve replacement). All patients undergoing isolated valve replacement in this period are included with exclusion of patients having combined operation (CABG or previous valve surgery). Written consent was taken from each patient, and the institutional ethical approval was taken.

Patients were divided randomly into two groups according to the suture technique used in valve replacement. Group I in which the conventional interrupted suture technique was used, and group II in which the semi-continuous suture technique was used. For all patients transthoracic echocardiography was done preoperatively, and the valvular lesion, cardiac function, and structure were evaluated in details.

Group I (76 patients), there were 43 males and 33 females, with a mean age 36.6 (17 to 60) years. 18 patients underwent isolated aortic valve replacement (AVR) (13 were predominantly aortic stenosis, and 5 with dominant aortic regurge), 36 underwent isolated mitral valve replacement (MVR) (20 were stenosis, 7 mitral regurge, and 9 combined lesion), and 22 patients underwent double valve replacement (DVR) (14 double stenosis, and 8 double regurge) table (1). Group II (55 patients), there were 27 males and 28 females, with a mean age 36.9 (17 to 63) years. 15 patients underwent isolated aortic valve replacement (AVR) (10 were predominantly aortic stenosis, and 5 with dominant aortic regurge), 24 underwent isolated mitral valve replacement (MVR) (15 were stenosis, 4 mitral regurge, and 5 combined lesion), and 16 patients underwent double valve replacement (DVR) (11 double stenosis, and 5 double regurge) table (1).

The etiology of valve lesions in the majority of patients in both groups was rheumatic, with 10 patients degenerative (6 in group I and 4 in group II), and 9 congenital bicuspid aortic valve (4 in group I and 5 in group II).

Patients data	Group I Interrupted	Group II Semi-continuous	P
Age (mean) ys	36.6	36.9	NS
Male / female	43 / 33	27 / 28	NS
Cardiac rhythm			
Sinus	55	43	NS
A.F	21	12	
NYHA class			
II	13	11	NS
III / IV	63	44	
Aortic lesion			
Stenosis	13	10	NS
Regurge	5	5	
combined	-	-	
Mitral lesion			
Stenosis	20	15	NS
Regurge	7	4	
combined	9	5	
Double valve			
lesion	14	11	NS
Stenosis	8	5	
Regurge			
LV ejection	59.5	59	NS
fraction %			

Table 1. Preoperative data in both groups (P value by Z test)

Operative technique

Endotracheal general anaesthesia, median sternotomy, aorto-bicaval cannulation, and cardiopulmonary bypass was instituted in the standard manner in all cases.

All cardiac valve prosthesis have been inserted in our study with the same technique (developed by Professor H. Sadeghi 1973)⁽⁶⁾, and its modification developed by Watanabe Go 2011⁽⁵⁾. We use an over-and-over semicontinuous suture with the valve prosthesis held above the native annulus. The prosthesis is secured with a “hoistlike” lowering technique. This method can be used in all situations encountered in valvular prosthetic operations for adults and children.

Generally after excision of the native and thorough annulus decalcification, three to four double-armed initial sutures of 2-0 Prolene on a 26-mm taper-cut needle are used for the aortic and four to six sutures for the mitral valve.

For the aortic valve the prosthetic valve was held firmly 5 cm above the native valve annulus. For the first suture,

the stitch was passed through the commissure between the right and left coronary cusps (R-L commissure), and then the stitch was passed from below the corresponding point of the prosthetic ring and up through the ring, in a counter clockwise direction, the next stitch was inserted into the aortic annulus and again passed through the prosthetic ring, and the suture was continued until one stitch before the commissure between the left coronary and noncoronary cusps (L-N commissure). The first suture was completed (Fig. 1). For the second suture, the first stitch was placed in the L-N commissure, and the stitches were passed through the prosthetic ring in a counterclockwise direction as described above, until reaching the N-R commissure. The third suture was also done as for the above sutures. During suturing it is important not to allow the sutures to slack but to maintain tension. Four to five stitches were made between the two commissures. At each stitch care was taken to anchor sufficient tissues including the ring.

Next the prosthetic ring was lowered into its position by manipulating the parachute suture. The prosthesis is lowered

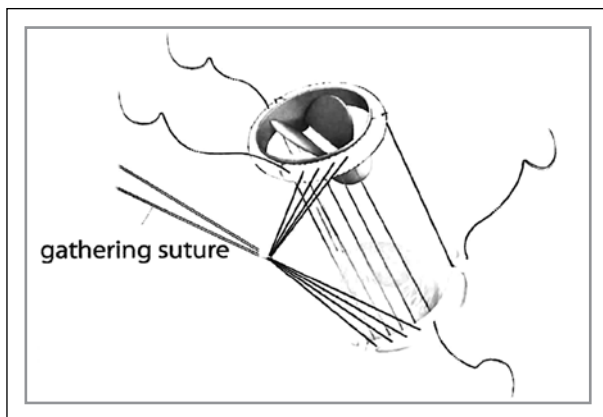


Fig 1. The first suture was completed (5).

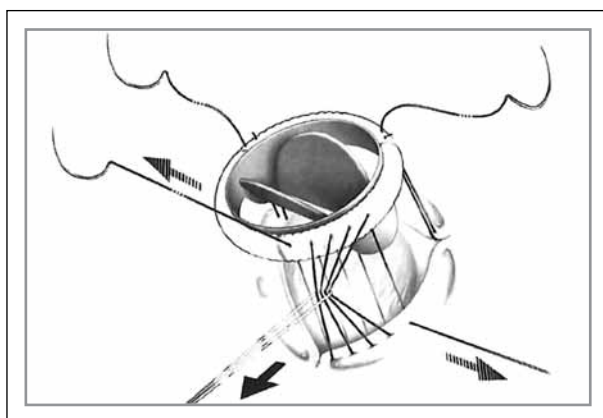


Fig 2. Lowering the prosthetic valve to its position by pulling the stitch ends and by counter traction (6)

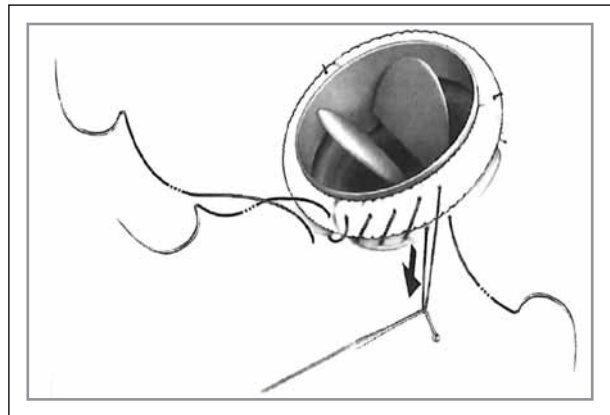


Fig 3. The suture is tighten carefully in a sequential manner using a nerve hook (9).

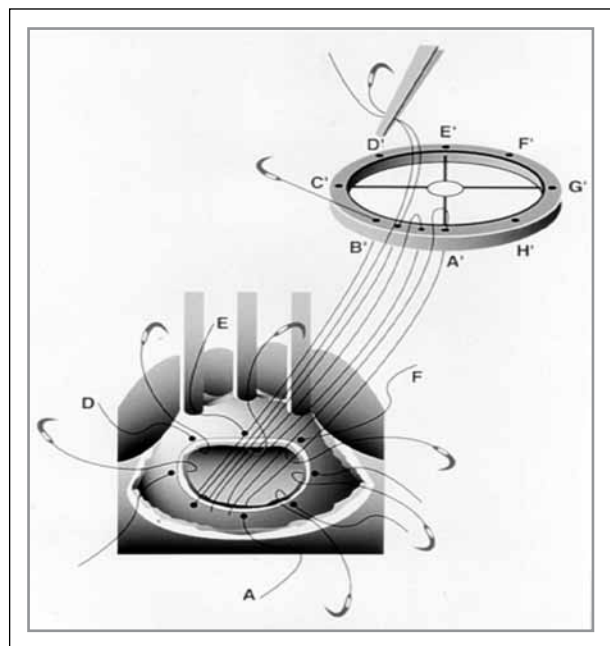


Fig 4. Mitral valve replacement. A left atriotomy is made. Eight initial sutures are placed (6).

onto the valve annulus by progressive gentle traction exerted sequentially on each end of the sutures. Countertraction is applied for uniform suture tension until the prosthesis is seated (Fig. 2). The valve holder is then removed. A thorough inspection of the superior and inferior surfaces of the sewing cuff is made, checking for any free loops that could be removed by gentle traction on the related suture. Each suture is tied, leaving a final three knots (Fig. 3).

For the mitral valve procedure we used the same technique but we recommend the use of four to six sutures. Commencing in the middle of the posterior leaflet: each continuous suture

progresses clockwise up to the next initial suture, each one covering one-fourth (or one sixth) of the sewing ring (Fig.4). After this the prosthesis is seated with the hoist method.

Intraoperative, early postoperative, and midterm (38 months) postoperative outcomes were obtained and compared for both groups.

Results

In this study there were no significant differences between both groups as regard age, sex, body weight, body surface area, valve lesion and concomitant surgical procedure, preoperative NYHA class, and early mortality. The types of valve implanted

in both groups were similar prosthetic bileaflet valves (St. jude 45, carbomedics 69, ATS 10, and sorin 45). The condition of patients in both groups were stable and uneventful during postoperative period, and there were no operative deaths.

Intraoperative findings, early and midterm outcomes of the two groups were shown in table (2). Statistical analysis showed that the aortic cross clamp time, cardiopulmonary bypass time (CBP), and operation time, were significantly decreased in group II (semicontinuous group), than in group I (conventional interrupted group). And the implanted valve size was significantly larger in group II. The ventilation time and hospital stay, although they are decreased in group II than in group I, the decrease is not significant.

	Group I Interrupted sutures (No. 76)	Group II Semicontinuous sutures (No. 55)	P value >0.05=NS <0.05=S
Cross clamp time (min)	64.6	50.5	0.001
Aortic	44.3	37	----
Mitral	51.6	39	----
Double	102	79.9	----
Cardiopulmonary bypass time	100.6	87	.005
Aortic	77	73.8	----
Mitral	85	74	----
Double	144	119.5	----
Postoperative intubation time (hs)	7.5	6.5	NS
Hospital stay (d)	9.4	9.3	NS
Size of implanted valve(mm)			S
Aortic	21.2	22.4	0.001
mitral	27.9	29	0.001
Perioperative death	0	0	---
Myocardial infarction	0	0	---
Pneumonia	2	1	NS
Ventricular fibrillation	3	1	NS
Stroke	0	0	---
Re exploration	2	1	NS
Paravalvular leakage			
Early	2(2%)	1(1%)	---
Late	0	0	
Infective endocarditis			
Early	0	0	---
Late	3(3%)	1(1%)	NS
thrombosis	5(6%)	4(7%)	NS

P value by Student's T-test

Table 2. Intraoperative, early, and midterm results of both groups

Patients of both groups were recovered satisfactorily without any complications associated with the suture technique or prosthesis. During the follow up period 38 months (from 10 to 48 months), which was completed in 92 % of patients, 2 patients in group I developed paravalvular leakage (one at the mitral position and one at aortic position), one of them was mild to moderate and improved by conservation and medical treatment as proved by transthoracic echocardiography, while one case was significantly severe necessitating surgical intervention (redo implantation) 3 months postoperatively. In group II, one patient developed severe paravalvular leakage (at the mitral position) two weeks postoperatively, redo implantation was done one week later on. There is no late postoperative leakage (during the follow up period) in both groups.

During the follow up period there is no recorded early postoperative prosthetic valve endocarditis in both groups, while 3 cases in group I presented by endocarditis late during the postoperative period, and one case in group II. As regard valve thrombosis in, 5 cases in group I were presented by valve thrombosis (malfunctioning and stucked valves), one case managed conservatively, while 3 needed intervention with good results, and one case died before intervention, in group II, 4 cases presented by valve thrombosis, intervention was done in 3 cases with good results, and one case died at the ICU.

Discussion

Continuous suture technique in aortic and mitral valve replacements has been described in the text book of cardiac surgery since a long time ago⁽⁵⁾. The use of continuous suture may be of benefit to the patients because the cardiac ischemic time is reduced by half with this technique, and myocardial injury is minimized. This may be important for patients with marginal cardiac reserve⁽⁸⁾. Moreover the continuous suture technique is effective method for aortic valve replacement, especially from the viewpoints of less thrombogenic materials around the prosthesis and lower risk of infection because a pledget is not used⁽⁵⁾.

Despite these advantages, many cardiac surgeons still tend to favor the interrupted suture technique, as the continuous suture method is technically difficult. In particular when tangling the sutures or tearing of tissue due to excessive tension occurs, adverse complications such as paravalvular leakage may develop⁽⁵⁾. To address these issues, various modifications for the continuous suture technique have been attempted^(6,9).

The semi-continuous suture technique is a modification of the continuous technique aiming to avoid the above technical disadvantages; this method combines advantages of the continuous and interrupted suture techniques. This method can be used in all types of valve prostheses. It is also suitable in the first row of sutures for the valvular homograft and stentless bioprosthesis⁽⁶⁾.

In our study we found that prosthetic valve replacement (mitral, aortic, or double replacement) using the semi-continuous suture technique there is significant reduction of the aortic cross clamp time, cardiopulmonary bypass time (CPB), and operation time, without postoperative complications related to the suture technique or midterm disadvantages.

Similar results were found in other studies, where in their series in 2011, Watanabe G and his group⁽⁵⁾, found that AVR using modified continuous suture technique markedly reduced operation time, CPB time, and aorta cross clamp time, without serious postoperative complication or long term disadvantages.

Ruchat et al in 1998⁽⁶⁾, applying the semi-continuous suture technique in all types of prosthetic valve replacement, found that the procedure is shortened by less instrumental handling and fewer knots to tie, therefore reducing the cross-clamping time.

Dalichau H., and Borst HG., in their study in 1993⁽¹⁰⁾, said that the use of continuous suture may be of benefit to the patients because the cardiac ischemia time is reduced by half with this technique, and myocardial injury is minimized, which may be important to patients with marginal cardiac reserve. Pluth JR and Curtis JJ in 1978⁽¹¹⁾, in their series found that, with the modified continuous suture technique, the open left atrial time is generally less than 30 minutes, exposure is good, and risk of disastrous regurgitation from suture break is minimized.

The incidence of arteriosclerotic aortic stenosis in the elderly (aged 75 years or older) continues to increase⁽¹²⁾. Furthermore, patients with small aortic annulus have also increased. In this population, less invasive surgery is desirable⁽¹³⁾. Although transcatheter aortic valve implantation may be an option in the future, complications of this procedure have been reported, and surgery definitely remains the first option⁽⁵⁾. In the semi-continuous suture technique, the prosthesis is seated on the aortic annulus rather than being wedged into it such as in the everting mattress technique. Moreover, similar to the interrupted single suture without pledget, a valve of a larger size can be fitted⁽¹⁴⁾.

In our study the size of the implanted prosthetic valve was definitely larger in the semi-continuous suture group, than in the conventional group ($P = 0.001$), at least by one size. And this is found in other similar studies, where watanabe G. et al in 2011⁽⁵⁾, found that a prosthesis one size larger than that used in the conventional interrupted mattress technique can be implanted smoothly on the patient's aortic annulus. Also Ricchi A and Ross DN in 1996⁽¹⁴⁾, found the same results.

There are some controversies about the incidence of perivalvular leak in continuous suture technique for AVR. Where Nair et al⁽¹⁵⁾, reported a higher incidence of paravalvular leakage when using continuous suture, both in aortic and mitral valve replacements. Hjelms et al⁽¹⁶⁾, reported an incidence of perivalvular leakage of 8.8% in 80 patients with pure aortic

insufficiency who underwent AVR using the continuous technique and suggested that the continuous suture technique is not suitable for patients with pure aortic insufficiency. In the other hand, Laks et al⁽¹⁷⁾ reported that the incidence of perivalvular leakage using the continuous suture technique was only 2.3% and that the incidence of perivalvular leak in aortic valve replacement was comparable in both continuous suture technique and conventional interrupted technique.

Qicai et al⁽¹⁸⁾, observed low incidence of both paravalvular leakage and infectious endocarditis with the continuous suture technique and reported the advantages of this method. Therefore, in case of aortic valve replacement, the occurrence of paravalvular leakage is probably not related to whether continuous suture or interrupted suture is used. Instead, reliable surgery, particularly whether stitches are made with firm anchoring to the tissue, is a factor that determines the outcome. The reason is that if paravalvular leakage is an inherent problem with continuous suture, then the use of continuous suture for proximal anastomosis in aortic root replacement using composite graft or homograft would not have been established^(19,20).

In our study, during the follow up period of patients 38 months (10 – 48 months), there was only one case of early paravalvular leakage (1%) in the semi-continuous group, where paravalvular leakage occurred in 2 cases in the interrupted group (2%). No detected late paravalvular leakage in both groups. These results are comparable with the results in other studies, where Ebetaz and colleagues⁽²¹⁾, in their study of 354 valves, found that the overall rate of early periprosthetic leakage was 0.8%. In another randomized study in 80 consecutive primary valve insertions, no detected periprosthetic leakage by Doppler echocardiography at 3 months⁽²²⁾.

These results are also comparable with those of Dhasmana and colleagues⁽²³⁾, who use an interrupted technique and 1-0 suture material. They have shown in a single and multivariate analysis that periprosthetic leakage without infection was independent of the suture technique (interrupted versus continuous), but was dependent on the suture size and annular calcification. This demonstrates the importance of meticulous annular decalcification in our technique using a 2-0 suture.

Another major advantage of the continuous suture technique is less thrombogenic material such as pledgets around the prosthesis compared with the conventional interrupted suture technique. Furthermore, our technique does not require a pledget inside the aorta, which further reduces complications associated with thrombogenic material. Prosthetic valve endocarditis is one of the common postoperative complications after cardiac valve replacement⁽²⁴⁾. Because there is no pledget in the aorta to expose the blood to foreign material, our modified continuous suture technique may help reduce the incidence of this severe complication⁽²⁵⁾.

In our study there is non-significant decrease in incidence of infective endocarditis in the semi-continuous technique group than in the conventional group, and nearly there is comparable incidence of thrombosis in both groups. We attribute this to the decrease in both educational and economic status of most patients, which in fact the cause of their decrease medical education and awareness about the importance of long life anticoagulation with close monitoring and follow up, and the most important is the importance of antibiotic prophylaxis before any minor or major surgical procedure.

Conclusion

Our conclusion is: the semi-continuous suture technique is suitable for all types of prosthetic valve replacement, especially those of rheumatic origin, and with small left atrium and aortic annulus. It is simple, with short period of valve implantation, associated with few postoperative complications, and especially suitable for patients in developing countries. It is reproducible and combines the advantages of interrupted and continuous suture techniques.

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Early Post- Operative Complications After Coronary Artery Bypass Grafting: on Pump Versus off Pump Technique: Controlled Randomized Study

M. Abdel-Fatah, MD.

Objective: This study was designed to compare on-pump CABG and off-pump CABG procedures in terms of completeness of revascularization and in-hospital postoperative complications.

Methods: Two hundred patients with coronary artery disease were prospectively randomized into 2 equal groups to either benefit from on-pump CABG under mild hypothermia and cardioplegic arrest with repeated infusion of warm blood cardioplegia (Group A) or from Off-pump beating CABG using the Medtronic Octopus suction stabilization system (Group B).

Results: There were 3 hospital mortalities (1.5%) that were unrelated to patients' groups. On-pump (Group A) patients benefited from significantly larger number of grafts (2.71 ± 0.61), compared to Group B patients (1.9 ± 0.85 ; $P < 0.001$). The on pump group needs significantly more blood transfusion ($P < 0.001$) and leaving the ICU with a significantly lower hematocrit value ($P < 0.001$), compared to Group B. On the other hand, on-pump group patients needed significantly longer mechanical ventilation time (29.36 ± 45.9 hours) and had a longer total hospital stay (8.2 ± 3.7 days), compared to off-pump group of patients 16.6 ± 12.8 hours ($P = 0.008$) and 6.4 ± 2.3 days ($P < 0.001$); respectively. Although respiratory complications were higher among on pump Group A patients ($P =$ non-significant), yet those complications were significantly related patients' demographics including; advanced patients' age, male sex, presence of diabetes mellitus, hypertension, hypercholesterolemia, smocking and an EF% of less than 50%; $P < 0.001$.

Conclusion: Although the off-pump technique was associated with shorter hospital stay and less complications, yet the classic on-pump CABG is still associated with significantly complete revascularization.

KEY WORDS: Coronary artery bypass, on-pump, off-pump.

Millions of people have coronary artery disease and many of these people have multivessel disease, which is best treated with coronary artery bypass grafting (CABG) which traditionally done with cardiopulmonary bypass (CPB). (1) Several physiologic derangements are associated with CPB, including thrombocytopenia, activation of complement factors, immune suppression, and inflammatory responses (24).

Furthermore, manipulating an atherosclerotic ascending aorta during cannulation and cross-clamping can potentially induce distal embolus formation, causing strokes. In an attempt to prevent CPB-related morbidity and minimize ascending aorta manipulation during surgical myocardial revascularization, surgeons developed off-pump coronary artery bypass (OPCAB), a revascularization technique that does not require CPB (1). With the growing interest in minimally-invasive techniques, there has been an increase in revascularization without CPB. In 1984, Rivetti and Gandra started to perform revascularization without CPB with the aid of a temporary intraluminal coronary device (shunt) in order to maintain blood flow in the artery, avoiding ischemia. (3) The development of commercially available cardiac stabilization devices resulted in several large, nonrandomized, retrospective case series demonstrating that CABG surgery can be performed safely without CPB (off-pump) and were suggestive of benefits when compared with conventional coronary artery bypass (CCAB) (5)

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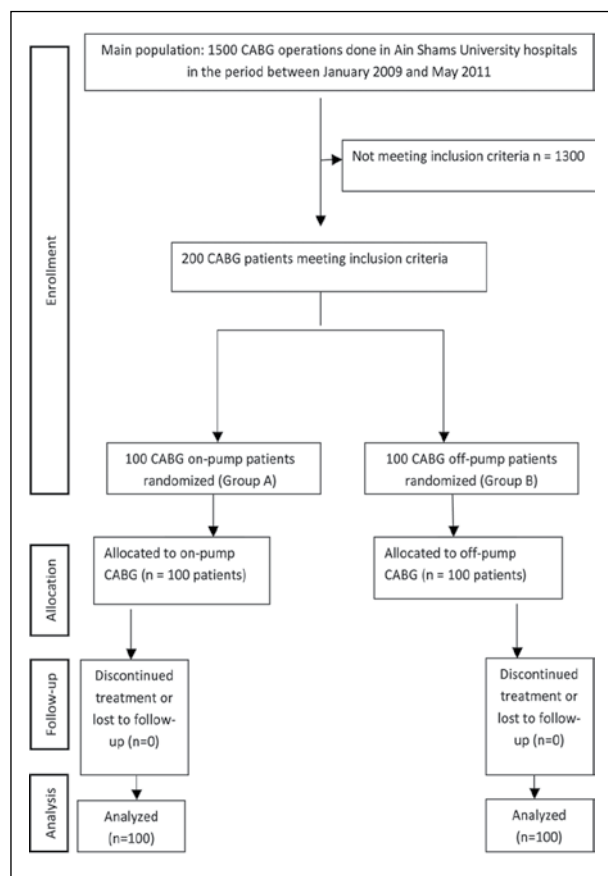


Fig 1. Consort flow diagram indicating patient screening and enrollment, treatment allocation, follow-up and analysis. n = number of patients.

Our study here is to compare between on-pump and off-pump early results to try to help other studies to confirm which technique is better than the other.

Material and Methods

In the period between January 1st 2009 and 31th of May 2011, 200 patients benefited from CABG at Ain Shams University Hospitals. Those patients were divided into 2 equal groups: A and B. Group A patients were operated upon classically using cardiopulmonary bypass, under mild hypothermia and repeated infusion of cold blood cardioplegia. Group B patients were operated upon off pump: In brief, after routine median sternotomy, half dose heparin, elevation and manipulation of the heart by a big towel fixed in the pericardium behind the heart, stabilization was by "Medtronic Octopus suction stabilization system" and control of bleeding from the coronary vessel by a silastic sutures. In both groups, LIMA was harvested skeletonized and the pleura was opened during harvesting. Long saphenous vein harvested from either

or both legs. Using an overrunning 7/0 proline sutures did all distal anastomoses. Using an overrunning 6/0 by proline sutures did all proximal anastomoses. Blood transfusion was done in case of bleeding more than 100 ml for 3 hours or in case of serum hemoglobin dropping below 10 gm%. Patients were prospectively followed up during their hospital stay so as to assess risk factors associated with hospital mortality and morbidity figures. Inclusion criteria include patients underwent elective CABG cases done by the same described techniques either off-pump or on-pump. Exclusion criteria include emergency CABG, CABG with other cardiac intervention and CABG that not done by same described techniques.

Statistical analysis

Data are presented as mean \pm SD or numbers and percentages, as indicated. Distribution of qualitative variables among patient's groups was analyzed by Chi-Square test or Fisher's exact test, as indicated. Means were compared using unpaired Student's test. A P value of 5% or less was our border line significance. SPSS statistical package version 19 was used for statistical analysis.

Results

Table 1 shows patient's demographic criteria, with no significant differences between compared groups. Table 2, shows outcomes in the 2 compared groups. Aortic cross clamp and bypass times in on-pump group were 65.5 ± 20.8 and 82.8 ± 24.8 minutes; respectively. In accordance, those patients benefited from significantly larger number of grafts (2.71 ± 0.61 graft/patient), compared to off-pump group (1.9 ± 0.85 graft/patient; $P < 0.001$). Respiratory complications were higher among on pump group, compared to off pump technique ($P =$ non-significant). The amount of blood loss was higher in the on pump group ($P =$ non-significant), with patients needing significantly more blood transfusion ($P < 0.001$) and leaving the ICU with a significantly lower hematocrit value ($P < 0.001$), compared to the off pump group. In fact, 81 patients (81%) in on-pump group needed blood transfusion, compared to only 21 patients (21%) in off pump group; $P < 0.001$. In concordance, on-pump group patients needed significantly longer mechanical ventilation time (29.36 ± 45.9 hours) and had a longer total hospital stay (8.2 ± 3.7 days), compared to off-pump group of patients 16.6 ± 12.8 hours ($P = 0.008$) and 6.4 ± 2.3 days ($P < 0.001$); respectively.

As shown in table 2, other complications including need for positive inotropic support, postoperative stroke, renal failure and hospital mortality were insignificantly different between compared groups. Interestingly, Table 3 shows that all 26 respiratory complications occurred in strictly male patients, were all smokers, diabetic, hypercholesterolemia and with low EF below 50%.

