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Please address all correspondence to:

Ezzeldin A. Mostafa, MD, Editor, In-chief

Journal of the Egyptian Society of Cardio-thoracic Surgery

330 El-Sudan St., Imbaba, Cairo, Egypt.

Telephone: (+202) 303 6634

Fax: (+202) 303 8054

E-Mail: jegyptscts@gmail.com

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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 original scientific articles; new technology papers; case reports, the way i do it articles, images; and review articles. The editor and/or associate editors review correspondence, invited commentaries, editorials, surgical heritage, 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

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 and relationship of the results to the existing literature. 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.

The following topics are offered to help guide the reviewer's assessment of an original scientific 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. 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. 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 and in proper format.

## New Technology

Articles describing new technology are necessarily descriptive and do not pose or test a hypothesis. These articles evaluate new devices, systems, 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.

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, The Way I 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. 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 topi-

cal 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.

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.

### **Footnote**

The reviewer remains anonymous. 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 additio



# Events of Interest

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## The 15th Annual Conference of the Egyptian Society of Cardiothoracic Surgery Cairo - Egypt

**Timing :** ..... **12 - 14 March 2008**  
**Location:** ..... **Cairo Sheraton Hotel**  
**Email :** ..... **egyicc@link.net**

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### ■ 15th Annual Echocardiographic Workshop on 2-D and Doppler Echocardiography-Vail, • Colorado—March 9-13, 2008

For more information on this meeting, contact Mayo Clinic, 200 First St, SW/GO-06-138SW, Rochester, MN 55905.

### ■ 5th Annual Course on Extracorporeal Membrane Oxygenation-Jeddah, Saudi Arabia—March 10-12, 2008

For more information on this meeting, contact Faiz Almalki, Rawdah Street (Khalediyah District), PO Box 40047 (MBC-J 16), Jeddah 21499, Saudi Arabia; telephone: (966-2) 667-7777, ext 2166; e-mail: faiz\_winner<§1 gmailcom or faizwinner@awalnet.net-sa; website: www.kfshrcj.org.

### ■ 15th Annual Mayo Clinic Arrhythmias and the Heart-Kauai, Hawaii—March 10-13, 2008

For more information on this meeting, contact Mayo Clinic, 200 First St, SW/GO-06-138SW, Rochester, MN 55905; telephone: (507) 266-0677; e-mail: cvcme@mayo.edu.

### ■ 16th Annual Meeting of the Asian Society for Cardiovascular Surgery-Singapore, Singapore—March 13-16, 2008

For more information on this meeting, contact ASCVS Congress Secretariat, c/o The Meeting Lab Pte Ltd, 176 B Joo Chiat Rd, Singapore 427447, Singapore; telephone: +65 63464402; fax: -65 63464403; e-mail: mice@themeetinglab.com; website: www.ascvs2008.com.

### ■ CTS Critical Care 2008-Washington, DC—March 27-29, 2008

For more information on this meeting, contact Alexander T. Taft III, Foundation for the Advancement of CTS Care, 616 E St NW, Suite 316, Washington, DC 20004; telephone: (202) 536-4822; fax: (202) 478-1669; e-mail: alextaft@facts-care.org; website: http://ctscriticalcare.ws.

### ■ American College of Cardiology 57th Annual Scientific Session-Chicago, Illinois—March 29-April 1, 2008

For more information on this meeting, contact American

College of Cardiology Foundation, Heart House, 2400 N St NW, Washington, DC 20037; telephone: (202) 375-6000; fax: (202) 375-7000; website: www.acc.org.

### ■ Houston Aortic Symposium: Frontiers in Cardiovascular Diseases-Houston, Texas—April 4-6, 2008

For more information on this meeting, contact Promedica International CME, 2333 State St, Suite 203, Carlsbad, CA 92008; telephone: (760) 720-2263; fax: (760) 720-6263; e-mail: houstonaortic@promedicacme.com.

### ■ International Society for Heart and Lung Transplantation 28th Annual Meeting and Scientific Sessions-Boston, Massachusetts—April 9-12, 2008

For more information on this meeting, contact International Society for Heart and Lung Transplantation, 14673 Midway Rd, Suite 200, Addison, TX 75001, telephone: (972) 490-9495; fax: (972) 490-9499; e-mail: ishlt@ishlt.org; website: www.ishlt.org.

### ■ Vascular and Endovascular Consensus Update-London, United Kingdom—April 12-15, 2008

For more information on this meeting, contact Chris Timmins, BIBA Medical Ltd, 44 Burlington Rd, London SW6 4NX, UK; telephone: 44 (0) 20 7736 8788; fax: 44 (0) 20 7736 8283; e-mail: info@cxsymposium.com; website: www.cxsymposium.com.

### ■ American Surgical Association 128th Annual Meeting-New York, New York—April 24-26, 2008

For more information on this meeting, contact American Surgical Association, 900 Cummings Center, Suite 221-U, Beverly, MA 01915; e-mail: asa@prri.com; website: www.americansurgical.info.

### ■ 57th International Congress of The European Society for Cardiovascular Sur-

**gery-Barcelona, Spain—April 24-27, 2008**

For more information on this meeting, contact Professor Claudio Mu-neretto, ESCVS Secretary General, UDA Cardiochirurgia, Spedali Civili PJe Spedali Civili, 25123 Brescia, Italy; telephone: +39 030 3996401; fax: +39 030 3996096; e-mail: munerett@med.unibs.it; website: www.escvs.org.

**■ 18th World Society of Cardiothoracic Surgeons World Congress-Kos Island, Greece— April 30-May 3, 2008**

For more information on this meeting, contact 18th WSCTS Congress Secretariat, 29 Sinopsis Str 11527, Athens, Greece; telephone: +30 210 7799261; fax: +30 210 7711768; e-mail: secretariat@wscts2008.com; website: www.wscts2008.com.

**■ Aortic Symposium 2008-New York, New York—May 8-9, 2008**

For more information on this meeting, contact American Association for Thoracic Surgery, 900 Cummings Center, Suite 221-U, Beverly, MA 01915; telephone: (978) 927-8330; fax: (978) 524-8890; e-mail: aats@prii.com; website: www.aats.org.

**■ 88th Annual Meeting of the American Association for Thoracic Surgery-San Diego, California—May 10-14, 2008**

For more information on this meeting, contact 900 Cummings Center, Suite 221-U, Beverly, MA 01915; telephone: (978) 927-8330; website: www.aats.org/annualmeeting.

**■ 16th World Congress of Cardiology 2008-Buenos Aires, Argentina—May 18-21, 2008**

For more information on this meeting, contact telephone: +54 11 4812-3444; e-mail: wcc2008@congresosint.com.ar; website: www.worldheart.org.

**■ 4th International Conference on Pediatric Mechanical Circulatory Support Systems, Pediatric Heart Transplantation, and Pediatric Cardiopulmonary Perfusion-Portland, Oregon— May 22-24, 2008**

For more information on this meeting, contact Perm State College of Medicine CME Department, PO Box 851, Herehey, PA 17033; telephone: (717) 531-6483; fax: (717) 531-5604; e-mail: continuing@hmc.psu.edu; website: www.hmc.psu.edu/ce/pe diatrics.

**■ Innovations in Treatment of Cardiac Structural Disease: The Mediterranean Meeting-Palermo, Sicily, Italy—June 6-7, 2008**

For more information on this meeting, contact University of Pittsburgh Medical Center, Division of Cardiac Surgery, The

Heart, Lung, and Esophageal Surgery Institute, UPMC Presbyterian, Suite C-700, 200 Lothrop sC Pittsburgh, PA 15213; telephone: (412) 802-6591; fax: (412) 648-6358; e-mail: espositogm@upmc.edu; website: http://ccehs.upmc.edu.

**■ Western Thoracic Surgical Association 34th Annual Meeting-Kona, Hawaii—June 25-28, 2008**

For more information on this meeting, contact Western Thoracic Surgical Association, 900 Cummings Center, Suite 221-U, Beverly, MA 01915; telephone: (978) 927-8330; fax: (978) 524-8890; e-mail: wtsa@prii.com; website: www.west-erthoracic.org.

**■ 14th World Congress on Heart Disease: International Academy of Cardiology Annual Scientific Sessions 2008-Toronto, Ontario, Canada-July 26-29, 2008**

For more information on this meeting, contact Asher Kimchi, MD, International Academy of Cardiology, PO Box 17659, Beverly Hills, CA 90209; telephone: (310) 657-8777; fax: (310) 659-4781; e-mail: klimedco@uda.edu; website: www.cardiologyonline.com.

**■ 22nd Annual Meeting of the European Association for Cardio-Thoracic Surgery-Lisbon, Portugal—September 13-17, 2008**

For more information on this meeting, contact EACTS Executive Secretariat, 3 Park St, Berkshire, SL4 1LU; telephone: +44 1753 832166; fax: +44 1753 620407; e-mail: info@eacts.co.uk.

**■ American College of Surgeons Annual Meeting-San Francisco, California—October 12-16, 2008**

For more information on this meeting, contact website: www.facs.org/index.html.

**■ 6th Triennial Brigham CardiaValve Symposium-Boston, Massachusetts-October 23-24, 2008**

For more information on this meeting, contact R. Morton Bolman III, MD, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115; telephone: (617) 732-6964; fax: (617) 732-6559; e-mail: ljaffel@partners.org; website: www.brigham-womens.org/ca rdi acsurge ry / e vents.aspx.

**■ Chest 2008-Philadelphia, Pennsylvania october 25-30,2008**

For more information on this meeting, contact American College of Chest Physicians, 3300 Dundee Rd, Northbrook, IL 60062-2348; telephone: (847) 498-1400; website: www.chestnet.org.

## WINDS OF CHANGE

Dear colleagues

In the last three years we tried as elected board to the Journal of the Egyptian Society of Cardio-Thoracic Surgery to make a difference; we hoped to the better.

We have built upon a strong base devised by Professor Mohamed ElFiki who took the initial difficult responsibility of mastering and cruising with our journal; great man who succeeded in a difficult task.

Winds of change brought another distinguished professor who took the lead and cruised again with our journal Doctor Ezz El Din Abdel Rahman Mostafa under whom I enjoyed working in the last three years.

We changed the journal look and format we tried to take a new shape imitating international journals

Reviewing of the articles by various professors was implemented anonymously ,correction and recorection with authors was an ongoing process and even a refusal of an article was honestly clarified to point of satisfaction for both parties.

We tried to ease the whole process of acceptance reviewing and publication while sticking at the same time to the rules in favor of the reader and the prestige of our journal.

Sometimes we met certain financial obstacles due to the scarcity of the adverts but with the aid of the society board our budget was supported.

Our journal is now electronic ie;online ([www.arabmedics.com](http://www.arabmedics.com)) and for free; a step which our readers looked for is finally achieved.

A real team work orchestrated this whole task: Mr. Ahmed Khalifa, Mr Ayman abdel Aziz , Dr Ezz Mostafa, Dr Ahmed Deebes, Dr Mohamed Othman and myself.

With the new elected board of the society again winds of change had to take place and one of the distinguished persons joined the boat as the new Co-Editor to the Journal Professor Ahmed Al Kerdani starting from 2008 and I have now to leave for another possible mission wishing him all the best and thanking Dr Magdi Mostafa , Dr Ezz Mostafa and all my seniors and colleagues for their help and all the readers who supported me either by encouragement or criticism

asking Almighty GOD to guide our ship of cardiac surgery to new horizons and shores.

Yasser M W Hegazy MD,FRCS  
Consultant Cardiac Surgeon.

# THE IMPACT OF MODERATE ISCHAEMIC MITRAL REGURGITATION ON PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING

Tamer Farouk MD,  
Omar Nawaytou MD,  
Mohamed Abuldahab MD,  
Yahia Balbaa MD,  
Magdy Gomaa MD.

**Background:** ischaemic mitral regurgitation (IMR) is distinctive valve disease in that, abnormalities of the left ventricle are not the consequence but the cause of the disease. Our aim is to study impact of moderate IMR in patients undergoing CABG on the immediate and early outcome and whether CABG alone can ameliorate moderate IMR.

**Methods:** In this study 35 patients with moderate IMR associated with coronary artery disease comprise the study group (IMR group), compared to 35 patients without IMR (control group), both undergoing CABG.

**Results:** 25 males (75.4 %) in the IMR group as compared to 23 (65.3 %) in the control group (p=NS). Mean age for the IMR patients was  $62.0 \pm 4.39$  and for the control group  $62.14 \pm 3.95$ . Preoperative echocardiographic of both groups showed no statistically significant differences. Mean jet area at follow up was  $3.65 \pm 3.55$  compared to a preoperative of  $5.88 \pm 0.94$ . CABG alone was able to decrease preoperative moderate IMR to mild or absent in 58.9% of our patients.

**Conclusion:** moderate IMR in patients undergoing CABG does not add any additional burden to the operative risk nor does it affect the immediate and early outcome of these patients. It can ameliorate moderate IMR in most patients postoperatively.

Ischaemic mitral regurgitation (IMR) is a distinctive valve disease in that, unlike with organic valvulopathies, abnormalities of the left ventricle (LV) are not the consequence but the cause of the disease (1). IMR is caused by myocardial infarction (MI). The leaflets and subvalvular apparatus are by definition normal (2).

The disease is a manifestation of post-infarction ventricular remodeling. The presentation may be either acute or develop insidiously over time (3). Different subgroups could be distinguished according to the distortion produced by ischaemia on the mitral valve (MV) apparatus (4). The presence of IMR after acute MI increases the likelihood of pulmonary edema, cardiogenic shock, and death. Mild to moderate grades of IMR double the 30-day and 3-year mortality to be approximately 15% and 20%, respectively, as compared to patients without mitral regurgitation (5). Even with revascularization, the presence of mild and moderate IMR increases the operative mortality to approximately 4% and 8%, respectively (6).

Should all patients with moderate IMR undergoing coronary artery bypass grafting (CABG) have an additional procedure addressing their mitral insufficiency? Can that be accomplished with an acceptable operative mortality and will this approach further improve the long-term outcome? This remains an

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Address reprint request to : Dr Tamer Farouk Department of Cardiothoracic Surgery, Kasr El Aini Hospital, Cairo University.

Email : tfrksm@yahoo.com.

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unresolved question (7).

The present operative strategy for management of IMR is as follows: the more severe forms (grade 3 and 4) are generally treated with CABG and a valve or annular procedure, while the milder forms (grade 1 and 2) are treated with CABG solely. This is supported in the majority of series (6,8&9). Others, range between a more aggressive attitude in associating CABG with a mitral valve procedure in cases of moderate IMR (10), to a more conservative attitude of CABG alone in patients with even severe mitral regurgitation (11).

### Patients and Methods

In this study 35 patients with moderate (4-8 cm2 regurgitant jet area) IMR associated with multivessel coronary artery disease comprise the study group (IMR group). To assess the effect of unrepaired moderate IMR on the early outcome of patients undergoing CABG, a cohort of 142 patients known to be without IMR, were used to propensity match the study group, this generated 35 patients for comparison (control group). Both groups were admitted to the Cardiothoracic Surgery Department at Kasr El-Aini Hospital, Cairo University, for CABG in the period between June 2004 and April 2007.

### Preoperative evaluation:

All patients were subjected to complete history taking, clinical examination, full laboratory investigations, plain chest X-ray, ECG, echocardiography and coronary angiography.

### Intraoperative procedure:

In all the patients routine anaesthetic techniques were used. There were 4 patients who were done using the off-pump technique in the study group and another 5 in the control group.

**Operative technique:** All the patients were routinely scrubbed and draped. After median sternotomy, harvesting of the left internal mammary artery (LIMA) was done in all the patients. Concomitantly, harvesting of the great saphenous vein and/or the left radial artery took place. Heparin 350U/Kg was administered prior to cannulation (half of that dose in off pump patients).

After cannulation and institution of cardiopulmonary bypass, perfusion was maintained at a flow rate of 2.5-3 L/m2/min. The patient's systemic temperature was allowed to drift to 32-34°C thus maintaining tepid systemic hypothermia.

The aorta is then clamped and myocardial protection was achieved by intermittent antegrade infusion of warm blood cardioplegia through the aortic root every

15-20 minutes.

After cardioplegia, a 4-5 mm arteriotomy is made in the selected coronary artery with a No. 11 scalpel. A continuous technique was used to perform the distal anastomoses using a No. 7/0 polypropylene suture. After distal anastomoses were completed, warm blood was infused antegradely in the aortic root at a rate of 300-500 ml/min for 3-5 minutes (hot shot) to allow the heart to regain contractility. The aortic root was deaired through the aortic root vent and the aortic clamp removed. Electrical and pharmacological cardioversion were used if the heart failed to regain contractility spontaneously. A vascular side occlusion clamp was applied to the ascending aorta to perform the proximal anastomoses. Polypropylene 6/0 suture using a continuous technique was used to perform the proximal anastomoses. During completion of the proximal anastomoses, the patient was rewarmed to 37°C and all electrolyte and acid-base imbalances corrected.

After completion of the proximal anastomoses, the patient's haemodynamics were assessed and if not satisfactory, pharmacological support, in the form of epinephrine infusion at a rate of 0.05 u/Kg/min and nitroglycerine 0.5-2.0 u/Kg/min, was instituted. If pharmacological support did not suffice, an intra-aortic balloon pump (IABP) was inserted for mechanical support. The patient was then weaned off bypass.

In this study, special consideration was paid to recording whether the operation was done on or off bypass, the total bypass and cross clamp times, the need for electrical cardioversion or antiarrhythmics to restore contractility, the need for inotropic or mechanical haemodynamic support to wean the patient off bypass. Intraoperative transoesophageal echocardiography (TEE) was used in the study group to assess the degree of mitral regurgitation and measure the jet area when possible.

Protamine was then administered, followed by decannulation, haemostasis, placement of epicardial pacemaker wires, and closure over a retrosternal and a left pleural drain.

For off pump cases: An Octopus vacuum-assisted coronary stabilizer is mounted on the sternal spreader. The target vessel is exposed by scratching as before, a silastic tape mounted on a blunt needle is used to attain proximal inflow occlusion.

The following variables were recorded in the operative technique: whether the operation was performed on or off pump, the number of grafts done, use of the LIMA to the LAD. All the patients were transferred to the cardiothoracic intensive care unit mechanically ventilated.



**Postoperative evaluation:****The following data were assessed,**

1. Intensive care unit: Postoperative haemodynamics, mechanical ventilation period, inotropic support, need for a postoperative IABP, ECG, total ICU stay in days and complications if present.

2. Postoperative echo: This was done at any day after drain removal and before hospital discharge. Stress was put on recording the LVEDD, LVESD, LA size, EF %, the presence and grade of IMR with measurement of the jet area.

3. Total hospital stay

4. Follow-up (3-6 months):

Patients were assessed for the following: Functional state, NYHA class and postoperative echocardiography.

**Results**

[A] Preoperative Data:

The demographic data of the two studied groups are shown in table(1)

**Table 1: Demographic data of the two studied groups**

	IMR group (n= 35)	Control (n= 35)	P value	Significance
Age (years)	62.0 ± 4.39	62.14 ± 3.95	0.887	NS
Male/Female	25/10 (71.4/28.6%)	23/12 (65.7/34.3%)	0.607	NS

**Table 1: Demographic data of the two studied groups**  
Data were expressed as mean ± standard deviation (SD) or number (%).

NS= Not significant

Thirty (85.7%) patients in the IMR group had a previous infarction with 12 of those having more than one infarction as opposed to 29 (82.9%) patients in the control group with a previous infarction and 14 of those sustaining more than one infarction (p=NS). Table 2 summarizes the risk factors for coronary heart disease in both groups. As can be seen, there were no significant differences between the two groups.

**Table 2: Risk factors in the two studied groups**

	IMR group (n= 35)	Control group (n= 35)	P value	Significance
Diabetes mellitus	21 (60%)	22 (62.9%)	0.806	NS
Hypertension	24 (68.6%)	21 (60%)	0.454	NS
Dyslipidaemia	9 (25.7%)	9 (25.7%)	1.00	NS
Smoking	25 (71.4%)	23 (65.7%)	0.607	NS
PVD	12 (34.3%)	14 (40%)	0.621	NS
COPD	5 (14.3%)	5 (14.3%)	1.000	NS

**Table 2: Risk factors in the two studied groups**

Data were expressed as number (%).

NS= Not significant

All the patients in both groups gave a history of angina. Thirty patients in the IMR group had some form of dyspnea, with a mean NYHA class of  $2.11 \pm 1.25$ . In the control group, 25 patients presented with dyspnea with the mean NYHA class being  $1.74 \pm 1.32$  (p=NS). As all the patients in the study group were verified to have ischaemia as the etiology of their mitral regurgitation, the onset of dyspnea followed that of angina or infarction in all the cases in the study group.