Variable	Total (n=200)	Group A (n= 100)	Group B (n = 100)	P value*
Age (years)	59 ± 5.67	59.5 ± 5.2	58.5 ± 6.1	Ns.
Male sex	170 (85%)	86 (86%)	84 (84%)	Ns.
Diabetes mellitus	98 (49%)	47 (47%)	51 (51%)	Ns.
Hypertension	112 (56%)	53 (53%)	59 (59%)	Ns.
hypercholesterolemia	136 (68%)	67 (67%)	69 (69%)	Ns.
Smocking	119 (59%)	57 (57%)	62 (62%)	Ns.
Preoperative hematocrit %	40.5 ± 4.1	40.6 ± 4	40.4 ± 4.6	Ns.
EF% below 50%	53 (26.5%)	30 (30%)	23 (23%)	Ns.
Parsonnet score:	11.23 ± 7.65	11.3 ± 7.3	11.2 ± 8	
0-4	37 (18.5%)	18 (18%)	19 (19%)	
5-9	61 (30.5%)	31 (31%)	30 (30%)	
10-14	47 (23.5%)	21 (21%)	26 (26%)	
15-19	27 (13.5%)	15 (15%)	12 (12%)	
20+	28 (14%)	15 (15%)	13 (13%)	Ns.

Values are presented as mean ± SD or numbers (%). Group A = patients undergoing CABG on pump, Group B = patients undergoing CABG off pump, n = number of patients, * = Chi-square test or Student's test, as indicated. Ns= non-significant.

Table 1. Selected demographic variables

Complications	Total (n=200)	Group A (n= 100)	Group B (n = 100)	P value*
Respiratory complications:				
Hypoxia	17 (8.5%)	11 (11%)	6 (6%)	Ns.
Pneumothorax	8 (4%)	6 (6%)	2 (2%)	Ns.
Pleural effusion	17 (8.5%)	11 (11%)	6 (6%)	Ns.
Bronchitis	22 (11%)	13 (13%)	9 (9%)	Ns.
Atelectasis	13 (6.5%)	9 (%)	4 (4%)	Ns.
Respiratory infection	25 (12.5%)	17 (17%)	8 (8%)	Ns.
Presence of 1 or more respiratory complications	26 (13%)	17 (17%)	9 (9%)	Ns.
Bleeding complications:				
Amount of blood loss (ml)	422.3± 250	452 ± 237	393 + 261	Ns.
Amount of blood transfusion (ml)	885 + 1229	1410 ± 1236	360 + 977	0.001
Hematocrit % upon discharge from ICU	0.344 ± 0.04	33.2 ± 3.5	35.3 ± 4.6	0.001
Postoperative renal failure	5 (2.5%)	4 (4%)	1 (1%)	Ns.
Postoperative stroke	3 (1.5%)	2 (2%)	1 (1%)	Ns.
Mediastinitis	3 (1.5%)	2 (2%)	1 (1%)	Ns.
Need of positive inotropic support	15 (7.5%)	11 (11%)	4 (4%)	0.06
Duration of mechanical ventilation (hours)	22.9 ± 34.1	29.36 ± 45.9	16.6 ± 12.8	0.008
Hospital stay (days)	7.3 ± 3.2	8.2 ± 3.7	6.4 ± 2.3	<0.001
Mortality	3 (1.5%)	2 (2%)	1 (1%)	Ns.

Values are presented as numbers (%). Group A = patients undergoing CABG on pump, Group B = patients undergoing CABG off pump, n = number of patients, * = Chi-square test or Fisher's exact test, as indicated. Ns= non-significant.

Table 2. Comparison of postoperative complications between group A and group B patients

Preoperative demographics	Patients presenting with ≥ 1 respiratory complication (n= 26)	Patients free from respiratory complications (n = 174)	P value
Age (years)	59 \pm 6	59 \pm 5.6	Ns.
Male sex	26 (100%)	0	0.001
Diabetes mellitus	26 (100%)	0	0.001
Hypertension	26 (100%)	0	0.001
hypercholesterolemia	26 (100%)	0	0.001
Smocking	26 (100%)	0	0.001
EF% below 50%	26 (100%)	0	0.001
Parsonnet score:			
0-4	3 (11.5%)	34 (19.5%)	
5-9	7 (26.9%)	54 (31%)	
10-14	8 (30.8%)	39 (22.4%)	
15-19	4 (15.4%)	23 (13.2%)	
20+	4 (15.4%)	24 (13.8%)	Ns.
CABG technique:			
On pump (group A)	17 (17%)	83 (83%)	
Off pump (group B)	9 (9%)	91 (91%)	Ns.

*Values are presented as mean \pm SD or numbers (%). Group A = patients undergoing CABG on pump, Group B = patients undergoing CABG off pump. n = number of patients, * = Chi-square test or Fisher's exact test, as indicated. Ns= non-significant.*

Table 3. Risk factors associated with the development of postoperative respiratory complications

Discussion

All preoperative data and risk factors have no statistical significant difference between the two groups, which makes the operative and postoperative factors and complications results reflect the effect of the presence or absence of the pump.

In our study there was significant statistical difference in the number of grafted vessels with more grafted vessels in on-pump group which is the same in most of the studies (2, 8, 11, 17), this is explained in our study and others by the difficulty of reaching the lateral OMs vessels in off-pump technique.

Although duration of mechanical ventilation was statistically significant longer in on-pump group, respiratory complications show no statistical difference between the two groups but they are more in on-pump group.

The majority of studies show that respiratory complications and duration of mechanical ventilation are more in on-pump patients (3, 19, 16, 18), others show the same respiratory results between off-pump and on-pump (15, 23) and other study shows less mechanical ventilation but more pulmonary complications in off-pump group (13). Less mechanical ventilation explained in off-pump group by the effect of the bypass machine on the lung tissue itself but the respiratory complications are affected

by other factors as the opened pleura, smoking, low EF, male sex, diabetes, hypertension, hypercholesterolemia or infections which are common in both groups.

Although the blood loss in our study doesn't give statistical significance it was much more in on-pump group which may explain the statistical significant difference in amount of blood transfusion less in off-pump group with more haematocrite concentration upon discharge from ICU in the same group. Other studies confirm our results (18, 19) while others in addition show statistical significant difference in amount of blood loss which was more in on-pump group (2).

In our study hospital stay was longer in on-pump group with statistical significant difference and this is explained by the longer mechanical ventilation and the more complications in this group. These results are confirmed mostly by all studies(4,13,18) and others show reflection of this on hospital cost (1,2). In our results renal impairment, stroke, mediastinitis and need for inotropes were more in on-pump group but without statistical significance. The majority of studies show better renal function results in off-pump patients (13, 19, 20) while others show no difference between the 2 groups in renal complications (14, 23). Also stroke has the same results in other studies with statistical difference that show less stroke

problems in off-pump patients (7, 9, 12, 14, 17, 18) but other studies that in general show no difference between on-pump and off-pump depending mainly on no difference in stroke and neurocognitive complications. (1, 5, 10, 15 21). In all cardiac centers due to infection control and good coverage of strong antibiotics wound infection and mediastinitis were rare to have difference between the 2 groups except in few studies (17). As other complications some studies show less use of inotropes and less low cardiac output in off-pump patients (4, 13) and others show no difference (1, 15) which may be explained by the less effect of CPB on the heart and the difference between studies come from the difference of the effect of cardioplegia on the heart.

In our study there were 3 cases of mortality, two of them in on-pump group and the third in off-pump group with no statistically significant difference. The 2 on-pump cases were preoperatively diabetics, smokers and hypertensive one of them had EF below 30% and died early postoperative from sever arrhythmia and the other died also in early postoperative period from low cardiac output. The mortality case of off-pump group had EF below 50%, diabetic, hypertensive, smoker and hypercholesterolemic and died from early postoperative low cardiac output after use of IABP.

The majority of studies as mine show no statistical difference in mortality between the two groups (1, 5, 7, 10, 13, 14, 23) with less of them show statistically different low mortality in off-pump patients (4, 11) and these results are in favor of that off-pump has no privilege on on-pump and some authors find that off-pump needs protocol to be safe and useful (6) while others find that on-pump is preferable that it has more complete and durable revascularization (8).

Conclusion

Although both on-pump and off-pump CABG appears to be comparatively safe. Although the off-pump technique was associated with shorter hospital stay and less complications, yet the classic on-pump CABG is still associated with significantly complete revascularization.

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CABG in Patients Over 70 Years: Perioperative Risks and Independent Predictors For Conversion to Atrial Fibrillation

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The aim of this work is to compare the perioperative risk of patients 70 years old or older to that associated with CABG in 50 years old patients or younger and to find the associated risk factors as well as independent predictors for perioperative conversion to AF after CABG in old age group. In the period between January 2009 and October 2011, we prospectively studied 50 consecutive patients ≥ 70 years who benefited from coronary artery bypass grafting (CABG) at Ain-Shams University and Ain-Shams Specialized hospitals (Group 1). Controls consisted of a randomly selected group of young 50 patients (≤ 50 years) who were offered CABG by our surgical team, in the same period (Group 2) and in same hospitals. Group 1 patients (≥ 70 years old) were significantly older ($P < 0.001$) and included significantly more females ($P = 0.025$), compared to Group 2 patients. On the other hand, the younger Group 2 patients had a lower preoperative EF% ($P = 0.002$) and included more patients with hypercholesterolemia ($P = 0.037$), compared to the older Group 1 patients. The older Group 1 patients suffered from significantly more neurological events (12 % versus 2%; $P = 0.05$) and a significantly larger proportion converted to AF (54% versus 16%; $P < 0.001$), compared to the younger patient group. Interestingly, the total postoperative blood loss was significantly less in the former, compared to the latter group (353.5 ± 204.5 versus 436.2 ± 159.2 ml; $P = 0.026$). Other outcomes were comparable among both groups. We had 4 cases of hospital mortalities (4%). 3 cases in old age group and 1 case in young age group without statistical difference. Old age (age group) was the only independent predictor of conversion to AF after CABG. We conclude that old age doesn't prevent us to operate on this age group, male sex and hypercholesterolemia were high risk factors and old age (age group) was the only independent predictor of conversion to AF after CABG.

Coronary artery bypass grafting (CABG) in 70 years or older patients is actually becoming part of our routine surgical workload. View the possible associated co-morbidities in the elderly, the aim of this work is to compare the perioperative risk of those patients to that associated with CABG in 50 years old patients or younger.

On the other, a higher proportion of those patients 40 to 50 % are reported to convert to AF, compared to only 5 to 20 % in younger patient group (1) and the second part of this study consists in finding the associated risk factors as well as independent predictors for perioperative conversion to AF after CABG.

Material and methods

In the period between January 2009 and October 2011, we prospectively studied 50 consecutive patients ≥ 70 years who benefited from coronary artery bypass grafting (CABG) at Ain-Shams University and Ain-Shams Specialized hospitals (Group 1). Controls consisted of a randomly selected group of young 50 patients (≤ 50 years) who were offered CABG by our surgical team, in the same period (Group 2). Main inclusion criteria were patients with coronary artery stenosis, 1-3 vessel disease, with stable angina and in Sinus rhythm. Exclusion criteria were patients with left main disease, associated peripheral arterial disease and cases necessitating additional cardiac procedure.

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Besides routine preoperative investigations, all patients benefited from carotid and femoral arterial duplex to exclude cases with significant arterial disease. All patients were operated upon classically through median sternotomy, under cardiopulmonary bypass, mild hypothermia, aortic cross-clamping and myocardial preservation with repeated infusion of warm blood cardioplegia, given after the completion of each distal anastomosis. LIMA was implanted to LAD in all cases; other vessels were classically targeted with venous grafts. Patients were then transferred to the surgical ICU, fully monitored and mechanically ventilated; till acquiring hemodynamic stability without the need of pharmacological or mechanical support, attaining full consciousness and efficiently breathing on their own. Definitions of hospital mortality and morbidity were those reported by STS database. The first part of the study involves the comparison of the 2 study groups 1 and 2. Age advancement was evaluated by relating preoperative demographics and operative variables to surgery outcomes; mainly hospital mortality and morbidity figures. In the case where the patients' advanced age was significantly related to the development of AF after surgery, the second part of the study involves finding other risk factors and possible independent predictors associated with the development of AF after surgery.

Statistical Analysis

Results are presented as mean \pm standard deviation or 95% confidence intervals. For comparisons between dichotomous variables, Chi-Square test or Fisher's exact test were used, as indicated. For comparisons of continuous variables by means the Student's *t* test was used, as indicated. Demographic and operative variables as well as in-hospital surgery outcome were compared among the 2 groups of patients.

Factors showing a trend to significance in univariate analysis ($p \leq 0.1$) were entered into a stepwise logistic regression model to determine independent risk factors for development of AF after surgery. The Coefficient B, SE, Wald statistics, exponential B and 95% confidence intervals for the predictors are displayed.

Results

One-hundred patients (11 females and 89 males) were included in the study. Their age ranged between 40 and 77 years with a mean age of 59.6 ± 13 years. Forty-eight patients had preoperative essential hypertension (48%), 32 patients were diabetic (32%), 41 were chronic smokers (41%) and a majority of 64 patients (64%) had preoperative hypercholesterolemia. Patients benefited from 1- 4 grafts, with a mean number of grafts of 2.56 ± 0.59 grafts per patient. The preoperative LV EF% ranged from 21 and 70%, with a mean EF% of 58.5 ± 15.9 %. The aortic cross clamp time ranged from 25 to 116 minutes, with a mean clamp time of 61.2 ± 20.39 minutes. The total bypass time ranged from 37 to 134 minutes, with a mean bypass time of 82.38 ± 23.9 minutes.

Table 1 shows the comparison between preoperative demographics and intraoperative variables of both groups. Group 1 patients (≥ 70 years old) were significantly older (<0.001) and included significantly more females ($P=0.025$), compared to Group 2 patients. On the other hand, the younger Group 2 patients had a lower preoperative EF% ($P=0.002$) and included more patients with hypercholesterolemia ($P=0.037$), compared to the older Group 1 patients. As shown in Table 1, other demographic and operative variables were comparable between the 2 groups of patients.

Positive inotropic support was used in as much as 44 patients (44%), view our anesthesiologist policy of liberally using positive inotropes after cardiopulmonary bypass. In 20 cases (20%), the use of the latter was prolonged for >24 hours, before being successfully tailed and discontinued. Mechanical support was judged necessary in 2 cases needing the use of intra-aortic balloon pump for less than 48 hours. The duration of mechanical ventilation ranged from 9 to 335 hours, with a mean duration of 59.6 ± 13 hours. There were 30 cases of prolonged ventilation due to mostly low cardiac output and longstanding smoking preoperatively and ended with extubation and discharge from ICU except for 2 cases mortality. Postoperative blood loss varied from as small as 120 ml to as large as 1410 ml (394.8 ± 187 ml), with the need of re-exploration in 2 patients only. We had 4 cases of hospital mortalities (4%). One of them was young age with preoperative EF 30%, hypercholesterolemia and very bad quality vessels; this patient underwent long operation with cross clamp time 113m. and bypass time 134m. and patient died from low cardiac output once transferred to ICU. The other 3 patients are of old age, 2 of them died from low cardiac output of them one was combined with neurological complications. The fourth patient died due to combined neurological complications and renal impairment.

Other in-hospital morbidity figures included 4 cases of renal impairment (4%) that necessitated dialysis in 2 cases and all of them ameliorated gradually till a normal creatinine level and discharged from ICU except one of the dialyzed patients died in ICU. Four patients developed deep sternal wound infection (4%) that necessitated reexploration and wound cleaning done very early in the infection course that helped in early cure and discharge from ICU and hospital. Three patients developed perioperative myocardial infarction (3%), 7 patients developed CVS (7%), in the form of delayed recovery in 4 patients and lateralization in 3 patients. One of the patients with delayed recovery died and the other three patients recovered and discharged from ICU. Those patients with lateralization one of them died in ICU and the other 2 patients recovered with residual hemiparesis. A large proportion of 35 patients developed AF either intra operatively (7patients, 7%) or postoperatively (28patients, 28%). 8 patients were controlled (8%), 26 patients reverted to sinus rhythm (26%) and one patient died from low cardiac output. The total hospital stay ranged from 5 to 41 days, with a mean hospital stay of 8.81 ± 4.86 days. 16 patients had a prolonged hospital stay >10 days due to LCO, renal impairment

or neurological complications and all of them discharged from the hospital.

Table 2 shows the comparison of surgery outcome in both groups of patients. The older Group 1 patients suffered from significantly more neurological events (12 % versus 2%; P=0.05) and a significantly larger proportion converted to AF (54% versus 16%; P<0.001), compared to the younger patient group. Interestingly, the total postoperative blood loss was significantly less in the former, compared to the latter group (353.5 ± 204.5 versus 436.2 ± 159.2 ml; P=0.026). As shown in Table 2, other outcomes were comparable among both groups.

Table 3 shows the repartition of patients' demographics, operative variables and surgery outcome between patients

converting to AF and those maintaining their sinus rhythm. There was a statistically significant difference between the mean age of the former and that of the latter group of patients: 67.5 ± 9.97 versus 55.7 ± 12.65 years; P<0.001. In comparison, patients converting to AF belonged more to Group 1 (74.3% versus 36.9%; P<0.001), as well as to the male sex (97% versus 74.3%; P=0.022) and included more patients with hypercholesterolemia (73.8% versus 45.7%; P=0.023); compared to patients maintain their sinus rhythm after surgery. As shown in Table 3, other demographics, operative variables and surgery outcomes were comparable among both groups. Statistically significant risk factors in univariate analysis were introduced in a binary logistic regression model (Patients in sinus rhythm versus patients in AF), with stepwise forward

Variable	Group 1	Group 2	P value
Age (years)	72.3 ± 1.65	46.9 ± 2.8	< 0.001
Female Sex	9 (18 %)	2 (4 %)	0.025
Preoperative hypertention	26 (52 %)	22 (44 %)	Non-significant
Preoperative diabetes mellitus	18 (36 %)	14 (28 %)	Non-significant
Preoperative hypercholesterolemia	27 (54 %)	37 (74 %)	0.037
Smoking	20 (40 %)	21 (42 %)	Non-significant
Preoperative EF	63.3 ± 14.1	53.6 ± 16.3	0.002
Number of grafts	2.54 ± 0.65	2.58 ± 0.54	Non-significant
Duration of aortic cross-clamp (min)	62.4 ± 18.4	59.9 ± 22.3	Non-significant
Bypass time (min)	84.5 ± 22.2	80.3 ± 25.6	Non-significant

Values are presented as n (%) or mean ± SD, as indicated. Group 1 = patients ≥ 70 years, group 2 = patients ≤ 50 years, * = Chi-Square test, (Fisher's exact test) or Student's test (Mann and Whitney tests), as indicated.

Table 1. Comparison of patients' groups: Demographic and operative variables

Variable	Group A	Group B	P value
Duration of mechanical intubation (hours)	35.4 ± 57.3	28.9 ± 43.1	Non-significant
Inotropic support	24 (48 %)	20 (40 %)	Non-significant
Postoperative low cardiac output	12 (24 %)	8 (16 %)	Non-significant
Need of IABP	1 (2 %)	1 (2 %)	Non-significant
Postoperative AF	27 (54 %)	8 (16 %)	< 0.001
Myocardial infarction	3 (6 %)	0	Non-significant
Neurological complications	6 (12 %)	1 (2 %)	0.05
Renal Impairment	3 (6 %)	1 (2 %)	Non-significant
Postoperative bleeding (ml)	353.5 ± 204.5	436.2 ± 159.2	0.026
Mediastinitis	3 (6 %)	1 (2 %)	Non-significant
Duration of hospitalization (days)	9.7 ± 5.8	8 ± 3.6	Non-significant
Hospital mortality	3 (6 %)	1 (2 %)	Non-significant

Values are presented as n (%) or mean ± SD, as indicated. Group 1 = patients ≥ 70 years, group 2 = patients ≤ 50 years, * = Chi-Square test, (Fisher's exact test) or Student's test (Mann and Whitney tests), as indicated.

Table 2. Comparison of patients' groups: Hospital mortality and morbidity

Cardiovascular

	Postoperative AF (n = 35)	Values	P value
Age (years)	Yes	67.5 ± 9.97	<0.001
	No	55.7 ± 12.65	
Group 1 patients	Yes	26 (74.3%)	<0.001
	No	24 (36.9%)	
Male sex	Yes	26 (74.3%)	0.022
	No	63 (97%)	
Hypercholesterolemia	Yes	16 (45.7%)	0.023
	No	48 (73.8%)	
Preoperative diabetes mellitus	Yes	7 (20%)	Non-significant
	No	25 (38.5%)	
Preoperative hypertension	Yes	17 (48.6%)	Non-significant
	No	31 (47.7%)	
Smocking	Yes	13 (37.1%)	Non-significant
	No	28 (401%)	
Preoperative EF%	Yes	60.1 ± 14.4	Non-significant
	No	57.7 ± 16.68	
No of Grafts	Yes	2.52 ± .62	Non-significant
	No	2.58 ± .58	
Duration of aortic cross- clamp (min)	Yes	62 ± 18.2	Non-significant
	No	60.8 ± 21.5	
Bypass time (min)	Yes	84.2 ± 22.7	Non-significant
	No	81.5 ± 24.63	
Duration of intubation (hours)	Yes	37.1 ± 63.4	Non-significant
	No	29.6 ± 42.9	
postoperative bleeding	Yes	403.5 ± 222.8	Non-significant
	No	390.1 ± 168.3	
Need of inotropes	Yes	16 (45.7%)	Non-significant
	No	28 (43.1%)	
Need of Intra-aortic balloon pump	Yes	0	Non-significant
	No	2 (3.2%)	
Neurological complications	Yes	2 (5.7%)	Non-significant
	No	5 (7.7%)	
Low cardiac output	Yes	7 (20%)	Non-significant
	No	13 (20%)	
Myocardial infarction	Yes	2 (5.7%)	Non-significant
	No	1 (1.6%)	
Mediastinitis	Yes	2 (5.7%)	Non-significant
	No	2 (3.2%)	
Renal impairment	Yes	3 (8.6%)	Non-significant
	No	1 (1.6%)	
Duration of hospitalization (days)	Yes	9.7 ± 6.2	Non-significant
	No	8.4 ± 4	
Hospital mortality	Yes	1 (2.75%)	Non-significant
	No	3 (4.8%)	

Values are presented as n (%) or mean ± SD, as indicated. AF = atrial fibrillation, Group 1 = patients ≥ 70 years, group 2 = patients ≤ 50 years,

* = Chi-Square test, (Fisher's exact test) or Student's test (Mann and Whitney tests), as indicated.

Table 3. Risk factors of conversion to AF After CABG.

	B	S.E.	Wald	df	Sig.	Exp. (B)	95% C.I.for EXP(B)	
							Lower	Upper
Group	-1.686-	.512	10.867	1	.001	.185	.068	.505
Hypercholesterolemia	.758	.482	2.467	1	.116	2.133	.829	5.492
Sex	.997	.702	2.016	1	.156	2.711	.684	10.737
Constant	.370	.826	.200	1	.654	1.447		

Group + patient groups 1 and 2, B = B coefficient, SE = standard error, Wald = Wald statistics = the ratio of B coefficient to its standard error, squared. Exp.(B)= Exponential (B) represents the ratio-change in the odds of the event of interest for a one-unit change in the predictor.

Table 4. Independent predictors of conversion to AF : After CABG.

analysis. The latter showed that being in Group 1 (70 years or older) is an independent predictor of converting to AF after CABG; P = 0.001. Table 4 shows the corresponding B coefficient, SE, Wald statistics and Exponential (B) ± 95% IC of the variables introduced in the equation.

Discussion

An increasing number of elderly individuals are now undergoing coronary artery bypass surgery. (2) Elderly patients, compared with patients of a younger age group, present for surgery with a greater burden of risk factors and reduced functional levels. (3) In our study all postoperative complications except postoperative bleeding amount and need for IABP were more in old age either statistically significant or not. Postoperative bleeding after CABG in the most of literatures is more in over 70s (4, 5, and 6) but may be the over care during closing our old patients is the cause of less bleeding in old age patients in our study.

The use of IABP was more in elderly in the most of literature (6), may be as a continuation of a routine preoperative insertion or the different management protocols in these cases in different departments.

Females were more in group of old age with a statistical difference which was the same in the majority of other studies (7). Other preoperative risk factors include hypertension and diabetes mellitus were higher in old age but without statistical difference. Preoperative hypercholesterolemia was significantly higher in young age indicating an important risk factor in this age group. Also preoperative EF was higher in old age group which means that the severity of the disease was higher in young age group.

Number of grafts was nearly the same in both groups aiding us to compare the real postoperative complications while it was more in old age in other studies (8), which may confirm that the severity of the disease may be more in young age that diseased

vessels were not doable in this study? Other operative data as cross clamping time and bypass time were more in old age but not statistically significant as in other study (8). But this also helped us to compare the postoperative complications in different age groups without the effects of intraoperative variations.

Postoperative wound infection (mediastinitis) was more in number in group of old age but didn't give statistical difference which was the case in many studies (9), while in others this number difference with higher infection rate in old age gave statistical difference (10). This indicates the low immunity and fragile tissues in old age with the effect of long standing diabetes mellitus.

Neurological complications presented as stroke and delayed recovery were statistically different in both groups as other studies (11), while even the other studies showed higher incidence of stroke and neurological complications there were no statistical difference. (8, 9, and 10). Nearly all these studies confirmed also that preoperative stroke is a high risk for postoperative complications in CABG in old age.

Hospital stay duration and ventilation duration in our study and nearly all studies were more in old age group either statistically significant or not (9, 10, 12 and 13). The explanations are the fragile organs in old age that need extra care after the exposure to the bypass, there is also the higher risk preoperative factors in old age group with longstanding diabetes and longer period of smoking that elongates the period of ventilation and period of hospitalization.

Cardiac complications presented as LCO and frequently the need for positive inotropes, cardiac infarction and ischemia and pericardial effusion were all nearly the same in all studies (14, 15, 9, 10, 12 and 13), and our study that they were more in old age group but without statistical significance. These results confirm the conclusions of these studies that CABG surgery for old age group is risky but statistical results encourage surgeons to do this operation to this age group.

Cardiovascular

As other complications in our study renal impairment was higher as a number in old age group without giving statistical significance which also was the same in other studies (**9 and 10**). Also as in other complications long standing diabetes and cardiac ischemia make renal impairment more liable to occur in old age, but absence of statistical difference encourage us to do CABG in old age group.

As other complications mortality was more in group of old age (3 cases) in comparison to group of young age (1 case) but without statistical difference.

Two cases of mortality in old age group were males and the third was female. The three cases died from low cardiac output and one of them was associated with renal impairment, another one associated with neurological complications and the third was bleeding. The duration of bypass time in the 3 cases was more than 100 minutes.

The mortality case in young age group was male with pre-operative EF 30 % and died from low cardiac output.

Other literatures are different in results for mortality in old age group, some of them didn't find difference between old age and young age groups for mortality (**9 and 10**). the majority of them are as our study found that mortality are higher in old age group but without statistical difference (**8, 11, 12 and 16**), while others found that mortality is higher in old age group with statistical significance (**7 and 13**). The cause of death in all previous studies was the same as our study which is mixture of low cardiac output, renal impairment and neurological complications. All the studies confirmed that old age is a risk factor for mortality in CABG but at the same time it doesn't prevent the operation.

Atrial fibrillation (AF) is one of the most common complications after coronary artery bypass graft surgery (CABG) and is associated with increased incidence of thromboembolic complications, prolonged hospital stay, and late mortality (**17**).

Advanced age, previous AF, and valvular heart operations are the most consistently identified risk factors for this arrhythmia (**1 and 18**). In our study old age, hypercholesterolemia and male sex were high risk factors for conversion to AF but old age (age group) was the only independent predictor of conversion to AF after CABG. Old age usually cause fibrosis of the cardiac tissues which help conversion to AF and hypercholesterolemia may affect the artery to SA node causing arrhythmia.