The preoperative ECG revealed that 74.3 % of the patients in the IMR group had either a posterior or an inferior infarction as opposed to 40 % in the control group (p=0.004). There were 9 patients with an anterior infarction and 6 with a lateral infarction in the IMR group as opposed to 18 and 10, respectively, in the control group (p=0.03). The preoperative echocardiographic data of both groups is summarized in table (3). The mean jet area for the 35 patients in IMR group was  $5.88 \pm 0.94$  cm<sup>2</sup>.

**Table 3: Preoperative echocardiographic data in the two studied groups**

	IMR group (n= 35)	Control group (n= 35)	P value	Significance
LVED	5.76 ± 0.58	5.79 ± 0.57	0.837	NS
LVES	4.02 ± 0.44	3.96 ± 0.52	0.603	NS
LA	3.87 ± 0.37	3.83 ± 0.44	0.705	NS
EF%	46.57 ± 14.30	45.94 ± 16.16	0.864	NS

**Table 3: Preoperative echocardiographic data in the two studied groups**

Data were expressed as mean ± standard deviation (SD)

NS= Not significant

[B] Operative Data: Out of the 35 operations in the IMR group, 31 (88.6 %) were done using cardiopulmonary bypass as compared to 30 (85.7 %) in the control group (p=NS). The total bypass and cross clamp times are shown in table (4).

**Table 4: Total bypass and cross clamp times in the two studied groups**

	IMR group (n= 31)	Control group (n= 30)	P value	Significance
Total Bypass Time	91.42 ± 16.47	96.17 ± 17.44	0.279	NS
Cross Clamp Time	57.45 ± 13.76	54.77 ± 11.73	0.416	NS

**Table 4: Total bypass and cross clamp times in the two studied groups**

Data were expressed as mean ± standard deviation (SD) or number (%).

NS= Not significant

Smooth weaning off bypass was achieved in 22 patients (71 %) of the IMR group and 21 patients (70 %)

of the control group (p=NS). The rest of the patients needed either, inotropic support, electrical cardioversion or an IABP.

During the operation the LIMA was used in all but 3 of the 70 patients in both groups. The mean number of anastomoses was  $3.31 \pm 0.63$  in the IMR group and  $3.40 \pm 0.69$  in the control group (p=NS). Figure (1) shows the number of anastomoses in both groups. Fig (1): The number of anastomoses performed and the percentage of patients in both groups

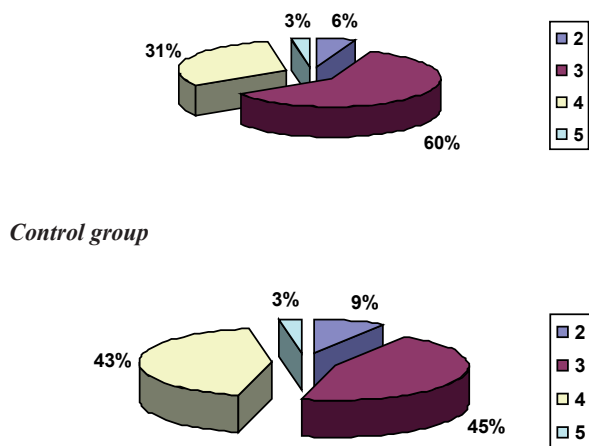


Fig 1: The number of anastomoses performed and the percentage of patients in both groups

TEE was used to assess the degree of regurgitation intraoperatively in 13 patients. It downgraded the degree of mitral regurgitation in 10 of the 13 patients measuring a mean jet area of  $3.13 \pm 1.33$  as opposed to  $5.85 \pm 0.85$  in their preoperative echo (p<0.001).

[C] Postoperative Data:

All the patients were discharged to the cardiothoracic ICU mechanically ventilated.

Table 5: Postoperative data in the two studied groups

	IMR group (n= 35)	Control group (n= 35)	P value	Significance
Mechanical ventilation (hrs)	$7.26 \pm 7.33$	$7.57 \pm 6.26$	0.848	NS
Inotropic support (hrs)	$20.72 \pm 13.05$	$24.9 \pm 12.71$	0.783	NS
Total blood loss (ml)	$847.50 \pm 411.13$	$731.17 \pm 355.21$	0.609	NS

Table 5: Postoperative data in the two studied groups Data were expressed as mean ± standard deviation (SD). NS= Not significant

In addition to the patients who were discharged from the operation room on inotropic support, 2 other patients in the IMR group needed that to be added in the ICU. Furthermore, 2 patients in the IMR group needed an IABP to be inserted in the ICU as opposed to one patient in the control group (p=NS). Three patients in the IMR group sustained a new perioperative infarction as shown by the postoperative ECG and elevated cardiac enzymes as compared to 4 in the control group (p=NS). Figure (2) shows the mean value of the total ICU stay in days of the patients in both groups (p=NS). Fig 2: Mean values of ICU stay (days) in the two studied groups.

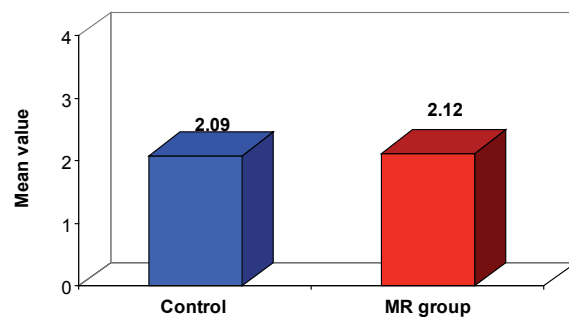


Fig 2: Mean values of ICU stay (days) in the two studied groups

There were 5 cases of postoperative morbidity in the IMR group and 8 in the control group. Table (6) depicts these complications.

Table 6: Postoperative morbidity in the two studied groups

	IMR group (n= 35)	Control group (n= 35)
Reoperation for bleeding	2	3
Arrhythmia	1	1
Renal failure	1	0
Wound Infection	1	3
Pneumonia	0	1

Table 6: Postoperative morbidity in the two studied groups

There was 1 (2.86 %) in-hospital mortality in the IMR group and 2 (5.71 %) in the control group (p=NS). All the cases occurred in the ICU. The mortality in the IMR group was a 53 year old female with a markedly dilated left ventricle preoperatively (LVEDD = 7.0, LVESD= 6.1) and poor contractility (EF= 33 %). She also had preoperative renal dysfunction (serum creatinine 3.3). After she had a three vessel bypass grafting, there was difficulty in weaning her off bypass and needed a large dose of inotropes. She was transferred to the ICU on

epinephrine 0.1 u/Kg/min. She passed into acute renal shutdown the next day of the operation, had peritoneal dialysis, and an IABP inserted in the ICU. She passed into a low cardiac output state and died. The first mortality in the control group was a 59 year old male with a preoperative ejection fraction of 40 %. He sustained an extensive anterior infarction on induction of anesthesia. There was very poor contractility after weaning off bypass. The second patient was a 62 year old female with a history of 2 previous extensive anterior and lateral infarctions that left her with a preoperative ejection fraction of 19 %. She passed into a low cardiac output state and died. Echocardiography was done for all the hospital survivors prior to discharge. Table (7) outlines the results of the postoperative echo. There were minute differences in the postoperative LVEDD, LVESD, and LA dimensions as compared to the preoperative echo in both groups. There was an improvement in the EF, with the IMR group sustaining a 4.69 % improvement and the control group a 5.3 % improvement (p=0.02). The degree of regurgitation postoperatively decreased to grade 0-1+ in 27 patients (79.4 %), remained 2+ in 6 patients (17.6 %) and increased to 4+ in one patient (2.9 %). The mean jet area postoperatively decreased to 2.41 cm<sup>2</sup> (p=0.04).

**Table 7: Postoperative echocardiographic data in the two studied groups**

	IMR group (n= 34)	Control group (n= 33)	P value	Significance
LVED	5.65 ± 0.54	5.77 ± 0.62	0.755	NS
LVES	4.02 ± 0.61	3.90 ± 0.57	0.542	NS
LA	3.84 ± 0.37	3.77 ± 0.48	0.671	NS
EF%	51.26± 17.21	51.24± 15.69	0.762	NS

**Table 7: Postoperative echocardiographic data in the two studied groups**

Data were expressed as mean ± standard deviation (SD)  
NS= Not significant

The mean hospital stay in days was 8.47 ± 2.11 in the IMR group and 8.24 ± 2.51 in the control group (p=NS).

[D]Follow up Data: Follow up was complete in 100% of the 67 hospital survivors. Patients were called after a mean period of 114.09 ± 29.37 days in the IMR group and 113.97 ± 28.98 days in the control group (p=NS).

In assessing the patients' functional state, the following was found; the average period for return to work was 100.23 ± 24.81 days in the IMR group and 105.93 ± 21.67 in the control group (p=NS). Dyspnea improved in both groups, with only 15 patients having dyspnea in the IMR group with a mean NYHA class of 0.62 ± 0.78 and 14 patients in the control group with a mean NYHA class of 0.73 ± 0.76. This was statistically signif-

icant when compared to the preoperative data (p=0.02), however the difference between both study groups was insignificant.

**Table (8) outlines the results of the follow up postoperative echo.**

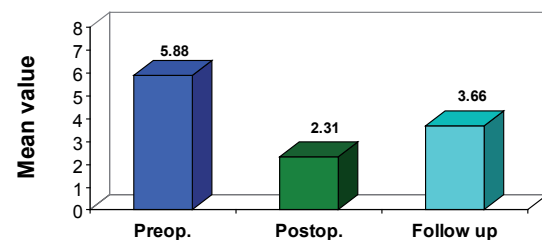
	IMR group (n= 34)	Control group (n= 33)	P value	Significance
LVED	5.46 ± 0.37	5.50 ± 0.42	0.805	NS
LVES	3.90 ± 0.46	3.91 ± 0.35	0.651	NS
LA	3.82 ± 0.27	3.79 ± 0.53	0.587	NS
EF%	51.26 ± 14.37	51.24 ± 15.49	0.734	NS

**Table 8: Echocardiographic data in the follow up period**  
Data were expressed as mean ± standard deviation (SD)  
NS= Not significant

**IMR group**

The degree of regurgitation as measured in the follow up echo was 0-1+ in 20 patients (58.9 %), 2+ in 11 patients (32.3%) and increased to 3-4+ in 3 patient (8.8 %). The mean jet area at follow up was 3.65 ± 3.55 as compared to a preoperative of 5.88 ± 0.94 (p=0.01).

Fig 3: The mean jet area as measured at different time periods in the IMR group



**Fig 3: Mean jet area as measured at different time periods in the IMR group**

**Discussion**

There is general agreement that patients with severe (3+ or 4+) IMR should undergo MV surgery at the time of CABG. However, the importance of moderate (2+) IMR in such patients is controversial. Therefore, we tracked the course of unrepaired moderate IMR after CABG surgery alone, regarding immediate and early outcome.

In our study, 74.3% of the IMR group patients had a previous posteroinferior MI (p=0.004). This validates data by other authors that states that, although anterior MI are more common to occur in IHD patients, the occurrence of IMR is more common after a posteroinferior MI (12). In their series on 102 patients with IMR, Calafiore and colleagues found that a posterior or inferior myocardial infarction occurred in 61.3% of their



patients (13). Explanation of this is that, posterior papillary muscle is supplied by one segmental artery and if occluded, it invariably infarcts thus producing tethering of the posterior mitral leaflet causing IMR.

The operative and postoperative results of our two studied groups were similar. There were no statistically significant differences as regards the use of on/off pump, the total bypass and ischaemic times, weaning off bypass, the dosage or length of time patients were on inotropic support, the need for IABP counterpulsation, the period of mechanical ventilation, the total blood loss, the perioperative morbidity or mortality, and the total period of ICU or hospital stay.

These results can conclude that the presence of moderate IMR does not add an additional burden to patients undergoing CABG in the operative and immediate postoperative periods. Strangely enough, this observation has not been thoroughly studied in the literature. A reason for this is that all the studies performed up to date are retrospective. Most authors address mid-term and long term survival and the late improvement in functional class to illustrate the impact of IMR on IHD patients and suffice with stating the in-hospital mortality to represent the immediate postoperative results. Our in-hospital mortality rate in the IMR group (2.9%) compares well with other series; 4.2% of the 168 patient cohort by Kim et al (14) and 2.9% in the study by Aklog et al (15).

Intraoperative TEE in our study downgraded 77% of our patients from a moderate preoperative regurgitation to no or mild regurgitation. The mean preoperative jet area of  $5.85 \pm 0.85$  decreased to  $3.13 \pm 1.33$ . This observation was also made by others. In the study by Aklog and coauthors (15), Intraoperative TEE downgraded the grade of regurgitation from moderate to mild or absent in 90% of the 38 patients. This is also substantiated by the study by Wong et al in which downgrading occurred in 56.8 % of their patients (16). The mechanism underlying this phenomenon is the unloading effect of general anesthesia. We found that CABG alone improved the clinical condition of patients in the IMR group. There were only 44% complaining of dyspnea at follow up as opposed to 86% preoperatively; the mean NYHA class improved from 2.11 preoperatively to 0.62 at follow up ( $p=0.02$ ). There was also an improvement in the ejection fraction, with the IMR group sustaining a 4.69 improvement ( $p=0.02$ ). Furthermore, CABG alone was able to decrease preoperative moderate IMR to mild or absent in 58.9% of our patients (20 out of 34). The grade remained moderate in 32.3%, and increased in only 8.8% of our cases. The mean jet area at follow up decreased to  $3.65 \pm 3.55$  ( $p=0.01$ ).

There is discrepancy in the literature as to agreement

with these results. In their study on 49 patients with mild to moderate IMR, Tolis and colleagues agree with our results. In their patients, the ejection fraction improved from 22.0% to 31.5% ( $p < 0.05$ ) after CABG. The mean degree of MR improved with CABG alone from 1.73 to 0.54 ( $p < 0.05$ ) as measured at a mean interval of 36.9 months from CABG. NYHA class improved from 3.3 to 1.8 ( $p < 0.05$ ) (17). In their study comparing 14 patients with moderate IMR to a similar cohort of 18 IHD patients who underwent CABG, Duarte and colleagues found no significant difference in the number of patients with angina or NYHA classification I or II versus III or IV between the two groups (11). Kim et al. found that the preoperative NYHA class of  $3.11 \pm 1.01$  decreased at 1 year to  $1.28 \pm 0.74$  (14). As regards improvement in the grade of regurgitation, Lam and colleagues found that moderate IMR improved to absent or mild in 73% of their patients on immediate postoperative echocardiograms and in 40% on follow up echocardiograms (18).

Disagreement however, arises in the proportion of patients who progressed to moderate-to-severe and severe mitral regurgitation. In the studies by Campwala et al., Lam et al., and Aklog et al., the proportion of patients in whom the grade of IMR progressed after CABG was 25%, 22%, and 40%, respectively (19), (18) & (15). These are however, certain points that need to be illuminated in these studies. In the study by Campwala and colleagues, the 37 patients (25%) in which the grade of IMR progressed had a statistically significant increase in their LV size postoperatively; the LVEDD increased by  $2 \pm 7$  mm and the LVESD by  $4 \pm 8$  mm. Also 15% of these patients had new perioperative infarctions and 9% had a new left bundle branch block on postoperative ECG. All these factors can change the preoperative characteristics of these patients. In the study by Lam et al. postoperative echocardiography was done in only 156 of their 467 patients at the discretion of the attending cardiologist. Therefore, it must be acknowledged that some of these echocardiograms may have been "clinically driven" by patient symptoms (heart failure) or physical examination (murmur); this would tend to cause over-representation of patients with more severe MR. Finally, the series by Aklog and coauthors defined moderate IMR as grade 3+, which is different than most series, including our own, which define it as 2+. Therefore, it can be argued that these investigators examined a cohort of patients with a more advanced grade of IMR preoperatively.

### Conclusion

The presence of moderate (2+) IMR in IHD patients undergoing CABG does not add any additional burden to the operative risk nor does it affect the immediate and early outcome of these patients. CABG alone can ame-

liorate moderate IMR in most patients postoperatively. This improvement is translated into an improvement in the functional class and the quality of life postoperatively. Moderate IMR progresses to more severe grades in only a minority of patients (5 %) in the early follow up period following CABG. Intraoperative TEE can frequently lead to downgrading of IMR.

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## SURGICAL RECONSTRUCTION OF RHEUMATIC ANTERIOR MITRAL LEAFLET PROLAPSE: MIDTERM RESULTS

Amr Rushdi, MD.  
Maged Salah, MD.

**Background:** Mitral valve repair for rheumatic disease still carries the worst results, although the characteristics of the usually underdeveloped and young population may still make it preferable to mitral valve replacement.

**Methods:** 23 patients had mitral valve repair for rheumatic pure mitral incompetence due to anterior mitral leaflet prolapse (AMLPL). They were operated upon between June 2003 and June 2007. Chordal transfer and artificial chordae with braided polyester sutures were the main techniques of repair. Intraoperative transesophageal echocardiogram was used to assess the efficiency of mitral repair.

**Results:** There was no mortality or valve related complications. In hospital echocardiography before discharge showed mild mitral regurge in 3 patients (13.1%) and trivial mitral regurge in 5 patients (21.7%). All patients were followed up by a clinical examination and serial echocardiograms, and the mean follow-up period was 25.6±16 months (range between 3-48 months). No patient required reoperation for structural valve failure at this period. There was a significant fall in the end-diastolic diameter (from 6.47±1.03 to 5.5±7.6 cm; p <0.001) and left atrial size (from 5.25±1.02 to 4.5±0.09 cm; p <0.001). Functional class was improved to 1.78±0.79. 12 patients (52.2%) had no residual mitral regurge (MR). 6 patients (26%) had trivial MR. 3 patients (13.1%) had mild MR and 2 patients (8.7%) had moderate MR. **Conclusion** mitral valve repair in rheumatic AMLPL entails stability with satisfactory midterm results.

Mitral valve repair was introduced in the late 1970s and early 1980s by the efforts of Carpentier<sup>1</sup>, Duran<sup>2</sup> and others. From that time many modifications were made to improve techniques of repair. Most surgeons now recognize its superiority, in terms of both early and late results<sup>3,4</sup>. However, repair for rheumatic disease still carries the worst results, although the characteristics of the usually underdeveloped and young population may still make it preferable to mitral valve replacement<sup>5</sup>.

Anterior mitral leaflet prolapse (AMLPL) can be treated with different techniques, such as chordal shortening, chordal transfer<sup>6</sup>, and chordal substitution<sup>7</sup>. The aim of this study is to address the possibility of repairing AMLPL in rheumatic patients and reviewing the success rate at mid-term.

### Methods

35 patients with rheumatic pure mitral incompetence were operated upon between July 2003 and July 2007. Anterior mitral leaflet prolapse was the main pathology in all patients. Intra-operative trans-esophageal echocardiography (TEE) was used to address the possibility of repair prior to skin incision. Mi-

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Address reprint request to : Dr Amr  
Rushdi Department of cardiothoracic  
surgery Cairo University

Email : amrrush@link.net

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tral valve replacement was done for 12 patients (34.3%). Extremely thickened or calcified leaflets and extreme fusion of subvalvular apparatus were the main causes of rendering the mitral valve irreparable. 23 patients (65.7%) had mitral valve repair with a variety of techniques. Those patients represent the study group.

### Operative technique

Median sternotomy was used in all patients to approach the heart, except two female patients who asked for submammary antero-lateral thoracotomy. Normothermic cardiopulmonary bypass was initiated in all patients. Myocardial protection was done with warm antegrade blood cardioplegia. Extended trans-septal approach was used in all patients to enhance mitral valve visualization.

Full analysis of the mitral valve apparatus was done including identification of the prolapsed segments. Chordal transfer was considered as the technique of choice. Adequate chordal support of the targeted area was checked in the posterior leaflet which is then detached as a triangle from posterior annulus. Then the excised portion of posterior leaflet was implanted to the free margin of the anterior leaflet with a double running 5/0 polypropylene suture enforced with pericardial pledgets. The residual defect of the posterior leaflet is closed using running 5/0 polypropylene suture.

If adequate chordal support was not justified, or other prolapsed points still exist, an artificial chorda was used. A double armed pledgeted braided polyester suture is passed twice through the fibrous portion of the papillary muscle head that anchors the elongated or ruptured chordae and is tied down. Both arms of the suture are then brought up to the free margin of the leaflet and passed through the point where the original chorda was attached. The needle is brought from the ventricular side of the leaflet to its atrial side and then passed once more through the leaflet. Two polypropylene stay sutures are then placed knotting just once to oppose the kissing edges of the leaflets. An indwelling line is inserted into the left ventricle across the mitral valve and saline is injected with a considerable pressure. When the opposite leaflet was also prolapsed, the lengths of the chordae were adjusted to align the edge of the leaflets with the mitral annulus. Once the length was adjusted, the suture was tied with the knot on the ventricular side.

The operation was completed by annuloplasty using either Carpentier-Edwards rigid incomplete ring or selective posterior annuloplasty with a glutaraldehyde-treated autologous pericardium strip just to commissural points. The annuloplasty band is sized according to the free margin length of the anterior leaflet using a ring

sizer. Valve competence was assessed by injecting saline into the left ventricle and, simultaneously, administering antegrade cardioplegia while the aortic valve was manually made incompetent to pressurize the left ventricle. The repair was considered acceptable when the regurgitation was less than trivial during testing.

A complete examination of the mitral valve by transesophageal echocardiography (TEE) was done through midesophageal four chamber, mitral commissural, midesophageal two chamber, midesophageal aortic long axis, transgastric basal and transgastric two chamber views with pulsed wave Doppler examination of left and right pulmonary veins.

2D examination aimed to confirm the diagnosis, look for the cause of regurge, and ensure that it is repairable. It aids in detection of the diseased leaflet and scallop, examination of the subvalvular apparatus and measurement of left atrial and ventricular size and function. Continuous wave Doppler was used to measure peak and mean trans-mitral gradient and pressure half time to measure mitral valve area.

Mitral incompetence was classified into Trivial (jet area less than 2 cm<sup>2</sup>), mild (jet area less than 3 cm<sup>2</sup>), moderate (jet area 3-6 cm<sup>2</sup>) and severe (jet area > 6 cm<sup>2</sup>). These data were measured after induction of anesthesia and after mitral repair. When the jet area was less than 3 cm<sup>2</sup>, the repair was considered acceptable, and when the area was more than 3 cm<sup>2</sup>, the repair was unacceptable and mitral valve replacement was considered.

### Thromboembolic prophylaxis

All patients received warfarin sodium for 3 months. Patients with atrial fibrillation or with giant left atrium received permanent anticoagulation. International normalized ratio (INR) was kept at 2-2.5.

### Follow-up and data collection

Data were collected antegradely in pre-prepared sheets. All data are expressed as mean and Standard Deviation. Student's t-test was used to analyze the data. Follow-up was conducted by clinical and echocardiographic evaluations 3 and 6 months after surgery and then annually until the end of follow up in September 2007. The last visit of each patient represents the end point of the follow up.

### Results

Preoperative patient characteristics were enlisted in table 1. AML chordal elongation was found in 16 patients while chordal rupture was found in 12 patients. No annular calcification encountered. The details of valves pathology were enlisted in table 2.



Age(years)	33.4±12.1
Sex(male: female)	9:14
NYHA Class	3.04±0.56
Atrial fibrillation	14/23(60.9%)
LVED	6.47±1.03
LVES	4.38±1.05
Ejection Fraction (%)	59±0.08(range 45-70)
Left atrium	5.25±1.02
Pulmonary artery pressure	46.96±16.08
Mitral valve area (cm2)	4.56±1.04
Jet area (cm2)	10.3±2.26

**Table 1: Preoperative patient characteristics**  
NYHA= New York heart association

Valve pathology	AML segment	Number of patients
Anterior mitral leaflet( AML) prolapse		23/23 (100%)
Single AML Chordal rupture		3/23(13.1%)
	A1	2
	A2	1
Multiple AML Chordal rupture		4/23 (17.9%)
	A1,A2	3/23(13.1%)
	A2,A3	1/23 (4.3%)
AML Chordal elongation		11/23 (47.8%)
	A1	3
	A2	4
	A3	2
	A1,A2	2
AML Chordal rupture(r) and chordal elongation (e)		5/23 (21.7%)
	A1(r) A2 (e)	2
	A1(r) A3 (e)	1
	A2(r) A1 (e)	1
	A3(r)A1,A2(e)	1
Posterior mitral leaflet prolapse		3/23(13.1%)
Posterior mitral leaflet hypoplasia		4/23 (17.9%)
Commissural fusion		2/23(8.7%)
Annular dilatation		10/23 (43.5%)
Subvalvular apparatus lesion		4/23 (17.9%)
Moderate to severe Tricuspid regurge		3/23(13.1%)
Mild to moderate Tricuspid regurge		6/23 (26%)

**Table 2: Operative findings (data in parentheses are percentages).**

AML= Anterior mitral leaflet  
r= chordal rupture  
e= chordal elongation

Artificial chordae were implemented in 17 patients (73.9%), while chordal transfer was done in 14 patients (60.9%). 8 patients (34.8%) required both chordal trans-

fer and artificial chordae. Quadrangular resection of the posterior leaflet and chordal transfer from posterior to anterior leaflet were done in 3 patients (13.1%) for bile-aflet prolapse. Commissurotomy was done in 4 patients (17.9%). Splitting of the commissural chordae was done in 3 patients. Cutting the secondary chordae of the posterior leaflet was done in two patients. Three patients (13.1%) required tricuspid segmental annuloplasty.

Carpnetier-Edwards ring was used in 14 patients (60.9%). Size 28 in 6 patients, size 30 in 5 patients, and size 32 in 3 patients. Selective annuloplasty with a pericardial strip was done in 9 patients (39.1%).

Intra-operative post-bypass TEE revealed trivial mitral regurge in 4 patients (17.9%). There was no operative mortality. One patient required 10 days of temporary pacing for low junctional rhythm. In hospital Trans thoracic echocardiography revealed mild mitral regurge in 3 patients (13.1%) and trivial mitral regurge in 5 patients (21.7%). No conversion to mitral valve replacement was needed. [fig.1]

### Follow up

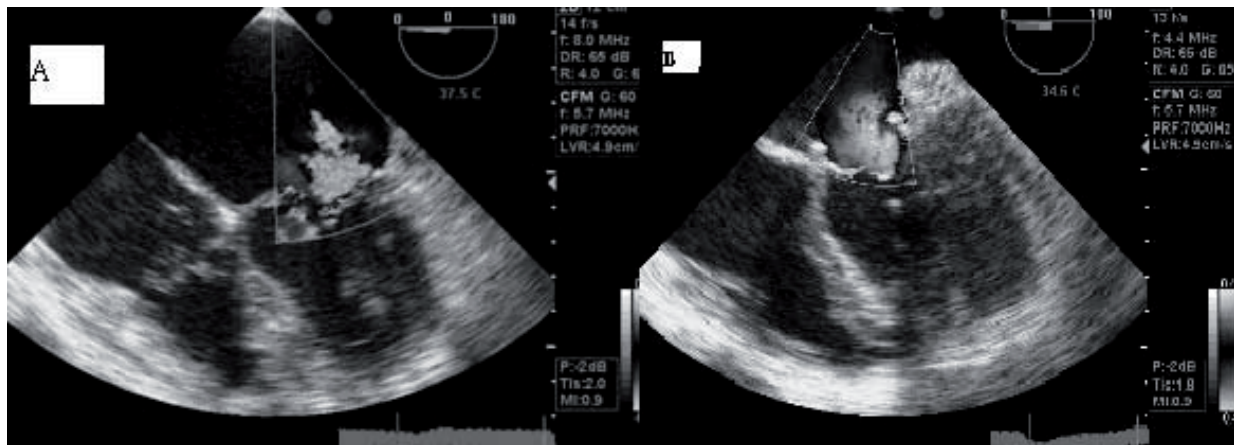
Patients were followed up for 25.6±16 months (range between 3-48 months). There was no mortality, no thromboembolic, or anticoagulant related complications. There were no episodes of infective endocarditis. No patient required reoperation for structural valve failure at this period. There was a significant fall in the end-diastolic diameter (from 6.47±1.03 to 5.5±0.76 cm; p <0.001) and left atrial size (from 5.25±1.02 to 4.5±0.09 cm; p <0.001). Functional class was improved to 1.78±0.79; p <0.01).

12 patients (52.2%) had no residual mitral regurge (MR). Of them, 10 patients had chordal transfer for AML chordal elongation, and two patients had chordal substitution for a single ruptured chorda. Moreover, 9 patients of those who had no residual regurge have had no annular dilatation, fused commissures or subvalvular apparatus affection.

6 patients (26%) had trivial MR. 3 patients (13.1%) had mild MR and 2 patients (8.7%) had moderate MR. All Patients with residual mild and moderate regurge had both chordal rupture and elongation of the AML. Three of them had fused commissures and four had annular dilatation.

### Discussion

Mitral valve repair represents a better alternative than valve replacement in terms of higher survival rate and significant reduction in mitral valve related complications 5.8.9.10. Reconstructive procedures for rheumatic



**Fig 1:** Mid-esophageal four chamber view of Trans-esophageal echocardiogram (TEE). (A) Showing a prolapsed anterior mitral leaflet with a posteriorly directed jet (mosaic). (B) Post mitral repair TEE with no regurgite.

mitral valve insufficiency remain controversial. The risk of reoperation is higher than degenerative diseases and long term studies proving the stability of these techniques are scarce<sup>3,11</sup>. Moreover, the variety of reconstructive techniques<sup>6,7,10,11</sup> together with the mixed patient population series created a mystery around this type of surgery.

In this series we tried to make our sample as homogeneous as possible regarding age, pathology and surgical techniques adopted. Only young age patients (mean 33 years) with rheumatic AML prolapse were studied. Historically, the repair of an AML prolapse has been technically demanding and less predictable than the repair of a posterior-leaflet prolapse. The traditional approach for the repair of anterior-leaflet prolapse due to elongated chordae has been either chordal shortening or chordal transfer. Chordal-shortening techniques, especially, may have the disadvantage of impaired durability by recurrent mitral insufficiency in a significant number of patients, caused by the rupture of shortened chordae.<sup>12,13</sup>

In 1983, Carpentier first described the chordal transfer from the posterior leaflet for AMLP<sup>8</sup>. Since then this technique gained popularity by many surgeons who have extended the use of chordal transfer to prolapse caused by chordal elongation<sup>9,10,11</sup>. Chordal transfer is an easier technique with good long term results<sup>11</sup>, but although the transferred chordae may have the correct length, they may be thin and fragile and consequently prone to rupture, resulting in failure of the repair.

Moreover, the effectiveness of this technique is limited to correct complex pathogenic cases such as multiple anterior ruptures, anterior rupture associated with posterior elongation, bilateral ruptures or global elongation. In our experience, these particular situations accounted for 73.9% of patients (17/23 patients) who required arti-

ficial chordae to achieve proper repair.

Frater and David introduced the use of polytetrafluoroethylene (PTFE) sutures for chordal replacement as part of mitral valve repair in patients with extensive mitral pathology. Neochordae can be used in all cases independent of the condition of the posterior leaflet. The only difficulty with this technique is finding the correct length<sup>13,14</sup>.

PTFE appears to be an ideal material for synthetic chordal replacement because of its biomechanical properties which ensure long-term durability and allow surface endothelialization. No calcification has been found in PTFE sutures explanted at various time intervals after implantation<sup>15</sup>. Braided polyester was used in this series, because of the unavailability of PTFE sutures in our center. At midterm, no fibrosis or calcification was found related to braided polyester artificial chordae.

Chauvaud and colleagues studied 951 patients with rheumatic mitral regurge over a period of 29 years. They found that surgery for anterior leaflet prolapse has a freedom from reoperation of 75% at 10 years and 66% at 20 years. Freedom from reoperation was different regarding the type of regurge. At 20 years, freedom as 65%, 63% and 46% for types IIa/IIIp, II, III respectively. The freedom from valve related events was 93%, 82%, 72%, and 52% at 5, 10, 15, and 20 years of follow up respectively<sup>3</sup>.

Salati and colleagues studied 89 patients who had chordal transfer for AMLP for a mean of 41 months. They had no mitral regurge (MR) in 45% of patients. 33% of patients had residual grade I MR, 17% of patients had residual grade II MR and 5% of patients had residual grade III MR<sup>16</sup>.

In our series, postoperative clinical results have been satisfactory, since 78% of the patients are in NYHA

functional class I-II and leading an active normal life. Complex original pathology necessitates complex forms of repair and worse midterm results. However, this issue represents only 21.8 % of patients who have only residual mild to moderate regurg at a mean follow-up of 25 months. 52.2% of patients had no MR and 26% of patients had trivial MR.

Selective posterior annuloplasty with a pericardial strip claimed to avoid a disadvantage of rigid rings relates to the change of the physiological saddle shape of the mitral annulus, leading to a more planar configuration<sup>16</sup>. Which predispose to the development of LV outflow tract obstruction by exacerbating mitral-leaflet systolic anterior movement (SAM), or by narrowing the intersection angle between the aortic and the mitral-valvular planes<sup>17</sup>.

### Conclusion

Mitral valve reconstructive surgery for rheumatic anterior mitral leaflet prolapse can be carried out with satisfactory early and midterm results. It allows improvement of the cardiac dimensions and functional class. These results also demonstrated the stability of repair, especially for patients with simple pathology.

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## RISK FACTORS FOR OUTCOME AFTER PROSTHETIC MITRAL VALVE DYSFUNCTION DUE TO INFECTIVE ENDOCARDITIS

Nasr Ezzat, MD,  
Ayman Gabal, MD,  
Ayman Sallam, MD,  
Mamdouh Elsharawy, MD,  
Ahmed Deebis, MD,

**Background:** prosthetic valve dysfunction due to valve endocarditis represent a catastrophic problem. Clinical features of valve dysfunction with fever and positive blood cultures are found in majority of patients.

**Methods:** 35 patients are reoperated due to prosthetic mitral valve endocarditis by mitral valve rereplacement through median resternotomy or right anterolateral thoracotomy.

**Results:** the time between primary operation and onset of valve dysfunction due to prosthetic valve endocarditis (PVE) range from 1-60 months with a mean  $30.6 \pm 10$  months. Age range from 20-39 years with a mean  $32 \pm 5.2$  years. There were 23 (65.7%) females & 12 (34.3%) males. Fever was present in all cases (100%). Dyspnea either mild to moderate in 21 patients (60%) and severe in 14 patients, (40%) congestive heart failure was moderate in 60% and severe in 40% of patients, low cardiac output was found in 19 patients (54%), 9 patients (25.9%) need preoperative endotracheal intubations and mechanical ventilation. There is non specific features as generalized fatigue, weight loss, anorexia, night sweats in 28 (80%) of patients. There is splenic enlargement in 21 (60%) patients. Blood culture was positive in 28 (80%) patients and staphylococci were the most commonly isolated organisms (13/28) (37.1%). Transesophageal echocardiography (TEE) is a good and sensitive tool for diagnosing valve dysfunction and detecting vegetations, ring abscess and paravalvular leak. Resternotomy done in 28 (80%) patients and right anterolateral thoracotomy done in 7 cases (20%).

**Conclusion:** this event is preventable in most cases, so all patients having mitral valve replacement should have antibiotic prophylaxis. Prevention of contamination in the operating theatre and intensive care unit (ICU). Use of adequate antibiotic prophylaxis for patients who have had mitral valve replacement during any diagnostic or therapeutic procedure causing bacteremia. Diagnosing of PVE should be suspected in dyspneic febrile patients with any mechanical valve with new cardiac murmur, leucocytosis, high ESR, splenomegally and positive preoperative blood culture. TEE is sensitive and effective diagnostic tool in PVE. Surgical intervention should be done in patients with low cardiac output (LCO) state, congestive heart failure, persistent sepsis, valve obstruction and paravalvular leak. Right thoracotomy approach is a good decision for reoperation due to PVE to decrease morbidity.

### Introduction

Prosthetic cardiac valve remain a substantial source of morbidity and mortality, reoperation for mitral valve is becoming part of routine practice of cardiac center. The over all operative mortality is still high in redo surgery due to PVE. ,(9).

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Address reprint request to Dr Nasr  
Ezzat

Department of Cardio-thoracic Surgery  
Zagazig University

E-mail: jegyptscts@gmail.com

Codex :04/ cord /51 B /0709



Risk factors of hospital mortality & morbidity after PVE by reoperation emphasized the role of functional class of the patients preoperatively and doing reoperation as early as possible to give best outcome, (8).

The prosthetic valve may produce hemolysis due to the valve itself or associated paravalvular leak. Morbidity associated with PVE such as valve thrombosis, embolisation, bleeding events and paravalvular leak, (9).

### Aim of the work

We aim to assess the effects of different risk factors on the prognosis of patients undergoing reoperation due to prosthetic mitral valve endocarditis and outcome of reoperation. We also aim to put parameters for reoperation and precautions preoperatively taken to obtain the best outcome.

### Methods

This study include 35 patients underwent reoperation due to PVE of mitral valve in cardiothoracic surgery department at Zagazig university hospitals during the period from Jan. 2001 to Jan. 2006. The patients were hospitalized with diagnosis of mitral valve dysfunction due to PVE.

The diagnosis of PVE based on clinical picture (fever, toxic look, pallor, leucocytosis, presence of new cardiac murmur, signs of peripheral septic emboli, splenomegaly), positive blood culture.

Preoperative study:- all patients are subjected to the following on admission:

1- History: complete history about medical, surgical treatment, history of surgical procedures as dental manipulations or gynecological procedures, history of post-operative complications as wound infection or fever.

2- Clinical examination:- complete general, cardiac and chest examination for signs of PVE.

3- Laboratory study:- full laboratory examination includes complete blood picture, liver & kidney function tests, coagulation profile, blood gases analysis and electrolytes, blood culture.

4- Resting ECG for all patients and analyzed for pulse rhythm, conduction abnormality, right or left ventricular hypertrophy and signs of ischemia.

5- Radiological study:- chest posteroanterior and lateral views.

6- Echocardiography:- for all patients either trans-thoracic or transesophageal to determine the following:

- Mitral valve study: movements of cusps, gradients across the valve, ring abscesses

- Presence of valve vegetations or thrombi, and their effects.

- Presence of paravalvular leak.
- Left atrial dimensions and thrombi inside it.
- Left ventricular study for dimensions & function.
- Degree of pulmonary hypertension.
- Associated valvular lesion as tricuspid valve lesion.

7- Once the diagnosis was confirmed either by strong suspicion or proved by culture, aggressive antibiotics were started intravenously.

\* Operative study:- all 35 patients were subjected to surgical intervention. Intraoperative monitoring lines were connected (arterial, central venous, peripheral venous, Foley's catheter, temperature probe). Induction of anesthesia was done and maintained as usual. Either median sternotomy was the incision used or right antero-lateral thoracotomy through 4th intercostals space. The right and left atria were exposed.

- In thoracotomy cases, we use femoral cannulation and deep hypothermia to 20°C.

- In sternotomy cases, we use cold crystalloid cardioplegia and systemic hypothermia to 28°C.

- In all patients, hemodilution was done and hematocrite reduced to 25%.

- After completing the procedure, deairing was done, then rewarming to 37°C was done when hemodynamics were stable, ABGs and electrolyte were satisfactory.

- Patients shifted to ICU and mechanically ventilated with monitoring the blood pressure, central venous pressure, pulse (rate, rhythm), blood loss and urine output. Patients need inotropic support in different concentrations and vasodilators were used in some patients with pulmonary hypertension.

- Weaning from mechanical ventilation was done when criteria of weaning were met with.

- in 1st postoperative day plain chest X-ray, ECG, complete laboratory investigations were routinely done for all patients.

- when patients become stable, patients shifted to ordinary ward and were followed up in the ward closely.

- patients were discharged from hospital when:

Wound clean, stable sternum, stable cardiovascular status, normal laboratory findings with coagulation profile in therapeutic level and no fever for at least one week before discharge.

Patients were regularly followed postoperatively in outpatients clinic monthly for 6 months and all preoperative studies were repeated except echocardiography which done to all patients before hospital discharge and then 6 months later and searching for left ventricular study (dimensions & function) compared to preopera-

tive findings, prosthetic valve profile as movement, gradients across the valve, vegetations, thrombi, ring abscess pulmonary artery pressure, other valvular lesions and pericardial effusion or adhesions.

### Statistical analysis:

\* Student's *t*-paired test was used to test difference between mean in numeric data.

\* Chi-square test used to detect difference between non numeric data.

\* Correlation of coefficient (r) used to denote relation between an independent and a dependent of follower.

\* P-value is significance if  $P < 0.05$ .

### Results

35 patients underwent reoperation due to prosthetic mitral valve endocarditis in the period from Jan. 2001 to Jan 2006.