One of the literatures (**19**), found that obesity is an independent predictor of postoperative AF which augment our results that impaired lipid profile cause postoperative AF. While we didn't follow the patients for late mortality in our study, many literatures found that AF is independent predictor of overall mortality after CABG especially late mortality (**1, 20 and 21**). For these reasons high risk factors for postoperative AF need aggressive prophylactic treatment (**22**).

Conclusion

Old age \geq 70 years old has more morbidity and mortality than those with young age either statistically significant or not but the results don't make us stop operating on this age group even with more AF conversion after CABG. Male sex and hypercholesterolemia were high risk factors and old age (age group) was the only independent predictor of conversion to AF after CABG.

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CABG in Acute Coronary Syndrome is Still A Vital Option

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Background: ACS(acute coronary syndrome) represents a life threatening manifestation of atherosclerosis. The complex process of plaque disruption, inflammation and hypercoagable state considered as the pathophysiological key for understanding the pathogenesis of ACS.

The strategy of management in NSTEMI-ACS Its management strategy is to alleviate ischaemia and is based upon a system of risk stratification.

In general speaking there is a world wide agreement for the management guidelines of surgical and medical management of STE-ACS, yet the NSTEMI-ACS management not yet fully understood with no sharp and clear results of CABG in high risk patient. In order to assess this complicated subject we did our study.

Aim of our study is to assess the Early clinical Outcome Of Coronary Artery Bypass Surgery Among high risk Patients With Non-ST Segment elevation Acute Coronary Syndrome.

Methods: From January 2010 till Oct 2012, 73 (7.52% of NSTEMI-ACS) patients of them was classified as a high risk population and they represented (3.98%) of the total ACS patient population.our inclusion criteria for the high risk NSTEMI-ACS population include: age 65-70 years , previous history of (coronary artery disease (CAD) , myocardial infarction (MI) , percutaneous coronary intervention (PCI) ,coronary artery bypass graft (CABG) ,congestive heart failure ,pulmonary oedema , mitral regurgitation ,renal insufficiency ,elevated inflammatory markers, ie C-reactive protein (CRP))and haemodynamic instability. GRACE(Global Registry of Acute Coronary Events risk score) is most commonly used score which is predictive of clinical outcome.

Results: Our Overall data suggest that the annual incidence of NSTEMI ACS is higher than that of STE ACS, without any clear explanation for the reasons. in our study it is 82.19% male gender, whereas in other studies the highest proportion of male were noted in the Netherlands and Argentina (74.8% and 74.6% respectively) with the lowest proportion in Canada (63.5% male). Cardiac risk factors varied markedly between countries as the lowest frequencies of hypertension and hypercholesterolemia were seen in United Kingdom (30.4% and 19.9% respectively) with the highest in Argentina (64.1% and 63.3% respectively), and in our study it was (68.49% and 54.79% respectively).Smoking prevalence varied from 32.5% in the Netherlands to 15.8% in France, but it is 56.16% in this study as we can notice the higher rate of smoking in our country and it is associated with the higher rate of males in our study.

Conclusion: The high risk NSTEMI-ACS that not controlled medically have a high risk to develop major cardiac event (death or infarction) must be a surgical subject, that should be considered by surgeons only. The more the earlier CABG in NSTEMI-ACS high risk population the best the result and the lesser the mortality.

KEY WORD : Acute coronary syndrome, CABG

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However the 'acute coronary syndromes' ACS, namely unstable angina and evolving myocardial infarction had the same anatomical sub-strate, unstable angina and myocardial infarction had a different clinical presentations that result from a common underlying pathophysiological mechanism.

Acute coronary syndrome (ACS) represents a life threatening manifestation of atherosclerosis. The complex process of plaque disruption, inflammation and hypercoagable state considered as the pathophysiological key for understanding the pathogenesis of ACS.

However The leading symptom that initiates the diagnostic and therapeutic cascade is a chest pain >20 min but the classification of ACS patients is based on (ECG). Two categories of patients may be encountered:

- (1) Patients with a persistent ST- segment elevation (or new-onset LBBB) STE-ACS.

It generally reflect an acute total coronary occlusion. Its therapeutic objective goal is to achieve a rapid and complete recanalization by fibrinolytic treatment or primary angioplasty (if technically feasible).

- (2) Patients with non ST- segment elevation NSTEMI-ACS ,

NSTEMI-ACS Patient do not have persistent ST-segment elevation and had persistent or transient ST-segment depression or T-wave inversion, flat T waves, pseudo-normalization of T waves, or non-specific ECG changes.

The strategy of management in NSTEMI-ACS Its management strategy is to alleviate ischaemia and is based upon a system of risk stratification, with serial electrocardiograms and repeat measurements of markers of necrosis (troponin) and to initiate appropriate therapy if the diagnosis is confirmed.

The clinical presentation of NSTEMI-ACS included a wide variety of symptoms: Prolonged (> 20 min) anginal pain at rest, or new onset angina (Class II or III of the Classification of the Canadian Cardiovascular Society)

Revascularization for NSTEMI-ACS relieves symptoms, shortens hospital stay, and improves prognosis. The indications and timing for myocardial revascularization and choice of preferred approach (PCI or CABG) depend on many factors that including the patient's condition, the presence of risk features, co-morbidities, and the extent and severity of the lesions as identified by coronary angiography

Surgery should be performed during the same hospital stay in patients with left main or three-vessel disease involving the proximal left anterior descending artery with acute coronary syndrome.

In general speaking there is a world wide agreement for the management guidelines of surgical and medical management

of STE-ACS, yet the NSTEMI-ACS management not yet fully understood with no sharp and clear results of CABG in high risk patient. In order to assess this complicated subject we did our study.

Our study is aimed to assess the Early clinical Outcome Of Coronary Artery Bypass Surgery Among high risk (NSTEMI-ACS) Patients With Non-ST Segment elevation Acute Coronary Syndrome.

Patients and Methods

We collected the data of all the patients presented with acute chest pain and diagnosed as ACS and admitted to the Coronary Care Unit CCU of Ain Shams University Hospital, Dar El Fouad Hospital, Sheikh Zayed Specialized Hospital, and Suez Health Insurance Hospital, from January 2010 till Oct 2012, depending on the history, clinical data, ECG interpretation, laboratory biomarkers results (troponin, CK, CK MB.), Imaging modalities (all are used to rule out or rule in differential diagnoses). 1832 patients were admitted with ACS. 123 patients had urgent therapeutic coronary intervention within the first six hours. 962 (52.19%) patients was diagnosed as NSTEMI-ACS , 73 (7.52% of NSTEMI-ACS) patients of them was classified as a high risk population and included in our study as they had an early invasive revascularization (early CABG) , they represented (3.98%) of the total ACS patient population.

The Indicators that predict the high risk NSTEMI-ACS or the high-risk for progression to myocardial infarction (MI) include: age 65-70 years ,history of any of the following (known coronary artery disease (CAD) ,previous myocardial infarction (MI),prior percutaneous coronary intervention (PCI) ,coronary artery bypass graft (CABG) ,congestive heart failure ,pulmonary oedema ,new mitral regurgitation murmur ,renal insufficiency ,elevated inflammatory markers, ie C-reactive protein (CRP) [CRP may be a valuable prognostic predictor in patients after ACS - early elevated blood CRP suggests increased long-term risk of recurrent cardiovascular events or death ongoing or recurrent ischaemia],dynamic spontaneous ST changes (more than 0.1 mV depression or transient elevation) ,deep ST depression in anterior leads V2-V4 indicating ongoing posterior transmural ischaemia, haemodynamic instability major ventricular arrhythmia .

There are many risk stratification scoring systems that can predict death or myocardial infarction in NSTEMI-ACS. the most commonly used score is GRACE(Global Registry of Acute Coronary Events risk score) which is obtained from "real life" observational registry. It is the most predictive of clinical outcome and validated as an independent external datasets.

GRACE score considered as Low risk <1%, Medium risk 1-9%, or High risk >9%

The diagnosis of (NSTEMI-ACS) is based on the basis of ECG, i.e. lack of persistent ST elevation and biomarkers

(negative troponin) which distinguished the NSTEMI and unstable angina patients. so we excluded any patients had +ve troponin or ST- elevation.

Our inclusion criteria included patients with prolonged (< 20 min) anginal pain at rest with the following criteria: ST-segment depression and persistent T-wave inversion, are the most reliable electrocardiographic indicators of unstable coronary disease was a new onset ST-segment depression >1 mm in two or more contiguous leads, or recent destabilization of previously stable angina with inverted T waves in two leads especially leads with predominant R-waves.

Patients with refractory angina, or hemodynamic and electrical instability or life-threatening arrhythmias (ventricular fibrillation or ventricular tachycardia, and very high risk patients to develop major cardiac events those patients are characterized by refractory angina despite maximum medical treatment indicating evolving MI without ST abnormalities. Patients with recurrent angina despite intense anti anginal treatment associated with ST depression (< 2 mm) or deep negative T waves, patients with early post-infarction unstable angina, patients with history of positive exercise test (with or without the results of nuclear imaging) and had transient ST segment elevation of ≥ 1 mm in 2 contiguous leads. Patients with chest pain and had new cardiac catheterization documenting coronary artery disease either left main disease or three vessels disease.

Patients with persistent chest pain despite pseudo normalization of previously inverted T waves.

All our patients had coronary angiography unless had major comorbidities or contraindication.

Coronary angiography was planned as soon as possible, but without undue urgency. In most cases coronary angiography was performed within the first 48 hours. In patients with lesions suitable for myocardial revascularization, the decision regarding the most suitable procedure was made after careful evaluation of the extent and characteristics of the lesions.

We performed multi disciplinary discussion between cardiology, anesthesia and cardiothoracic surgery to identify which patient should be admitted to surgical interference and those who have high risk factors to develop major cardiac events.

All our high risk NSTEMI-ACS patients are operated within the 48 -72 hs from the presentation.

Results

From Jan 2010 to Oct 2012 we had 1832 patients admitted with chest pain that diagnosed as Acute Coronary Syndrome ACS, 123 patients had therapeutic coronary intervention within the first six hours, 962 of the total population had non ST-segment elevation ACS (NSTACS) 52.19%, 73 (7.52%) patients

of them was classified as a high risk population and included in our study as they had an early invasive revascularization (early CABG), they represented (3.98%) of the total ACS patient population. they represented (6.2%) of the total number of the CABG patients (1172 patients) who operated in the same period of time in the mentioned four medical centers.

The mean age of our group was 54.78 ± 5.2 yrs, there were (82.19%) male, (45%) of those patients were diabetics, (54.79%) were hyperlipidemic (68.49%) were hypertensive and (56.16%) were smokers.

Their history according to previous cardiac events was as follow, 67.1% had previous angina pectoris, but 32% was their first presentation, 15 patients (20.54%) had previous Myocardial Infarction (MI), and 8 (10.96%) had previous percutaneous coronary intervention (PCI).

58.9% of the 73 patients had left main disease while the others had triple vessels disease, of the 73 patients (16.43%) needed preoperative mechanical support in the form of Intra-Aortic Balloon Counter pulsation (IABP), 10.95% had preoperative persistent arrhythmia, (12.35%) had hemodynamic instability with systolic pressure < 90 mmHg, and two (2.74%) were intubated preoperatively, 61.64% were on aspirin medication preoperatively, and 49.32% had at least two antiplatelet medication, all of our patients were admitted to the Coronary Care Unit and transferred to the Operating Room within 48-72 from admission.

As regards the Intraoperative data, the mean number of the distal grafts was 2.64, the bypass time was 84.86 ± 43.14 min and the cross clamp time was 55.5 ± 28.49 min, 49.3% had smooth postoperative weaning off the bypass, 42.47% needed minimal support < 50ng adrenaline, and 6.84% needed high inotropic support, while 14 (19.17%) had IABP.

The average amount of the postoperative drainage was 782.78 ml, while 5.48% of the patients needed reexploration for high drainage or for tamponade, 4.1% had prolonged ventilation, 6.85% had moderate renal impairment (S Cr. > 3) who improved within 72 hours with no need of dialysis in any patient, neurological complication occurred in two 2.73% as a behavioral changes without any deficit, 6.85% had deep wound infection or Mediastinitis needed re operation, the total ICU time was 51.53 hs, total postoperative hospital stay was (10.12 days), and the total mortality rate was 8.2% vs. 2.7% among our total mortality of the conventional CABG patients in the same period (p-value <0.005), while the in-hospital mortality rate of the 962 patients who had NSTACS but subjected to medical treatment rather than early surgical interference was 6.8% (p-value = 0.83 >0.05).

Variables	NST-ACS high risk early CABG 73 patients
Age	54.78±5.2 ys
Diabetes	45%
Hypertension	68.49%
Hypercholesterolemia	54.79%
Smokers	56.16%
History of previous cardiac events	
Previous angina pectoris	67.1%
Previous MI	20.54%
Previous PCI	10.96%
Left main disease	58.9%
Preoperative mechanical support (IABP)	16.43%
Preoperative persistent arrhythmia	10.95%
Hemodynamic instability with systolic pressure < 90 mmHg	12.35%
Intubated preoperatively	2.74%
Aspirin medication preoperatively	61.64%
At least two antiplatelet medication	49.32 %

Table 1. Preoperative Patients Demographics

Variables	NST-ACS high risk early CABG
Cross clamp time	55.5 ± 28.49 min
Total bypass time	84.86 ± 43.14 min
No. of Grafts	3.2± 1.8

Tables 2. Operative variables

variables	High risk NSTEMI-ACS
ICU stay in Hours	51.53 ± 6 hs
Total post operative stay	10.12 ± 3days
Average amount of bleeding	782.78± 6.9 ml
Reopening	5.48%
Reintubation	4.10%
High Inotropic Support& moderate renal impairment (cr. >3)	6.84%
No Inotropic Support	49.30%
IABP	19.17%
Neurological complications	2.73%
Deep wound infections	6.85%
Mortality	8.20%

Tables 3. Postoperative variables

Variables	Early CABG in high risk NSTEMI-ACS 73 PATIENTS	Conservative medical treatment 962 patients WITH NSTEMI ACS	P value
Mortality rate	8.2%	6.8 %	>0.5

Table 4. Comparison of early CABG high risk NSTEMI-ACS mortality rate with conservative treatment mortality rate:

Variables	Early CABG in high risk NSTEMI-ACS 73 PATIENTS	Conservative medical treatment 962 patients WITH NSTEMI ACS	P value
Mortality rate	8.2%	6.8 %	>0.5

Table 5. Comparison of early CABG high risk NSTEMI-ACS mortality rate with the Elective CABG patients group done in Same period had the same preoperative demographic criteria mortality.

Variables	Early CABG in high risk NSTEMI-ACS 73 PATIENTS	Elective CABG IN Same period with same preoperative demographic criteria 115 PATIENT	p-value
age	54.78±5.2 ys	56.4 ± 3.2ys	0.9
Diabetes	45%	43.20%	0.92
Hypertension	68.49%	62.40%	0.82
Hypercholesterolemia	54.79%	52.60%	
Smokers	56.16%	57.20%	0.9
total bypass time	94.8 min	88.63 min	0.95
cross clamp time	55.5 min	54.9 min	0.9
No. of Grafts	2.60%	2.70%	0.9
INR	1.30%	1.20%	0.9
PT	13.20%	13.30%	0.94
PTT	34 seconds%	32 seconds	0.97
Serum Creatinine	1.40%	1.20%	0.98
hemoglobin	10.80%	11.20%	0.98

Table 6. Compare of the Early CABG in high risk NSTEMI-ACS group (73 PATIENTS) with the Elective CABG patients group done in Same period had the same preoperative demographic criteria (115 patients)

Variables	Early CABG in NSTEMI-ACS 73 PATIENTS	Elective CABG IN Same period with same preoperative demographic criteria 115	p-value
ICU stay in Hours	51.53 ± 6 hs	34.7 ± 4 hs	0.005
Total post operative stay	10.12 ± 3days	7.2 ± 4days	0.03
Average amount of bleeding	782.78± 6.9 ml	698.32± 4.6 ml	0.003
Reopening	5.48%	4.10%	0.89
Reintubation	4.10%	1.40%	0.002
High Inotropic Support	6.84%	2.74%	0.003
No Inotropic Support	49.30%	63%	0.002
IABP	19.17%	2.74%	0.0004
Neurological complications	2.73%	1.37%	0.02
Mortality	8.20%	2.70%	0.0002

Table 7. Compare of the postoperative variables of Early CABG in high risk NSTEMI-ACS group (73 PATIENTS) with the Elective CABG patients group done in Same period (115 patients)

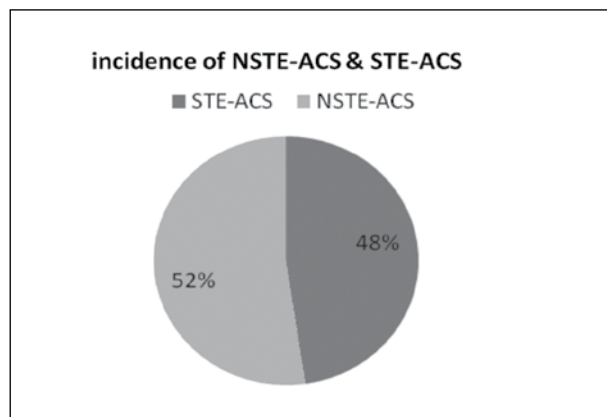
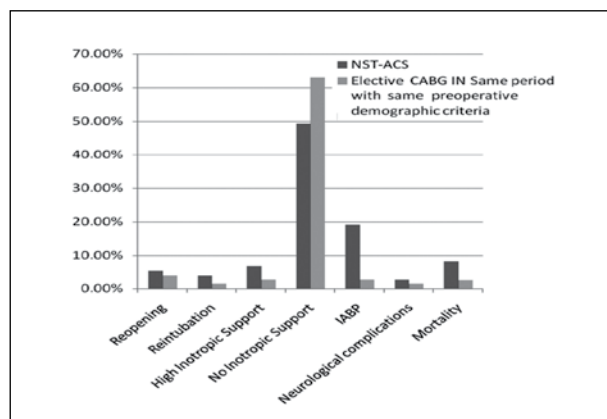
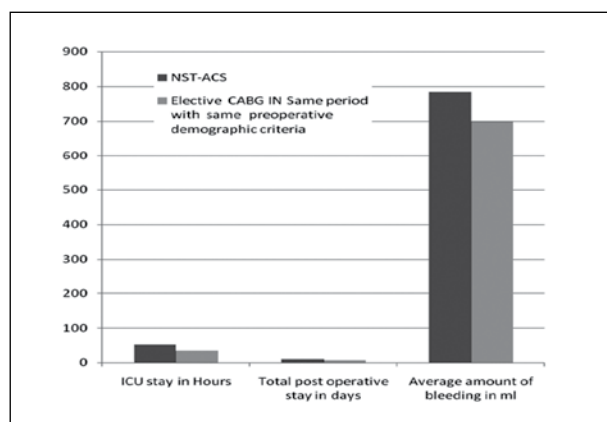


Fig 1. Incidence of NSTEMI-ACS and STEMI-ACS



(a)



(b)

Fig. 2 a&b. Compare of the postoperative variables of Early CABG in high risk NSTEMI-ACS group (73 PATIENTS) with the Elective CABG patients group done in Same period (115 patients)

Comment

In general ACS includes different subgroups of patients (ST-segment MI, non ST-segment MI, non ST-segment elevation ACS and undetermined ECG ACS). General speaking ST-MI needs rapid revascularization by thrombolytic therapy and it is mainly a cardiologist concern or surgical problem with in the first 6 hours or after minimum of 3-14 days in post infarction state in stable patients according to the guidelines or the task force report (1).

While the non ST-segment elevation ACS (troponin – ve) unstable angina that not controlled medically in patients have high risk to develop major cardiac event (either death or infarction) is a surgical subject, that should be considered by surgeons with a concept that the more the earlier and the invasive procedure to be done the best the result and the lesser the mortality (2,4).

The prevalence of NSTEMI-ACS, relative to STEMI, has been determined from multiple surveys and registries⁶⁻¹⁵. Overall, data suggest that the annual incidence of NSTEMI ACS is higher than that of STE ACS. The ratio between NSTEMI-ACS and STEMI has changed over time, as the rate of NSTEMI-ACS increased relative to STEMI, without any clear explanation for the reasons behind this evolution.¹⁶

In one study (46%) of the ACS patients was diagnosed as NSTEMI-ACS with a ratio approximately of 1.2:1, while it was 41.9% of the entire Euro Heart Survey ACS cohort study, resulting in a ratio of unstable angina to myocardial infarction of 0.8, which is lower than the 1.2 ratio, while in our study 52.19% of all the ACS patients was diagnosed as NSTEMI-ACS or unstable angina which is more or less is similar to the 1.2:1 ratio. Enact and adam.

There are world wide acceptance that the demographic characteristics of those subgroup is quite different from region to region but male gender is more common in those patients, in our study it is 82.19% male gender, whereas in other studies the highest proportion of male were noted in the Netherlands and Argentina (74.8% and 74.6% respectively) with the lowest proportion in Canada (63.5% male). (2&13)

Also there were considerable differences in the frequency of prior manifestations of coronary artery disease. For instance, the highest rates of prior myocardial infarction in those patients who presented later on by non ST-segment ACS were noted in the United Kingdom (54.5%) and the lowest in France (38.3%), while in ours was (32.87%), whilst the highest frequency of prior angina was seen in Canada (73.8%) closely followed by United Kingdom (72.8%), with the lowest frequency found in Argentina (54.3%), and in our study it was (67.1%) which is in the average rate.

Documented cardiac risk factors also varied markedly between countries. For example, the lowest frequencies of hypertension and hypercholesterolemia were seen in United

Kingdom (30.4% and 19.9% respectively) with the highest in Argentina (64.1% and 63.3% respectively), and in our study it was (68.49% and 54.79% respectively).

Smoking prevalence varied from 32.5% in the Netherlands to 15.8% in France, but it is 56.16% in this study as we can notice the higher rate of smoking in our country and it is associated with the higher rate of males in our study.

While the principal aim is to prevent death, early reperfusion helps to minimize the patient's discomfort and distress, and to limit the extent of myocardial damage in patients with ACS (6). Understanding the changes associated with progressive ischemia and the mechanisms of reperfusion injury are the keys for understanding the role of revascularization strategies (7).

In patients with ACS, current indications for emergency CABG, briefly, are limited to those presenting with evolving myocardial ischemia refractory to optimal medical therapy, presence of left main stenosis and/or 3-vessel disease, ongoing ischemia despite successful or failed PCI, complicated PCI, or cardiogenic shock accompanied by complex coronary anatomy(2,13). Surgery puts forward the advantage of controlled reperfusion and complete revascularization in the setting of myocardial ischemia. (11, 34, 35)

Surgery, currently, is the only means of applying controlled reperfusion in the setting of ACS (12). Clinical data have confirmed the experimental data showing the superiority of controlled reperfusion methods, especially in high-risk patients(11).

The pathogenesis of ACS nearly always involves acute thrombosis superimposed on a disrupted atherosclerotic plaque (8). The onset of ischemia is accompanied by rapid changes in myocardial metabolism because of its extreme dependence on aerobic respiration. Myocardial ischemia leads to increased intracellular calcium, diminished amino acid precursors, and decreased ATP production. Reperfusion reverses these deleterious changes (3).

Reperfusion limits infarct size, protects threatened myocardium and rescues hypoperfused border areas that can become arrhythmogenic foci, and thus resulting in mortality reduction. The open-artery hypothesis suggests that the sooner normal flow can be restored in an occluded coronary artery; the better will be the short, medium and longer-term outcome for the patient with MI.

Surgical revascularization is also indicated in the setting of mechanical complications of such as free-wall rupture, acute ischemic mitral insufficiency, and ventricular septal defect. The efficacy of surgery has been demonstrated in patients with cardiogenic shock complicating AMI, although the reported mortality rate is never less than 20% (4, 11, 12). Early surgical revascularization may be beneficial by limiting infarct size,

reducing LV dysfunction, and increasing patient survival. Nevertheless, delay in surgery may potentially lead to extension the infarction and worse long-term prognosis.

There is indirect evidence that identifying higher risk individuals following faster selection of patients for early investigation and intervention benefits of early surgical interference. Data from the TACTICS and FrISC II trial in patients with non-ST elevation acute coronary syndromes suggest that the short term (6-12 months) benefits of invasive strategy is much better.

Lastly, a recent report from the SHOCK Trial and Registry showed a clear survival advantage for CABG over PCI at 30-day follow-up in patients with left main coronary disease (37).

In unselected patients admitted for ACS, performance of early CABG, despite being performed in higher-risk patients, is associated with very low in-hospital mortality, even when compared with the mortality of lower-risk population not submitted to early CABG. Therefore, early performance of this procedure should be considered more often in eligible patients, although those patients were more often on mechanical ventilation and intra-aortic pump and they had more in-hospital complications (31.1% versus 18.7%), namely recurrent angina, re-infarction, and mechanical complications. They had a more severe coronary anatomy and the culprit lesion was more frequently on the left main (7.7% versus 2.2%). However, their in-hospital mortality was significantly lower (2.2% versus 6.8%; $P < 0.001$).

The CRUSADE investigators¹¹ clearly showed that an early invasive strategy (involving early angiography, usually followed by PCI or CABG) is the best in ACS, even in an unselected population. This result is in line with a recently published substudy of the GUSTO IV-ACS trial, which also compared ACS patients submitted or not to early revascularization (PCI or CABG).

Recently published results of a EuroHeart Survey on Acute Coronary Syndromes substudy¹³ also shows a trend toward lower in-hospital mortality, leading the authors to conclude that "CABG remains an effective and safe means to achieve revascularization among ACS patients in current clinical practice".

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The IABP counter pulsation is beneficial for the initial stabilization of patients with cardiogenic shock, and is favored over the use of vasopressors and inotropes alone. In our study we actually used the IABP once we saw that the patient was in need to it with out any hesitation, and we can see that it was used in (19.17%) of the patients. and observational studies suggest that preoperative intra-aortic balloon counter pulsation may improve clinical outcomes, also GUSTO-I and III, Hudson et al. demonstrating a clear relationship between

increased intra-aortic balloon pump use in the United States and improved survival from post-myocardial infarction cardiogenic shock[17].

204, 205 other Studies have shown that IABP use results in initially hopeful clinical and hemodynamic responses; however, death was only delayed by this modality in the majority of studies (32). As clinical trial evidence is lacking, the recommendations on the use of intra-aortic balloon counter pulsation in patients with ACS are based on clinical experience of efficacy, and biased observational data and potentially considered expert opinion.

In the CURE study, 1822 patients of the clopidogrel group underwent bypass surgery. Overall, there was no significant excess of major bleeding after CABG (1.3% vs 1.1%) but in the 912 patients who stopped clopidogrel within 5 days before surgery, the rate of major bleedings was higher in the clopidogrel group (9.6% vs 6.3%, $P=0.06$)[41].

A meta-analysis of seven trials reported the superiority of early invasive strategy in comparison with a conservative approach in patients with unstable angina and non-ST elevation acute coronary syndrome that the overall mortality in one year was reduced (5.5% vs 6.0; 8% relative RR, 95% confidence interval).