We tried to evaluate the surgical outcome of the patients and studying various risk factors affecting outcome of surgery.

\* Age: the mean age was  $32 \pm 5.2$  years with a range from 20-39 years.

\* Sex: we have 24 females (68.5%) and 11 males (31.5%).

\* The time elapsed from 1st operation till second reoperation range from 1-60 months with a mean of  $30.6 \pm 10$  months.

An identifiable source of infection and/or predisposing factors were elicited in 30 patients (85.7%) as dental procedure in 10 (28.6%) patients, gynecological procedure in 11 patients (31.4%), postoperative fever in 3 patients (8.6%), wound infection in 2 patients (5.6%), breast procedure in 4 patients (11.4%) and unknown cause or source in 5 patients (14.2%) (Table I).

History	No.	%
- Dental procedure	10	28.6%
- Gynecological procedure	11	31.4%
- Postoperative fever	3	8.6%
- Wound infection	2	5.6%
- Breast procedure	4	11.4%
- Unknown source of infection	5	14.2%

**Table (1): Shows the predisposing causes of endocarditis in PVE.**

- Clinical findings:- The initial clinical presentation in all cases was fever which is either low grade in 25 patients (71.4%) or high grade fever in 10 patients (28.6%). Generalized non specific manifestations in the form of fatigue, weight loss, and night sweats were pres-

ent in 28 patients (80%).

- Congestive heart failure symptoms were present in all patients (mild to moderate in 21 (60%) patients and severe in 14 patients (40%).

- There is new murmur and loss of metallic sounds in 4 patients (11.4%) muffling of prosthetic valve sound in 25 patients (71.4%) and no change of valve sounds in 6 patients (17.2%).

- Congestive heart failure and pulmonary congestive symptoms were present in 18 patients (51.4%), 7 patients (20%) need preoperative mechanical ventilation and two patients (5.7%) had cardiopulmonary arrest with successful resuscitation. (table 2).

Clinical feature	No	%
*Dyspnea		
a-NYHA class III	21	60%
b-NYHA class IV	14	40%
*Fever *****		
a- low grade	25	71.4%
b- high grade	10	28.6%
* Congestive Heart Failure*****		
a- Moderate	21	60%
b- Severe	14	40%
*Metallic sound		
a-present	4	11.4%
b- Muffled	25	71.4%
c- Absent	6	17.2%
*Spleen enlargement	21	60%
*Mechanical ventilation	7	20%
*Cardiopulmonary arrest	2	5.7%

**Table (2): Clinical findings in patients with PVE.**

\* Laboratory findings : patients with PVE had hypoxia, hypercapnea, metabolic acidosis, variable degree of normochromic anemia, high ESR, leucocytosis, disturbed renal function was found in 9 patients (25.7%) hepatic dysfunction with elevated serum bilirubin in 11 patients (31.4%), blood culture was positive with isolated organism in 28 patients (80%) and in 7 patients blood cultures were either -ve or contaminated (20%).

- staphylococci were the most common isolated organism. It was isolated from 15/28 cases (53.6%).

- Streptococci were isolated from 7/28 patients (25%) either alone or mixed with other organisms.

- Gram- ve organisms were isolated from 4/28 case (14.3%) either alone or mixed( table 3)

Variable	No. of patients	%
Blood culture:		
* - ve.	7	20%
* + ve.	28	80%
Organisms:		
1* staphylococci	15	53.6%
2* streptococci	7	25%
3* gram-ve.	3	10.7%
4* mixed infection.	3	10.7%
5* no growth.	7	20%

**Table (3): Shows preoperative blood culture result**

\* Echocardiography findings: the study showed:

- Restricted prosthetic valve movement in 31 patients (88.6%).

- Mean diastolic pressure gradient was 14.6±3 mmHg with a range between 9-18 mmHg.

\* Vegetations: there was statistically significant difference between TEE & TTE regarding detection of vegetations in case of PVE, TEE is more sensitive with sensitivity up to 92.8% versus 60.7% with TTE.

\* Vegetations were found totally in 28 patients, but 26 patients (74.3%) detected by TEE&TTE (preoperatively) but the other two cases (7.1%) detected intraoperatively.

\* Echocardiography detect paravalvular leak in 12 cases (34.2%) TEE is more accurate than TTE in detecting this lesion.

\* Echocardiography give good study about ventricular dimensions & function (Table 4).

Variable	Min	Max	Mean	SD
1- Mean diastolic pressure gradient mmHg	9	18	14.6	±3
2- Left ventricular E.F%	36	58	48.4	±7
3- Valve movement	No	%		
a*Restricted	31	88.6%		
b*Normal	4	14.6%		
4-Ejection fraction				
a-Good	14	40%		
b-Fair	12	34.3%		
c-poor	9	25.7%		

**Table (4): Shows echocardiography findings in PVE.**

Surgical intervention: 20 patients need emergency reoperation versus 15 patients operated on less emergency bases

All patients receive course of medical treatment in

ICU which included broad spectrum antibiotics (parenteral) either according to culture & sensitivity of isolated organism or empirical in cases no causative organisms isolated. Duration of medical treatment ranged between 2-19 days with a mean 9±3.1 days.

Redo median sternotomy was used in 25 patients (71.4%) while right thoracotomy approach was used in 10 patients (28.6%).

The surgical technique used was removal of infected prostheses, debridement of infected annulus and removal of all friable and necrotic tissues.

Prosthetic valve replacement was use in all cases and fixed in the original annulus.

Aortic cross clamping time in resternotomy ranged from 60-110 minutes with a mean 83±260 min with a mean 180±40 minutes. In right thoracotomy aortic cross clamp time ranged between 80-140 min with a mean 150±43 min.

Weaning from cardiopulmonary bypass was smooth in 22 patients (62.9%), difficult in 10 patients (28.6%) and need more support and high doses of inotropes. In the other three cases weaning from CPB with in possible with intra operative deaths (8.6%).

\* Total blood loss ranged from 430 – 1260 ml with a mean of 530± 170 ml. 4 cases (11.4%) need reexploration due to excessive bleeding.

\* stay in ICU ranged from 3-14 days with a meant of 4.4 ± 1.3 days. 5 cases died postoperatively in ICU due to sepsis, acute renal failure and multiple organ failure with septicemic shock.

\* Early postoperative complications include: low cardiac output in 11 patients (34.4%), excessive postoperative bleeding in 4 patients (12.5%), prolonged mechanical ventilation in 8 patients (25%), ventricular arrhythmia in 8 patients (12.5%) , neurological complications in 3 patients (9.4%), renal impairment in 4 patients(12.5%)and wound infection in 4 patients(12.5) ( table 5)

Item	No. of patients	%
1-Low cardiac output.	11	34.4%
2-Excessive postoperative bleeding	4	12.5%
3- prolonged mechanical ventilation	8	25%
4- ventricular arrhythmia	8	25%
5- Renal impairment.	4	12.5%
6- wound infection.	4	12.5%
7- neurological complications	3	9.4%

**Table (5): shows early post operative complications**

## Discussion

Prosthetic valve endocarditis (PVE) remains a substantial source of morbidity and mortality, Elective or emergency operation for patients with mitral PVE become part of daily work due to this complication.

35 patients underwent reoperation due to mitral PVE were included in this study. .

- Regarding sex in our study no significant female predominant, it was 68.5% female and 31.5% males.

- The mean interval between time elapsed from 1st operation till second operation range between 1-60 months with a mean  $30.6 \pm 20$  this also reported by .(5)

that no sex difference in their study. The prevalence of females in our study may be due to history of gynecological procedures without antibiotic cover.

- In our study the source of infection in (PVE) was dental procedure in 10 cases (28.6%), Gynecological procedure in 11 cases (31.4%), postoperative fever in 3 cases (8.6%), wound infection in 2 cases (5.6%), breast procedure in 4 cases (11.4%) and the source of infection was unknown in 5 cases (14.2%).

Calderwod et al., stated that mouth and nasopharynx are the most likely sources of contamination in streptococcal infection and Bayer et al., emphasized the role of gynecological and obstetric procedures in the development of mitral PVE. .(3,4)

- In our study the clinical findings and routine laboratory investigation in patients with mitral PVE were non specific as fever, new murmur, leucocytosis, high ESR and anemia. It is difficult to diagnose early postoperative PVE in the presence of wound infection, pneumonia, phlebitis, urinary tract infection and postcardiotomy syndrome.

- These findings were also reported by Jones et al., and Wolff et al., who stated that microbiological examination by blood culture is essential in the diagnosis of mitral PVE as the clinical picture and the laboratory findings are almost non specific and have no clinical judgment in the presence of negative blood culture. .(12,21)

In our study causative organisms were isolated in 80% of patients by bacteriological examination. the blood culture is -ve or contaminated in 20% of patients

- In our study causative organisms were isolated in 80% of patients by bacteriological examination. The blood culture is -ve or contaminated in 20% of patients. Staphylococcal organisms were the most common pathogen isolated from +ve culture 15 (53.6%), streptococci in 7 cases (26%), gram -ve organisms in 3 cases (10.7%), mixed infection in 3 cases (10.7%) and no growth in 7 cases (20%).

- the same results were reported by., .(21,3) who stated that staphylococci were the microorganism most

commonly involved in PVE and virulence group constitute the second most common organism responsible for PVE especially late onset, Jones et al. .(13), also reported the same results and findings. Griggetal. and Marguat et al. .(11,15) recommended that all patients suspected to have PVE should undergo TTE&TEE as the later is superior and sensitive than TTE. This is with our study that result of TEE is superior when analyzed with operative findings in detecting vegetations, paravalvular leak, and masses on the atrial surface of the valve, left atrial appendages or in the body of the left atrium itself.

This is also reported by .(15,6) There is initial period of medical treatment before surgery. In the presence of persistent fever, sepsis, valve obstruction, severe pulmonary venous congestion, pulmonary edema, heart failure, vegetations, paravalvular leak and low cardiac output with hemodynamic instability. Akowauh et al., and Baumgartner et al., reported that the main indication of surgery in these patients were congestive heart failure, uncontrolled sepsis and septic emboli. .(1,2)

The difference may be due to delayed referral of patients from other hospital and condition of our patients were poor. Our medical treatment range from 2-19 days with a mean of  $9 \pm 3$  days.

This is also reported with .(1,2) . However Wilson et al., reported that no correlation between surgical success and duration of preoperative antibiotics. .(23). The over all mortality in our study were 8 patients (22.9%). The mortality was affected by emergency surgery, advanced NYHA class, left ventricular dysfunction, prolonged cross clamping time (CCT) and total bypass time (TBT).

This also reported by.(7,10,14,16,18)

Redo through re sternotomy in our series is risk factor causing early complications postoperatively. This is also reported by.(17). So right thoracotomy in reoperation is preferred to avoid these complications. This is also reported by ,(19).

## Conclusion

PVE is a preventable problem, so all patients with prosthetic valve should have good antibiotic prophylaxis with the antibiotic chosen should be directed against the commonest isolated organisms and guided by antibiotic sensitivity data.

- Contamination in ICU and operation theatre should be prevented and all procedures to be done under complete aseptic precautions.

- Diagnosis of PVE should be suspected in any patients acutely febrile dyspneac one.

- Postoperative echocardiography is essential in all patients with regular follow up examination at least



yearly.

- Attempts to perform elective reoperation with any patients with progressive symptoms before deterioration in ventricular function.

- All patients with suspected prosthetic valvular dysfunction should undergo TTE as well as TEE if available

- Aggressive antibiotic should be started once the diagnosis is suspected

- Surgical intervention should be recommended in patients with hemodynamic instability, sepsis, vegetations and unstable prosthesis with paravalvular leak.

- Reoperation should be done by senior surgeons to reduce (ACT,TBT) to reduce operative mortality and postoperative morbidity and mortality.

- Right thoracotomy approach is a good decision for reoperation to reduce morbidity& mortality.

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## CONVERSION TO CARDIOPULMONARY BYPASS IN PLANNED OFF- PUMP CORONARY ARTERY BYPASS GRAFTING: EFFECT OF TIMING ON OPERATIVE MORBIDITY AND MORTALITY

Mohamed Essa MD,  
Ehab Yehia MD,  
Ashraf Esmat MD,  
Ahmed Abd El-Aziz MDS,

**Background:** Timing of conversion in off-pump coronary artery bypass surgery (OPCAB) was crucial to avoid serious outcomes and has not been extensively studied. Our aim was to evaluate operative morbidity and mortality according to timing of conversion in patients initially scheduled for OPCAB and subsequently converted to cardiopulmonary bypass (CPB).

**Methods:** In this prospective multicenter study, all planned non emergent isolated OPCAB done between December 2004 to August 2007 were included. We classified timing of conversion according to the urgency of the conversion as either (1) Semi-elective (Early) conversion or (2) Emergency (Delayed) conversion. All preoperative, intraoperative and in-hospital postoperative data of all patients were collected and analyzed and groups were compared.

**Results:** From a total of 480 patients operated, 26 patients converted semi-electively and 21 needs emergency conversion. Emergency conversion group patients had serious complications incidence of 33.3% versus 7.7% and 6 % in semi-elective conversion and non- conversion groups respectively, which is highly statistically significant ( $p < 0.01$ ). Patients converted semi-electively had overall mortality rate of 3.8 % whereas it increased to 28.6% in those undergoing emergency conversion, which is highly statistically significant ( $P < 0.01$ ). Statistically, there was no significant difference as regard operative morbidity and mortality between the semi-electively conversion group and the non-conversion group ( $p =$  not significant).

**Conclusion:** Emergency conversion to CPB during OPCAB surgery results in significantly higher operative morbidity and mortality. Early conversion semi-electively under controlled circumstances is a safe and good option.

Off-pump coronary artery bypass surgery (OPCAB) has gained significant popularity in an effort to reduce patient morbidity related to cardiopulmonary bypass and has become a widely accepted procedure for surgical myocardial revascularization [1-5]. One of the limitations of beating heart surgery is that in some instances the procedure cannot be completed safely without resorting to cardiopulmonary bypass (CPB) [6-16]. The most common reasons for conversions to CPB include: ischemia, inability to visualize a target vessel, and hemodynamic instability [17, 18]. The reported incidence of conversion has varied from 0 % to 25% [6-16].

Several groups have reported that converted patients have significantly higher mortality and morbidity than patients not requiring conversion [6-16]. Emergency conversion significantly increased major morbidity and mortality [12-16], meanwhile, early elective conversion without hemodynamic compromise has been reported not to increase mortality and morbidity [6, 9]. Although, timing of conversion was crucial to avoid serious outcomes; it has not

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Address reprint request to Dr Mohamed  
Essa

Department of Cardio-thoracic Surgery  
Zagazig University .

E-mail: messacts1@gmail.com

codex : 04 / cord / 52 / 0706

been extensively studied [8, 9]. There are no published studies that have been specifically addressed the operative outcomes according to timing of conversion [8, 9, 14].

The aim of this study was to evaluate operative morbidity and mortality according to timing of conversion in patients initially scheduled for OPCAB and subsequently converted to cardiopulmonary bypass (CPB) as these outcomes have major implications regarding the correct guideline for timing of conversion during OPCAB.

## Methods

In this prospective multicenter study, all planned non emergent isolated OPCAB done between December 2004 to August 2007 in Zagazig university hospital, El-kaser El-Ainy hospital and Ain-shams hospital were included. All procedures were performed by experienced surgeons. Also, anaesthesia was exclusively managed by experienced anaesthesiologists.

We classified timing of conversion according to urgency of conversion; as either (1) Semi-elective (Early) Conversion (Group I): was defined as conversion to cardiopulmonary bypass before hemodynamic collapse. Situation where we were not able to maintain systolic blood pressure of 100 mm of Hg (unresponsive to Trendelenburg position, atrial pacing, intravenous fluid infusion, or inotropes (dopamine 5-8  $\mu\text{g}/\text{kg}/\text{min}$  or norepinephrine 0.025-0.05  $\mu\text{g}/\text{kg}/\text{min}$ ), Unexplained tachycardia (heart rate more than 120/min), unexplained arrhythmias, rise in LVEDP, fall in the urine output less than 1cc Kg body weight & blood loss requiring more than two units of blood; or (2) Emergency (Delayed) Conversion (Group II): was defined as conversion to cardiopulmonary bypass after hemodynamic collapse (severe hypotension, bleeding ) or severe electrical disturbance (ventricular tachycardia or fibrillation, heart block, severe bradycardia, or cardiac arrest.) or severe ischemia (as detected by ST-segment or wall-motion changes). We considered non- converted patients as Group III.

We did not include patients who underwent CPB electively because of coronary anatomy (diffusely diseased vessels, small-caliber vessels, and intramyocardial vessels), problems obtaining adequate exposure, adhesions or enlarged heart as they are not true conversions because they depend on the surgeon's preference [12].

**Surgical Procedure:** All patients received the same general anesthetic technique with standard monitoring included intra-arterial and central venous pressures. All patients were operated via median sternotomy. After harvesting of conduits, heparin was given at a dose of 1 mg/kg of weight (maintain the activated clotting time at approximately 300 seconds).

Deep retracting sutures, the placement of a warm moist laparotomy sponge in the posterolateral aspect of the pericardial sac, the apical suction cardiac positioning device Xpose (Guidant Corporation, Cupertino, Calif) and Trendelenburg position, and right tilt were used to facilitate exposure of the lateral, posterior, and inferior vessels of the heart. Octopus tissue suction stabilizer (Medtronic, Inc., Minneapolis, MN, USA) was used to stabilize the myocardium. Distal anastomoses were always constructed before proximal anastomoses. The left internal thoracic artery to left anterior descending coronary artery anastomosis was always performed first. During the construction of all anastomosis, target vessel hemostasis was obtained with intracoronary shunts (Anastafloa, Research Medical, Midvale, UT, USA), proximal and distal silicone rubber (Silastic; Dow Corning, Midland, Mich) vessel loops. The anastomoses were constructed with a single running stitch of 7-0 or 8-0 polypropylene (Prolene<sup>TM</sup>, Johnson & Johnson, New Brunswick, NJ, USA) and visualization was improved with use of a continuous air/saline blower. Most proximal anastomoses were performed with partial clamping of the ascending aorta.

## Conversion to CPB:

When conversion to CPB was necessary, after full heparinization (at a dose of 3 mg/kg), aortic cannulation and two-stage right atrial cannulation were done while supportive measures were taken for the few minutes required to shift to CPB (100% oxygen ventilation in all patients, internal cardiac massage and attempts to cardioversion if necessary). CPB was established at mild hypothermia (32°C) with the use of membrane oxygenator and a roller pump. Arterial flow was adjusted to 2.2-2.4L/min/m<sup>2</sup>, and blood pressure was maintained between 50 and 70mmHg. Haematocrit level was kept at >22%. Myocardial preservation was achieved by intermittent (every 20 min) antegrade cold (4°C) crystalloid and in some cases blood cardioplegia.

All the preoperative, intraoperative and in-hospital postoperative data, of all patients were collected and analyzed. Comparison of variables between Semi-elective conversion, delayed conversion and non-conversion groups was done.

**Statistical Analysis:** Values of variables were expressed as mean  $\pm$  standard deviation, unless otherwise indicated. Groups were analyzed and compared. Descriptive statistics included continuous and discrete variables, which were analyzed accordingly with an unpaired t-test, Wilcoxon rank sum test, chi-square test, and Fisher exact test. Statistical significance was defined as a p value of less than 0.05. Statistical analyses were

performed using SPSS for Windows version 11.5 statistical package (SPSS, Inc, Chicago, Ill).