In the PURSUIT trial, in patients who underwent surgery and who were initially treated with aggressive antiplatelet treatment: a total of 78 patients underwent immediate CABG within 2 h of cessation of the antiplatelet drug major bleeding was not different between groups occurring in 64% of patients receiving placebo and 63% of patients receiving eptifibatid[12]. The rate of blood transfusion was also similar (57% vs 59%). Similar observations were made by Bizzarri with tirofiban[193]. In our study the incidence of reopening was (5.8 % vs 4.1%) in the group of NSTEMI-ACS where the patients received two antiplatelet drugs before surgery vs the control group with a p-value < 0.05 which is not significant, and this also be explained as one theory of the ACS is an acute inflammatory process with a hypercoagulable state justified the no significant incidence of reopening despite the higher dose and antiplatelet drugs before surgery in ACS.

In a large database analysis of unselected patients admitted for ACS, performance early CABG, even in high risk patients, was associated with low in-hospital mortality.

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Early Postoperative Outcome of Off Pump CABG Using Bilateral Skeletonized Internal Mammary Arteries in Type II Diabetic Patients.

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Objectives: CABG in diabetic patients using bilateral skeletonized internal mammary arteries (BIMA) has long term survival and patency rates.

Methods: Retrospective study to evaluate the outcome of off pump CABG using bilateral skeletonized mammeries in type II diabetics.

Results: 69 type II diabetics patients had off pump CABG with bilateral skeletonized mammeries (Group I) compared to 69 diabetics patients with single skeletonized mammary artery (Group II). There was no statistically significant difference between both group regarding preoperative and demographic data. No significant difference in operative time (212.73 ± 7.26 min in Group I minutes versus 197.50 ± 6.85 min in group II, $P = 0.06$). No difference in ventilation time (10.32 ± 2.24 hours in Group I versus 9.28 ± 2.03 hours in Group II, $P = 0.07$). There was no significant difference in postoperative chest tube drainage (546.61 ± 294.86 ML in Group I versus 465.50 ± 256.07 ML in Group II, $P = 0.08$). Three patients in Group I (4.34%) re-opened for bleeding versus two patients (2.89%) in Group II with no significant difference, $P = 0.29$. No significant value regarding incidence of wound infection, 4 patients (5.79%) had superficial wound infection in Group I versus 3 patients (4.34%) in Group II, $P = 0.68$. Two patients had mediastinitis (2.89%) in Group I versus one patient (1.44%) in Group II, $P = 0.55$. There was no significant difference in hospital stay (8.13 ± 1.0 days in Group I versus 7.85 ± 0.91 days in Group II, $P = 0.09$).

Conclusion: Off pump CABG using BIMA in type II diabetics can be done safely without significant increase in postoperative complications.

Keywords: OFF PUMP, BIMA, DIABETICS.

The incidence of diabetes mellitus especially type II (insulin dependent) had reached an epidemic incidence in some western countries. ⁽¹⁾ In the developing countries the situation is even worse. A country like Saudi Arabia the overall prevalence of DM in adults is 23.7% of the total population. ⁽²⁾

Due to diffuse and aggressive nature of coronary atherosclerosis in diabetics patients coronary artery bypass grafting has a better survival, relief of symptoms and less incidence to repeat revascularization when compared to PCI. ⁽³⁾

Grafting the left internal mammary artery to the left anterior descending artery is the "gold standard" for coronary artery revascularization due to high patency rates ranging from 90% to 95% at ten years follow up compared to only 30% patency rate in saphenous vein grafting. ⁽⁴⁾

Although using bilateral mammary thoracic artery (BIMA) grafts is proved to have long term survival and patency rates in diabetics when compared to single internal mammary artery (IMA) and saphenous vien ⁽⁵⁾. Many surgeons still reluctant in routine using of bilateral mammary arteries in diabetics to avoid the relatively high incidence of postoperative sternal wound and healing problems ^(6,7). This deprive those patients from the gaining long-term benefits of BIMA grafts. Only 12 % of the surgeons in Europe use BIMA while in the USA the percentage is only 4% ^(8,9).

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Right internal mammary artery (RIMA) can be used as free graft, Y graft with LIMA or used in situ. RIMA grafting strategy differs from center to another; it can be grafted to left circumflex artery, diagonal, left anterior descending or proximal right coronary arteries. ⁽¹⁰⁾ Another argument that is often used against BIMA when composite grafting is higher incidence of graft occlusion or string sign in up to 20% of the patients due to competitive flow ⁽¹¹⁾. But this is proved to be more in mildly stenosed target vessels while other studies proved that skeletonization of the internal mammary artery provides significant higher flow capacity and better graft flow reserve ⁽¹²⁾.

Skeletonization gives more length to mammary artery and flow capacity when compared to pedicled one ⁽¹³⁾. Also skeletonization decreases the postoperative pain and dysarthria ⁽¹⁴⁾ but most importantly it preserve the microcirculation of the sternum and decrease the venous congestion which is reflected on better healing power and less incidence of sternal wound infection ⁽¹⁵⁻¹⁶⁾.

Using the off pump technique in diabetics can decrease the postoperative complications including the sternal wound infection when compared to CABG with conventional bypass machine ⁽¹⁷⁾.

Along with the surgical techniques, perioperative tight control of blood sugar with strict infection control measure can decrease the incidence of postoperative sternal wound infection in diabetic patients ⁽¹⁸⁾.

PATIENTS AND METHODS

From 2007 till end of 2012 total 1758 patients had elective CABG in our center, 651(37.03 %) of those patients were diabetics. We had this retrospective study to evaluate the outcome of using bilateral skeletonized mammary artery versus single skeletonized mammary use in elective off pump CABG in type II diabetic patients,

The choice of single or double IMAs was guided by patient's age, clinical status and surgeon's preference. From clinical experience BIMA patients are usually younger and with incidence of multi vessel disease and a lower incidence of chronic renal failure, so we used a matching score guided by the preoperative demographic data of the patients to match 69 patients with type II diabetic mellitus who underwent off pump elective CABG using bilateral mammary artery (group I) with another 69 patients with type II diabetic mellitus under went off pump elective CABG using single skeletonized LIMA (Group II).

Inclusion criteria

- 1- Type II diabetes mellitus.
- 2- EF \geq 35%.
- 3- Elective CABG.

- 4- Off pump CABG
- 5- Using bilateral skeletonized mammary arteries.

Exclusion criteria:

- 1- Non diabetic patients
- 2- Type I Diabetic patients
- 3- EF $<$ 35%.
- 4- Emergency or urgent CABG.
- 5- CABG plus other surgeries
- 6- Redo CABG.
- 7- Associated valvular lesion.
- 8 - Patients converted from off pump to on pump.
- 9- Pedicled internal mammary arteries.

Surgical technique

All Patients were anaesthetized with Propofol and Fentanyl using a target-controlled intravenous anesthesia protocol. Each patient had a central venous catheter and Swan-Ganz catheter with invasive monitoring of blood pressure. All patients had median sternotomy.

Internal mammary artery harvesting technique

After midline sternotomy low electro-cautery (40-50 watt) was used for haemostasis of the pre-sternal tissues with minimal use of bone wax. The pleurae were not opened routinely. Endothoracic fascia is incised medially to expose the IMA from its accompanying vein. The dissection of the IMA was done with low settings (10–20 W) on the electro-cautery. Arterial branches were ligated with haemostatic clips from the distally bifurcation of the IMA to the first rib.

The right IMA was harvested in an identical fashion to the left IMA. Distal IMA The division is made at the bifurcation of the IMA and systemic heparin is given before this division. Both the superior epigastric and musculophrenic arteries are ligated with haemostatic clips and with silk surgical tie for double check. Both IMAs were warped in gauze soaked with warm saline with Papaverine solution.

If the left internal mammary artery (LIMA) was planned to be used in-situ graft is preferred bypassed to the left anterior descending artery (LAD).The plan for using right internal mammary artery (RIMA) differs. In some cases it was used in-situ for bypass to the LAD, diagonal or the circumflex artery and rarely to the proximal part of right coronary artery. In other group of patients the free RIMA graft were used as a composite 'Y' graft with the LIMA used for revascularization of both the LAD and circumflex arteries or diagonal artery.

During anastomosis, a suction type mechanical stabilizer (Octopus Evolution AS; Medtronic, Minneapolis, MN) was used to immobilize the target site of the coronary artery. Distal myocardial perfusion was maintained using an intracoronary shunt tube (ClearView®; Medtronic, Minneapolis, MN).

Before closure of the sternum, haemostasis was done with minimal use of low setting electro cautery and bone wax. The sternum was closed using at least of 6 stainless steel wires size 5-6 French. Closure of subcutaneous tissues was done with two layers of continuous absorbable sutures and skin closed with continuous intracutaneous absorbable suture.

Data collection and statistical analysis

All preoperative and demographic variables including age, sex, body mass index, hypertension, chronic obstructive pulmonary disease, renal failure on dialysis, hepatic failure, previous myocardial infarction, smoking history, carotid disease and peripheral vascular disease along with all preoperative laboratory tests including HBA1C level are collected and analyzed.

All operative data including operative time, graft distribution site, mean number of the graft per patients, intra operative use of intra-aortic balloon pump (IABP) and any intra-operative event are collected and analyzed. All follow up data for 3 months from discharge home.

As the major clinical end points analyzed in this study sternal wound infection rate so *sternal wound classification* was done according to the guidelines of the Centers for Disease Control and Prevention as follows:

1. Superficial sternal wound infection: defined as wound erythema and purulent discharge without evidence of sternal or mediastinal involvement.
2. Deep sternal wound infection: defined, with patients meeting at least one of the following criteria:
 - (a) Isolation of an organism from culture of mediastinal tissue or fluid.
 - (b) Evidence of mediastinitis during sternal re-exploration.
 - (c) Chest pain, sternal instability, or fever present in combination with purulent discharge from the mediastinum or an isolated organism from blood or tissue cultures.

Mortality is defined as death during a hospitalization for surgery, regardless of length of stay, or within 30 days from surgery.

Values of continuous variables were expressed as mean standard deviation. Non-parametric tests (Mann-Whitney test and Fisher’s exact test) were used for comparison between both groups of patients. Values of *P* less than 0.05 were

considered significant. Statistical analyses were performed with computerized statistical packages (SPSS 18.0 software, SPSS, Chicago, IL, USA).

Results

There was no statistical significant difference between both group regarding preoperative and demographic data. Mean EF was 45.15±6.34% in Group I (double mammary arteries) versus 44.23±5.91% in Group II (single mammary artery), *P* = 0.37. No significant difference in EURO SCOREII (1.76±0.50 in Group I versus 1.90±0.51 in Group II, *P* = 0.10).

Table (1) summarizes all preoperative and demographic data of the two groups.

Variable	Group I (n=69)	Group II (n=69)	P value
Age	57.40±5.70	57.20±5.81	0.83
Male, n (%)	51(73.91%)	50(72.46%)	0.37
Female, n (%)	8(11.59%)	7(10.14%)	0.48
Hypertensive, n (%)	23(33.33%)	20(28.98%)	0.78
BMI	23.26±2.84	23.41±2.89	0.75
CREATININE	1.24±.28	1.33±.32	0.29
HBA1C	7.11±0.39	7.08±0.36	0.67
Smokers, n (%)	20(28.98%)	17(24.63%)	0.26
Old MI, n (%)	37(53.62%)	34(49.27%)	0.27
LEFT MAIN LESION	9 (13.04 %)	11 (15.94%)	0.86
EF	45.15±6.34	44.23±5.91	0.37
PVD	3(4.34%)	4 (5.79%)	0.73
CAROTID STENOSIS>50%	4(5.79%)	5 (7.24%)	0.34
EUROSCORE II	1.76±0.50	1.90±0.51	0.10
Previous PCI	15(21.73%)	14(20.28%)	0.32

PVD: peripheral vascular disease, EF: ejection fraction, BMI: body mass index.

Values of P less than 0.05 were considered significant.

Table 1. Preoperative Demographic Data of the Two Groups.

No radial or inferior epigastric arteries were used in any patients. No need for intra operative IABP insertion in both groups. No significant difference in operative time (212.73±7.26 min in Group I minutes versus 197.50±6.85 min in Group II, *P* = 0.06) Table (2) summarizes operative data of the two groups.

Table 3 shows arrangements of BIMA and graft Combinations in Group II.

Cardiovascular

Variable	Group I (n=69)	Group II (n=69)	P value
Operative Time (minutes)	212.72±7.26	197±6.50	0.06
Mean No. of Grafts/Patient	2.88±0.60	2.72±0.53	0.10

Values of P less than 0.05 were considered significant.

Table 2. Operative Data of the Two Groups.

BITA group(69)	
Y graft (12)	
LIMA TO LAD	12
RIMA TO DIAGONAL	3
RIMA TO CX	9
IN SITU BIMA (57)	
LIMA TO LAD	48
RIMA TO LAD	9
RIMA TO CX	36
RIMA TO DIAGONAL	10
LIMA TO DIAGONAL	9
RIMA TO PROXIMAL RCA	2

Table 3. Graft Arrangements in BIMA Group (Group I).

LIMA: left-side internal mammary artery; RIMA: right-side mammary thoracic artery; CX: circumflex artery; LAD: left anterior descending artery.

No early postoperative mortality in both groups. Postoperatively there was no significant difference regarding the ventilation time (10.32±2.24 hours in Group I versus 9.28±2.03 hours in Group II, $P = 0.07$). There was no significant difference regarding the first 24 hours postoperative chest tube drainage (546.61±294.86ML in Group I versus 465.50±256.07 ML in Group II, $P = 0.08$).

There was no significant difference in packed RBCS transfusion 0.45±1.25 units in Group I versus 0.28±0.92 units in Group II, $P = 0.15$. There was no significant regarding the FFP transfusion (0.62±1.90 units in Group I versus 0.47±1.43 units in Group II, $P = 0.23$). There was no significant regarding the platelets transfusion (1.25±2.88 units in Group I versus 0.92±1.84units in Group II, $P = 0.13$).

Three patients in Group I (4.34%) were re-opened for bleeding versus two patients (2.89%) in Group II, $P = 0.29$.

In Group I four patients (5.79%) had postoperative Atrial fibrillation (POAF) versus five patients (7.24%) in Group II with no significant difference between both groups, $P = 0.47$. No patients needed continues renal replacement therapy (CRRT) for renal impairment postoperatively in both groups. There was no significant difference between both groups regarding ICU stay 43.13±43.24 hours in Group I versus 40.50±41.15hours in Group II, $P = 0.23$.

Four patients (5.79%) had superficial wound infection in Group I versus three patients (4.34%) in Group II with no significant value, $P = 0.68$. Two patients had deep wound infection and need re-wiring (2.89%) in Group I versus one patient (1.44%) in Group II, $P = 0.55$.

There was no significant difference between both groups regarding the hospital stay (8.13±1.0 days in Group I versus 7.85±0.91days in Group II, $P = 0.09$).

Table 4 summarizes all post-operative data of the two Groups.

VARIABLE	GROUP I (n=69)	GROUP II (n=69)	P value
Ventilation Time, Hours	10.32±2.24	9.28±2.03	0.51
CHEST Drainage, ML	546.61±294.86	465.50±256.07	0.08
PRBCS (unit)	0.45±1.25	0.28±0.92	0.15
FFP (unit)	0.62±1.90	0.47±1.43	0.23
PLATLETS (unit)	1.25±2.88	0.92±1.84	0.13
Reoperation for Hameostasis, N (%)	3(5.26%)	2(289.38%)	0.97
POAF	4(4.79%)	5(7.24%)	0.47
Intensive Care Unit Stay, Hours	43.13±43.24	40.50±41.15	0.23
Superficial Wound Infection	3(4.34%)	4(5.79%)	0.68
Mediastinitis	3(4.34%)	2(3.38%)	0.55
Hospital Stay, Days	8.13±1.0	7.85±0.91	0.09

POAF: postoperative atrial fibrillation, PRBCS: packed red blood cells, FFP: fresh frozen plasma.

Values of P less than 0.05 were considered significant.

Table 4. Post-Operative Data of the Two Groups.

Discussion

Recent evidence suggests that CABG using bilateral mammary arteries in diabetics has better outcome with than percutaneous coronary intervention⁽¹⁹⁾, but CABG in diabetics - especially in insulin dependent type II - is associated with higher perioperative morbidity and mortality when compared to non diabetics⁽²⁰⁾.

Many recent of studies found superior long term patency rates of bilateral internal mammary arteries when compared to single mammary artery in diabetics CABG patients^(5,21-22).

As Diabetes is a well known major risk factor for decess sternal bone healing with slight increase in the incidence of postoperative mediastinitis ,some studies argue about increase the incidence of postoperative sternal wound infection in diabetic when BIMA are used when compared to non diabetic patients but more recent studies did not found the significant difference between diabetics and non diabetics regarding the rate of sternal wound infection when using BIMA specially when skeletonized mammeries with off pump technique are used.⁽²³⁻²⁶⁾

In our study the mean operative time was longer in BIMA group by 16 minutes but with no significant statistical difference between both groups which was found by other studies which found up to 23 minute longer in operative time⁽²⁷⁾.

Although there was increase in the amount of chest tube drainage in group I -which is expected as two mammary beds are exposed -but there was no significant difference between groups.

Also there was no significant difference regarding the postoperative incidence of reopening and the need for blood products transfusion.

In our study there was no significant difference regarding the ventilation time which differs from Taggart et al in Arterial Revascularization Trial (ART)⁽²⁷⁾ who found that using BIMA increases the ventilation hours but in only 6.1% of their patients were diabetics on insulin and 40% were done off pump and the study did not mention any thing about the harvesting technique of the mammary arteries which does not match with our patients population nor surgical technique used in our study.

Although the rate of postoperative superficial and deep sternal wound infection in BIMA group was relatively higher in our study when compared to single mammary patients but with no statistical significant difference same found by other studies which proved no significant increase in incidence of postoperative sternal infection when using BIMA skeletonized mammeries in diabetics specially when using off pump technique.^(7, 23-26)

Other studies found that female gender, old age above 70 years, COPD patients and body mass index (BMI) between 27

to 30, are considered risk factors for postoperative mediastinitis in use of bilateral mammeries in diabetics⁽²⁸⁻²⁹⁾.

In our study 10.14 % from patients were female with mean body mass index 23.41 in and no COPD patients were included in the study which could explain the relatively low incidence of sternal wound infection in BIMA group.

Conclusion

Off pump CABG using skeletonized BIMA can be used in type II diabetics safely without increase in the in the early postoperative outcome specially the incidence of sternal wound infection.

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PERICARDIAL PATCH ENLARGEMENT WITH FRAGMENTATION OF THE POSTERIOR LEAFLET: A NOVEL TECHNIQUE FOR REPAIR OF RHEUMATIC MITRAL REGURGITATION.

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Background: Repair of severe rheumatic mitral regurgitation is a surgical challenge for a disease that is frequently faced in our region. Posterior leaflet retraction is a common pathologic feature of this disease for which posterior leaflet augmentation with an autologous pericardial patch has been advocated. However, due to concerns about the creation of mitral stenosis, we propose a new modification to this technique consisting of an extensive fragmentation of the posterior leaflet.

Material & methods: Between April 2005 and July 2012, 76 consecutive patients with severe rheumatic mitral regurgitation due to posterior leaflet retraction (Carpentier type IIIa) underwent mitral valve repair with pericardial patch enlargement of the posterior leaflet. The surgeries were performed at Cairo University Hospitals and the Nasser Institute by the same team. The patients were divided into 2 groups: in the control group or group A (n=32), the patch was sutured to the intact posterior leaflet. In the study group or group B (n=44), the technique of posterior leaflet fragmentation was used. Both groups were comparable in terms of age, gender, functional classification, atrial fibrillation and echocardiographic measurements. There was a higher incidence of recent or ongoing rheumatic activity in group A (5 or 15.6% versus 0%, p=0.01).

Results: There was one operative mortality in each group. No patient was discharged with residual mitral regurgitation or stenosis. Follow-up period ranged between 3 months and 98 months (8.1 years). The mean follow-up period was 4.2 years. There was 1 delayed mortality in group A and 2 in group B. The survivors in both groups showed significant functional improvement, freedom from mitral regurgitation and reduction of left ventricular dimensions relative to their preoperative state. Only group B patients achieved significant reduction of left atrial diameter and pulmonary artery systolic pressure. They also enjoyed larger mitral valve areas and lower mean pressure gradients than group A patients. The incidence of severe mitral stenosis requiring reoperation was significantly higher in Group A (6 cases or 18.8% versus 1 case or 2.3%, p=0.01). Multivariate analysis revealed that assignment to group A was the only risk factor for the development of delayed mitral stenosis.

Conclusion: It was concluded that pericardial patch augmentation of the posterior leaflet is an effective technique for the repair of severe mitral regurgitation in rheumatic heart disease, with good midterm results at 4.2 years. Fragmentation of the posterior leaflet improves the outcome and protects from the occurrence of severe mitral stenosis, and is recommended for the routine conduct of this operation.

Key words: Rheumatic valve disease - Mitral valve repair - Pericardial patch - Leaflet augmentation.

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Rheumatic heart disease is still the prevailing aetiology of severe mitral regurgitation in our surgical practice. Although mitral valve replacement is the more expedient option and yields more consistently reliable results on the short term, compared with repair, it is associated in western literature with higher morbidity and mortality on the long term (1). In our part of the world, Gometza and coworkers reported a particularly alarming mortality after mechanical valve replacement in a young Saudi population, reaching 25% at 4 years (2).

Over the years, mitral valve repair has established itself as the procedure of choice in rheumatic valvulopathy, whenever feasible, although the durability of repair is shorter for rheumatic heart disease relative to degenerative pathology. In degenerative mitral valve disease, redundant tissues are often present, allowing for the creation of large surfaces of coaptation. By contrast, rheumatic valves are most commonly characterized by a paucity of tissues, due to leaflet retraction and fibrosis (3). The most frequent lesion encountered is posterior leaflet retraction, resulting in a type IIIa mitral regurge in the Carpentier classification, occurring in 42 to 60% of surgical series, either alone or in combination with anterior leaflet prolapse (Carpentier type II). This has inspired Chauvaud and associates in 1991 to launch the concept of posterior leaflet extension with an autologous, glutaraldehyde-preserved pericardial patch (4). In 2001, they reported very good long term results in 65 patients, with a 10-year freedom from reoperation of 70% (5). In 2007, they refined the technical details of this procedure, emphasizing the importance of creating very large patches, with heights of at least 3 cm, to ensure large coaptation reserves (6).

One major concern has been expressed regarding the use of large pericardial patches, namely the creation of mitral stenosis. Carpentier warned that if the patch height is not kept below a maximum of 1.5 to 2 cm, it results in a large immobile mass, a situation which he calls "a curtain effect", leading to elevated transmitral gradients (7). Looking further into this problem, Dion and associates observed that in many cases, the posterior leaflet is shrunken not only in height but also in width, with loss of the indentations between the scallops and a tense and shortened free edge. If the leading edge of a large pericardial patch is directly attached to a posterior leaflet with such morphology, it acquires the characteristic of an aortic cusp, which has, unlike the normal mitral leaflet, a free edge that is shorter than the base of implantation. The thus reconstructed posterior leaflet behaves like an aortic cusp, moving forward in diastole and obstructing the mitral valve inlet, instead of moving downwards and backwards towards the posterior wall of the left ventricle. This observation was dubbed "the aortic cusp effect". As a solution to this problem, Dion and associates make a brief, undetailed outline of a technique by which the posterior leaflet is divided into several fragments that are individually reattached to the free edge of the patch, aiming at increasing its length and subsequently its mobility, and thus

decreasing transmitral gradients. To this date, however, they have not yet published any results. (8)

We have first learned about the concept of posterior leaflet fragmentation in 2008 from Dr. Dion himself (9) and we have been using it extensively for our posterior leaflet augmentations ever since. The following study is aimed at comparing the midterm results of two techniques of posterior leaflet pericardial patch enlargement in our hands: the original method of continuous suturing of the patch to the intact posterior leaflet, as described by Zegdi et al. (6), and the fragmentation of the posterior leaflet based on the concept proposed by Dion and coworkers (8).

Material and methods

Group assignment

Between April 2005 and July 2012, 76 consecutive patients with severe rheumatic mitral regurgitation due to posterior leaflet retraction (Carpentier type IIIa) underwent mitral valve repair with pericardial patch enlargement of the posterior leaflet, at Cairo University Hospitals and the Nasser Institute, and were all managed by the same team consisting of the two authors. The patients were divided into 2 groups: in the control group or group A, the patch was sutured to the intact posterior leaflet. In the study group or group B, the technique of posterior leaflet fragmentation was used. Group assignment was done in three stages. In the initial stage between April 2005 and March 2008, all patients (n=25) were systematically operated on by keeping the posterior leaflet intact and were thus assigned to group A. This was followed by an intermediate period between April 2008 and April 2009 during which a selective approach was used, depending on intraoperative surgical assessment of the transverse span of the free edge of the posterior leaflet. If after the leaflet was incised from its annular attachment, its free edge was found to be of normal redundancy, the leaflet was not fragmented and the patient was assigned to group A. Seven patients were added to group A in this manner. On the other hand, if after leaflet incision, its leading edge was judged to be tense and shortened from side to side, the technique of leaflet fragmentation was employed, assigning the patient to group B. Fourteen patients were thus assigned to group B. Finally, during the latest stage of the study, between May 2009 and December 2012, leaflet fragmentation was used exclusively, adding 30 patients to group B. The total number was therefore 32 patients in group A and 44 in group B.

Patient population

Preoperative clinical characteristics are summarized in table I. The two groups were matched regarding the mean age (26.6 ± 13.2 years in group A, 27.2 ± 10 years in group B, $p=0.4$) and regarding the male to female distribution (26 females or 81.2% in group A, 39 females or 88.6% in group B, $p=0.3$). The mean functional class was also similar for both groups (2.8 ± 0.7 versus 2.9 ± 0.5 , $p=0.4$). There was a comparable incidence of

AF (atrial fibrillation) in both groups (15 patients or 46.8%, versus 14 patients or 31.8%, $p=0.18$). The only significant difference was the presence of 5 patients (15.6%) in group A diagnosed with recent (within 1 month) or ongoing rheumatic activity, compared to none in group B ($p=0.01$).

The preoperative echocardiographic findings are listed in table II. The echocardiographic measurements were equivalent in terms of the left ventricular, left atrial and right ventricular dimensions, the ejection fraction, grade of mitral regurgitation, mitral valve area (MVA), mitral valve score and pulmonary artery systolic pressure. There were also no differences in the incidence of significant mitral stenosis, defined as a mitral valve area (MVA) smaller than 1.5 cm² either by planimetry or pressure half time, nor in the prevalence of significant tricuspid regurgitation nor significant aortic regurgitation.

	Group A (n=32)	Group B (n=44)	p value
Females	26 (81.2%)	39 (88.6%)	0.3
Age	26.6 years (± 13.2)	27.2 years (± 10)	0.4
AF	15 (46.8%)	14 (31.8%)	0.18
NYHA class			
I	2 (6.2%)	1 (2.2%)	0.3
II	5 (15.6%)	5 (11.3%)	
III	20 (62.5)	35 (79.5%)	
IV	5 (15.6%)	3 (6.8%)	
mean	2.8 \pm 0.7	2.9 \pm 0.5	0.4
Rheumatic activity	5(15.6%)	0(0%)	0.01

(AF=atrial fibrillation, NYHA=New York Heart Association. Values are expressed as percentage or as mean \pm standard deviation)

Table I. Patient characteristics.