Groups	Semielective conversion group (I) [N= 26]	Emergency conversion group (II) [N=21]	Non conversion group (III) [N=433]	P value
Age	54±4.7	58±4.9	57±4.6	NS
Female gender	6 (23.1%)	6 (28.6%)	108 (24.9%)	NS
Body surface area	2.0±0.12	1.9±0.14	2.0±0.2	NS
NYHA Class	2.7±0.4	2.8±0.6	2.6±0.8	NS
Congestive cardiac failure	2 (7.7%)	1 (4.8%)	7 (1.6%)	NS
Previous MI	9 (34.6%)	7 (33.3%)	109 (25.2%)	NS
Preoperative EF	51.6±15.2	50.9±13.4	52.0±12.9	NS
Hypertension mellitus	18 (68.4%)	14 (66.7%)	285 (65.8%)	NS
Diabetes	8 (30.8%)	6 (28.6%)	98 (22.6%)	NS
Hypercholesterolemia	19 (73.1%)	15 (71.4%)	287 (66.3%)	NS
COPD	4 (15.4%)	7 (33.3%)	37(8.5%)	< 0.05
Renal insufficiency	2 (7.7%)	1 (4.8%)	21(4.8%)	NS
Peripheral vascular disease	1 (3.8%)	1 (4.8%)	6 (1.4%)	NS
Preoperative AF	7 (26.9%)	4 (19.1%)	86 (19.9%)	NS
Left main disease	(11.5%)	2 (9.5%)	35(8.1%)	NS

**Table 1. Patients' demographic data.**

*NYHA=New York Heart Association; MI=Myocardial infarction; EF=ejection fraction; COPD=chronic obstructive pulmonary disease; AF=Atrial fibrillation; n= number.*

## Results

From a total of 480 patients operated, 433 patients underwent OPCAB without conversion (Group III) and 47 patients required conversion to CPB. The overall conversion rate was 3.1%. From 47 patients required conversion, 26 patients converted semi-electively (Group I) and the remaining (21 patients) needs emergency conversion (Group II). Demographic data of all patients are shown in Table (1). The mean age of all patients was 56.7±4.7years. One hundred and twenty patients (25%)

were women. There was no significant difference in pre-operative and intraoperative variables between the three groups except that; there was significant incidence of chronic obstructive pulmonary disease (COPD) in emergency conversion group (Group II) than other groups (Group I&III) ( $p < 0.05$ ).

In Table 2, we have presented operative and in-hospital postoperative data and outcomes of all patients. As for morbidity, the overall incidence of complications (which includes all minor or major complications) was the same for Group II patients and the matched Group I and Group III. the overall incidence of complications was 57.1% (12 of 21) in Group II patients versus 42.3% (11 of 26) and 44.3% (192 of 433) in Group I and Group III respectively ( $p =$  not significant). However, when comparing incidence of individual complications, some significant differences emerged. Also when comparing incidence of serious complications (i.e. stroke, Myocardial infarction [MI], Gastro-intestinal [GI] bleeding, etc.), patients who required emergency conversion (Group II) had significantly higher incidence of serious complications as compared with patients in Group I and Group III. Group II patients had 33.3% incidence (7 of 21) of serious complications versus 7.7% (2 of 26) and 6 % ( 26 of 433) in Group I and Group III respectively ( $p < 0.01$ ). Statistically there was no significant difference between the serious complications incidence of the semi-electively conversion group (Group I) and the non-conversion group (Group III) ( $p =$  not significant).

The incidence of the use of intraoperative and /or postoperative intra-aortic balloon pump support, use of postoperative inotropes, pulmonary complications and dialysis were significantly higher in the emergency conversion group (Group II) as compared with Group I and Group III( $p<0.05$ ). We also found that, Group II patients had a markedly increased incidence of ischemic complications. The most common ischemic complications were stroke and perioperative myocardial infarction which achieved significance ( $p<0.02$ ). Also, patients converted emergently had a significantly higher incidence of post-operative cardiac arrest ( $p< 0.001$ ) and multisystem organ failure than other patients ( $p < 0.03$ ).

The number of patients requiring prolonged intensive care unit (ICU) stay and hospitalization were significantly higher in the emergency conversion group (Group II) than in Group I and Group III ( $p< 0.05$ ).

Although, overall mortality rate in the conversion groups (Group I and Group II) was 14.9 % as compared to 2.5 % in the non-conversion group (Group III), which is statistically significant ( $P<0.02$ ), however, Conversion urgency was a significant factor in patient death. Patients converted semi-electively



Groups	Semielective conversion group (I)[N= 26]	Emergency conversion group (II) [N=21]	Non conversion group (III) [N=433]	P- value		
				I VS III	II VS III	I VS II
-Distal anastomoses/patient,n	2.8±1.04	2.6±1.09	2.4±1.02	NS	NS	NS
-Intraoperative or postoperative IABP	1 (3.8%)	5 (23.8%)	6 (1.4%)	NS	<0.001	<0.001
-Inotropic support [n(%)]	18 (68.4%)	19 (90.5%)	295 (68.1%)	NS	<0.05	<0.05
- Blood loss complications						
Blood transfusion [n(%)]	6 (23.1%)	7 (33.3%)	72 (16.6%)	NS	<0.05	NS
Reoperation for bleeding	1 (3.8%)	2 (9.5%)	8 (1.9%)	NS	<0.05	NS
- Pulmonary complications						
Prolonged ventilation >12hs	6 (23.1%)	10 (47.6%)	86 (19.9%)	NS	<0.05	<0.05
Reintubation	2 (7.7%)	4 (19.1%)	19 (4.4%)	NS	<0.05	<0.05
Postoperative pneumonia	1 (3.8%)	3 (14.3%)	7 (1.6%)	NS	<0.01	<0.05
-Cardiac arrhythmia complications						
Postoperative AF, SVT, VT	7 (26.9%)	9 (42.9%)	99 (22.9%)	NS	<0.05	<0.05
Postoperative cardiac arrest	0 (0.00%)	3 (14.3%)	3 (0.6%)	NS	<0.001	<0.001
- Renal complications						
Postoperative dialysis	1 (3.8%)	3 (14.3%)	6 (1.4%)	NS	<0.01	<0.01
-Ischemic complications						
Perioperative MI	0 (0.00%)	3 (14.3%)	5 (1.1%)	NS	<0.01	<0.001
Stroke	1 (3.8%)	2 (9.5%)	3 (0.6%)	NS	<0.05	NS
-Other serious complications						
GI bleeding	0 (0.00%)	2 (9.5%)	3 (0.6%)	NS	<0.05	<0.05
Multi-organ failure	1 (3.8%)	3 (14.3%)	5 (1.1%)	NS	<0.05	<0.05
Deep sternal infection	0 (0.00%)	2 (9.5%)	3 (0.6%)	NS	<0.05	<0.05
-Length of ICU stay (>1 day)	8 (30.8%)	14 (66.7%)	109 (25.2%)	NS	<0.01	<0.05
-Length of postoperative hospital stay (>7 days)	12(46.2%)	16 (76.2%)	181 (41.8%)	NS	<0.05	<0.05
- Mortality						
Intraoperative mortality	0 (0.00%)	2 (9.5%)	3 (0.6%)	NS	<0.05	<0.05
Postoperative mortality (in hospital)	1 (3.8%)	4 (19.1%)	8 (1.9%)	NS	<0.01	<0.01
Overall mortality	1 (3.8%)	6 (28.6%)	11 (2.5%)	NS	<0.001	<0.001

**Table 2. Operative and postoperative data and outcomes.**

**IABP = intra- aortic balloon pump; n= number; MI=Myocardial infarction; AF=Atrial fibrillation; SVT= Supraventricular tachycardia; VT = Ventricular tachycardia; GI=Gastro-intestinal; ICU=Intensive care unit**

(Group I) had overall mortality rate of 3.8 % (1 of 26) whereas it increased to 28.6% (6 of 21) in those undergoing emergency conversion (Group II), which is highly statistically significant ( $P<0.01$ ). Statistically there was no significant difference between the overall mortality rate of the semi-elective conversion group and the non-conversion group ( $p=$  not significant).

## DISCUSSION

Surgeons in the last few years have been increas-

ingly used OPCAB in an effort to eliminate the morbidity associated with CPB. OPCAB has been shown to be a safe procedure with similar or better outcomes to conventional on pump coronary artery bypass grafting (ONCAB) [1-5]. However, manipulation of the heart required to do OPCAB can bring about hemodynamic and electrical changes and occasionally there are situations where conversion becomes mandatory and the patient must be placed on CPB in order to safely complete the operation [6-16]. Emergency conversion to CPB is the most feared complication in OPCAB surgery [6]. In the

early days, conversion rates were as high as 25% [6]. However, in more recent literature; the rate varies between 0 to 9.2% [7-16].

Common reasons mandating conversion from an off-pump to an on-pump procedure include hemodynamic instability, bleeding, circulatory collapse due to severe ischemia, critical arrhythmias or cardiac arrest, heart failure and failure to adequately expose the target vessel, deep intramyocardial course of the target vessel [6-16]. Hemodynamic compromise and ultimately collapse during OPCAB is likely the result of substantial changes in the existing blood flow and/or the normal geometry of the heart [17]. However, significant hemodynamic compromise occurs when ischemia is compounded by mechanic alterations such as right ventricular compression, reduction in right ventricular outflow size and reduction in left ventricular preload, as can be caused in exposing the posterolateral wall. When allowed to continue, this may result in a down-turning spiral (ischemia causing worsening cardiac function and worsening cardiac function resulting in further ischemia) that may not be salvageable without immediate cardiopulmonary bypass [18].

Several studies do indicate that patients who require conversion may experience a higher rate of morbidity or mortality than those whose operation was successfully completed off-pump [6-11]. Mujanovic and colleagues [8] reported that timing of conversion was crucial to avoid serious outcomes. Surprisingly, there were no published studies that have been specifically addressed the results of conversion according to timing of conversion, although it has been discussed secondarily in a few series. Some studies included elective conversions while others did not and it has not been extensively studied [6-9, 10, 14]. The available data did not allow emergency conversions to be distinguished from other, non-emergency conversions [14].

The surprising finding is that, according to the available data, emergency conversion significantly increased major morbidity and mortality [12-16], meanwhile, early elective conversion without hemodynamic compromise has been reported not to increase mortality and morbidity in comparison with non-converted OPCAB group [6, 9]. The patients converted early electively had a mortality rate in the range of 4.2 to 6.1% and major morbidity rate in the range of 0.1% to 4.5% [6, 9], whereas, they were increased to the range of 7.8 to 45% and the range of 1.8 to 10.0% respectively in those underwent emergency conversion [12-16]. Also, it has been reported that emergency converted OPCAB have a 12-fold and an 8-fold higher mortality in hospital than ONCAB patients [9] and unconverted OPCAB patients [12].

Compared with unconverted OPCAB patients, emergency converted patients also had a six-fold increased risk of stroke and similar increased risks of other serious post-operative complications [12].

A higher risk of mortality after emergency conversion had also been observed in a large cardiac registry [13]. So, conversion urgency was a significant factor in patient morbidity and death [6-16].

Also, delay in conversion can be very detrimental and early conversion before hemodynamic collapse can be rewarding [8, 9].

Our study showed that, there was significant incidence of COPD in emergency conversion group than other groups ( $p < 0.05$ ). Tabata et al. [15] and Landoni et al. [16] reported that COPD was independent predictor of emergency conversion. The most important finding in our study was the poorer outcome of emergency conversion group patients, as shown by significantly increased major morbidities and overall mortality rates ( $p < 0.01$ ); meanwhile, semi-elective (early) conversion had not increase operative morbidity and mortality in comparison with non-converted group ( $p =$  not significant).

As for morbidity in our study, the overall incidence of complications was not different between the converted and non-converted groups when counting all major and minor complications. However, when comparing incidence of individual complications, some significant differences emerged. Also when comparing incidence of serious complications (i.e. stroke, MI, GI bleeding, etc.), patients who required emergency conversion had significantly higher incidence of serious complications compared with patients in other groups. Emergency conversion group patients had 33.3% incidence of serious complications versus 7.7% and 6% in semi-elective group and non-converted group respectively ( $p < 0.01$ ). This led to significant differences in the number of patients requiring prolonged ICU stay and hospitalization between the emergency conversion patients and the patients who did not need ( $P < 0.05$ ). Accordingly, patients who converted urgently from off-pump to CPB had a more complicated hospital course (Table 2).

Although, overall mortality rate was 14.9% in the conversion groups as compared to 2.5% in the non-conversion group, however, in the conversion groups, the overall mortality rate was 28.6% in the emergency conversion group as compared to 3.8% in the semi-elective conversion group, which is highly statistically significant ( $P < 0.01$ ).

According to our results, conversion urgency was a significant factor in patient death and morbidity. Also, patients who underwent early conversion semi-electively under controlled circumstances had better surgical

outcomes. So, early elective conversion to ONCAB may be a safe and good option when the risk of conversion outweighs the benefit of OPCAB [15]. Surgeons threshold for conversion may be important and they should have a low threshold to electively convert to ONCAB early in the procedure if there are any early indicators of electrical or hemodynamic instability rather than waiting to the last minute [9,14]. An expert team recognizes patients who cannot tolerate luxation or coronary snaring early and safely switches rapidly to CPB operation [16]. Careful attention to detail is important, and if conversion becomes necessary, it must be performed prior to cardiac arrest. In borderline cases with unstable hemodynamics, an early elective conversion to CPB or at least the priming of the CPB machine is indicated. This step will shorten the time necessary to initiate CPB [8].

Additionally, in our study we found that judicious use of cardiac monitoring could provide an insight into predicting emergency conversions. Early changes in patient hemodynamics can be noticed before serious compromise and early elective conversion could be chosen in such cases [8, 15]. The creation of the anastomosis requires the full attention of the surgeon while the anesthesiologist carefully monitors and treats ischemia [6]. The main tools for detecting ischemia are electrocardiography and monitoring hemodynamic status. Visual inspection of the contractility of the heart is also important [8, 15, 18].

To conclude, emergency conversion to CPB during OPCAB surgery results in a significantly higher operative morbidity and mortality. Early conversion semi-electively under controlled circumstances to CPB during OPCAB surgery is a safe and good option as delay in conversion can be detrimental. Judicious cardiac monitoring and hemodynamic assessment can give signals for early conversion before serious hemodynamic collapse.

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## HYBRID SURGERY FOR MANAGEMENT OF PATIENTS WITH MULTISEGMENT THORACIC AORTA DISEASE WHO REQUIRE ASCENDING AORTA RECONSTRUCTION

Amro R. Serag, MD  
 Patrice Bergeron, MD  
 Xavier Mathieu, MD  
 Vincent Piret, MD  
 Andranik Petrosyan, MD  
 Joël Gay, MD

**Background:** Re-operation after ascending aorta reconstruction (AAR) represents a technical challenge that carries higher mortality and morbidity than primary reconstruction. We present the technique and outcome of hybrid surgical and endovascular therapeutics.

**Methods:** The study included 12 patients, mean age of 67.3±2.6 years, who had multisegment thoracic aorta disease and required AAR. Four patients had a previous Bentall procedure, 7 had ascending aorta replacement and one had ascending aorta and arch replacement. Etiologies of aortic diseases were post-operative aortic pseudoaneurysm (n=1), aneurismal dilatation and/or extended dissection to the aortic arch (n=7) and type B aortic dissection in 4 patients (3 of them had proximal type I endoleak after TEVAR). Nine patients underwent total arch transposition (TAT), 2 patients had hemiarch transposition (HAT), while one had a first HAT followed by TAT. Subsequent aortic arch exclusion using endovascular graft was done in all patients.

**Results:** There were no neurological adverse events after the surgical stage. Stent graft deployment was successful in all cases. Completion angiography and discharge CT scan showed patent thoracic false lumens after stentgrafting in 3 patients. One patient had a proximal type I endoleak due to a short proximal neck and underwent embolization via the left subclavian artery. One patient died (8.3%) after the endovascular stage and 2 patients had minor strokes (16.6%). During a mean follow-up of 11.9±3.9 months, one patient with pre-operative chronic obstructive pulmonary disease (COPD) died at 3 months from respiratory failure. No stent graft complications were seen. One patient had a new distal endoleak successfully treated by graft extension. Another patient with a persisting endoleak also underwent endograft extension, while another patient remained under surveillance for a clinically non significant endoleak.

**Conclusions:** Hybrid therapeutic solution is a less invasive and safe option for management of patients with multisegment thoracic aorta disease requiring AAR. However a change in the surgical paradigm will depend on the improvement of endovascular grafting technologies. Long term results of such hybrid therapeutics will eventually identify patients who could better benefit from open repair or hybrid management.

**A**scending Aorta reconstruction (AAR) for treatment of aortic aneurysm or dissection is a complex surgical procedure which has undergone major technical modifications over decades. In parallel, operative mortality has improved (1) and good early results were reported (2). However, this procedure carries a potential risk of various late complications, mainly evolutive peri-prosthetic false aneurysms, and residual aorta dissection and/or aneurysm (3) in patients

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Address reprint request to : Dr Amro R. Serag

Department of Cardiothoracic surgery,  
 Faculty of Medicine, Tanta University,  
 Egypt

Email : amroserag@yahoo.com

Codex : 04 / cord / 53 / 0709



whose disease, nonetheless, remains a surgical challenge. These complications and or residual abnormalities contributed to the non significant improvement in long-term survival after AAR (4) and frequently warrant surgical re-intervention. Re-operation may present a formidable technical challenge that requires dissection through previous scarred operative sites in patients who are likely to have more comorbidities than that with primary aortic surgery. The mortality of re-operations is up to 17.9% (5) while it is up to 5% for the elective primary reconstructive surgery in recent series (1).

Many surgeons advocated more radical treatment of the aortic pathology at the initial operation in the form of root replacement and partial or complete aortic arch replacement to reduce the need for further re-operation (6). Recently, this has been recommended for event-free long-term survival (7). However, in the setting of an emergency operation, this has been identified as an independent risk factor for postoperative mortality (2, 4). This is the main argument for less invasive strategies. Recent enthusiasm for innovative endovascular therapies to treat aortic disease has spurred many centers to investigate endoluminal grafting of the thoracic aorta. Here, we present the technical considerations and clinical outcome of using hybrid therapeutic solution (transposition of aortic arch great vessels combined with arch endografting) in 12 patients who had multisegment thoracic aorta disease and required AAR.

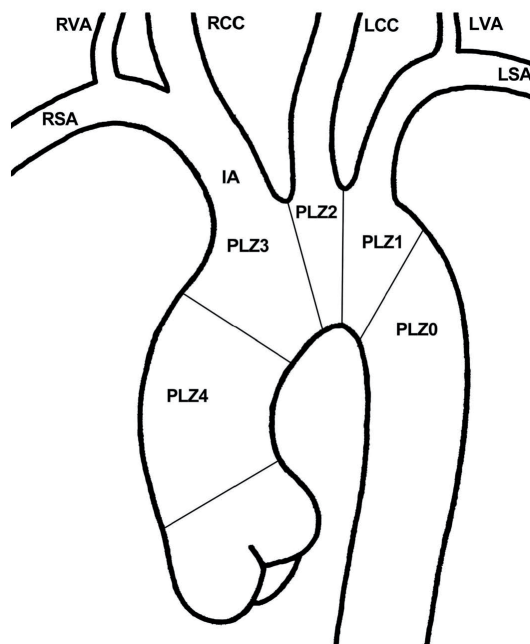
## Methods

Between May 2000 and December 2006, 69 patients were treated with open surgical reconstruction of the ascending aorta. In 12 patients, mean age of (67.3+ 2.6 years), hybrid therapeutic solution was used to manage their multisegment thoracic aorta disease and post AAR false aneurysm. The male to female ratio was 11:1. Data of these 12 patients were reviewed retrospectively. All patients had AAR either for repair of aortic dissection (n=11) or aortic aneurysm (n=1). Clinical assessment before hybrid therapeutic solution included evaluation of patients' risk factors. Medical histories of the patients included either chronic obstructive pulmonary disease (COPD) (n=3), hypertension (n=10), diabetes mellitus (n=2), renal insufficiency (n=2), coronary artery bypass surgery and percutaneous transluminal coronary angioplasty (PTCA) (n=3), myocardial infarction (n=1), arrhythmia (n=2), cardiac valvulopathy and valve surgery (n=5), or previous intervention for abdominal aortic aneurysm (AAA) (n=1). All patients were classified as American Society of Anaesthesiology (ASA) class 4 on the basis of pre-existing disease. Radiological survey before hybrid therapeutic solution also included imag-

ing and sizing (CT scan + calibrated aortography) of the aorta and iliac arteries, duplex scanning of carotid and vertebral arteries and consensual final surgical strategy was decided. Endografts were oversized by 20% for aortic aneurysms and 10% for aortic dissections.

## Operative Strategy

**Great Vessels Transposition** We propose a retrograde classification of arch zone (fig1) that has evolved from our previous PLZ classification which has been previously reported (8).



**Figure 1** Figure 1. Our “retrograde landing zone classification” has been developed to illustrate the need of great vessels transposition. Z0 is the ideal situation where the proximal landing zone allows the deployment of the endograft without any adjunctive procedure. Z1 relates to the case in which the diseased aortic portion includes the ostium of the LSA or when the proximal neck is less than 2cm and does not allow the landing of the endograft. If the aortic aneurysm extends to Z2, the left CCA & LSA must be transposed to the right CCA (left hemi-arch transposition), prior to endovascular completion. If the diseased portion of the aorta extends to Z3, the 3 supra-aortic vessels have to be bypassed to the ascending aorta (total-arch transposition) before the endovascular intervention. Diseases lying in Z4 can be treated without adjunctive procedures, provided landing zones are suitable; if not, the transposition of the IA to the left CCA (right hemi-arch transposition) may be useful, as illustrated on figure 2. RSA: Right Subclavian Artery; LSA: Left Subclavian Artery; RVA: Right Vertebral Artery; LVA: Left Vertebral Artery; IA: Innominate Artery; RCC: Right Common Carotid artery; LCC: Left Common Carotid artery; PLZ: Proximal Landing Zone

This classification is based on pathophysiology and reflects the extension of the disease and case complexity, with respect to the number of great vessels to be transposed (Table 1). The details of the operative procedures were already reported (9).