Anesthesia and intraoperative trans-esophageal echocardiography (TEE)

A written informed consent was obtained from every patient or his family regarding the operative procedure but not regarding group assignment. All patients were managed by a standard anesthetic protocol. After sedation with midazolam 0.02 - 0.07 mg/Kg, local anesthesia was used for the insertion of a wide bore peripheral intravenous cannula and a radial arterial catheter. Induction of anesthesia was accomplished with sodium thiopental 2-3 mg/kg, fentanyl 7-10 μ g/kg and pancuronium 0.12 mg/kg. Anesthesia was maintained with isoflurane 0.6 - 1% in 100% oxygen. Continuous monitoring included ECG, pulse oxymetry, invasive arterial and central

venous pressure measurements, urinary catheter output, and nasopharyngeal temperature. Intra-operative trans-esophageal echocardiographic (TEE) assessment was carried out before cardiopulmonary bypass by the anesthesiologist with a Hewlett-Packard Sonos 5500 machine (Hewlett-Packard, Palo Alto, California). A comprehensive TEE examination was performed with special emphasis on leaflet thickness, height and mobility, commissural fusion, state of the subvalvular apparatus, annular dilatation, extent of calcification, gradient across the valve, direction of the regurgitant jet, presence of left atrial thrombus, biventricular function, pulmonary artery systolic pressure and associated tricuspid or aortic valve disease.

	Group A	Group B	p value
MR grade	3.6 \pm 0.5	3.6 \pm 0.4	0.4
LVEDD	6.4 \pm 1.4 cm	6.1 \pm 0.8 cm	0.18
LVESD	4.3 \pm 1.2 cm	4 \pm 0.7 cm	0.13
EF	56.3 \pm 13.9%	60.7 \pm 8%	0.09
LA	5.7 \pm 1.3 cm	5.6 \pm 1.3 cm	0.47
RV	1.9 \pm 0.4 cm	2.2 \pm 0.7 cm	0.17
PASP	58.3 \pm 23.4 mmHg	52.2 \pm 14.2 mmHg	0.06
PASP \geq 60 mmHg	9(28.1%)	7(15.9%)	0.19
MVA	2 \pm 0.6 cm ²	2.4 \pm 0.6 cm ²	0.1
Significant MS	6(18.8%)	3(6.8%)	0.1
Echo score	7.5 \pm 1.5	6.6 \pm 0.9	0.07
Severe TR	4(12.5%)	7(15.9%)	0.67
Severe AVD	3(9%)	7(15.9%)	0.4

(MR=mitral regurgitation, LVEDD=left ventricular end diastolic diameter, LVESD=left ventricular end systolic diameter, EF=ejection fraction, LA=left atrium, RV=right ventricle, PASP=pulmonary artery systolic pressure, MVA=mitral valve area, MS=mitral stenosis, TR=tricuspid regurgitation, AVD=aortic valve disease. Values are expressed as percentage or as mean \pm standard deviation)

Table II. Preoperative echo findings.

Operative technique

All of the operations were performed by the same surgeon. After median sternotomy, mildly hypothermic (32°C) cardiopulmonary bypass was established through aorto-bicaval cannulation. An autologous pericardial patch was harvested, thoroughly cleaned of all fibrofatty tissue and immersed in a 0.6% glutaraldehyde solution for 8-10 minutes, then rinsed twice in normal saline. Myocardial protection was achieved by antegrade, intermittent, cold blood-enriched, crystalloid

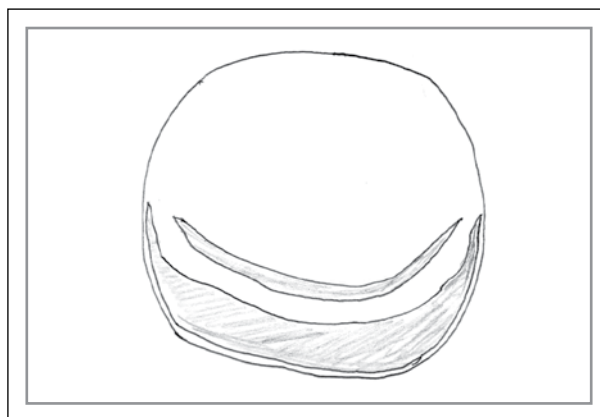
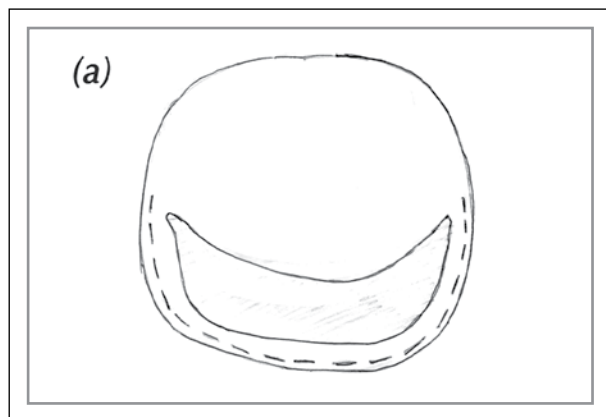


Fig 1. Disinsertion of the posterior leaflet (a) and the resultant defect (b).

cardioplegia. Access to the mitral valve was through a standard left atriotomy incision. Following routine valve analysis, the annuloplasty sutures were all placed, using 2/0 braided polyester, and put under traction to enhance the exposure. The repair was started first by a commissurotomy, a papillotomy, or correction of anterior leaflet prolapse by either chordal transfer or artificial chordae, if any of these manoeuvres was deemed necessary.

The decision was made to augment the posterior leaflet if the leaflet height was less than 1.5 mm, or whenever the leaflet appeared to have restricted motion in the TEE exam, especially if there was a posteriorly directed regurgitant jet unexplained by an anterior leaflet prolapse. The posterior leaflet was then disinserted from the annulus by a curvilinear incision running 1-2 mm away from and parallel to the annulus and extending well around both commissures (figure 1). An ovoid pericardial patch was fashioned with a width of 2-3 cm and a length corresponding to the intercommissural distance. It was sutured to the annulus in all cases using two 4/0 polypropylene running sutures, each starting at one commissure and meeting each other at the middle of the posterior annulus. The suturing was done in a continuous and locking fashion to avoid a purse string effect on the patch. In group A, the detached posterior leaflet was kept intact and the leading edge of the patch was sutured to its posterior edge, again using a continuous locking 4/0 polypropylene suture (figure 2).

In group B, the posterior leaflet was fragmented into several fragments (typically numbering 5-7), each fragment consisting of an islet or button of posterior leaflet tissue bearing its chordal attachments. The most medial and the most lateral fragments were kept attached to their corresponding commissural tissues (figure 3a). The fragments were then sutured to the free edge of the pericardial patch by means of one 5/0 polypropylene mattress suture for each fragment, maintaining equal distances of unsupported pericardium between the fragments (figure 3b).

A complete rigid annuloplasty ring (Carpentier-Edwards classic ring, Edwards Lifesciences, Irvine, California) was then

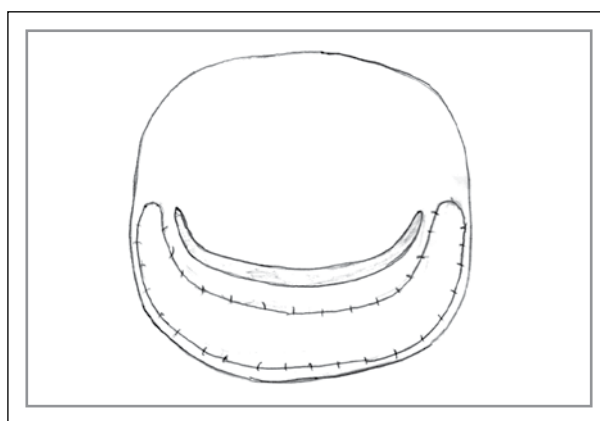


Fig 2. Final appearance of the pericardial patch when sutured to the intact posterior leaflet in group A.

implanted. Ring sizing was based on the height of the fully unfurled A2 segment of the anterior leaflet, with an inclination to oversize by one size in order to take advantage of the bulk of tissue provided by the newly reconstructed posterior leaflet. Ring sizes ranged between 28 and 38 and the mean ring size was smaller in group A, compared to group B (32.4 ± 1.7 , versus 34.1 ± 2.4 , $p=0.01$). Saline testing of the valve, closure of the atriotomy and any additional aortic or tricuspid valve procedures were then performed in the usual manner. TEE evaluation was repeated after separation from bypass, with special attention to biventricular function, mitral valve competence and length of coaptation. The mean pressure gradient was always investigated using continuous wave Doppler. Operative procedures and post-bypass TEE findings are summarized in table III.

Transthoracic echocardiography was performed by the anaesthetist just before hospital discharge, then by the referring cardiologist 3 months after hospital discharge and at 6 months intervals. All the patients were followed up by the surgeon at the outpatient clinic.

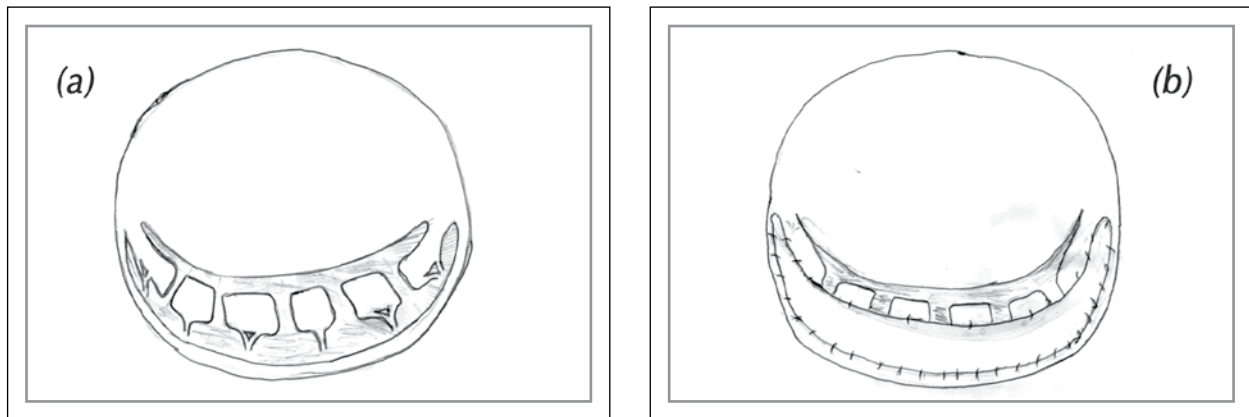


Fig 3. Fragmentation of the posterior leaflet (a) and reattachment of the fragments along the free edge of the pericardial patch (b) in group B.

	Group A	Group B	p value
Ring size	32.4±2.7	34.1±2.4	0.01
Commissurotomy	11(34%)	13(29.5%)	0.6
ALrepair	3(9%)	8(18.1%)	0.28
TV repair	5 (15.6%)	8(18.1%)	0.7
AV procedure	3(9%)	7(15.9%)	0.4
Post-bypass TEE			
MR grade	0.3±0.5	0.1±0.4	0.2
Coaptation length	11.1±2.4 mm	11.2±2.8 mm	0.4
Mean PG	3.9±1.2 mmHg	4.2±1.4 mmHg	0.6

(AL=anterior leaflet, TV=tricuspid valve, AV=aortic valve, TEE=trans-esophageal echocardiography, MR=mitral regurgitation, PG=pressure gradient. Values are expressed as percentage or as mean ± standard deviation)

Table III. Intraoperative data.

Statistical analysis

Data are expressed as percentages or as mean values ± standard deviation. Group comparison was done using the paired Student’s t-test for continuous variables and the Pearson chi-square test for categoric variables. P values lower than 0.05 were considered significant. Multivariate analysis by logistic regression was performed when needed.

Results

Regarding operative procedures, there was no difference in the number of patients requiring a mitral commissurotomy, anterior leaflet repair, concomitant tricuspid annuloplasty or concomitant aortic valve procedure in both groups. Only one patient in group A and none in group B required a second pump run to correct a residual severe mitral regurgitation. Post-bypass

TEE readings showed no difference between the two groups in terms of mitral regurgitation grade, the length of coaptation between the anterior and posterior mitral leaflets, and the mean diastolic pressure gradient across the mitral valve. (Table III)

There was one operative mortality in each group (3.1% and 2.2% respectively, p=0.06). A 19-year old male in group A, with severe preoperative congestive hepatomegaly and elevated serum bilirubin, underwent mitral and tricuspid valve repair and died one week later of fulminant hepatitis. A 9-year old female in group B who underwent concomitant aortic valve replacement died of left sided heart failure on the second postoperative day. There was no incidence of stroke, complete heart block or mediastinitis.

	Group A	Group B	p value
MR grade	0.3±0.4	0.4±0.6	0.6
MVA	1.9±0.5 cm ²	2.2±0.3 cm ²	0.1
MPG	3.6±0.4 mmHg	4.3±1.9 mmHg	0.2

(MR=mitral regurgitation, MVA=mitral valve area, MPG=mean pressure gradient. Values are expressed as mean ± standard deviation)

Table IV. Discharge echocardiographic findings.

Discharge echocardiographic findings are listed in table IV. The values were comparable in both groups concerning the grade of mitral regurge (MR), the mitral valve area and the mean diastolic pressure gradient across the mitral valve. MR grade was either 0 or 1 for all patients, except for one patient in group B who was discharged with grade 2 MR. No patient in either group had a mean pressure gradient greater than 8 mmHg at discharge.

The follow-up data are summarized in table V. The mean follow-up duration for both groups combined had a mean of 50.9±20.5 months (4.2±1.7 years). In group A, the

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follow-up period ranged between 3 and 98 months with a mean of 68.8 ± 14.9 months. Five patients were lost to follow-up, which was thus 83.8% complete. In group B, the follow-up duration ranged between 5 and 64 months with a mean of 40.8 ± 15.1 months. Four patients in that group were lost to follow-up, which was 93% complete. One patient died of heart failure at 11 months in group A. Two patients died of infective endocarditis at 5 and 6 months in group B and one patient died of an undiagnosed cause at one year. The combined overall survival was therefore 94.7%. One patient in group B who was in atrial fibrillation developed a non-fatal thromboembolic stroke at 18 months, due to cessation of oral anticoagulant therapy. The mean NYHA class at latest follow-up was comparable in both groups (2 ± 0.7 , versus 1.5 ± 0.6 , $p=0.1$). For both groups however this represented a significant improvement over the preoperative mean NYHA class ($p=0.002$ for group A and $p<0.0001$ for group B). The prevalence of atrial fibrillation was similar in both groups and was unchanged compared to baseline values.

Seven patients or 21.8% needed a reoperation in group A, compared to 3 patients or 6.8% in group B, but the difference in the overall rate of reoperation was not statistically significant ($p=0.11$). The freedom from reoperation was therefore 78.2% for group A, 93.2% for group B and 86.8% for the both groups combined. In group A, the mean time to reoperation was 27 ± 14 months or 2.2 ± 1.1 years and the indication for reoperation was severe MS (mitral stenosis) in 6 cases (18.8%) and severe MR (mitral regurgitation) in one case (3.1%). Five of the reoperations in this group were performed by the initial surgeon, but the operative findings for all of the 7 were available. The cause of repair failure was attributed to progression of the rheumatic pathology in 2 of them, and to de novo MS in five cases in whom the following recurring findings were observed: the pericardial patch was intact except for occasional areas of dotted calcification, the commissures were not significantly fused and the anterior leaflet mobility was preserved, but an extensive pannus had formed at the free edge of the patch, leading to severe limitation of diastolic motion of the posterior leaflet. On the other hand, in group B, the mean time to reoperation was 43 ± 29 months and the mode of repair failure was severe MS in one patient (2.3%) and severe MR in 2 patients (4.6%). The cause was attributed to underlying disease progression in one case and to technical errors in 2 cases. In one patient, lack of annuloplasty was the cause. In the other, the polypropylene sutures used for chordal reattachment to the free edge of the patch had perforated the patch at 3 points, leading to severe prolapse, at 3 months of follow-up. Retrospective analysis of the TEE recording of the case revealed that the patch was unduly oversized with excessive systolic billowing. This has presumably led to increased tension at the sites of chordal reinsertion, according to the law of Laplace, and eventual rupture. All of the patients subjected to reoperation had their mitral valves successfully replaced, without any major complication.

	Group A	Group B	p value
Follow-up duration	68.8 ± 14.9 months	40.8 ± 15 months	< 0.001
Delayed mortality	1(3.1%)	2(4.5%)	0.7
Reoperation	7(21.8%)	3(6.8%)	0.1
NYHA class	$2 \pm 0.7^*$	$1.5 \pm 0.6^{**}$	0.1
AF	17(53%)•	17(38%)••	0.3

(AF=atrial fibrillation, NYHA=New York Heart Association. Values are expressed as percentage or as mean \pm standard deviation.

* $p=0.002$ group A follow-up versus group A preoperative,

** $p<0.0001$ group B follow-up versus group B preoperative, • $p=0.4$ group A follow-up versus group A preoperative, •• $p=0.7$ group B follow-up versus group B preoperative)

Table V. Clinical follow-up data.

The echocardiographic findings at latest follow-up are listed in table VI. There were no differences in the left ventricular or left atrial dimensions, nor in the mean grade of MR or mean ejection fraction between the two groups. The incidence of severe MS necessitating redo surgery was significantly higher in group B (6 cases or 18.8%, versus 1 case or 2.3%, $p=0.01$). Multiple logistic regression analysis including gender, age younger than 20 years, preoperative NYHA class, atrial fibrillation, recent or ongoing rheumatic activity at the time of surgery, $PASP \geq 60$ mmHg, preoperative associated severe MS, associated significant tricuspid or aortic valve disease, the need for commissurotomy, concomitant anterior leaflet repair and annuloplasty ring size failed to identify any independent risk factor for the occurrence of severe MS during follow-up other than assignment to group A. The patients in group A had also higher mean pressure gradients across the mitral valve (7.8 ± 3.7 mmHg, versus 4.2 ± 1.9 mmHg, $p=0.001$), smaller mitral valve areas (1.76 ± 0.4 cm², versus 2.4 ± 0.6 cm², $p=0.001$) and higher pulmonary artery systolic pressures (50.6 ± 12.7 mmHg, versus 39.7 ± 20.2 mmHg, $p=0.04$).

Compared to the preoperative measurements, both groups exhibited significant reduction in terms of MR grade, and left ventricular end diastolic and end systolic dimensions. However, only group B showed evidence of reduced left atrial dimensions relative to baseline levels (4.1 ± 0.6 cm, versus 5.6 ± 1.3 cm, $p=0.001$).

Discussion

Mitral valve repair offers many advantages over replacement in rheumatic heart disease, including better preservation of left ventricular function, fewer thromboembolic episodes and lower incidence of anticoagulant related hemorrhage. The higher rate of reoperation is balanced by the increased long term survival.(1) In our study, we have observed a 94.7% survival

	Group A	Group B	p1 value	p2 value	p3 value
MR grade	0.9±1.2	1.1±1.5	0.6	<0001	<0001
Severe MS	6(18.8%)	1(2.3%)	0.01	0.9	0.1
MVA	1.76±0.4 cm ²	2.4±0.6 cm ²	0.001	0.8	0.8
MPG	7.8±3.7 mmHg	4.2±1.9 mmHg	0.001	N.A	N.A
LVEDD	4.7±0.4 cm	4.8±0.5 cm	0.8	<0001	<0001
LVESD	2.7±0.2 cm	3.1±0.6 cm	0.14	<0001	0.001
EF	60.4±6.5	58.2±10.5	0.17	0.2	0.43
LA	5.3±1.3 cm	4.1±0.6 cm	0.3	0.77	0.001
PASP	50.6±12.7 mmHg	39.7±10.2 mmHg	0.04	0.78	0.29

(MR=mitral regurgitation, MS=mitral stenosis, MVA=mitral valve area, MPG=mean pressure gradient, LVEDD=left ventricular end diastolic diameter, LVESD=left ventricular end systolic diameter, EF=ejection fraction, LA=left atrium, PASP=pulmonary artery systolic pressure, p1=group A versus group B, p2=group A follow-up versus preoperative, p3=group B follow-up versus preoperative)

Table VI. Follow-up echocardiographic findings.

at 4 years, which is comparable to 5-year survival rates ranging from 87.5% and 96.5% reported in the literature. (5,10,11) This survival rate however has a clear advantage over the 4-year survival of 75% after mechanical valve replacement described in a young rheumatic population. (2)

Posterior leaflet retraction is a common pathology in rheumatic mitral regurgitation. The other surgical options for the correction of this lesion are division of secondary chordae coupled with an undersized annuloplasty (4) and leaflet peeling (12). The undersized annuloplasty in our opinion yields coaptation surfaces that are often suboptimal, since they are limited by the already reduced posterior leaflet tissue. Regarding leaflet peeling, it is a technically difficult manoeuvre, which frequently leads to leaflet perforation in our hands. In addition, we find that it increases the pliability of the posterior leaflet when the latter is thickened but has a preserved height of at least 1.5 cm. If the height is reduced, the peeling technique has little benefit in our opinion. On the other hand, pericardial patch augmentation yields invariably generous areas of coaptation, which was manifested by the high mean coaptation lengths of 11.1 mm and 11.2mm measured respectively in the post-bypass TEE in groups A and B of our study. It was not uncommon for us to witness coaptation lengths of up to 20 mm in some cases. These measurements safely exceed the 8 mm mark generally acknowledged as a strong predictor of repair durability.(3) This was substantiated at 4 years of follow-up by the freedom from MR, the marked symptomatic improvement, and the significant reduction in left ventricular dimensions in both arms of the present study.

The creation of early mitral stenosis during posterior leaflet augmentation necessitating a return to cardiopulmonary bypass is always a valid concern. This phenomenon was described as a “curtain effect” by Carpentier, who recommends limiting the

height of the patch to 1.5-2 cm to avoid it.(7) It was described as an “aortic cusp effect”, as previously detailed, by Dion et al who proposed fragmentation of the posterior leaflet to increase the length of its free edge.(8) Both are intraoperative phenomena that would lead to immediate failure of the repair, and we have observed neither of them in any of our patients, as confirmed by the low gradients in both groups in the immediate TEE and in the discharge echocardiograms. On the other hand, we recorded a significantly higher incidence of delayed stenosis in the non-fragmentation group (6 cases or 18.8% requiring re-intervention, versus 1 case or 2.3%, p=0.01), occurring at a mean interval of 2.2±1.1 years. This was paralleled by the observation that lack of fragmentation was associated with higher mean pressure gradients across the mitral valve (7.8±3.7 mmHg, versus 4.2±1.9 mmHg, p=0.001), smaller mitral valve areas (1.76±0.4 cm², versus 2.4±0.6 cm², p=0.001) and higher pulmonary artery systolic pressures (50.6±12.7 mmHg, versus 39.7±20.2 mmHg, p=0.04) at latest follow-up. Mitral stenosis after a previous mitral repair is usually attributed to evolution of the rheumatic process and is characterized by fibrosis involving the leaflets, the commissures and the subvalvular apparatus. In a large series of repair for isolated rheumatic mitral regurge, mitral stenosis was identified as the cause of repair failure in 16% of reoperations and it occurred at a mean interval of 9.3 years. (5) However in our operative findings, the fibrosis was localized to the suture line between the patch and the native leaflet, making the free edge markedly shortened and tense and making the patch, in spite of its preserved height, unable to open freely in diastole, while sparing the rest of the valve. It also occurred at a much earlier stage of follow-up, with a mean delay of 2.2 years and in one case as early as 3 months. We believe therefore that this fibrotic reaction is unrelated to the rheumatic process, but is an inherent complication of the surgical technique, whereby increased initial tension on the

suture line generates an area of turbulence to the flow which leads to progressive pannus formation at the free edge of the patch, much in the same way that turbulence at the commissure makes it the seat of maximal fibrosis and calcification in native mitral stenosis, and that turbulence at the point of insertion of a mitral clip in a percutaneous edge-to-edge procedure leads to fibrosis and calcification at the clip. To our knowledge, this phenomenon of *de novo* stenosis has never been described before as a complication of pericardial patch augmentation of the posterior leaflet. Fragmentation of the posterior leaflet on the other hand seems to abolish this effect altogether, probably through a better distribution of tension across the longer free edge that it creates.

It was demonstrated before by Chauvaud et al. that mitral repair performed during rheumatic activity is related to a decline in the 10-year freedom from reoperation from 82% to 71%. (5) In our study, recent or ongoing rheumatic activity at the time of surgery was not associated with an increased risk of reoperation. Still the difference in this outcome may be due to the smaller sample and the shorter duration of follow-up.

Some concerns have been voiced about the risk of inducing SAM or systolic anterior motion of the mitral valve with this technique. (10) It was stated however that SAM does not occur after posterior leaflet augmentation, due to the tendency to oversizing of the ring but mainly due to the pliability of the pericardial patch which seems unable to push the anterior leaflet into the outflow tract. (8) We have not encountered a single case of SAM in our patients, in spite of our use of relatively large patches, and we therefore concur with the latter opinion.

On a final note, we are also convinced that the reported method of glutaraldehyde fixation of the autologous pericardium reliably protects it from calcification and shrinkage. Our intraoperative findings in the reoperated patients, as well as the echocardiographic follow-up of the rest suggest the absence of any significant deterioration of the patch. This is in concert with the follow-up reported by others. (5,10,11,13) Of particular interest is the recent publication of Shomura et al., where the patch was found intact up to 19 years after implantation. (14)

Conclusion

We conclude that posterior leaflet augmentation using a glutaraldehyde treated autologous pericardial patch is an effective operation for the repair of severe rheumatic mitral regurgitation resulting from leaflet retraction. It can be performed with low operative morbidity and mortality and, at a mean follow-up of 4.2 years, yields excellent midterm survival, coupled with freedom from mitral regurgitation, significant relief of symptoms and reverse left ventricular remodeling. The proposed modification of posterior leaflet fragmentation adds the advantage of preventing *de novo* mitral stenosis, and significantly reduces left atrial dimension and pulmonary artery systolic pressure. It is therefore recommended as the technique of choice for performing this operation.

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PREDICTORS OF RESIDUAL OR PROGRESSIVE TRICUSPID REGURGITATION AFTER SUCCESSFUL MITRAL VALVE SURGERY

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Background: Functional tricuspid regurgitation or TR is frequently associated with left sided valve lesions. Contrary to previously held belief, it does not always regress spontaneously following a successful mitral valve surgery. In some patients, functional TR will even continue to progress. Residual TR even if moderate was shown to significantly affect mid term survival and functional capacity. This work intends to investigate the factors predicting the course of untreated TR after mitral valve operations.

Material and methods: In the period between March 2011 and October 2012, 39 consecutive patients with no or mild TR undergoing isolated elective mitral valve surgery for rheumatic heart disease by the same surgeon, at the Cairo University Hospitals and the Nasser Institute were studied prospectively. Two-dimensional transthoracic echocardiography was performed within the week before surgery and 6 months postoperatively. In addition to routine measurements, tissue Doppler imaging was used to calculate the following parameters of right ventricular (RV) function: the fractional area change or FAC, the tricuspid annular plane systolic excursion or TAPSE, the lateral tricuspid annular systolic wave velocity or LASWV and the RV myocardial performance index or MPI.