Arch zones covered by the endograft	Complementary surgical step			
Z0	No			
Z0+Z1	Coverage or transposition of LSA		Hemi-arch transposition (HAT)	
Z0+Z1+Z2	Carotido (CCB)	Carotid Bypass	Hemi-arch transposition (HAT)	
Z0+Z1+Z2+Z3	Bypass	From ascending aorta to IA and left CCA through median sternotomy	Total arch transposition (TAT)	
Z0+Z1+Z2+Z3+Z4	Bypass	From ascending aorta to IA and left CCA through median sternotomy	Total arch transposition (TAT)	
Z3+Z4	Transposition of IA to ascending aorta. Carotido – carotid bypass		Hemi-arch transposition (HAT)	
Z4	No			

**Tables Table 1: Complementary surgical procedures to prepare proximal landing zone for the endograft**

We only recommend transposition of the left subclavian artery (LSA) when it supplies coronary circulation through the left internal mammary artery (LIMA), when the contralateral vertebral artery (VA) is stenosed or hypotrophic and when there is an incomplete fusion of both VAs at C1. We also recommend transposing the LSA in association with left common carotid artery (LCCA) when they are included in the aneurysm, except during total transposition since the LSA is difficult to reach by median sternotomy. Moreover, a patent LSA may serve as access to the aneurysm when coiling is necessary to treat a residual type I endoleak. In all other cases, LSA transposition is only required later if the coverage becomes symptomatic.

**Endovascular procedures (EVP)** Endovascular procedures (9) were performed generally within 2-4 weeks after great vessel transposition. They were performed under general anaesthesia in the operating room equipped with C-arm fluoroscopy and digital subtraction angiography. Either percutaneous or open femoral or iliac artery access was used. Transesophageal echocardiography (TEE) and intravascular ultrasound (IVUS) were mainly used during treatment of aortic dissections to monitor stentgraft deployment.

Devices Four patients received Talent endoprosthesis

(Medtronic, Minneapolis, MN, USA), in another 4 patients, Endofit devices (LeMaitre Vascular, Burlington, MA, USA) were deployed while in 3 patients, we used TAG (WL Gore & associates, Flagstaff, CA, USA) stentgraft. In one patient who underwent successive interventions to manage his extensive thoracic aorta disease; all 3 types of the previously mentioned devices were used.

Surveillance Protocol Three-D CT scan and X-Ray examinations were obtained for all patients before their discharge to serve as control images. Surveillance after hospital discharge included physical examination at clinic visits, regular contact either by mail or telephone. It also included 5 phase contrast-enhanced spiral CT scans at 3, 6, 12, 18 and 24 months post-operatively, and yearly thereafter.

## Results

### Primary interventional procedure

The primary intervention was surgical in 11/12 patients for management of Type A aorta dissection (n=10) and aneurysm of ascending aorta and aortic arch (n=1). One/12 patient underwent EVP at the start for treatment of Type B aorta dissection and 9 months later he required AAR with hybrid therapeutic solution for management of Non A Non B chronic dissection and proximal endoleak of his previous stentgraft in the descending thoracic aorta. Four/12 patients had Bentall operation, 7/12 patients underwent AAR and in one case, ascending aorta and aortic arch were replaced under hypothermic circulatory arrest (HCA).

### Hybrid therapeutic solution

Nine patients/12 underwent total arch transposition (TAT). TAT was done either as a one-step procedure (n=5) or a 2-step procedure (n=4). Performance of one-step procedure includes transposition of innominate artery (IA) and LCCA to the ascending aorta tube through sternotomy of the primary surgical intervention (AAR) (n=3) or by performance of re-sternotomy (n=2). Two-step procedure includes transposition of IA to the ascending aorta tube through sternotomy and followed by cervical carotido-carotid bypass (CCB) as a second step.

Two patients out of 12 had hemiarch transposition (HAT). In only 1/12, HAT was done first then followed by TAT and in this patient; the TAT procedure was done through re-sternotomy.

All cases of great vessels transposition were followed by deployment of endovascular stentgraft.

The details of the primary and subsequent interventions in all patients are shown in (Table 2). Immediate

	Indication	1ry	Indication	2ry	Latency	Indication	3ry	Latency.	Out
	1 ry operation	Operation.	2ry interven- tion	Intervention	Period	3ry interven- tion	Interven- tion	Period	come
1	Type A Dissec- tion	Bentall	False aneurysm	CCB +EVP	4 years				Died
2	Type A Dissection	AAR	Ao-LA Fistula	Close + Transpose IA	2 months	Type B Dissection	CCB + EVP	2 months	Died
3	Type A Dissection	AAR	Type B Dissection	EVP	One month	Type I Endoleak	CCB + LSA transp + EVP	One week	OK
4	Aorta Dissection	Bentall +TAT	Dissecting aneurysm Arch + Aorta	EVP	1.5 year				OK
5	Type B Dissection	EVP	Type Non A Non B Dis + Type I endoleak	AAR+TAT+ EVP	9 months				OK
6	Acute Dis Tho- racic Ao	AAR	aneurysm Arch + Aorta	TAT	4 years				OK
7	AA+Arch aneurysm	Bentall + TAT + EVP							OK
8	Type A Dissection	AAR+ Arch Replacement	Type B Dissection	LSA to LCCA+EVP	2 months	Arch False Aneurysm	EVP	2 months	OK
9	Type A Dissection	Bentall + LIMA to LAD	Aortic Arch Aneurysm	TAT	8 years	LIMA to LAD	LSA to LCCA + EVP	One month	OK
10	Type A Dissection	AAR + IA transposition	Aortic arch extension	CCB+LSA to LCCA +EVP	2 months				OK
11	Type A Dissection	AAR + IA transposition	False aneurysm	Surgical control	One month	Aortic arch extension	CCB+ EVP		OK
12	Type A Dissection	AAR + IA transposition	Aortic arch extension	CCB+ EVP	7 months				OK

**Table 2: Details of primary and subsequent interventions**

results:

There was no intra-operative mortality, while 1/12 in-hospital mortality after the endovascular step of HAT was recorded giving an incidence of 8.3%. This is a fatal catheter-related complication due to an iliac artery rup-

ture worsened to multi-organ failure within 3 days. The surgical transposition step was complicated by massive hemothorax in one patient who required re-sternotomy for TAT. This was drained effectively by intercostal tube with underwater seal drainage. Also, this patient had



coronary artery bypass surgery with LIMA to the left anterior descending (LAD) coronary artery and he required a left subclavian to left common carotid artery bypass to avoid myocardial ischemia after exclusion of the aortic arch and coverage of his LSA. This step was complicated by excessive lymph drainage which necessitates re-exploration for control. However, there was no immediate major neurological adverse event after the surgical step.

During the endovascular step, the stentgraft deployment was successful in all patients and we had no misplacement of the endografts. But we observed 2/12 minor strokes (16.6%) after EVP during the in-hospital course. One patient had minor stroke within 48 hours due to the

occlusion of left CCA bypass tube, which was resolved by a cervical CCB. The other patient developed aphasia within 24 hours of EVP that improved gradually. Both patients had TAT. Local wound complications in the form of groin lymphorrhea occurred in 2/12 (16.6%) patients after the endovascular step.

Until discharge, patent thoracic false channels after aortic dissection coverage were found in 3/11 patients (27.3%). Await-and-see policy was followed and the next CT scan was planned for 3 months later. In patient No. 9, who had previous Bentall operation and underwent TAT, a proximal type I endoleak was detected after endograft deployment due to the short PLZ. Later on, he underwent an embolization through his patent LSA.

Follow-up period During an average follow-up period of 11.9 + 3.9 months, no patient was lost to follow-up. One patient had new distal endoleak in his stentgraft of the descending aorta that was treated by graft extension. Two out of 3 patients who had minor endoleak on discharge had follow-up surveillance and the endoleak was persistent. In one patient, stentgraft extension was justified while in the other patient, the endoleak remained stable and did not lead to aneurysmal expansion of the aorta over 40 mm nor true channel compression over 1/3. No endograft migration or fracture nor stentgraft related complications were diagnosed and all patients were free from new cerebral neurological adverse events or paraplegia. Late mortality was encountered in one patient who had preoperative COPD and he died 3 months after the procedure from acute respiratory failure.

## Discussion

Conventional AAR for repair of aortic aneurysm or dissection is generally a durable procedure. A consensus is emerging that optimal surgical treatment of extensive thoracic aorta disease requires more than one surgical procedure. However, extended aortic resection is associ-

ated with major peri-operative risks (10) and has a substantial cumulative mortality (>20%) especially for aortic dissection (11). In recognition of these risks, surgical strategies have been modified progressively and inclusion of the endovascular repair of thoracic aorta disease has proliferated at a dramatic pace. Surgical series in the literature indicated that most re-operations after AAR are needed because of post-operative false aneurysm or true aneurysm and or extension of the dissection process (4).

Post-operative aortic false aneurysm Post-operative aortic false aneurysm is a serious complication with variable incidence that can occur several months to years after the initial operation. It has the possibility of rupture or dissection and warrants surgical intervention. However, surgical repair has a mortality rate up to 18% (12, 13). Since mortality rate in open pseudoaneurysm repair is high, the endovascular repair of these lesions could provide an extra-advantage for these patients. In recent literature, endovascular repair of pseudoaneurysm after AAR was published as a case report (14). In this study, we encountered 3/12 (25%) patients with postoperative pseudoaneurysm. One of them was treated surgically, and another one that developed after AAR and aortic arch replacement was treated using an endovascular stent. In the third case, we combined CCB and endografting of the ascending aorta to treat a false aneurysm that had developed 4 years after Bentall procedure (figure 2). The carotid transposition (HAT) allowed us to deploy a short stentgraft excluding the pseudoaneurysm. Of note, the endovascular procedure was technically demanding as it required a reversal of the stentgraft in its sheath and the shortening and reshaping of its tip to allow proper deployment. However, there was no reported early morbidity or mortality.

It has to be pointed out that whether EVR will ever be the preferable technique for repair of postoperative thoracic aorta pseudoaneurysm is not yet predicted.

Aortic arch exclusion, Thanks to the benefit of combined surgical and endovascular technique, it was possible to exclude the aortic arch safely in 4 patients who had aneurysmal enlargement of the aortic arch after AAR. Providing adequate global cerebral protection and prevention of embolization during reconstruction of the aortic arch are decisive determinants of outcome. The arch reconstruction requires cardiopulmonary bypass (CPB), hypothermic circulatory arrest (HCA) and selective cerebral perfusion (SCP) that are invasive techniques. There remains an unsettling risk of cerebral damage as well as other complications that can lead to a 25% risk of stroke and death (15). Great vessels transposition allows anastomo-

sis to the arch vessels cephalad to the area of most obvious atherosclerotic disease; therefore significantly decrease the risk of embolization. Vessels free of disease can almost always be reached by extending sternotomy incision. Also, the transposition of great vessels obviates the need for HCA. In our current series, an adverse outcome including permanent neurological damage was not reported in relation to the surgical step.

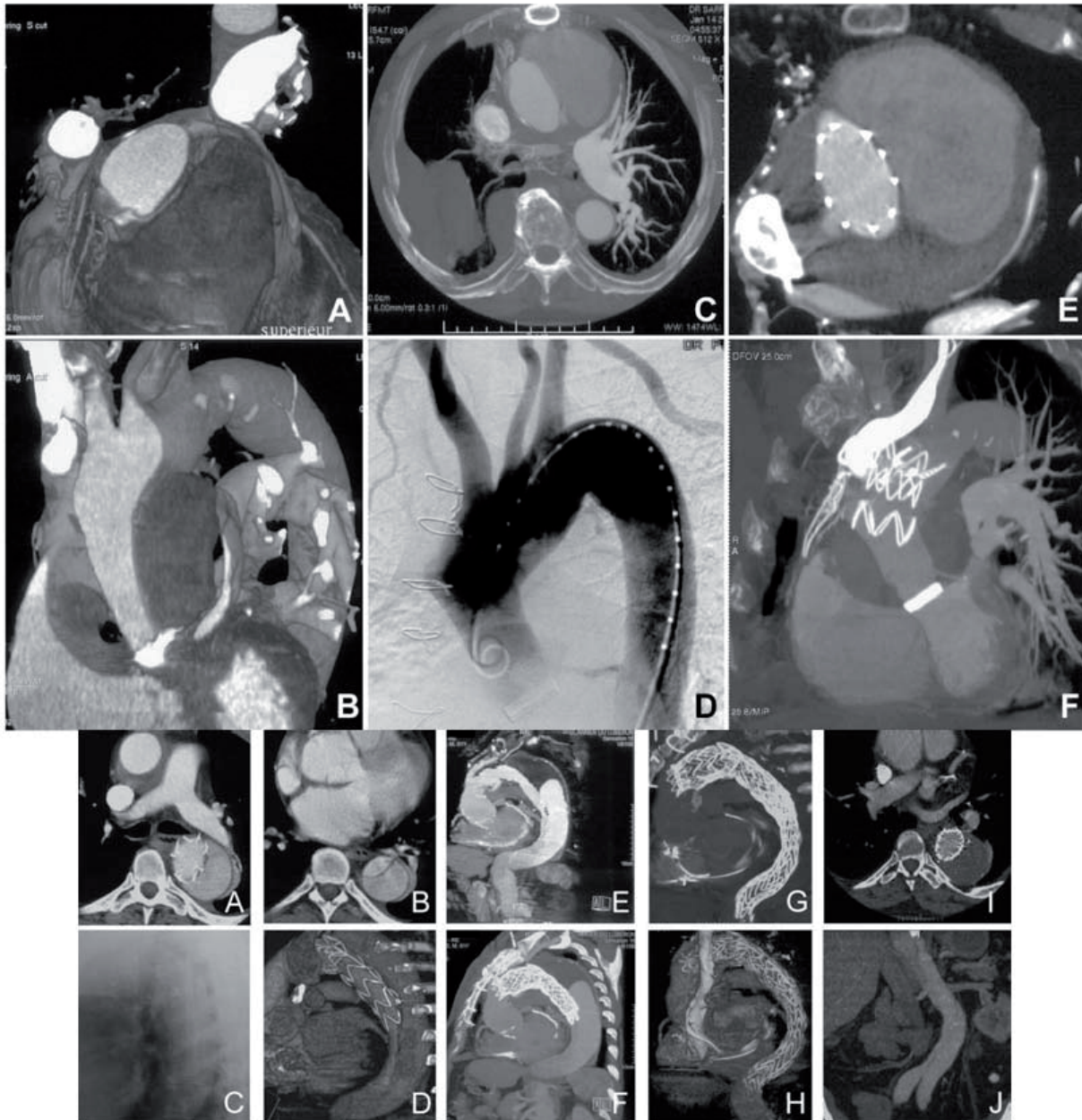


Figure 2. This 83-year old male patient had a previous Bentall operation in 2000. When he was admitted in November 2004, this patient was suffering from an effort dyspnea that had begun 3 months earlier. The angio CT scan showed a large 93-mm bulge surrounding the ascending aorta immediately distal to the replaced aortic valve (A-D). A limited right pleural effusion was also observed (C). A hybrid strategy was decided consisting in a preliminary transposition of the IA to the left CCA. The intra-operatively TEE showed that the aneurysm was poorly circulating and its posterior half was almost thrombosed; its blood flow was estimated to originate from the distal anastomosis of the aortic graft. Two months later the patient came back to our department to receive the aortic endograft. A

Cardiovascular

Talent stentgraft (Medtronic, Minneapolis, MN, USA) was used that was reversed prior deployment. The tip of the sheath was also reshaped and shortened to allow its precise positioning in the ascending aorta. The control images showed a good exclusion of the aneurysm, although the poor pre-exclusion aneurysmal blood flow did not allow a definite answer (E-F).

Figure 3. This male patient underwent a replacement of the ascending aorta due to an acute type A dissection in March 2000. Two months later, the descending dissecting false lumen evolved to an aneurysm and an endograft was placed in the descending aorta after the previous transposition of the LSA to the left CCA (A-C). As seen in picture D, the false lumen was still circulating 3 years later and the maximum aortic diameter reached 63mm; the entry tear was found to be at the proximal end of the implanted stentgraft. However, due to a sudden heart failure, this patient had a defibrillator implanted in priority. In March 2004 the patient had a total-arch transposition performed and the endograft was extended proximally 6 months later (E-F). This proximal extension did not resolve the perfusion of the false lumen from distal entry tears (E-F). The patient then came back in September 2005 and underwent a distal endograft extension with a tapered device (G), which sealed distal reentries (H-I) and left all visceral branches patent (J).

However, we have an incidence of 16.6% of minor stroke after the endovascular step. Nonetheless, earlier reports from our institution demonstrated the safety of the hybrid therapeutic strategy in high risk patients with aortic arch disease with results as good as conventional surgery for low risk patients (8, 9). Based on our encouraging clinical and surgical results, a new approach to manage patients with acute type A dissection during emergency repair has evolved (16). We are combining the AAR with the transposition of the IA to the ascending aortic graft (right HAT). This allows secondary arch coverage and cervical CCB for recalcitrant dissection. The goal of our specific strategy is to salvage the patient during the first surgical stage and to allow unhurried aortic arch exclusion.

We applied this technique in 7 patients up till now, three of them were included in this study as they underwent the second step of the hybrid therapeutic strategy and all had a favorable outcome with no mortality or major neurological complications. Although, it could be argued that the risk of sudden rupture and death between the two stages constitutes a theoretical drawback, good outcome in our patients is consistent with the idea that this technique represents a significant advance.

**Endoleak after endovascular stent graft deployment**  
The endovascular stent graft technology presents choices and complications previously unknown with standard open repair. A choice of commercially available endografts and the potential complications of endoleaks in addition to vascular catheterization problems are examples in which this modality differs from the traditional approach. We applied the hybrid therapeutic strategy in 4 patients with type B aortic dissection who required AAR and 3 of them developed proximal endoleak of the stentgraft used to treat the aortic dissection. The great vessels transposition prepared a landing zone of enough length and allowed the safe deployment of an extension endograft to the aortic arch.

Most inadequate seals (Type I endoleak) can be corrected by balloon angioplasty or by additional stent-graft component. Sometimes, a primary type I endoleak resists endovascular repair. In these cases, surveillance is advised in the literature (17), because most of these endoleaks seal spontaneously (18). This spontaneous resolution may be temporary, thus in case of a persistent primary type I endoleak, immediate intervention should be considered. It is worthwhile to mention patient No 8 who was a high risk patient for surgery. He had a type A aortic dissection and he underwent AAR. This was followed by the development of Type B dissection which necessitated LSA transposition to create a safe landing zone for the stentgraft of descending aorta. Later on he developed a retrograde chronic aneurysm of the proximal arch that was excluded by a short stentgraft after TAT through re sternotomy. Recently he showed a persistent perfusion of the false lumen in the descending aorta was treated by distal graft extension (figure 3).

This provides an insight into the flexibility of hybrid therapeutic strategy as well as it demonstrates the pitfall of endovascular stent grafting. The endograft excludes the diseased aorta segment but it neither eliminates nor prevents the progression of the disease process in the aortic wall. That is why long-life surveillance is advised.

## Conclusion

Hybrid therapeutic solution is an appealing less invasive and safe option for management of patients with multisegment thoracic aorta disease requiring AAR. Change of the surgical paradigm regarding treatment of thoracic aorta diseases is dependent on improvement of the endovascular graft technologies. Long term results of hybrid therapeutic strategy will eventually make clear if there are patients in whom open repair is indicated and which patients will benefit most from this challenging strategy.



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## COMPARISON OF POSTOPERATIVE OUTCOME OF TWO MYOCARDIAL PROTECTION STRATEGIES IN PATIENTS WITH LEFT MAIN STEM DISEASE.

Mohamed F. Ibrahim, MD.  
Amal A. Refaat, MD.  
Tamer Elghobary, MD.  
Ayman Ammar, MD.