Results: Although the overall grade of TR was significantly decreased at follow-up, 18 patients or 46% showed evidence of residual or progressive TR. Multivariate analysis defined atrial fibrillation ($p=0.002$), a tricuspid annulus > 3.4 cm ($p=0.04$), and a left atrial diameter > 4.1 cm ($p=0.04$) as strong predictors of residual TR. The degree of pulmonary hypertension, TAPSE and LASWV were all reduced postoperatively, but none of them had an impact on TR progression. The type of surgery performed (repair versus replacement with preservation of both leaflets) did not have an impact either.

Conclusion: It was concluded that, in patients with rheumatic heart disease, with preserved left ventricular function and less than moderate tricuspid regurgitation undergoing isolated mitral valve surgery, atrial fibrillation, tricuspid annular enlargement and left atrial dilatation are independent risk factors for residual or progressive tricuspid regurgitation, regardless of right ventricular function or pulmonary artery pressure.

Key words: Rheumatic heart disease, tricuspid regurgitation, tricuspid annuloplasty, tissue Doppler imaging, right ventricular function.

Functional tricuspid regurgitation (TR) is a common condition associated with left sided valvular lesions undergoing surgery. Its incidence in mitral valve patients with rheumatic heart disease is reported to be as high as 30-51% [1]. Contrary to traditional belief [2], TR does not always regress spontaneously after a successful mitral valve operation [3]. It was demonstrated that a substantial number of patients would continue to suffer from TR or even develop de novo TR after a variable interval from mitral repair or replacement [4]. Predicting which patients are likely not to have their TR improved is of paramount importance, since any residual TR that is more than mild was proven to significantly worsen mid-term survival and functional class [5].

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Many factors have been investigated as predictors of residual or de novo TR after mitral valve surgery, like advanced age, rheumatic aetiology, female gender, atrial fibrillation, left atrial enlargement, left ventricular dysfunction, tricuspid annulus diameter, grade of preexisting TR, pulmonary artery pressure, extent of subvalvular preservation during mitral replacement and prosthetic valve dysfunction [6]. Even though TR is known to be affected by preload, afterload and right ventricular or RV function, there is little information in the literature about the effect of right ventricular function on the course of functional TR after mitral valve surgery [7].

This work is aimed at investigating the possible clinical and echocardiographic variables predicting residual or progressive tricuspid regurgitation after a successful mitral valve operation in patients with rheumatic heart disease, with special emphasis on echocardiographic criteria of right ventricular function.

Material and methods

Patient selection

In the period between March 2011 and August 2012, 50 consecutive patients undergoing isolated elective mitral valve surgery for rheumatic heart disease, at the Cairo University Hospitals and the Nasser Institute were studied prospectively. They were operated upon by the same surgeon. The exclusion criteria were the following: other than rheumatic pathology, moderate or severe tricuspid regurgitation requiring tricuspid annuloplasty, more than mild aortic valve disease, pre- or postoperative left ventricular (LV) dysfunction defined as LV ejection fraction <50%, and inadequate correction of the mitral valve lesion.

Echocardiographic examination

Transthoracic echocardiography was performed twice for each patient: within one week before the operation and 6 months postoperatively. A commercially available machine was used (Vivid S5, General Electric Healthcare, Wauwatosa, WI). Every study consisted of the routine evaluation of a valvular patient by standard M-mode, two-dimensional and continuous wave Doppler techniques, with particular attention to tricuspid annular and RV dimensions. TR was graded according to the ratio of the regurgitant jet area or RJA to the surface area of the right atrium or RA: TR was considered mild if the RJA was < 20% of the RA, moderate if the RJA was between 20-50% of the RA, and severe if the RJA was > 50% of the RA. Pulmonary hypertension (PHT) was classified according to the following scaling of the pulmonary artery systolic pressure or PASP: it was described as mild if the PASP was between 30-44 mmHg, moderate if the PASP was between 45-59 mmHg, and severe if the PASP was \geq 60 mmHg. With the addition of tissue Doppler imaging or TDI, the following indices of RV function were also recorded: fractional area change or FAC (defined as end

diastolic area – end systolic area / end diastolic area x 100), tricuspid annular plane systolic excursion or TAPSE, lateral tricuspid annular systolic wave velocity or LASWV, and RV myocardial performance index or MPI (defined as isovolumetric relaxation time + isovolumetric contraction time / ejection time).

Operative procedures

A written and informed consent was obtained from every patient or his next of kin. The same surgeon, under transoesophageal echocardiographic or TEE guidance, performed all of the operations. After median sternotomy, mildly hypothermic (32°C) cardiopulmonary bypass was established through aorto-bicaval cannulation.

Myocardial protection was achieved by antegrade, intermittent, cold blood cardioplegia. Access to the mitral valve was through a standard left atriotomy incision. Following routine valve analysis, the decision to repair or replace the valve was taken at the surgeon's discretion. All the replacements were done using a standard interrupted suturing technique and a variety of commercially available bileaflet mechanical valves were implanted. Preservation of the subvalvular attachments of both leaflets was systematically performed. In case of mitral valve repair, standard techniques were employed, including commissurotomy, papillotomy, posterior leaflet augmentation with an autologous pericardial patch, leaflet decalcification or peeling, secondary chordal transfer and artificial chordae. The repair was always concluded by a rigid ring annuloplasty. Three patients underwent an unplanned tricuspid annuloplasty and were thus eliminated from the study. By TEE examination, all the patients had adequately functioning prosthetic valves or adequate repairs.

Statistical analysis

The SPSS statistical software package (version 20; SPSS Inc, Chicago, IL) was used for data analysis. Continuous variables were presented as mean \pm standard deviation and categorical variables as frequencies and percentages. Comparisons between the groups were made by Student's t-test for continuous variables and chi-square test for categorical variables. Multivariate analysis by stepwise logistic regression was done using Pearson's chi-square test or Spearman's rank correlation coefficient as indicated. Results were considered significant when probability (p) was \leq 0.05. Receiver operating characteristic curves or ROC curves were constructed to calculate cutoff values when needed with their respective sensitivity and specificity.

Results

Eleven patients were eliminated from the study due to the following reasons: there were 2 operative deaths, 3 patients underwent an unplanned tricuspid annuloplasty, one mitral repair patient had grade 2 mitral regurgitation at follow-up,

and 5 patients had impaired LV function (ejection fraction < 50%) at follow-up. Therefore, 39 patients remained for analysis and they constitute our study population. There were 24 females (61.5%) and 15 males (38.5%). Their age ranged from 20 to 60 years with a mean of 34.8±11.1 years. The incidence of atrial fibrillation was 13 patients or 33.3%. The original mitral valve lesion was regurgitation in 30 patients (76.9%), stenosis in 5 patients (12.8%) and mixed in 4 patients (10.3%). Baseline tricuspid regurgitation was absent in 14 cases (35.9%) and mild in 25 cases (64.1%). Twenty-one patients (53.8%) had no pulmonary hypertension or PHT, 10 patients (25.6%) had mild PHT, 7 patients (17.9%) had moderate PHT, and one patient (2.6%) had severe PHT. Mitral valve replacement was done in 23 patients or 59%, with preservation of both leaflets in 19 cases and preservation of only the posterior leaflet in 4 cases, whereas mitral valve repair was performed in 16 patients or 41%.

Echocardiographic follow-up at 6 months was 100% complete. The findings are summarized in tables I and II. No patient had prosthetic mitral valve dysfunction or an inadequate mitral valve repair, except for the one patient with moderate mitral regurgitation who was excluded from the study as mentioned before. There were 21 patients (53.8%) with no TR, 14 patients (35.9%) with mild TR, 4 patients (10.3%) with moderate TR and none with severe TR. Even though, compared to the preoperative state, the overall TR grade was significantly reduced (p=0.004), 18 patients (46%) were still identified with mild or moderate TR. They were clustered together for later multivariate analysis. The changes in TR grade at 6 months are illustrated in figure 1. With 31 patients (79.5%) having no PHT, 4 patients (10.3%) showing mild PHT, another 4 (10.3%) having moderate PHT, and none with severe PHT, the PHT grade at follow-up was also significantly lower, relative to the preoperative levels (p=0.002). There was also a significant decrease in left atrial diameter from a preoperative mean of 4.3±0.6 cm to a mean of 4.1±0.5 cm (p=0.03). Right ventricular (RV) dimensions remained unchanged, as well as the FAC and the MPI, while the TAPSE and the LASWV indices were both significantly depressed postoperatively (from 2.1±0.4 cm to 1.8±0.3 cm, p=0.002 and from 0.12±0.02 m/s to 0.1±0.01 m/s, p=0.04 respectively). The patients were divided according to the postoperative TR grade into 2 groups. The first group comprised 21 patients who were free of TR, 9 of whom had no TR preoperatively and 12 in whom TR improved from mild to none. The second group consisted of 18 patients with mild or moderate TR, among whom mild preoperative TR persisted in 9 patients, and preoperative TR progressed from none to mild in 5 patients and from mild to moderate in 4 patients. To investigate predictors of residual or progressive TR, the 2 groups were compared by stepwise logistic regression for the following factors: age, sex, atrial fibrillation, the original mitral valve lesion, preoperative TR grade, left atrial diameter, RV diameters, tricuspid annular diameter, preoperative evidence of depressed indices RV function (FAC, MPI, TAPSE and LASWV) according to

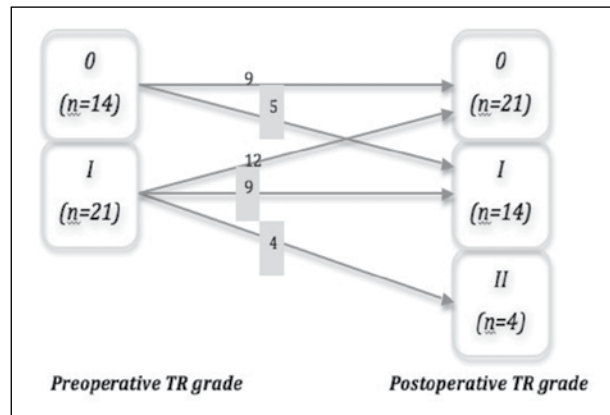


Fig 1. Changes over time in tricuspid regurgitation (TR) grade.

the thresholds formulated by Rudski et al. [8], preoperative pulmonary hypertension grade, postoperative improvement in pulmonary hypertension grade, and the type of surgery performed. The findings are listed in table III. Independent predictors of residual or progressive TR were atrial fibrillation (p=0.002), left atrial enlargement (p=0.04) and tricuspid annular dilatation (p=0.04). FAC impairment showed a trend of being associated with residual or progressive TR, but this trend did not reach statistical significance (p=0.09). ROC curve analysis yielded cutoff values of 4.1 cm for left atrial diameter (sensitivity=0.77, specificity=0.57), 3.4 cm for tricuspid annular diameter (sensitivity=0.78, specificity=0.67) and 31% for the FAC (sensitivity=0.85, specificity=0.56).

	Preoperative n=39	Postoperative n=39	p value
TR grade			
No TR	14 (35.9%)	21 (53.8%)	p=0.004
Mild	25 (64.1%)	14 (35.9%)	
Moderate	0 (0%)	4 (10.3%)	
Pulmonary Hypertension			
None	21 (53.8%)	31 (79.5%)	p=0.002
Mild	10 (25.6%)	4 (10.3%)	
Moderate	7 (17.9%)	4 (10.3%)	
Severe	1 (2.6%)	0 (0%)	

(TR=tricuspid regurgitation. Values are expressed as frequency and percentage)

Table I. Pre- and postoperative tricuspid regurgitation & pulmonary hypertension.

	Preoperative n=39	Postoperative n=39	p value
LA diameter	4.3±0.6 cm	4.1±0.5 cm	0.03
RV diameter			
Basal	3.7±0.6 cm	3.7±0.6 cm	p=0.2
Mid level	2.8±0.6 cm	2.9±0.5 cm	p=0.4
Longitudinal	6.9±0.8 cm	6.9±0.7 cm	p=0.6
FAC	37±12 %	42±13 %	p=0.2
MPI	0.44±0.13	0.45±0.12	p=0.4
LASWV	0.12±0.02 m/s	0.1±0.01 m/s	p=0.04
TAPSE	2.1±0.4 cm	1.8±0.3 cm	p=0.002

(LA= left atrial, RV=right ventricular, FAC=fractional area change, MPI= myocardial performance index, LASWV= lateral tricuspid annular systolic wave velocity, TAPSE=tricuspid annular plane systolic excursion. Values are expressed as mean ± standard deviation or as frequency and percentage)

Table II: Pre- and postoperative LA & RV diameters and function indices.

	No TR n=21	Residual/ progressive TR n=18	p value
Age > 30 years	14(66%)	15(83%)	0.2
Female	12(57%)	12(66%)	0.4
Atrial fibrillation	2(9%)	11(61%)	0.002
LA > 4.1 cm	9(43%)	14(78%)	0.04
TA > 3.4 cm	4(19%)	12(66%)	0.04
Dilated RV	2(9%)	3(16%)	0.3
Preoperative PHT	8(38%)	10(56%)	0.4
Improved PHT	8(38%)	4(22%)	0.2
FAC < 31%	10(47%)	14(78%)	0.09
Impaired TAPSE	4(19%)	3(16%)	0.2
Impaired LASWV	4(19%)	5(28%)	0.2
Impaired MPI	2(9%)	4(22%)	0.3
Repair /replacement	9(43%) /12(57%)	7(39%) /11(61%)	0.8

((LA= left atrial, TA=tricuspid annulus, RV=right ventricle, PHT= pulmonary hypertension, FAC=fractional area change, LASWV= lateral tricuspid annular systolic wave velocity, TAPSE=tricuspid annular plane systolic excursion, MPI= myocardial performance index. Values are expressed as frequency and percentage)

Table III. Predictors of postoperative residual or progressive tricuspid regurgitation.

Discussion

It has been increasingly recognized that intraoperative grading of tricuspid regurgitation or TR by TEE is not the most reliable method to determine the need for a tricuspid annuloplasty in conjunction with a mitral valve operation. This is due to the knowledge that TR is heavily dependent on preload and afterload, which are usually affected by operative conditions such as volume depletion by prior diuresis or the long period of fasting, and the vasodilator effect of general anaesthetic agents [9]. Consequently, other parameters emerged as more reliable indicators of tricuspid valve function; the most frequently embraced being the tricuspid annular diameter, made popular by Raja and Dreyfus [10]. There is no consensus however on the cutoff value which ranges between 3.4 to 4 cm [11]. The cutoff value of 3.4 cm which we have reached seems in agreement with the most aggressive trend in accurate evaluation [12]. Since two-dimensional echo seems to underestimate the tricuspid annulus, some authors also suggested the use of three-dimensional echo for tricuspid annular measurement [9]. It is noteworthy however that all of the previous estimates rely on measuring the anteroposterior dimension of the annulus, while it has been proposed that direct surgical measurement of the anteroposterior diameter of the annulus which is almost invisible by two dimensional echo, with a limit of 7 cm, would be more reliable and is indeed part of the routine practice of some teams in every mitral valve operation [9,10].

It has been our surgical strategy to perform a concomitant tricuspid annuloplasty in left sided valve procedures whenever the degree of TR is moderate or severe. This explains why, in recruiting patients for the present study, only those with no TR or mild TR were enrolled. Since this patient population would appear to be, for practical purposes, virtually free of TR to start with, it would have been expected that, at such a short period of follow-up, no discernible effect would be detected. Nevertheless, there were detectable changes already at 6 months of follow-up, with

18 patients or 46% showing persistent or progressive TR, in spite of good LV performance and adequate mitral valve function. It seems then that these patients, as explained by Dreyfus and coworkers, were not actually free from tricuspid regurgitation but were in the first stage of the disease where the annulus dilates and leaflet coaptation decreases. The second stage is characterized by more annular enlargement and overt regurgitation, and the third stage by papillary muscle displacement leading to leaflet tethering. Apparently, once this disease process sets in, it does not always regress spontaneously after correction of the mitral lesion but becomes independent from it. [13]

It could be argued that our finding of 4 patients or 10.2% with moderate TR at 6 months of follow-up is not a heavy burden. However, it was demonstrated that a moderate residual

TR decreases 8-year survival from 90% to 78% after a mitral valve operation [5]. This is therefore not an entirely benign condition as the number

We have not observed any impact for the type of surgery performed on the mitral valve, meaning repair versus replacement, on TR progress. This is explained by the fact that most of the replacements were done with preservation of the subvalvular attachments of both leaflets. In a large series of 801 patients with less than moderate TR undergoing isolated mitral valve replacement, Garcia Fuster and coworkers reported that the incidence of late progressive TR decreased from 10.8% with preservation of the posterior leaflet alone to 2.4% with preservation of both leaflets [7]. Since the deleterious effect of mitral replacement on TR progression seems to be related to lack of leaflet preservation, it appears therefore that total preservation possibly bridges the gap between replacement and repair regarding this issue.

Although we started out with a patient population with preserved RV function, we observed a slight decline in two of the RV functional parameters at 6 months, namely the LASVW and the TAPSE, that was statistically significant, even if numerically it was not severe enough to characterize these ventricles as impaired [8]. We hypothesize that mitral valve surgery by itself might impart a certain damage to RV function, either due to the ischemia / reperfusion injury of aortic cross-clamping, the effect of the pericardiotomy on RV loading conditions, or the postoperative paradoxical septal wall motion which could lead to RV embarrassment. We did not observe however any correlation between RV function or pulmonary artery pressure and TR progress. This finding is similar to widely held views in the literature [14,15].

Also in harmony with previously published reports, we were able to identify atrial fibrillation and left atrial enlargement as strong predictors for residual TR [5-7]. This has made a valid reason for the systematic performance of a Maze procedure in mitral patients with AF, which was shown to significantly decrease the incidence of progressive TR, especially in the patients in whom not only normal electric atrial activity but also mechanical atrial activity was restored [16]. One unexpected others [5-7]. In any case, it could make an argument for an aggressive policy of left atrial plication in mitral valve surgeries and it could be the basis for future research on the impact of such a policy on TR progression.

Conclusion

We conclude that, in patients with rheumatic heart disease with preserved left ventricular function and less than moderate tricuspid regurgitation undergoing isolated mitral valve surgery, atrial fibrillation, tricuspid annular enlargement and left atrial dilatation are independent risk factors for residual or progressive tricuspid regurgitation. A subtle decrease in right ventricular function and a

significant reduction in pulmonary hypertension were noted in these patients, but were both of no effect on the outcome. A liberal indication for tricuspid annuloplasty is recommended in these cases, independently of right ventricular function or pulmonary artery pressure. If the mitral valve is to be replaced, complete subvalvular preservation seems to be equal to repair regarding its impact on tricuspid valve function and therefore should be attempted in every case.

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Recurrent Achalasia After Cardiomyotomy

Thoracic

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Background: From the many surgical options available, there is no consensus about how persistent or recurrent dysphagia after myotomy should be treated. In this study we evaluated our experience with reoperation following previous surgery.

Methods: We reviewed the medical records of 14 patients (8 men and 6 women; mean age 49 years) who underwent reoperations for achalasia between January 2000 to August 2010.

Results: The mean interval between the two surgeries was 56 months. In all patients the abdominal approach was done . Mean satisfaction score was 8 (out of 10) and 86% had an improvement in symptoms.

Conclusions: Selecting surgical procedures based on the causes and conditions of recurrence led to symptomatic improvement and acceptable outcomes.

The term Achalasia, which means failure of the lower esophageal sphincter (LES) to relax, was given by Sir Arthus Hurst in 1927, it was known before as cardiospasm. The incidence is 1 per 100,000 persons.⁽¹⁾ The condition can occur at any age, with no gender predilection, and was described from infancy to the 9th grade with the majority of patients between 20 and 40 years. Achalasia is a primary esophageal motor disorder characterized by impaired relaxation of the lower esophageal sphincter, and loss of esophageal body peristalsis. In South America many patients have infestations by *Trypanosoma cruzi* as an underlying pathogenesis Chagas disease.^(1,2)

Histologically, the most common finding is a decrease or loss of myenteric ganglionic cells. The cause of ganglion cell degeneration is unknown, although an association with class II HLA antigen DQw1, implicating an autoimmune mechanism has been described. The ganglionic loss leads to selective loss of inhibitory nerves that results in unopposed stimulation of the smooth muscle fibers of the LES.⁽²⁾

The predominant symptoms of dysphagia are secondary to progressive relative obstruction at the gastroesophageal junction. Treatment is directed at lowering the resistance of the LES. Interventions for achalasia include surgery open or endoscopic, dilatation, botulinum toxin injection and pharmacological therapy, but surgical treatment is the most effective.^(1,3)

Recurrent achalasia after surgical relief constitute a considerable challenge to the surgical team, It occurs in 10-20% of cases.^(4,5) Causes includes an incomplete myotomy, adhesions from previous surgery, fibrosis around the gastroesophageal junction and a tight fundoplication. The risk of perforations is higher. Being a rare disease, there are few reports on reoperations after surgery for achalasia.⁽⁵⁾

In this study we reviewed 14 patients who needed reintervention after surgery for persistent or recurrent dysphagia.

Patients and Methods

From January 2000 to August 2010, 312 patients underwent modified Heller myotomy for achalasia by surgeons from the Cardiothoracic Surgery Department, Alexandria University. 14 patients required reintervention, 2 patients underwent their primary surgery elsewhere. All patients were investigated with barium swallow x-

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ray, upper gastrointestinal endoscopy fiberoptic and rigid. The reoperative strategy was determined by the preferences of the operating surgeon. From the 14 patients five patients had previous balloon dilatation.

The surgical steps included reversal of any previous fundoplication, mobilization of the anterior and lateral aspects of the distal part of the esophagus. A re-myotomy was performed and extended from approximately 4cm below to 12 cm above the gastroesophageal junction.

We evaluated the approaches used for the primary operation, surgical procedures, timing of the reoperation, indications for reoperation, surgical procedure at reoperation, and postoperative courses.

After reoperation, patients were contacted by phone, they were asked about: dysphagia, odynophagia, chest pain, heart burn and cough (scale= never, once a month, few times a week and daily). Overall satisfaction with the result was determined (0= totally dissatisfied; 10 = totally satisfied)

Results

From June 2002 to September 2011, 14 patients were referred for recurrent dysphagia after the initial procedure. Two patients were referred to us following primary surgery at another location. The primary operation were laparoscopic Heller myotomy in 8 patients (57%), open Heller-Dor cardioplasty in 3 (21%) patients and open Heller myotomy without an anti-reflux procedure 3 patients. There were 6 women and 8 men, and the age ranged from 28-73, with mean age of 49 years. Three patients had a previous thoracic approach and 3 patients via the abdomen. Symptoms occurred within the first year after

surgery in 8 patients (57%), and in fact two of them stated that there dysphagia did not change after surgery. Three patients had moderate improvement in dysphagia after the first myotomy but worsened in the following 2 years, the remaining three patients had an initially good result but then developed recurrent symptoms 4-5 years after. These symptoms included dysphagia, heartburn, chest pain or a combination of these complaints. Recurrence occurred between 1 and 60 months (mean 18 months) after the initial operation.

All 14 patients were investigated with a preoperative barium swallow x-ray, In 12 of them a dilated esophagus was identified. The extent ranged from mild dilatation to an elongated tortuous sigmoid esophagus. They all underwent upper gastrointestinal endoscopy.

Re-myotomy was performed after one year to 10 years, abdominal approach was our choice in 12 patients while in two patients pneumatic dilatation (Balloon dilatation) was done, due to previous three laparotomies in one patient and partial gastrectomy with gastro-jejunostomy for the management of perforated gastric ulcer in the second patient. Operating time ranged 90 to 235 minutes (mean 149 minutes), the median blood loss was 120 ml. The median postoperative hospital stay was 5 days (range 4-11 days)

Factors contributing to failure of the primary surgery included inadequate myotomy (57%) (n=8), adhesion or fibrosis and a band of scar tissue at the gastroesophageal junction (21%) (n=3). Slipped Nissen in two patients. In the eight patients with incomplete myotomy a further myotomy was undertaken, taking care to extend this well onto the stomach, and as far proximally as possible, the mean length of the new myotomy was 12cm.

No	Age	Sex	First Approach	First surgery	Reason for failure	Time of Symptoms
1	44	F	Lap	Heller	Incomplete myo	2 months
2	28	M	Abdomen	Heller-Dor	Myotomy fibrosis	2 years
3	56	M	Abdomen	Heller-Dor	slipped nissen	3 months
4	73	M	Lap	Heller	Poor emptying, thick muscle	1 month
5	39	F	Lap	Heller	Incomplete myotomy, diverticulum	2 years
6	47	M	Chest	Heller	Myotomy fibrosis	4 years
7	55	F	Chest	Heller	Incomplete myotomy	6 months
8	62	M	Chest	Heller	Incomplete myotomy	12 months
9	30	M	Abdomen	Heller-Dor	Scar tissue at GEJ	5 years
10	41	M	Lap	Heller	Incomplete myotomy	6 months
11	48	F	Lap	Heller	adhesion	4 years
12	58	M	Lap	Heller	Incomplete myotomy	7 months
13	66	M	Lap	Heller	Incomplete myotomy	6 months
14	42	M	Lap	Heller	Incomplete myotomy	4 months

Table 1. Clinical characteristics of patients

Pt No	Procedure Performed	Time after first Surgery	Operative Time (min)	Complications
1	Re-myotomy	4 years	160	None
2	Re-myotomy	6 years	185	None
3	Repair of hiatal hernia	9 years	140	None
4	Re-myotomy	1 year	130	Bleeding
5	Ballon dilatation ,	10 years	153	None
6	Remyotomy	5 years	98	None
7	Remyotomy	1 year	111	None
8	Re-myotomy	5 years	90	None
9	Remyotomy	7 years	230	None
10	Re-myotomy	1 year	149	None
11	Balloon deletions	8 years	235	None
12	Re-myotomy	2 years	124	None
13	Balloon deletion	6 years	144	Bleeding
14	Re-myotomy	3 years	138	None

Table 2. Operative detail

Follow-up for patients was done for 5 years . Symptoms after redo surgery is shown in Fig 3. Nine patients were able to eat an unrestricted diet. All patients except one experienced an improvement in the overall outcome (including dysphagia, odynophagia, heartburn and chest pain). This patient with persistent dysphagia underwent a trial of pneumatic dilatation .