**Background:** Myocardial protection is a major contributing factor in the results of CABG surgery. We aimed to compare the early postoperative outcome of two myocardial protection techniques in patients with left main stem disease, namely: intermittent cross-clamp fibrillation (ICCF) and antegrade cold blood cardioplegia (ACBC).

**Methods:** From January 1993 to February 2002 615 patients were operated upon for left main stem stenosis. We divided these patients into two groups, group A: 127 patients, ICCF was used, and group B: 488 patients, ACBC was used.

**Results:** There were 8 mortalities in group A (6.3%) and 14 (2.9%) in group B. Mean bypass time was more (87.9 min.  $\pm$  22.1) vs (74.6 min.  $\pm$  34.8) and Cross clamp time was less (35 min.  $\pm$  11.3) vs (45.2  $\pm$  20.7) in Group A than in Group B. In group A six patients (4.7%) needed IABP vs seventeen patients (3.5%) in group B. By multivariate logistic regression analysis, the type of myocardial protection was not an independent factor to predict the occurrence of postoperative complications, prolonged ICU stay or mortality.

**Conclusion:** ICCF is a method of myocardial protection that can be used safely in patients with left main stem disease.

The type and the efficacy of myocardial protection is a major contributing factor in the immediate and long term results of coronary artery surgery. Despite the increasing world-wide use of beating heart surgery, the majority of coronary artery surgery all over the world continues to be done on-pump. Two of the commonly used types of myocardial protection are ante grade/retrograde cold blood cardioplegia (ACBC) and intermittent cross-clamp fibrillation (ICCF). Some studies have compared the postoperative outcome of using these methods of myocardial protection, but to our knowledge, no studies have compared the use of these two methods in patients with left main stem (LMS) disease. The objective of this study was to analyse and compare the clinical postoperative outcome of using the two myocardial protection strategies in patients with left main stem disease.

### Methods

From January 1993 to February 2002 six hundred and fifteen patients were operated upon for LMS stenosis. All patients with LMS disease more than 50% were included in the study including elective, urgent and emergency patients. Surgery was performed by all surgeons of the institution. Data was collected prospectively using our Patient Analysis and Tracking System (PATS) database.

Retrospectively, we divided these patients into two groups, (group A): 127

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Address reprint request to : Dr. Mohamed F. Ibrahim Department of Prince Salman Heart Centre, King Fahd Medical City, Riyadh, Saudi Arabia  
Email : jegyptscts@gmail.com  
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patients for which ICCF was used, and (group B): 488 patients for which ACBC was used. Both groups were compared preoperatively, intraoperatively, and immediate postoperatively. Clinical data, hemodynamic status, morbidity and mortality were studied.

The anaesthetic technique was similar in both groups. Cardiopulmonary bypass was established in a similar way for the two groups using aortic cannula and double stage single venous cannula (or Ross basket). Moderate systemic hypothermia (32-33 °C) was maintained during bypass in all cases.

The cardioplegia solution in group B consisted of St. Thomas solution number 1. Following cross-clamp application; ante grade instillation was done through aortic root cannula at a pressure of 100 -120 mm Hg. The first dose of 15 ml per kg was followed by 200-300 ml every 20 minutes. All bottom ends were anastomosed with the aorta cross-clamp and while the myocardium is arrested. Top ends were constructed after de-clamping of the aorta and during partial clamping while the heart starts beating again.

In group A, ventricular fibrillation (VF) was induced using 10 mA alternate current (AC) through a fibrillator prior to cross-clamping of the aorta for bottom-end anastomosis. On completion of each bottom end the aorta was declamped, and the heart perfused and defibrillated with 10-15 J. direct current (DC) shock before the corresponding top end was anastomosed. This sequence was repeated with each graft.

Systemic rewarming was commenced during the final distal anastomosis in both groups and weaning from the bypass machine was attempted when the core temperature reached 36 °C.

The baseline characteristics of both groups are shown in Table 1. Both groups were comparable in terms of age, Canadian Cardiac Society (CCS) angina score, pulmonary disease, renal disease, smoking, diabetes, hypertension, peripheral vascular disease, cerebro-vascular stroke, previous and recent myocardial infarction, left ventricular function, previous thrombolysis and PTCA. Although non statistically significant, group A had more patients with CCS angina score III+IV, more patients with pulmonary disease, more current smokers, more patients with non insulin-dependant diabetes, more patients with hypertension and peripheral vascular disease, more patients with previous stroke and more patients with recent MI less than 30 days. Also the LVF was generally lower in group A. On the other hand, group B had more female patients, more patients with CCS angina score IV, more patients with renal disease, more ex-smokers, more patients with insulin-dependant diabetes. Also group B had more patients with transient

ischemic attacks (TIA), more patients with thrombolysis and previous PTCA.

Variable	Group A (ICCF) N= 127	Group B (ACBC) n= 488	p value
Age	65.4 ± 8.7	65.2 ± 8.6	0.3
Gender M:F	2.6:1	3.1:1	0.02
BSA	1.8 ± 0.2	1.9 ± 0.1	0.6
BMI	27.3	27.3	0.1
CCS Angina Class			0.1
0	1.6%	3.9%	
I	4.7%	7.6%	
II	26.8%	30.4%	
III	59.8%	38.8%	
IV	7.1%	19.3%	
III+IV	66.9%	58.1%	
Pulmonary ds.(COPD)	18.9%	12.3%	0.02
Renal ds.			0.7
s.cr. > 200	0.8%	1%	
dialysis	0	0.4%	
Smoking			0.7
Current	29.1%	19.3%	
Ex	44.1%	57.2%	
Diabetes			0.3
Diet control	4.7%	2%	
Oral hypoglycemic	11%	6.7%	
Insulin dependent	3.1%	4.3%	
Hypertension	65.4%	54%	0.03
Peripheral Vascular ds.	21.3%	17%	0.04
CVA			0.7
TIA	4.7%	4.9%	
Stroke	3.9%	3.3%	
Previous infarction	40.5%	50.8%	0.03
Recent infarction (30 days)	11.8%	8.6%	0.02
Thrombolysis	1.6%	4.1%	0.1
Previous PTCA	4.7%	6.2%	0.3
LVF			0.2
Fair	37.8%	34.4%	
Poor	11.8%	7.7%	

Table 1. Preoperative data

BSA= Body surface area; BMI= Body mass index; CCS= Canadian Cardiovascular Society; CVA= Cardiovascular accident; LVF= Left ventricular function; PTCA= Percutaneous transluminal coronary angioplasty; TIA= Transient ischemic attack.

### Statistical analysis

The SPSS version 10.5 for Windows was used for statistical analysis. Chi-square test and Fisher's test was used for categorical data while the Student's t-test was used for numerical data. Statistical significance was set



at  $p < 0.05$ . Variables entered for multivariate logistic regression analysis to identify predictors of complications were, age, gender, angina grade, pulmonary disease, renal disease, smoking, diabetes, hypertension, peripheral vascular disease, LV function, timing of operation (elective, urgent or emergency), number of grafts, type of myocardial protection, total bypass time, cross-clamp time, the need for inotropic support, IABP usage, post-operative renal and neurological complications.

## Results

Both groups were comparable in terms of age, Canadian Cardiac Society (CCS) angina score, pulmonary disease, renal disease, smoking, diabetes, hypertension, peripheral vascular disease, cerebro-vascular stroke, previous and recent myocardial infarction, left ventricular function, previous thrombolysis and PTCA. Although non statistically significant, group A had more patients with CCS angina score III+IV, more patients with pulmonary disease, more current smokers, more patients with non insulin-dependant diabetes, more patients with hypertension and peripheral vascular disease, more patients with previous stroke and more patients with recent MI less than 30 days. Also the LVF was generally lower in group A. On the other hand, group B had more female patients, more patients with CCS angina score IV, more patients with renal disease, more ex-smokers, more patients with insulin-dependant diabetes. Also group B had more patients with transient ischemic attacks (TIA), more patients with thrombolysis and previous PTCA.

Intra-operative variables are shown in table 2. The two groups were comparable in terms of number of grafts. Group A had more patients who underwent urgent and emergency surgeries and less elective surgeries. Group A had less cross-clamp time. Group B had more bilateral mammary artery utilisation, less total bypass time.

Variable	Group A (ICCF) n= 127	Group B (ACBC) n= 488	P value
Timing of surgery			0.009
Elective	35.4%	49.6%	
Urgent	55.1%	46.3%	
Emergency	9.5%	4.1%	
BIMA	11%	37.7%	0.008
Average no. of grafts	3.06	3.14	0.01
TBT (minutes)	87.9 ± 22.1	74.6 ± 34.8	0.006
XCT (minutes)	35 ± 11.3	45.2 ± 20.7	0.007

Table 2. Intra-operative data

**BIMA= Bilateral internal mammary artery; TBT= Total bypass time; XCT= Cross-clamp time**

Postoperative variables are shown in table 3. The

two groups were comparable in terms of postoperative IABP, the need for ventricular assisted devices and inotropic utilisation, overall complications, neurological complications, hours of ventilation, hours in ICU, total hospital stay as well as mortality. Though not statistically significant, group A had less hours of ventilation, less ICU stay.

Multivariate logistic regression analysis identified pre-operative renal dysfunction, previous myocardial infarction, pre-operative left ventricular dysfunction, age, prolonged total bypass time, cross-clamp time, post-operative IABP, VAD, and inotropes utilisation, duration of inotropic utilisation, to be predictors of post-operative complications. The predictors of mortality were: pre-operative renal dysfunction, angina grade, hypertension, emergency surgery, recent myocardial infarction, pre-operative left ventricular dysfunction, prolonged total bypass time, post-operative IABP, VAD, and inotropes utilisation, duration of IABP.

The type of myocardial protection was not an independent factor to predict the occurrence of post-operative complications, prolonged ICU stay or mortality

Variable	Group A (ICCF) n= 127	Group B (ACBC) n= 488	P value
POIABP	4.7%	3.5%	0.5
IABP duration (hrs.)	20.2 ± 6.8	30 ± 4.5	0.02
POVAD	0.8%	0.4%	0.5
PO inotropes	18.1%	18.2%	0.9
Duration of inotropes (hrs.)	5.7 ± 4.0	15.7 ± 3.0	0.008
Complications	32.3%	37.4%	0.2
Neurological complications			0.01
Transient	0%	1.7%	
Stroke	1.6%	2.7%	
Hours in ICU	17.1 ± 8.9	20.6 ± 13.6	0.04
Hours of ventilation	7.9 ± 4.2	9.4 ± 11.6	0.1
Hospital stay (days)	11.4 ± 5.8	11.1 ± 9.0	0.2
Hospital mortality			0.049
Early (<30 days)	5.5%	2.9%	
Late (>30 days)	0.8%	0%	

Table 3. Postoperative data

**POIABP= Post-operative intra-aortic balloon pump; POVAD= Post-operative ventricular assisted device**

## Discussion

The principle of cardioplegic arrest is to minimize cellular metabolism and maximize cellular energy preservation without causing myocardial injury. In addition

to variations of temperatures and compositions of cardioplegia, different perfusion strategies to maximize coronary distribution can be adopted [1-6]. Simply arresting the heart reduces the myocardial oxygen demand by nearly 90%; by cooling the myocardium cold cardioplegia significantly reduces the remaining 10%. The technique of intermittent cross-clamp fibrillation depends on reducing myocardial oxygen demand by moderate hypothermia and simultaneous work-load reduction by emptying the heart [7-8]. The effect of short periods, 15-20 minutes, of ischemia can be rapidly reversed by coronary reperfusion on releasing the aortic cross-clamp. In elective as well as in non-elective cases the advantages of blood cardioplegia over intermittent cross-clamp fibrillation are not so clear cut [9-13]. The relevance of using clinical end points, especially the immediate post-operative clinical outcome, morbidity and mortality, lies in the fact that poor outcome is usually a manifestation of injury to a critical mass of myocardial tissue beyond the compensatory capacity of the uninjured myocardium.

In our study the post-operative outcome of both groups were essentially comparable in terms of number of grafts, post-operative IABP, ventricular assisted devices and inotropes utilisation, overall complications, neurological complications, hours of ventilation, hours in ICU, total hospital stay as well as mortality.

The type of myocardial protection was not an independent factor to predict the occurrence of post-operative complications, prolonged ICU stay or mortality.

Multivariate logistic regression analysis identified pre-operative renal dysfunction, previous myocardial infarction, pre-operative left ventricular dysfunction, age, prolonged total bypass time, cross-clamp time, post-operative IABP, VAD, and inotropes utilisation, duration of inotropic utilisation, to be predictors of post-operative complications. The predictors of mortality were: pre-operative renal dysfunction, angina grade, hypertension, emergency surgery, recent myocardial infarction, pre-operative left ventricular dysfunction, prolonged total bypass time, post-operative IABP, VAD, and inotropes utilisation, duration of IABP.

Although total bypass time was considerably higher in group A; cross-clamp time was significantly lower. Interestingly, studies from Musumeci and associates [8] and Anderson and colleagues [11] found lower levels of cardiac creatine kinase and troponin T in patients with intermittent cross-clamp fibrillation compared with cold-blood cardioplegic arrest. These results may be related to the significantly shorter ischemic time in patients with intermittent cross-clamping than in patients with cardioplegic arrest. The longer total bypass time

was not reflected by an increase in post-operative inotropic or IABP utilisation or the occurrence of any other complication.

Neurological complications, either transient or prolonged, was similar in both groups in spite of the fact the removing and applying the aortic cross-clamp may increase the incidence of embolic strokes. Bonchek and associates [12] reported a low incidence of transient and permanent neurologic events in a series of 3000 patients operated on with repeated aortic cross-clamping. Musumeci and co-workers [8] showed that in patients with no preoperative evidence of aortic or cerebrovascular disease, repetitive clamping of the aorta is not associated with a higher rate of cerebrovascular events compared with the single-clamp technique.

The higher incidence of mortality in group A is probably related to the pre-operative higher CCS angina class III & IV, more patients with recent myocardial infarction, hypertension, smoking, pulmonary disease, and lower left ventricular function. Also it may be related to the higher incidence of urgent and emergency surgeries in group A.

## Conclusion

We conclude that on the basis of clinical outcome; intermittent cross-clamp fibrillation is a safe and effective method of myocardial protection even in cases of left main stem stenosis.

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## SURGICAL REVASCULARIZATION AFTER ACUTE MYOCARDIAL INFARCTION, IS IT RUNNING AGAINST THE CLOCK?

Mohamed A. Alaal, MD,  
 Nezar Elnahal, MD,  
 Mamdouh Sharawy, MD,  
 Mostafa Alsabban, MD,  
 Osama Abbas, MD,  
 Bakir M. Bakir, MD,  
 Ahmed Al-Saddique, MD,  
 Mohammed Fouda, MD,  
 Ahmed Alshaer, MD,

**Background:** The optimal timing for surgical revascularization after acute myocardial infarction (MI) remains controversial. Higher mortality for emergency coronary artery bypass grafting (CABG) after acute myocardial infarction (AMI), ranging from 5% to 30%, has been documented since the early 1970.

**Methods:** We examined our experience retrospectively in 278 patients who underwent CABG between 2005 and 2007 at king Fahad cardiac center in king khaled university hospital, Riyadh, Saudi Arabia and cardiothoracic surgery department in faculty of medicine, Zagazig university. We had three groups one who underwent CABG within 24 hours (group 1), group 2 between 1 to 3 days and last group 3 after 14 days.

**Results:** The operative mortality associated with increasing time intervals between MI and CABG were 11.68%, 7.05%, 2.5%, for group 1 (within 24 hours), group 2 and 3 respectively. In comparison, the incidence of cerebrovascular (CVA) and atrial fibrillation (AF) were greater in group 1 and the length of ICU stay was longer for patients undergoing CABG early after MI (within 24 hours).

**Conclusions:** emergency coronary artery bypass grafting (CABG) after AMI (group 1) hours has a significantly higher risk. Non-emergency surgical revascularization can be done safely at any time interval after acute myocardial infarction, certainly after 72 hours, without increase in operative mortality and acceptable morbidity.

The optimal method to achieve early reperfusion is a matter of controversy and a subject of ongoing studies. (1) Evolving ischemia, cardiogenic shock, PCI failure, and structural complications such as papillary muscle rupture, ventricular septal defect, or severe left ventricular mechanical dysfunction are indications for emergency operation to maximize myocardial salvage and reduce the impact of severe hemodynamic compromise on other organs. (2) Higher mortality for emergency coronary artery bypass grafting (CABG) after acute myocardial infarction (AMI), ranging from 5% to 30%, has been documented since the early 1970s. (3) However, the ideal timing of coronary artery bypass grafting (CABG) after an AMI remains controversial. (4) Patients without risk factors have an expected operative mortality similar to elective CABG. However, in patients with multiple risk factors, hospital mortality may reach 30 to 40 percent. (5) Some studies have found early CABG to be an acceptable therapy, whereas others have recommended a waiting period. Numerous interventions have also been suggested to improve the surgical outcome. (6,7) Some of these recommendations have included better selection of patients, timing of the operation, and preoperative support with intraaortic balloon counterpulsation (IABP). (8)

The objective of the present study was to delineate the relationship between

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Address reprint request to :

Dr Mohamed A. Alaal

Department of cardiothoracic surgery

Email : jegyptscts@gmail.com

Codex: 04 / cord / 54B / 0709

the timing of CABG after acute MI and mortality and short-term postoperative outcomes in series of patients.

### Methods:

The data for this report are obtained from our database registry which is reporting system that registers all data of every patient undergoing a cardiac operation at King Fahad Cardiac Center in King Khaled University hospital at Saudi Arabia and Zagazig university hospital, faculty of medicine, Zagazig university. The data of 278 patients who underwent conventional CABG as the sole procedure between January 2005 and December 2007 were identified and selected for analysis. Seventy seven of them underwent emergency operations for evolving MI, performed during the first 24 hours (group 1) after onset of pain with cardiogenic shock, or those with hemodynamic instability and complications related to cardiac catheterization, eighty five patients underwent CABG 1-3 days of AMI (group 2) who were hemodynamically stable and 116 patients after 2 weeks (group 3).

The diagnosis of AMI was made by conventional electrocardiographic (ECG) and enzyme criteria, and confirmed by coronary angiography which showed occluded vessel(s) with a regional wall-motion abnormality on the left ventriculogram. Patients who underwent concomitant valve replacement redo-CABG or other combined operative procedures were excluded from the analysis.

Information regarding each patient's demographic data, preoperative medical history (number and time of previous MIs, diabetes mellitus, smoking history, renal insufficiency, hypertension, and peripheral vascular disease), operative procedure (urgency of operation, cardiopulmonary bypass time, aortic cross-clamp time, the number of distal bypasses performed, and use of the IABP), and postoperative outcomes (operative death, cerebrovascular accident (CVA), postoperative atrial fibrillation, and number of days spent in the intensive care unit and hospital stay) were gathered retrospectively from the medical record.

The most commonly used myocardial protection technique was the administration of antegrade, intermittent cold blood cardioplegia, but some patients also received warm blood cardioplegia, especially in group operated within 24 hrs. for myocardial energy resuscitation. A warm dose of blood cardioplegia (hot shot) was given at the end of the final distal anastomosis was used in some patients.

Standard cardiopulmonary bypass techniques were used, including moderate systemic hypothermia (28 to 32C) and blood cardioplegia. Internal mammary artery graft and saphenous vein graft anastomosis were performed in most of patients.

### Timing of Surgery

All patients received maximal medical therapy for stabilization. Nitrates, bed rest and use of an IABP were maximally used to stabilize patients with unstable angina prior to surgery. Patients with symptoms of heart failure were treated with afterload reduction, diuretics and on occasion an IABP to optimize their condition prior to surgery. The exact timing of surgery was based on several variables, but the following guidelines were generally employed. The indication for urgent surgery were unstable symptoms not responding to maximum medical therapy (group 1). Patients without evidence of ongoing ischemia received aggressive medical treatment up to 3 days to optimize their condition and allow recovery of potentially "stunned" myocardium (group 2). Patients who had uncomplicated hospital courses were operated on electively at the first available time, (group 3)

### Statistical Analysis

Statistical calculations were made using SAS. Descriptive data were reported as mean  $\pm$  one standard deviation. Comparisons between continuous variables were made using Student's t test. Multiple group means were compared using analysis of variance. In all cases, differences were considered to be significant for a p value of 0.05 or less.

### Results:

The demographics of patients were similar in all groups. Mean age of patients was  $59.2 \pm 12.4$  years (range, 42 to 92 years). There were 210 men (75.5%) and 68 women (24.5%). The mean left ventricular ejection fraction was  $40.9\% \pm 14.5\%$ . Mean number of vessels bypassed in each patient was  $3.2 \pm 0.9$ , with a mean aortic cross-clamp time of  $59.2 \pm 28.5$  minutes and a mean cardiopulmonary bypass time of  $95.3 \pm 39.8$  minutes. Overall in-hospital mortality for all patients was 6.47% (18 pts.)