Discussion

Around 10 to 15% of patients have persistent or recurrence of symptoms after the initial procedure^(5,6,7). Most of these patients have clinically important symptoms of dysphagia with or without reflux symptoms, and these symptoms improved significantly in most patients. (Fig. 3)

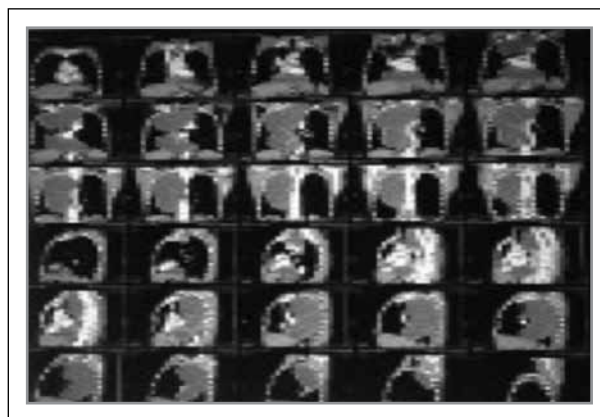


Fig. 2. CT of the same patient



Fig. 1 Chest X ray for patient with huely dilated esophagus

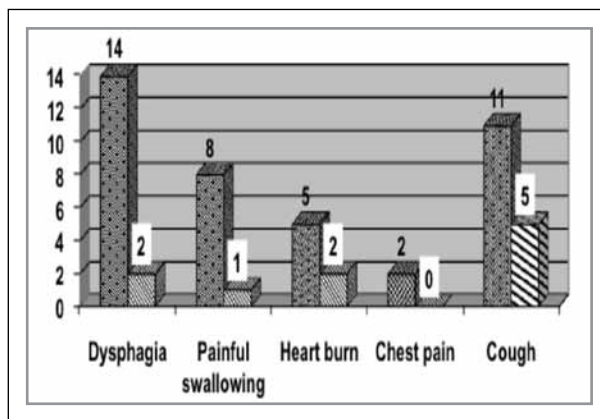


Fig. 3 Symptomatic result

Thoracic

Endoscopic dilatation is considered as the first option in association with medical treatment with proton pump inhibitors when symptoms of gastroesophageal reflux is present. There are few reports on reoperation because of the limited number of surgical cases of achalasia, and even fewer reports on redo surgery after laparoscopic surgery, which was introduced in 1991.⁽⁶⁾

In this series of patients, it was the decision of our institution to choose the abdominal approach whatever the first approach was, because our early experience showed that there is always adhesions in the lower end of the esophagus that may be attached to the liver, which can be accessed safely from the abdominal approach.

The reported causes for reoperation for achalasia include incomplete myotomy, myotomy fibrosis (scarring of the myotomy), fundoplication disruption, tight fundoplication new onset reflux symptoms, mega-esophagus and incorrect diagnosis.^(7,8,9) It is difficult to differentiate inadequate myotomy and readhesion or fibrosis after myotomy from preoperative investigations such as endoscopy and barium. An incomplete myotomy or a band of scar tissue at the gastroesophageal junction were thought to be the cause of recurrent or persistent dysphagia in most of our patients. However in 2 cases the exact reason could not be identified maybe a combination of both factors. This was sometimes because we undertook all the revision surgery from the abdomen, and in cases with previous thoracotomy operation the myotomy is on the left posterolateral part of the esophagus while we do the myotomy on the anterior wall of the esophagus from the laparotomy. Hence, our strategy is to extend the myotomy as far as possible both proximally and distally irrespective of whether the previous myotomy was thought to have been adequate or not.

In many reviews, the ideal length of myotomy that relieves dysphagia and minimizes the occurrence of reflux is controversial. Most reports describe from 5 mm to 2 cm gastric myotomy, in our patients the distal myotomy was performed until 4 cm below the gastroesophageal junction which provide good results and similar to other studies.^(4,9,10)

However, it was done in only three patients because in our institution the incidence of reflux is low after the primary surgery, and we are afraid that it may contribute to dysphagia, and if there is any reflux it is treated medically with good results.

It is known that symptoms of dysphagia due to incomplete myotomy or adhesions and scarring recurs early in the first 3 years.^(11,12,13)

We followed the patients 3 months to 6 years showed that 2 patients still experience some symptoms of dysphagia and or odynophagia. The mean overall satisfaction score of 8 in our patients and they stated that they made the right decision to undergo a redo surgery after multiple trial of pneumatic dilatation. In most improvement was achieved. This is comparable with results from other studies, where between 80 to 100% of patients have benefited from surgical revision.⁽⁵⁾ Balloon dilatation has been reported to achieve a variable success rate, ranging from 33% to 80%,⁽⁴⁾ and it is short term improvement.

In conclusion

Reoperation for persistent or recurrent achalasia is a safe operation, resulting in a good outcome, however the timing of the operation is not clear and the results of the investigation should be taken with caution, taking into consideration each patient's individual symptoms. Although the great enthusiasm on laparoscopic myotomy, we found that recurrence of symptoms due to inadequate myotomy was higher with laparoscopic approach we recommend that it should be done only with experienced surgeon taking care to extend the myotomy to the required length. Finally we recommend the abdominal approach even if it is used before because of the dense adhesion that may connect the lower esophagus to the liver which can be accessed only with this approach

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Management of Malignant Pleural Effusion: Comparative Study Between Doxycycline, Bleomycin and Povidone-Iodine

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Background: Malignant pleural effusions are commonly managed with tube thoracostomy drainage followed by chemical pleurodesis. Doxycycline, bleomycin and povidone-iodine have been shown to be effective for intrapleural injection, although no agent has definitively proved advantages over the other. The aim of the present study was to compare these three agents in terms of response rate and side effects.

Patients and methods: A prospective, randomized trial was carried out between May 2008 and March 2011. One hundred twenty patients with proved malignant pleural effusion received either intrapleural doxycycline (0.5 g), bleomycin (60 mg) or povidone-iodine 10% (20 mL in 30 mL saline 0.9 %) after the same drainage procedure. Demographic and clinical data were comparable in all groups. Response was evaluated at 1, 3 and 6 months after pleurodesis.

Results: Time to relapse did not differ between all groups. No statistically significant differences were found in terms of efficacy at different intervals of follow up. Overall recurrence of pleural effusion was 22 (55 %), 17 (42.5 %) and 22 (55 %) during follow-up in the doxycycline, bleomycin and povidone-iodine groups respectively. Additional drainage procedures were needed in 6 (15 %), 6 (15 %) and 7 (17.5 %) in the doxycycline, bleomycin and povidone-iodine groups respectively. Fever was noted only in bleomycin-treated patients while pain was most frequent in the doxycycline group without statistical significance.

Conclusion: Since no agent was superior to the other in this trial, we suggest that suspected anaphylaxis and drug availability should be considered in the choice of a sclerosing agent.

KEYWORDS: Malignant pleural effusion- pleurodesis- doxycycline- bleomycin- povidone iodine.

Recurrent and symptomatic pleural effusions are common in patients with malignancy. Up to 25% of patients with lung cancer and 50% of patients with breast cancer will develop a pleural effusion. Mesothelioma, breast and lung cancer, account for the majority of malignant pleural effusions [1]. A minority of effusions remains asymptomatic and few cancers involving the pleura can be cured by specific antineoplastic or hormonal treatment. Therefore, the majority of patients will need a procedure to remove the fluid and prevent recurrence. A therapeutic drainage should be performed. This usually leads to symptomatic relief and reliefs trapped lung. However, pleurodesis is considered the best palliative therapy for the treatment of recurrent malignant pleural effusions [2].

Pleurodesis with a chest tube drainage and intrapleural instillation of a chemical agent is the most effective methods for controlling a malignant pleural effusion (3,4). A wide variability exists in the choices of sclerosing agents. Talc, tetracycline and bleomycin have been widely used for pleurodesis. Considering these agents, povidone-iodine, an iodine based topical antiseptic, is extensively used as an sclerosing agent (2). Many studies have shown the effectiveness of povidone-iodine to achieve a complete response rates 80-90% in the management of pleural effusion. On the other hand some side effects including thyroiditis and even visual loss has been reported (5), however it is the cheapest agent available. Previous studies have compared the effectiveness of

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talc with other agents including tetracycline, doxycycline and bleomycin (6). Bleomycin is widely used; however it is much more expensive compared to povidone-iodine. Besides there is not enough evidence demonstrating the efficacy of bleomycin compared to povidone-iodine and doxycycline. The purpose of this study was to compare the choice of the sclerosing agent, which is not only determined by the efficacy of the agent but also by its cost, accessibility, safety, ease of administration and the efficacy to achieve a complete response .

Patients and Methods

A prospective randomized trial was carried out between May 2008 and March 2011. One hundred twenty patients with proved malignant pleural effusion received either intrapleural doxycycline (0.5gm), bleomycin (60 mg) or povidone-iodine 10% (20 mL in 30 mL saline 0.9 %) after the same drainage procedure. Response was evaluated at 1, 3 and 6 months after chemical pleurodesis.

All Patients were subjected to detailed clinical evaluation including history talking and examination, plain chest X-ray postero-anterior (P-A), while computed tomography (CT) was done for few cases. The preoperative demographic data of study patients in the three groups is shown in table (1) without any statistical significant difference between groups.

In our study, the following symptoms (dyspnea, pain, cough and hemoptysis) were the presenting symptoms where as dyspnea was present in all patients, while hemoptysis was rarely present. Radiological evaluation of the amount of pleural effusion, other opacities or loss of lung volume were done. Table (2) shows these details.

The criteria for diagnosis of malignant pleural effusions were based on the evidence of malignant disease in the chest or else where in the body , positive cytological examination for malignant cells in the pleural fluid and/or positive lymph node biopsy for metastatic or pleural biopsy for primary tumour or secondary invasion.

	Doxycycline	Bleomycin	Povidone-Iodine	P value
Age yrs	59±15	58±11	60±12	0.879*
Male/female	17/23	18/22	19/21	0.904*
Primary site of tumour n				
Mesothelioma	9 (22.5 %)	13(32.5 %)	11(27.5 %)	
Breast	13 (32.5 %)	9 (22.5 %)	10 (25 %)	
Lung	3 (7.5 %)	5 (12.5 %)	4 (10 %)	
Stomach	2 (5 %)	1 (2.5 %)	1 (2.5 %)	
Rectal	0 (0 %)	1 (2.5 %)	0 (0 %)	0.928*
Ovarian	2 (5 %)	2 (5 %)	1 (2.5 %)	
Lymphoma	2 (5 %)	2 (5 %)	3 (7.5 %)	
Osteosarcoma	2 (5 %)	3 (7.5 %)	2 (5 %)	
Thyroid	0 (0 %)	1 (2.5 %)	1 (2.5 %)	
Melanoma	0 (0 %)	1 (2.5 %)	0 (0 %)	
Unknown	7 (17.5 %)	2 (5 %)	7 (17.5 %)	
Metastatic sites n				
0	9 (22.5 %)	8 (20 %)	7 (17.5 %)	
1	16 (40 %)	14 (35 %)	13(32.5 %)	0.919*
2	9 (22.5 %)	10 (25 %)	9 (22.5 %)	
≥3	2 (5 %)	5 (12.5 %)	5 (12.5 %)	
Unknown	4 (10 %)	3 (7.5 %)	6 (15 %)	
Prior surgery	14 (35 %)	13 (32.5 %)	13 (32.5%)	0.963*
Prior chemotherapy	18 (45 %)	17 (42.5 %)	18 (45 %)	0.967*
Prior irradiation	9 (22.5 %)	10 (25 %)	12 (30 %)	0.737*

*: Data is not statistically-significant

Table 1. Characteristics of patients in treatment groups

	Doxycycline	Bleomycin	Povidone-Iodine	P value
Symptoms				
Dyspnoea	40 (100 %)	40 (100 %)	40 (100 %)	-
Chest pain	21 (%)	23 (%)	21 (%)	0.874*
Cough	24(%)	22(%)	25(%)	0.786*
Hemoptysis	3(%)	3(%)	4(%)	0.897*
Chest X-ray				
Effusion only	14(%)	15(%)	13(%)	
Pulmonary nodules	9(%)	10(%)	11(%)	0.994*
Pleural masses	10(%)	8(%)	8(%)	
Loss of lung volume	7(%)	7(%)	8(%)	
Size of effusion				
Moderate	23(%)	25(%)	24(%)	
Massive	17(%)	15(%)	16(%)	0.901*

*: Data is not statistically-significant

Table 2. Presenting symptoms and radiographic features

Exclusion criteria

Previous attempts at pleurodesis with other agents, known hypersensitivity to any sclersant material, incomplete re-expansion of the lung after tube thoracotomy and/or patients with known thyroid disease.

Technique

The insertion of intercostal tube was indicated clinically and radiologically. In all of our patients, the 5th intercostal space in midaxillary line was site for the tube insertion. The tube was allowed to drain the pleural fluid continuously. Some of our patients were distressed and suffered from severe dyspnea due to rapid evacuation of the pleural fluid and the associated rapid expansion of the underlying lung. This necessitated an intermittent withdrawal of the fluid by clamping the tube every few minutes to allow gradual evacuation. The complete evacuation of the pleural space was confirmed by mild oscillation of the fluid column in the underwater tube which denoted that the lung has expanded to occupy the place of the withdrawn fluid, auscultation of the chest would reveal marked improvement of air entry after removal of the fluid and X-ray of the chest was also necessary to show if there was any residual fluid remaining in the pleural space and if the underlying lung expanded completely.

Then the tube was clamped close to the chest wall and disconnected from the underwater seal bottle. Premedication in the form of 2mg/kg lidocaine (xylocaine) in 50 ml of normal saline was injected through the chest tube. Doxycycline (500 mg) diluted in 20cc distilled water then injected into pleural cavity through chest tube in 40 patients. While povidone-iodine

pleurodesis solution contains mixture of 20 ml of 10% iodopovidine and 80 ml normal saline was injected into pleural cavity through tube in another 40 patients. In the 3rd group, 60 mg of bleomycin diluted in 100 ml normal saline solution was instilled. Then the patient was allowed to change his position repeatedly every 10-15 minutes for 2-3 hours to permit complete dispersal of the drug over the whole pleural surfaces.

The chest tube was strictly observed to avoid its blockage by clot or kink or slipping. The patient was followed up with chest x-ray to show the degree of clearance of the fluid and the expansion of the lung and then the tube was removed. The patient was then followed up clinically and by radiologically after removal of the chest tube. The patient was then discharged to be followed up by clinical and radiological examination.

Statistical analysis

Data were collected, tabulated, statistically analyzed by computer Using SPSS version 16. Quantitative data expressed in. mean (x) and standard deviation (SD).and analysed by *k-test*: to study statistical relation between more than two quantitative none normally distributed variables.

Results

In our study groups, adverse effects of chemical pleurodesis were chest pain, fever, nausea and / or vomiting and hypersensitivity reactions. There were no statistically significant differences as shown in table (3). Chest pain was the main adverse effect in Doxycycline group, while fever was only present in Bleomycin group. Povidone-iodine group was the least to show adverse effects (table 3).

The efficacy of pleurodesis was defined as: complete (absence of pleural fluid re-accumulation), partial (residual pleural fluid or asymptomatic fluid re-accumulation, which did not require additional procedures), or failure (additional pleural procedures were required). Table (4) shows the response of different groups to chemical pleurodesis after 1, 3 and 6 months. Time to relapse did not differ between all groups. No statistically significant differences were found in terms of efficacy at different intervals of follow up. Overall recurrence of pleural effu-

sion was 22 (55 %), 17 (42.5 %) and 22 (55 %) during follow-up in the doxycycline, bleomycin and povidone-iodine groups respectively. Additional drainage procedures were needed in 6 (15 %), 6 (15 %) and 7 (17.5 %) in the doxycycline, bleomycin and povidone-iodine groups respectively. Only one patient in povidone-iodine group showed partial resolution after 3 months duration and then required drainage procedure after 6 months (added to failure of pleurodesis in this group after 6 months). All groups showed no statistical significant difference.

	Doxycycline	Bleomycin	Povidone-Iodine	P value
Pain during instillation	13 (32.5 %)	8 (20 %)	7 (17.5 %)	0.236*
Fever	0 (0 %)	7 (17.5 %)	0 (0 %)	-
Nausea/vomiting	2 (5 %)	3 (7.5 %)	1 (2.5 %)	0.59*
Hypersensitivity reaction	0 (0 %)	1 (2.5 %)	3 (7.5 %)	0.164*

*: Data is not statistically-significant

Table 3. Adverse effects of chemical pleurodesis

St. group	Doxy		Bleo		Povi.		p
	No	%	No	%	No	%	
1 month							
NA	0	0.0	0	0.0	0	0.0	0.785*
CR	18	45.0	23	57.5	19	47.5	
PR	16	40.0	11	27.5	14	35.0	
Failure	6	15	6	15	7	17.5	
3 month							
NA	3	7.5	3	7.5	4	10.0	0.787*
CR	15	37.5	22	55.0	17	42.5	
PR	16	40.0	10	25.0	14	35.0	
Failure	6	15	5	12.5	5	12.5	
6 month							
NA	7	17.5	8	20.0	7	17.5	0.642*
CR	14	35.0	20	50.0	13	32.5	
PR	14	35.0	8	20.0	15	37.5	
Failure	5	12.5	4	10.0	5	12.5	

NA: not available (patient lost to follow-up, or death); PR: partial response; CR: complete resolution.

*: Data is not statistically-significant

Table 4. Response to chemical pleurodesis

Discussion

Malignant pleural effusion is a major common problem leading to a significant dilemma regarding quality of life due to symptoms such as dyspnea and cough. Palliative management of malignant pleural effusion should aim at improving the quality of life with minimal complications. Optimal outcome as definition and as a mode of management entails variety of controversies. The aim of pleurodesis in these patients is to prevent reaccumulation of the effusion and avoid the need for repeated thoracentesis or intercostal tube drainage.

Pleural effusion is a common complication of malignant diseases occurring in 50% to 70% of all malignancies in the course of their illness (7). Carcinoma of the lung is the most common malignancy to invade the pleura (30%) and produce malignant and para malignant effusions (8). Carcinoma of the breast is second in incidence (25%) (9). The frequency declines markedly with ovarian and gastric cancer representing 5% or less of malignant pleural effusions. Lymphoma accounts for approximately 20% of the malignant pleural effusions and is the most common cause of chylothorax (10). A less common cause of malignant pleural effusion other than metastatic carcinoma, is malignant mesothelioma (11). Unlike ours, mesothelioma is the most common cause in our series. Mesothelioma and breast cancer constituted more than half of our studied cases. This difference may be attributed to early diagnosis of mesothelioma and bronchogenic carcinoma. An early manifestation of malignant mesothelioma is pleural effusion that is reabsorbed or organized and then largely replaced by tumor and fibrosis while malignant effusion is a late manifestation in bronchogenic carcinoma.

Patients with carcinoma involving the pleura most often present with symptoms attributable to a large pleural effusion, dyspnea on exertion and cough (12). The presence and degree of dyspnea depends on the size of the effusion and the patient's pulmonary function. Thoracentesis or intercostal tube thoracostomy results in relief of dyspnea in most of the patients (13). These results were similar to ours, in which dyspnea was present in all of our patients, while chest pain and cough were present in slightly more than fifty percent of our patients. The mechanism of dyspnea caused by a large pleural effusion probably entails a decrease in the compliance of the chest wall, a contra-lateral shift of the mediastinum, and a decrease in ipsilateral lung volume. Also endobronchial lesion that causes atelectasis or an infiltrative malignant disease of the pulmonary parenchyma may also contribute to dyspnea and cough (10).

Since malignant involvement of the pleura signifies advanced disease, these patients commonly have weight loss and appear chronically ill. Chest pain is often present because of the involvement of the parietal pleura, ribs or chest wall. However, 25% of patients may be asymptomatic at the time of presentation (12). Unlike us, others found that chest pain is the most common presenting symptom and occurs in 60-70% of patients. Dyspnea and cough were found about 20-25% of patients (10).

Variation in the definition of recurrence (radiological and clinical) may account for some discrepancies among studies. Mohsen and associates (14) found povidone—iodine pleurodesis as a safe and also effective alternative means of preventing the recurrence of malignant pleural effusion at 30 days post-procedure. Povidone—iodine is a topical antiseptic, and is less commonly used as a sclerosing agent. The reported success rates range from 64% to 96% (15, 16), whereas Moshen and associates (14) found the success rate 85%.

Chest pain and fever are the most common adverse effects of all pleurodesis agents. The iodine—povidone population tended to have less analgesic requirements and no recorded pyrexia incidents but these did not reach statistical significance. Concerns that povidone—iodine might be associated with visual loss were reported by Wagenfeld et al. (5) in three cases during VATS. However, authors used an unusual amount of 200—500 ml of 10% povidone—iodine 'Jodobac'. They also noted that the safe amount to be used is 20 ml of 10% iodine, which is actually the amount that we have used in our study. As an additional safety practice, we administered this dose in a diluted form (in normal saline). Moreover, Wagenfeld et al. (5) reported that they used Jodobac in patients who had normal pleura (patients who had pneumothorax), which might have increased absorption and toxicity (5). In our study (as others (14)), we used iodine only in malignant effusions with pathological pleura that has a poor absorption potential (that could partly explain the pathophysiology of accumulated pleural effusion). We strongly believe that this practice has significantly increased povidone safety in our study, as none of our patients encountered any loss of vision.

There was not any statistical significant difference between groups in pain after procedure and other adverse effects and the recurrence of pleural effusion in one month follow up after procedure. Ali and coworkers (17), also reported nearly same results in their study comparing iodine and bleomycin.

The mechanism by which povidone-iodine works is not clear; it is thought to be related to the low pH of the sclerosing solution. On the other hand bleomycin is an anti-neoplastic antibiotic. It has sclerosing properties which is widely used for pleurodesis. It has minimal toxic reactions and is cleared by kidneys (4, 18-20).

Previous studies have repeatedly shown the efficacy of povidone-iodine and bleomycin in the management of malignant pleural effusion separately (21-24). In a meta analysis conducted by Agrawal and associates (6) the success rate of povidone-iodine pleurodesis was 90.6% which is almost equal to the efficacy of talc pleurodesis. Furthermore they showed that this effectiveness was regardless of the etiology or the techniques used to perform the pleurodesis (6, 25). On the other hand it is showed that talc is the most effective chemical agent for the management of malignant pleural effusion (24, 26, 27). Kelly-Garcia and coworkers (16) in a clinical trial of 20 patients, compared the efficacy of bleomycin with povidone-iodine in

the management of malignant pleural effusion. They showed that povidone-iodine is as effective as bleomycin in the management of malignant pleural effusion in cases of recurrence.

This was similar with our finding that there was not any significant difference in the effectiveness of bleomycin compared to povidone-iodine. Many studies have demonstrated that the significant side effects of povidone-iodine are the occurrence of the chest pain, postoperative visual loss and thyroiditis (5,6, 18-21). We did not find any significant difference in the reported chest pain between our patients whereas doxycycline group showed some increase regarding the incidence of chest pain.

Tetracycline and doxycycline are commonly used for pleurodesis and have similar success rates, although they are associated with intense pleuritic pain (28, 29), there are also reports of acute renal failure, anaphylaxis and acute respiratory failure after tetracycline pleurodesis(30, 31). Alternative methods of pleurodesis should be always considered if sensitivity is suspected.

Conclusion

Since no agent was superior to the other in this trial, we suggest that suspected anaphylactic reactions and drug availability should be considered in the choice of a sclerosing agent.

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Primary Bony Chest Wall Tumors. Experience in One Center

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Background: Primary chest wall tumor is a rare tumor that originates from different structure of the chest wall. The aim of this study is to evaluate experience of our center for management of primary bony chest wall tumors.

Methods: From 2002 to 2012, twenty three patients with the diagnosis of 1ry bony chest wall tumors were operated in our center (cardiothoracic surgery department-Zagazig University). Chest wall resection and reconstruction with synthetic polypropylene mesh and local muscle flaps was performed on one stage surgical procedure.

Results: the median age was (41±3) years(range 21-62) with male to female ratio (1.6 : 1). The common presentations were palpable mass in 17 patients (73.9%) and pain in 15 patients (65.22%). Nine patients (39.1 %) had malignant lesions and fourteen patients (60.9 %) had benign lesions. we used double layer polypropylene mesh in six patients, one of them needed semitendaneous tendon to repair the sternoclavicular joint ,successful primary closure of the chest wall done in 16 patients and one patient needed muscle flap for chest wall reconstruction. follow up of the patients showed recurrences occurred in a female patient with osteosarcoma after 6 months from the resection.

Conclusion: Surgical treatment of primary bony chest wall tumors, when malignancy confirmed, wide radical resection of the tumor performed . If malignancy was not proved surgery should consist of resection of the tumors with free margins in order to provide the best chance for cure in both benign and malignant lesions.

Key word: chest wall, bony tumor, thoracic surgery.

P rimary chest wall tumor is rare and represents about 5% of all thoracic neoplasms. It encompasses tumors of various origins, including bone, cartilage, soft tissue such as muscle, vessel, nerve and even some hematologic disease.

Only 8% of primary bone tumor occurs in chest wall ^(1,2).

Methods:

From 2002 to 2012, twenty three patients with the diagnosis of 1ry bony chest wall tumors were operated in our center at cardiothoracic surgery department, Zagazig University hospitals , Egypt.

Among 85 patients who presented with chest wall tumors, only 23 patients had bony chest wall tumors were included in our study.

Patients with metastatic chest wall lesions, chest wall invasion from nearby malignancy (e.g. breast cancer, lung cancer, mesothelioma), soft tissue tumors , chest wall infection (e.g. cold abscess) and chest wall inflammation were excluded.

Medical charts for patients with bony chest wall tumors were retrospectively reviewed.

Clinical data including age, sex distribution, medical history (smoking, diabetes mellitus, hypertension and chronic obstructive pulmonary disease), clinical symptoms,

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image findings (chest x ray {CXR}, computed tomography {CT}, bone scan), tumor size, tumor location, operation methods, pathological reports and outcome were collected. (fig.1).



Fig. 1. Aneurysmal bone cyst of the right first rib.

Follow up period range from 1-60 month (mean 39 ± 6), and included recurrence, function class and mortality .

Pathological diagnosis was made by non-excision biopsy (fine needle aspiration and/or incisional biopsy)and histopathological examination from excised specimen.

Our treatment policy for benign chest wall lesions was total excisional biopsy under general anesthesia and if suspicion of malignancy or if the tumor proved by frozen studies during surgery to be malignant a wide radical resection of the affected ribs with at least 4-5 cm free margin proximal and distal to the tumor and resection of the portions of the ribs immediately above and below the tumor, the adjacent muscle and the pleura.

Chest wall reconstruction done by, primary closure of the chest wall, double layer polypropylene mesh or muscle flap according to the size of the defects .

We used semitendinosus tendon graft in one patient for fixation of sternoclavicular joint after resection (fig. 2).



Fig. 2. Use of semitendinosus tendon graft for fixation of sternoclavicular joint after resection.

Semitendinosus tendon harvested using small incision of medial aspect of knee joint, exposure of tendon by blunt dissection , use of tendon stripper, rotation and traction on the tendon till extracted .

After that multiple holes done in the upper end of the sternum and medial end of the clavicle by bone drill, tendon passed through holes by nerve hook , tight in figure of eight (8), finally, the ends of tendon is fixed in each other by ethibond No. 5 .

Concomitant partial pleural resection and lung resection done when the tumor extend inside the thoracic cavity(fig 3).



Fig. 3. Bony chest tumor extend inside the thoracic cavity.

One case(4.34%) with aneurysmal bone cyst of right first rib needed resection of the first rib only through trans cervical supraclavicular approach

Statistical analysis

Results were analyzed using SPSS version 15.0 (Statistical Package for Social Science, SPSS Inc., Chicago, IL, USA). Continuous variables, such as age were expressed as the mean ± S.D. Categorical variables were expressed by number (n) and frequencies (%).

Results

Twenty three patients with 1ry bony chest wall tumor with median age (41±3) years(range 21-62years)with male to female ratio was(1.6 : 1) .

As regard medical history, thirteen patients were smoking, Nine were DM, Eleven were hypertensive and Ten were COPD.

The common presentations were chest wall palpable mass in 17 patients (73.9%) and pain in 15 patients (65.22%) table 1.

Nine patients (39.1 %) had malignant lesions and fourteen patients (60.9 %) had benign lesions .

In the patients with benign lesion, eight patients (34.78%) complained from swelling (palpable mass), ten patients (43.47%) complained from pain and one patient (4.34 %) accidentally discovered.

	Number of patients	23
Age	21-62	
Sex(male/female)	14/9	
Medical history		
Smoking	13 (56.52%)	
DM	9 (39.1%)	
Hypertension	11(47.8%)	
COPD	10(43.47%)	
Clinical presentation		
Accidentally discovered	1(4.34%)	
Pain	15(65.2%)	
Mass	17(73.9%)	
Cough	2 (8.69%)	
Tumor location		
Anterior chest wall	12(52.1%)	
Posterior chest wall	5(21.7%)	
Lateral chest wall	6(26%)	

Table 1. demographic data and clinical presentation

In the patients with malignant lesions, Nine patients (39.1%) complained from palpable mass (swelling), 6 patients (26 %) complained from pain and 2 patients (8.69 %) from cough (table 2).

The patients with benign lesions, five patients (21.7%) had osteochondroma, six patients (26%) had chondroma, two pa-

tients (8.69%) had giant cell tumor and one patient (4.3%) had aneurysmal bone cyst.

Patients with benign lesions, were 7 male and 7 female while in malignant lesions, 7patients were male and 2 patients were female (table 3).

Nine patients with malignant tumors. Five of them (21.7%) had chondrosarcoma, three (13%) had osteosarcoma and one patient (4.3%) had Ewing's sarcoma.

Chest wall resection and reconstruction with synthetic polypropylene mesh and local muscle flaps were performed safely and effective in one stage surgical procedure. We don't find any difficulty in chest wall closure. We had 12 patients with anterior chest wall tumor, the number of the resected ribs ranged from 2 to 3 ribs. Successful primary closure done in Nine patients , use of double layer polypropylene mesh in two cases, and one patient needed double layer of polypropylene mesh with semitendaneous tendon to repair the sternoclavicular joint.

Six patients with lateral chest wall defect ; the number of the resected ribs were 2-3 and successful primary closure done in 3 patients and 2 patients needed double layer polypropylene mesh and one patient needed latissimus dorsi flap.

Five patients with posterior chest wall defect; the numbers of the resected ribs were 1-4, successful primary closure done in 4 cases and one patient needed double layer polypropylene mesh (table 4) .

Concomitant partial pleural resection done in 2 cases (8.69%), lung wedge resection in 4 cases (17.39 %) and partial resection of T1 spinous process in one case (4.34 %).

Two patients were lost to follow-up, one patient died in the intervening period due to causes not related to mass resection. The remaining 20 cases (86.9%) continue on follow-up, recurrences occurs in a female patient with osteosarcoma after 6 months from resection. fourteen (14) patients were in functional class I while six (6) patients were in functional class II, and no radiological abnormalities in 19 patients(table 5).

Pathology	Palpable mass	Pain	Accidentally discovered	Cough
a- malignant				
Chondrosarcoma	5	3		1
Osteosarcoma	3	3		
Ewing's sarcoma	1			1
b- benign				
Osteochondroma	4	4	1	
Chondroma	3	3		
Giant cell tumor	1	2		
Aneurysmal bone cyst		1		

Table 2. clinical presentation of different pathological types

Pathological type	Total number	%	Male	Female
a-malignant				
Chondrosarcoma	5	21.7	4	1
Osteosarcoma	3	13	2	1
Ewing's sarcoma	1	4.3	1	
b- benign				
Osteochondroma	5	21.7	2	3
Chondroma	6	26	3	3
Giant cell tumor	2	8.69	1	1
Aneurysmal bone cyst	1	4.3	1	

Table 3. Pathological findings of the resected specimens correlated with patient sex

Anatomic site of the lesion	No of ribs resected	No of primary closure	No of Usage of prosthetic material	No of usage of semi-tendinous tendon	Use of muscle flap
Anterior chest wall tumor	2-3	9	3	1	
Lateral chest wall tumor	2-3	3	2		1
Posterior chest wall tumor	1-4	4	1		

Table 4. Correlation of surgical procedures with anatomic lesion

Morbidity and mortality	Malignant toumer	Benign toumer
Recurrence	1	0
Mortality	1	0
Function class		
Class I	5	9
Class II	4	2

Five-year survival rate were 95.4%.

Table 5. Mobidity and mortality

Discussion

Primary tumors of the chest wall are uncommon and require preoperative diagnosis to plan the best management.

Malignancy in primary chest wall tumors is approximately 50% (4). In this study, it was 39.1 % (9 patients) while benign lesions had 60.9 % (14 patients).

Most frequent symptoms were palpable mass and pain; in our study 4.34 % of the patients with benign tumors were as-

ymptomatic, whereas all patients with malignant tumors were symptomatic.

It had been reported that primary chest wall tumors occur mostly in the 5th and 6th decades of life with equal gender distribution and possibility of benign or malignancy, (1-5). In our study mean age was (41±3) years and patients with malignant tumors were significantly older than those with benign tumors.

Imaging feature of chest wall tumors are nonspecific but this imaging methods (CXR and CT) were useful in determining the extent of tumor invasion, surgical treatment planning and follow up (6,7).

The role of needle aspiration or non-excision biopsy for the diagnosis of primary chest wall tumors is controversial (3, 6, 8).

Some authors suggest that, all patients with primary chest wall tumors should receive at least excision biopsy, whereas those with high suspicion of malignancy should receive wide radical resection or subsequent resection for safe margin (1,9 10).

In our study, 16 patients (69.56%) received non excision biopsy for initial diagnosis. Definite diagnosis was obtained in 12 of 16 patients.

In our study; Chondroma ,Osteochondroma, Giant cell tumor, Aneurysmal bone cyst were the benign tumors. All these patients received surgical excision and recovered well.

Enchondroma of the rib account for 2-12%of primary rib tumors ⁽¹¹⁾.

In our study, the rate of enchondroma was 6 patients (26%) with equal male to female ratio.

Osteochondroma is the second common benign tumor and account for 2-8% of primary rib tumors ⁽¹¹⁾.

In our study, the rate of this lesion was 5 patients (21.7%) and female more dominant than male. Aneurysmal bone cyst is expansile , osteolytic lesion consisting of blood filled cystic spaces separated by connective tissue septa containing bone or osteoid and osteoclast giant cells. Aneurysmal bone cyst involving the rib is very rare ⁽¹²⁾.

In our study, there was one patient (4.3%) with aneurysmal bone cyst of right first rib.

Chondrosarcoma was the most frequent malignant tumor; all 5 patients with Chondrosarcoma received wide surgical excision. Recurrence after excision developed in one patient 25 months after first excision, repeated excision and radiotherapy were carried out .this patients is still alive and under regular follow up. Broccoli et al ⁽⁷⁾ reported 16 cases with chondrosarcoma and found recurrence in 6 of 16patients after wide excision and that it may occur as late as 68 months after operation.

Osteosarcoma is the second most frequent malignant rib tumor, in our study, incidence rate of osteosarcoma was 13 % (3patients), and more common in male.

Ewing sarcoma is relatively rare malignant bone tumor that usually occur in children and young adults .the ribs are frequent sites of primary Ewing sarcoma accounting for about 10-12 % of all cases ⁽¹³⁾.

In our study, there was one male patient (4.3%) had Ewing sarcoma.

The numerous advances in chest wall reconstruction over the years with introduction of muscle and musculocutaneous flaps have made them the mainstay in chest wall reconstruction⁽¹⁴⁻¹⁶⁾.

In our study , one patient needed latissimus dorsi flap to cover lateral chest wall defect. Also we use double layer of polypropelene mesh with the use of semitendaneous tendon to repair the sternoclavicular joint in one patient with anterior chest wall defect.

Le Roux and Shama⁽¹⁷⁾ had the ideal characteristics of a prosthetic material: rigidity to abolish paradoxical chest motion, inertness to allow in-growth of fibrous tissue and decrease likelihood of infection, malleability so that it can be fashioned to the appropriate shape at the time of operation, and radiolucency to allow radiographic follow up of the underlying problem.

Reconstruction of large chest wall defect indicated with use of polypropelene mesh in 6 cases; 3 to cover anterior chest wall defect, 2 to cover lateral chest wall defect, one to cover posterior chest wall defect.

Finally; our limited experience in the management of primary bony chest wall tumors showed that the number of the patients with benign lesions were more than the patients with malignant lesions. Males were predominant in malignant lesions while males and females were equal in benign one.

Surgical treatment of primary malignant bony chest wall tumors, when confirmed, was wide radical resection of the tumor with safety margin. If malignancy was not proved surgery should consist of resection with tumor free margins in order to provide the best chance for cure in both benign and malignant lesions. Careful postoperative evaluation were mandatory for patients with malignant tumors especially who were at high risk of tumor recurrence after surgical resection.

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Management of malignant pleural effusion: comparative study between doxycycline, bleomycin and povidone-iodine

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Background: Malignant pleural effusions are commonly managed with tube thoracostomy drainage followed by chemical pleurodesis. Doxycycline, bleomycin and povidone-iodine have been shown to be effective for intrapleural injection, although no agent has definitively proved advantages over the other. The aim of the present study was to compare these three agents in terms of response rate and side effects.

Patients and methods: A prospective, randomized trial was carried out between May 2008 and March 2011. One hundred twenty patients with proved malignant pleural effusion received either intrapleural doxycycline (0.5 g), bleomycin (60 mg) or povidone-iodine 10% (20 mL in 30 mL saline 0.9 %) after the same drainage procedure. Demographic and clinical data were comparable in all groups. Response was evaluated at 1, 3 and 6 months after pleurodesis.

Results: Time to relapse did not differ between all groups. No statistically significant differences were found in terms of efficacy at different intervals of follow up. Overall recurrence of pleural effusion was 22 (55 %), 17 (42.5 %) and 22 (55 %) during follow-up in the doxycycline, bleomycin and povidone-iodine groups respectively. Additional drainage procedures were needed in 6 (15 %), 6 (15 %) and 7 (17.5 %) in the doxycycline, bleomycin and povidone-iodine groups respectively. Fever was noted only in bleomycin-treated patients while pain was most frequent in the doxycycline group without statistical significance.

Conclusion: Since no agent was superior to the other in this trial, we suggest that suspected anaphylaxis and drug availability should be considered in the choice of a sclerosing agent.

Keywords: malignant pleural effusion- pleurodesis- doxycycline- bleomycin- povidone iodine.

Recurrent and symptomatic pleural effusions are common in patients with malignancy. Up to 25% of patients with lung cancer and 50% of patients with breast cancer will develop a pleural effusion. Mesothelioma, breast and lung cancer, account for the majority of malignant pleural effusions [1]. A minority of effusions remains asymptomatic and few cancers involving the pleura can be cured by specific antineoplastic or hormonal treatment. Therefore, the majority of patients will need a procedure to remove the fluid and prevent recurrence. A therapeutic drainage should be performed. This usually leads to symptomatic relief and relieves trapped lung. However, pleurodesis is considered the best palliative therapy for the treatment of recurrent malignant pleural effusions [2].

Pleurodesis with a chest tube drainage and intrapleural instillation of a chemical agent is the most effective methods for controlling a malignant pleural effusion (3,4). A wide variability exists in the choices of sclerosing agents. Talc, tetracycline and bleomycin have been widely used for pleurodesis. Considering these agents, povidone-iodine, an iodine based topical antiseptic, is extensively used as an sclerosing agent (2). Many studies have shown the effectiveness of povidone-iodine to achieve a complete response rates 80-90% in the management of pleural effusion. On the other hand some side effects including thyroiditis and even visual loss has been reported (5), however it is the cheapest agent available. Previous studies have compared the effectiveness of

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talc with other agents including tetracycline, doxycycline and bleomycin (6). Bleomycin is widely used; however it is much more expensive compared to povidone-iodine. Besides there is not enough evidence demonstrating the efficacy of bleomycin compared to povidone-iodine and doxycycline. The purpose of this study was to compare the choice of the sclerosing agent, which is not only determined by the efficacy of the agent but also by its cost, accessibility, safety, ease of administration and the efficacy to achieve a complete response .

Patients and methods

A prospective randomized trial was carried out between May 2008 and March 2011. One hundred twenty patients with proved malignant pleural effusion received either intrapleural doxycycline (0.5gm), bleomycin (60 mg) or povidone-iodine

10% (20 mL in 30 mL saline 0.9 %) after the same drainage procedure. Response was evaluated at 1, 3 and 6 months after chemical pleurodesis.

All Patients were subjected to detailed clinical evaluation including history taking and examination, plain chest X-ray postero-anterior (P-A), while computed tomography (CT) was done for few cases. The preoperative demographic data of study patients in the three groups is shown in table (1) without any statistical significant difference between groups.

In our study, the following symptoms (dyspnea, pain, cough and hemoptysis) were the presenting symptoms where as dyspnea was present in all patients, while hemoptysis was rarely present. Radiological evaluation of the amount of pleural effusion, other opacities or loss of lung volume were done. Table (2) shows these details.

	Doxycycline	Bleomycin	Povidone-Iodine	P value
Age yrs	59±15	58±11	60±12	0.879*
Male/female	17/23	18/22	19/21	0.904*
Primary site of tumour n				
Mesothelioma	9 (22.5 %)	13(32.5 %)	11(27.5 %)	
Breast	13 (32.5 %)	9 (22.5 %)	10 (25 %)	
Lung	3 (7.5 %)	5 (12.5 %)	4 (10 %)	
Stomach	2 (5 %)	1 (2.5 %)	1 (2.5 %)	0.928*
Rectal	0 (0 %)	1 (2.5 %)	0 (0 %)	
Ovarian	2 (5 %)	2 (5 %)	1 (2.5 %)	
Lymphoma	2 (5 %)	2 (5 %)	3 (7.5 %)	
Osteosarcoma	2 (5 %)	3 (7.5 %)	2 (5 %)	
Thyroid	0 (0 %)	1 (2.5 %)	1 (2.5 %)	
Melanoma	0 (0 %)	1 (2.5 %)	0 (0 %)	
Unknown	7 (17.5 %)	2 (5 %)	7 (17.5 %)	
Metastatic sites n				
0	9 (22.5 %)	8 (20 %)	7 (17.5 %)	0.919*
1	16 (40 %)	14 (35 %)	13(32.5 %)	
2	9 (22.5 %)	10 (25 %)	9 (22.5 %)	
≥3	2 (5 %)	5 (12.5 %)	5 (12.5 %)	
Unknown	4 (10 %)	3 (7.5 %)	6 (15 %)	
Prior surgery	14 (35 %)	13 (32.5 %)	13 (32.5%)	0.963*
Prior chemotherapy	18 (45 %)	17 (42.5 %)	18 (45 %)	0.967*
Prior irradiation	9 (22.5 %)	10 (25 %)	12 (30 %)	0.737*

*: Data is not statistically-significant

Table 1. Characteristics of patients in treatment groups

	Doxycycline	Bleomycin	Povidone-Iodine	P value
Symptoms				
Dyspnoea	40 (100 %)	40 (100 %)	40 (100 %)	-
Chest pain	21 (%)	23 (%)	21 (%)	0.874*
Cough	24(%)	22(%)	25(%)	0.786*
Hemoptysis	3(%)	3(%)	4(%)	0.897*
Chest X-ray				
Effusion only	14(%)	15(%)	13(%)	
Pulmonary nodules	9(%)	10(%)	11(%)	0.994*
Pleural masses	10(%)	8(%)	8(%)	
Loss of lung volume	7(%)	7(%)	8(%)	
Size of effusion				
Moderate	23(%)	25(%)	24(%)	
Massive	17(%)	15(%)	16(%)	0.901*

*: Data is not statistically-significant

Table 2. Presenting symptoms and radiographic features

The criteria for diagnosis of malignant pleural effusions were based on the evidence of malignant disease in the chest or else where in the body, positive cytological examination for malignant cells in the pleural fluid and/or positive lymph node biopsy for metastatic or pleural biopsy for primary tumour or secondary invasion.

Exclusion criteria

Previous attempts at pleurodesis with other agents, known hypersensitivity to any sclersant material, incomplete re-expansion of the lung after tube thoracotomy and/or patients with known thyroid disease.

Technique

The insertion of intercostal tube was indicated clinically and radiologically. In all of our patients, the 5th intercostal space in midaxillary line was site for the tube insertion. The tube was allowed to drain the pleural fluid continuously. Some of our patients were distressed and suffered from severe dyspnea due to rapid evacuation of the pleural fluid and the associated rapid expansion of the underlying lung. This necessitated an intermittent withdrawal of the fluid by clamping the tube every few minutes to allow gradual evacuation. The complete evacuation of the pleural space was confirmed by mild oscillation of the fluid column in the underwater tube which denoted that the lung has expanded to occupy the place of the withdrawn

fluid, auscultation of the chest would reveal marked improvement of air entry after removal of the fluid and X-ray of the chest was also necessary to show if there was any residual fluid remaining in the pleural space and if the underlying lung expanded completely.

Then the tube was clamped close to the chest wall and disconnected from the underwater seal bottle. Premedication in the form of 2mg/kg lidocaine (xylocaine) in 50 ml of normal saline was injected through the chest tube. Doxycycline (500 mg) diluted in 20cc distilled water then injected into pleural cavity through chest tube in 40 patients. While povidone-iodine pleurodesis solution contains mixture of 20 ml of 10% iodipovidine and 80 ml normal saline was injected into pleural cavity through tube in another 40 patients. In the 3rd group, 60 mg of bleomycin diluted in 100 ml normal saline solution was instilled. Then the patient was allowed to change his position repeatedly every 10-15 minutes for 2-3 hours to permit complete dispersal of the drug over the whole pleural surfaces.

The chest tube was strictly observed to avoid its blockage by clot or kink or slipping. The patient was followed up with chest x-ray to show the degree of clearance of the fluid and the expansion of the lung and then the tube was removed. The patient was then followed up clinically and by radiologically after removal of the chest tube. The patient was then discharged to be followed up by clinical and radiological examination.

Statistical analysis

Data were collected, tabulated, statistically analyzed by computer Using SPSS version 16. Quantitative data expressed in. mean (x) and standard deviation (SD).and analysed by *k-test*: to study statistical relation between more than two quantitative none normally distributed variables.

Results

In our study groups, adverse effects of chemical pleurodesis were chest pain, fever, nausea and / or vomiting and hypersensitivity reactions. There were no statistically significant differences as shown in table (3). Chest pain was the main adverse effect in Doxycycline group, while fever was only present in Bleomycin group. Povidone-iodine group was the least to show adverse effects (table 3).

The efficacy of pleurodesis was defined as: complete (absence of pleural fluid re-accumulation), partial (residual pleural fluid or asymptomatic fluid re-accumulation, which did not require additional procedures), or failure (additional pleural procedures were required). Table (4) shows the response of different groups to chemical pleurodesis after 1, 3 and 6 months. **Time to relapse did not differ between all groups. No statistically significant differences were found in terms of efficacy at different intervals of follow up. Overall recurrence of pleural effusion was 22 (55 %), 17 (42.5 %) and 22 (55 %) during follow-up in the doxycycline, bleomycin and povidone-iodine groups respectively. Additional drainage procedures were needed in 6 (15 %), 6 (15 %) and 7 (17.5 %) in the doxycycline, bleomycin and povidone-iodine groups respectively.** Only one patient in povidone-iodine group showed partial resolution after 3 months duration and then required drainage procedure after 6 months (added to failure of

	Doxycycline	Bleomycin	Povidone-Iodine	P value
Pain during instillation	13 (32.5 %)	8 (20 %)	7 (17.5 %)	0.236*
Fever	0 (0 %)	7 (17.5 %)	0 (0 %)	-
Nausea/vomiting	2 (5 %)	3 (7.5 %)	1 (2.5 %)	0.59*
Hypersensitivity reaction	0 (0 %)	1 (2.5 %)	3 (7.5 %)	0.164*

*: Data is not statistically-significant

Table 3. Adverse effects of chemical pleurodesis

Evaluation time	St. group	Doxy		Bleo		Povi.		p
		No	%	No	%	No	%	
1 month								
NA		0	0.0	0	0.0	0	0.0	0.785*
CR		18	45.0	23	57.5	19	47.5	
PR		16	40.0	11	27.5	14	35.0	
Failure		6	15	6	15	7	17.5	
3 month								
NA		3	7.5	3	7.5	4	10.0	0.787*
CR		15	37.5	22	55.0	17	42.5	
PR		16	40.0	10	25.0	14	35.0	
Failure		6	15	5	12.5	5	12.5	
6 month								
NA		7	17.5	8	20.0	7	17.5	0.642*
CR		14	35.0	20	50.0	13	32.5	
PR		14	35.0	8	20.0	15	37.5	
Failure		5	12.5	4	10.0	5	12.5	

NA: not available (patient lost to follow-up, or death); PR: partial response; CR: complete resolution.

*: Data is not statistically-significant

Table 4. Response to chemical pleurodesis

pleurodesis in this group after 6 months). All groups showed no statistical significant difference.

Discussion

Malignant pleural effusion is a major common problem leading to a significant dilemma regarding quality of life due to symptoms such as dyspnea and cough. Palliative management of malignant pleural effusion should aim at improving the quality of life with minimal complications. Optimal outcome as definition and as a mode of management entails variety of controversies. The aim of pleurodesis in these patients is to prevent reaccumulation of the effusion and avoid the need for repeated thoracentesis or intercostal tube drainage.

Pleural effusion is a common complication of malignant diseases occurring in 50% to 70% of all malignancies in the course of their illness (7). Carcinoma of the lung is the most common malignancy to invade the pleura (30%) and produce malignant and para malignant effusions (8). Carcinoma of the breast is second in incidence (25%) (9). The frequency declines markedly with ovarian and gastric cancer representing 5% or less of malignant pleural effusions. Lymphoma accounts for approximately 20% of the malignant pleural effusions and is the most common cause of chylothorax (10). A less common cause of malignant pleural effusion other than metastatic carcinoma, is malignant mesothelioma (11). Unlike ours, mesothelioma is the most common cause in our series. Mesothelioma and breast cancer constituted more than half of our studied cases. This difference may be attributed to early diagnosis of mesothelioma and bronchogenic carcinoma. An early manifestation of malignant mesothelioma is pleural effusion that is reabsorbed or organized and then largely replaced by tumor and fibrosis while malignant effusion is a late manifestation in bronchogenic carcinoma.

Patients with carcinoma involving the pleura most often present with symptoms attributable to a large pleural effusion, dyspnea on exertion and cough (12). The presence and degree of dyspnea depends on the size of the effusion and the patient's pulmonary function. Thoracentesis or intercostal tube thoracostomy results in relief of dyspnea in most of the patients (13). These results were similar to ours, in which dyspnea was present in all of our patients, while chest pain and cough were present in slightly more than fifty percent of our patients. The mechanism of dyspnea caused by a large pleural effusion probably entails a decrease in the compliance of the chest wall, a contra-lateral shift of the mediastinum, and a decrease in ipsilateral lung volume. Also endobronchial lesion that causes atelectasis or an infiltrative malignant disease of the pulmonary parenchyma may also contribute to dyspnea and cough (10).

Since malignant involvement of the pleura signifies advanced disease, these patients commonly have weight loss and appear chronically ill. Chest pain is often present because of the involvement of the parietal pleura, ribs or chest wall. However,

25% of patients may be asymptomatic at the time of presentation (12). Unlike us, others found that chest pain is the most common presenting symptom and occurs in 60-70% of patients. Dyspnea and cough were found about 20-25% of patients (10).

Variation in the definition of recurrence (radiological and clinical) may account for some discrepancies among studies. Mohsen and associates (14) found povidone-iodine pleurodesis as a safe and also effective alternative means of preventing the recurrence of malignant pleural effusion at 30 days post-procedure. Povidone-iodine is a topical antiseptic, and is less commonly used as a sclerosing agent. The reported success rates range from 64% to 96% (15, 16), whereas Moshen and associates (14) found the success rate 85%.

Chest pain and fever are the most common adverse effects of all pleurodesis agents. The iodine-povidone population tended to have less analgesic requirements and no recorded pyrexia incidents but these did not reach statistical significance. Concerns that povidone-iodine might be associated with visual loss were reported by Wagenfeld et al. (5) in three cases during VATS. However, authors used an unusual amount of 200–500 ml of 10% povidone-iodine 'Jodobac'. They also noted that the safe amount to be used is 20 ml of 10% iodine, which is actually the amount that we have used in our study. As an additional safety practice, we administered this dose in a diluted form (in normal saline). Moreover, Wagenfeld et al. (5) reported that they used Jodobac in patients who had normal pleura (patients who had pneumothorax), which might have increased absorption and toxicity (5). In our study (as others (14)), we used iodine only in malignant effusions with pathological pleura that has a poor absorption potential (that could partly explain the pathophysiology of accumulated pleural effusion). We strongly believe that this practice has significantly increased povidone safety in our study, as none of our patients encountered any loss of vision.

There was not any statistical significant difference between groups in pain after procedure and other adverse effects and the recurrence of pleural effusion in one month follow up after procedure. Ali and coworkers (17), also reported nearly same results in their study comparing iodine and bleomycin.

The mechanism by which povidone-iodine works is not clear; it is thought to be related to the low pH of the sclerosing solution. On the other hand bleomycin is an anti-neoplastic antibiotic. It has sclerosing properties which is widely used for pleurodesis. It has minimal toxic reactions and is cleared by kidneys (4, 18-20).

Previous studies have repeatedly shown the efficacy of povidone-iodine and bleomycin in the management of malignant pleural effusion separately (21-24). In a meta analysis conducted by Agrawal and associates (6) the success rate of povidone-iodine pleurodesis was 90.6% which is almost equal to the efficacy of talc pleurodesis. Furthermore they showed that this effectiveness was regardless of the etiology or the tech-

niques used to perform the pleurodesis (6, 25). On the other hand it is showed that talc is the most effective chemical agent for the management of malignant pleural effusion (24, 26, 27). Kelly-Garcia and coworkers (16) in a clinical trial of 20 patients, compared the efficacy of bleomycin with povidone-iodine in the management of malignant pleural effusion. They showed that povidone-iodine is as effective as bleomycin in the management of malignant pleural effusion in cases of recurrence.

This was similar with our finding that there was not any significant difference in the effectiveness of bleomycin compared to povidone-iodine. Many studies have demonstrated that the significant side effects of povidone-iodine are the occurrence of the chest pain, postoperative visual loss and thyroiditis (5,6, 18-21). We did not found any significant difference in the reported chest pain between our patients whereas doxycycline group showed some increase regarding the incidence of chest pain.

Tetracycline and doxycycline are commonly used for pleurodesis and have similar success rates, although they are associated with intense pleuritic pain (28, 29), there are also reports of acute renal failure, anaphylaxis and acute respiratory failure after tetracycline pleurodesis(30, 31). Alternative methods of pleurodesis should be always considered if sensitivity is suspected.

In conclusion, Since no agent was superior to the other in this trial, we suggest that suspected anaphylactic reactions and drug availability should be considered in the choice of a sclerosing agent.

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