Overall hospital mortality was 6.47% (18 pts.). Hospital mortality decreased with increasing time interval between CABG and AMI: 11.68% (9 pts) in group (1), 7.05% (6 pts) in group (2), and 2.58% (3 pts.) in group (3). The graphic representation of the data is shown in Figure 1.



Table (1) shows the prevalence of co-morbidities in patients with history of myocardial infarction. Comparison of percentage of patients in the all AMI groups. The percentage of patients with ejection fraction less than 30%, recent history of congestive heart failure, requirement of intraaortic balloon pump, and renal dialysis in the group 1 were significantly higher than those of the other groups. The IABP was used most frequently in association with operations performed early after MI, with as many as 43.9% of patients receiving an IABP in group 1 and 2.

There was no statistical difference in the incidence of the number of distal bypass grafts in all the patient groups. In particular, fewer grafts were performed for patients who underwent operation early after MI. The mean times required for cardiopulmonary bypass and aortic cross-clamping fell within a narrow range for the patient groups, from 109.2 to 124.2 minutes ( mean 95.3± 39.8 min) and 42.3 to 69.9 minutes( mean 59.2± 28.5 minutes)respectively (figure 2).

The incidence of CVA, and atrial fibrillation were not uniform among the patient groups, it was statistically different in group 1. The postoperative length of stay in the intensive care unit was not similar for the patient groups. There was no statistically difference in the length of hospital stay. In general, there was a longer intensive care unit stay for patients with short time intervals between MI and CABG as in group 1 and 2 (table 2).

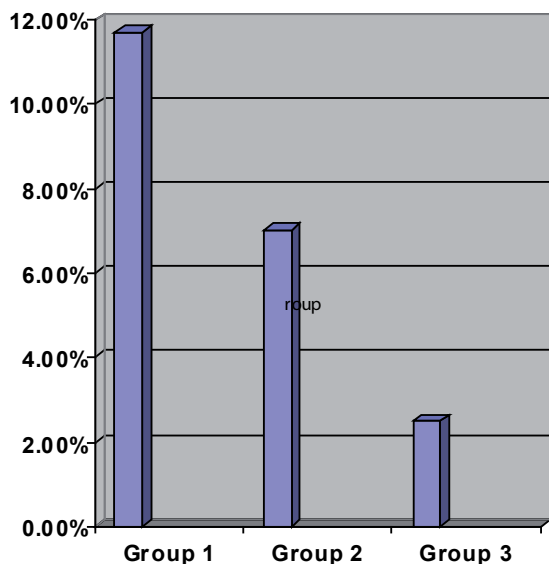


Figure: 1 showed mortality rate in all patients.

Characteristic	Group 1 (n = 77)	Group 2 (n = 85)	Group 3 (n = 211)	P value
Age	62.3 ± 12.0	65.0 ± 11.3	65.1 ± 10.5	NS
Smoking	81.8%	66.7%	66.3%	NS
Diabetes mellitus	0.0%	30.3%	30.7%	NS
Hypertension	54.5%	58.3%	60.9%	NS
Renal insufficiency	18.2%	6.8%	10.2%	HS
Urgent/emergent	100%	78.8%	16.1%	HS
EF< 30%	25.97% (20pts)	15.29% (13pts)	5.2% (11pts)	HS
IABP	42.9% (33pts)	27% (23pts)	20.37% (43pts)	HS
Congestive heart failure	19.48% (15pts)	4.7% (4pts)	-	HS

Table 1: displayed Preoperative risks

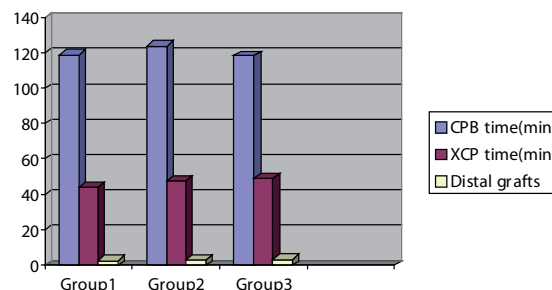


Figure2: displayed operative data

Outcome	Group 1 (n = 77)	Group 2 (n = 85)	Group 3 (n = 211)	P value
CVA	9.1%	3.8%	2.9%	HS
Atrial fibrillation	44.0%	35.6%	22.5%	HS
Postoperative ICU days	8.1 ± 4.4	4.4 ± 1.4	2.8 ± 1.9	HS
Hospital days	9.8 ± 10.6	9.5 ± 10.0	8.1 ± 6.6	NS

Table 2: Short-Term Postoperative Outcomes for All Patients

CVA: cerebrovascular accident; ICU: intensive care unit, MI: myocardial infarction. NS: non significant, HS: highly significant p < 0.01

**Discussion:**

The optimal method to achieve early reperfusion is a matter of controversy and a subject of ongoing studies. The optimal timing of surgery depends upon why it is being performed. As an example, ongoing ischemia, cardiogenic shock, PCI failure, and structural complica-



tions are indications for emergency operation to maximize myocardial salvage and reduce the impact of severe hemodynamic compromise on other organ systems (9, 10).

The surgical management of AMI has been an issue of ongoing debate. In the setting of AMI and acute coronary occlusion, there are some who have advocated emergency revascularization, but others remained unconvinced and suggested a variable period of waiting before surgical intervention.(11,12)

Some data suggest that revascularization performed within the first six hours after acute MI results in a greater degree of reperfusion injury and increased mortality.(13) This observation was supported by clinical studies showing increased morbidity and mortality when CABG was performed in the first 12 to 24 hours after acute MI due both to reperfusion injury and to the unstable clinical state (14).

Our retrospective study evaluated 278 patients undergoing CABG after myocardial infarction over a three year time span. The hospital mortality decreased with increasing time between the MI and surgery; 11.68% in group 1(within 24 hours), 7.05 % for in group 2 (1- to 3 days), 2.5% for group 3(> 15 days). Operative mortality was less for patients undergoing operation electively compared to emergency surgery. Lee et al;2001(15) coincided with our results as they reported that the hospital mortality decreased with increasing time between the MI and surgery; 11.8 percent for <6 hours, 9.5 percent for 6 to 23 hours, 4.3 percent for one to seven days, 2.4 percent for 8 to 14 days, and 2.6 percent for 15 days. Mortality for the transmural group remained high during the first 24 hours after AMI before trending downward. Creswell et al;1995(16) reported that the operative mortality associated with increasing time intervals between MI and CABG were 9.1%, 8.3%, 5.2%, 6.5%, and 2.9%, for less than 6 hours, 6 hours to 2 days, 2 to 14 days, 2 to 6 weeks, and more than 6 weeks, respectively, so correlation between time of operation and mortality in the AMI patients is more striking as a result of these different patterns.

DeWood and colleagues 1989(17), have been advocates of early operations after transmural AMI. Their conclusions were derived from a retrospective study of 440 patients with transmural AMI from 1971 to 1981. In that study it was reported that patients started on cardiopulmonary bypass within 6 hours of an AMI had significantly lowered short-term and long-term mortality. Although these results were impressive, the majority of these patients only had 1- or 2-vessel disease.

Another prospective randomized study of 302 patients from 1993 to 1998 by Hochman and colleagues(18)

showed improved survival in patients undergoing early revascularization after AMI complicated by cardiogenic shock. However, methods of revascularization in this study included either CABG or PTCA.

Hirose H. et al; 2000(19) reported that short-term risk analysis demonstrated a high in-hospital mortality rate among the subsets of patients with preoperative cardiogenic shock (3 of 19, 15.8%), and no mortality in those without cardiogenic shock (0 of 28, 0.0%). In our study, 15 patients of 77 ( 19.48%) of patients in group1 were in cardiogenic shock and mortality rate was 11.68%. The presence of cardiogenic shock impairs coronary blood supply, which may result in extension of the impending necrosis of the myocardium.

Statistically, the risk of mortality would be the same whether one waits 3 days or 7 days. Early surgical intervention has the advantage of limiting infarct expansion and adverse ventricular remodeling.(20) However, there is a potential risk of ischemia-reperfusion injury, which might lead to hemorrhagic infarct extension, resulting in additional myocardial injury. Some have advocated the use of mechanical support to stabilize and allow elective rather than emergent surgery.(21)

It is unclear why surgical intervention within 3 days of transmural AMI might be an added risk for mortality. It has been reported that serum C-reactive protein (CRP), a marker of acute inflammatory response that increases precipitously after transmural AMI, plateaued on day 3 after the infarction. In addition, this peak level is a strong indicator of prognosis after a first transmural AMI. One might speculate that surgical revascularization within 3 days of an AMI, during the rising phase of CRP, might further augment such a systemic inflammatory response and affect prognosis because CABG is known to cause an increase in serum CRP level with or without cardiopulmonary bypass. With improved myocardial protection, anesthesia, and surgical techniques, recent reports have mortality that is lower when compared with earlier studies.(22)

Sintek C. F. et al; 1994(23) mentioned in their study that the timing of CABG after AMI is controversial, even though CABG can provide a better outcome in patients with AMI than medical treatment. They had no hospital mortality among the patients who underwent emergency CABG within 24 hours after the onset of AMI, despite the fact that 14 patients (43.8%) had triple vessel disease and 11 patients (34.4%) were in cardiogenic shock.

In conclusion, this study revealed, emergency coronary artery bypass grafting (CABG) after AMI (within 24) hours has a significantly higher risk. Nonemergency surgical revascularization can be done safely at any

time interval after acute myocardial infarction, certainly after 72 hours, without increase in operative mortality and acceptable morbidity. In the absence of clear indications for emergency surgical intervention, such as severe hemodynamic instability in spite of maximum medical treatment and evolving ischemia, a 3-day waiting period before CABG should be considered. There are important questions remained to be answered, such as the role of thrombolytic therapy, early PTCA, and controlled surgical reperfusion in the management of AMI. These questions require the cooperation of our cardiology colleagues in multi-institutional, prospective, randomized clinical trials.

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## STERNOTOMY COMPLICATIONS AFTER CABG RISK FACTORS

B. M Ibrahim MD,

***Background:*** The development of a sternotomy complication is multifactorial and numerous studies point to a multitude of patient- and procedure-related variables as underlying factors in this complication.

***Methods:*** Retrospective study analysis of 132 patients operated upon coronary artery bypass grafting.

***Results:*** Sternal wound complications occurred to 19 patients (14.4), statistical analysis of the results demonstrated that prolonged mechanical ventilation, post operative blood loss and transfusion, prolonged bypass time, and diabetes mellitus was significant predictor risk factors for sternal wound complications risk factors.

***Conclusion:*** Identification of both patients related risk factors and procedures related risk factors for sternal wound infection is very beneficial. Patients related factors should be lessened as much as possible while procedures related factors should be eliminated to abort any chance for sternal wound complication.

Median sternotomy is still the most commonly used approach in cardiac surgery. But patient who undergo median sternotomy continue to suffer morbidity and death from sternal wound complication especially after CABG surgery. Sternal wound infection, dehiscence, mediastinitis and extensive wound necrosis can complicate the postoperative course (Sung et al., 1998) (1). Sternal wound complications, i.e. instability and or infection, following median sternotomy are infrequent yet potentially devastating events following cardiac surgery, leading to prolonged hospitalisation, increased hospital costs and high associated morbidity and even mortality (Ivert et al., 1991) (2).

The reported incidence of sternal wound infection can range between 1 and 10% (Ottino et al study., 1987) (3), and mediastinitis can occur in up to 8% of patients (Culliford et al., 1976) (4).

The development of a sternotomy complication is multifactorial and Numerous studies point to a multitude of patient- and procedure-related variables as underlying factors in this complication (Parisian Mediastinitis Study., 1996) (5). This highlights the importance of identifying those patients at greater risk of developing sternal wound infections prior to coronary artery bypass surgery, with the potential for risk factor modification when possible as Risk factor identification permits the assessment of factors that may be modifiable. Therefore, several risk stratification systems are defined to evaluate the results of surgery in acquired heart disease (Parsonnet et al., 1989) (6) and Higgins et al., 1992) (7).

Accepted for publication July 7, 2007  
Address reprint request to : Dr Ibrahim  
B.M  
Departement of cardiothoracic  
surgery, faculty of medicine Tanta  
university  
Email : messacts  
Codex : 04 / cord /55 /0707

Also recent univariate and multivariate models were developed to compute the risk for sternal complications but these models ultimately provided low sensitivity and low predictive value (Lozonoff et al., 2002)(8).

Preoperative risk factors for sternal wound dehiscence may include old age, male gender, diabetes mellitus, chronic obstructive airway disease, obesity, New York Heart Association class 3, renal pathology, peripheral vascular diseases and smoking ( Loop et al.,1990)(9).

Other studies reported that chronic steroid use, chronic renal failure (on dialysis), previous median sternotomy; recent cerebrovascular accident (between median sternotomy and sternal wound reconstruction), perioperative acute myocardial infarction and placement of an intra- aortic balloon pump (IABP) are risk factors for sternal wound complications (Jones et al., 1997)(10)

This study aimed to assess the risk factors for sternotomy complications for patients underwent CABG.

## Methods

This retro and prospective study includes all patients who have underwent consecutive coronary artery bypass graft surgery through midline sternotomy. Patients were selected to this study after institutional and informed consent according to the following inclusion and exclusion criteria.

### Inclusion criteria:

All patients who have underwent coronary artery bypass graft surgery either on or off cardiopulmonary machine.

### Exclusion criteria:

1. Patients who have underwent compound procedures as coronary by pass graft surgery with valvular surgery.
2. Patients who died either intraoperative or during their stay in intensive care unit immediately postoperative due to causes not related to sternal complications.

### the patient suffering sternal wound complications will be subdivided into 4 subgroups :

1. Superficial wound infection invading skin and subcutaneous tissue.
2. Sternal dehiscence without infection.
3. Sternal dehiscence with infection.

4. Mediastinitis involving the deepest layer.

### Patients were subjected to the following:

A) History taking: a thorough history was taken as regards age, sex, obesity, diabetes, priority of surgery & chronic obstructive airway disease.

B) Physical examination: a complete clinical; general & local examination was performed.

C) Investigations:

- \*completeLaboratory investigations
- \*Radiological investigations
- \* Electrocardiogram
- \* Echocardiogram
- \*Coronary Angiography and Ventriculography

D) Preoperative counseling:

In the preoperative visit prior to surgery, a brief explanation of the steps of the operation, the postoperative events and the intensive care stay was done.

E) Preoperative preparation:

All patients received their morning dose of cardiac medications. Intramuscular 0.1 mg/kg morphine sulphate before transfer to the operating theatre was given to all patients.

F) Intra-operative procedure:

Patients were showered and shaved the day of their operation. All patients received intravenous 1gm cefotaxime preoperatively and for at least 6 days postoperatively. The operative field was painted with povidone-iodine solution and the skin was covered with an iodiform-impregnated adhesive plastic sheet.

The skin was incised with a scalpel and electrocautery was used to open the presternal layers and pericardium. Patients underwent surgery via median sternotomy with standard Cardiopulmonary bypass and moderate hypothermia at 30 to 34°C. Bone wax was used only if sternal bleeding was profuse. Internal thoracic arteries were harvested as a pedicled or skeletonised and used for coronary bypass.

Myocardial protection during aortic cross clamping was provide with initial warm blood cardioplegia and maintained by cold crystalloid cardioplegia. 2 retrsternal drains were placed, and chest tubes were inserted into the pleural spaces if opened. The sternum was closed



with stainless steel wires.

The presternal space was obliterated with two layers of absorbable suture, and the skin was closed with a subcuticular absorbable suture. Patients were extubated when they were hemodynamically stable, normothermic, and ventilating spontaneously.

Reoperation for early postoperative bleeding was generally performed when drains exceeded 500ml/h during the first 2 hours of surgery or continuous bleeding for 200ml/h.

All drains were removed when drainage was less than 25 mL/h.

**Our special consideration to:**

- \*Operative procedure as type of the saw, type of stainless steel wire, technique of sternal closure.
- \*Ischemic time and total bypass time.
- \*Total operation time.
- \*Problems in homeostasis.
- \*Use of inotropic support.
- \*Haemodynamics of the patient.

**G) Postoperative:**

**Our special consideration to:**

- Blood loss
- Ventilatory support.
- Blood transfusion
- Re- operation for bleeding.

All patients in this study were followed up during their monthly visits.

Sternal wound infection was defined according to the guidelines of the centers for disease control and prevention:

- An organism is isolated from culture of mediastinal tissue or fluid.
- Evidence of mediastinitis is seen during operation.

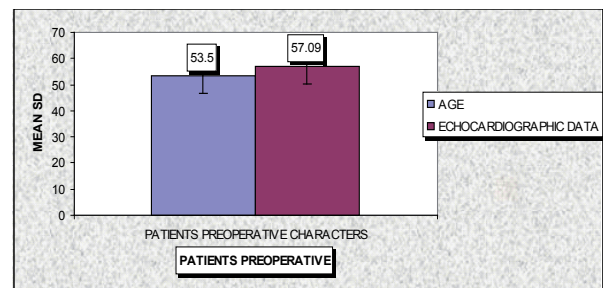
- One of the following symptoms; chest pain, sternal instability or fever > 38 °C and there is either purulent discharge from the mediastinum or an organism isolated from culture of drainage of the mediastinal area.

**Results**

- Preoperative characteristics of the patients under study:

Patients preoperative characteristics	Number of patients (n=132 patients) % within study
*Age	53.5±7.023 range (31- 69 ys)
*Sex	Male 116(87.9 %) Female 16(12.1 %)
*Overweight & Obese	43(32.6 %)
* Smokers	92(69.7 %)
*Preoperative chest problems	18(13.6%)
*Hypertensive	45(34.1%)
*Hypercholestermia	23(14.4%)
*Diabetics on oral therapy	42(31.8 %)
*Diabetics on Insulin therapy	24(18.2 %)
*Cerebrovascular stroke	8(6.1 %)
*Unstable angina	13(9.8%)
* Renal impairment (Creatinine > 2 gm/dl)	4(3.1 %)
* Echocardiographic data E.F% (Mean ± SD)	57.09±7.05% range (45-70%)
*Angiographic data	
Left main stenosis	4(3%)
One vesseles diseased	34(25.8 %)
Two vessels diseased	38(28.8 %)
Three vessels diseased	60(45.4 %)

**Table (1) Demographic and preoperative characteristics of the patients under study:**



**Fig (1): Means of ages and ejection fractions of patients within study.**

- Intraoperative and postoperative characteristics of patients under study:

- \*Emergency: Two patients (1.5%) was an emergent case and did not develop sternal wound complications.
- \*Off Pump Surgery: Four patients (3%) had underwent coronary artery bypass graft surgery off pump and did not develop sternal wound complications.
- \*Number of grafts: 46 patients (34.9%) had

underwent one graft surgery, 42 patients (31.8%) had underwent two grafts surgery, 42 patients (31.8%) had underwent three grafts surgery and only two patients (1.5%) had underwent four grafts surgery.

\*Types of grafts & conduits: 86 patients (65.2%) were revascularised by left internal mammary arterial conduit while 44 patients (33.3%) were revascularised by venous grafts without usage of arterial conduit and two patients (1.5%) was revascularised by radial artery conduit. So in this study, 86 LIMAs was harvested, 176 venous grafts were used and only two radial arteries were harvested and used.

\*Postoperative Pulmonary Complications: 48 patients (36.4%) developed postoperative pulmonary complications.

\*Sternal Wounds Complications: 113 patients (85.6%) did not develop sternal wound complications and 19 patients (14.4%) did. Furthermore, these 19 complicated patients are subdivided into 3 subgroups:

\*Subgroup 1: Patients with superficial sternal wound infection (S.S.W.I.). This subgroup included 4 patients (3.0%).

\*Subgroup 2: Patients with sternal dehiscence or Instability (SD/SI). This subgroup included 7 patients (5.3%).

\*Subgroup 3: Patients with deep sternal wound infection (D.S.W.I.). This subgroup included 8 patients (6.06%).

Of patients with sternal wound complications, only one case (0.76%) died due to mediastinitis leading to multisystem organ failure and generalized septicemia after 22 days.

• Mean operative time (hours)	5.33±0.56 h range (4-9hs)			
• Mean Cross-clamping time (minutes)	77.88±25.28 ms range (50-120 minutes)			
• Mean CBP time (minutes)	99.23±26.98 ms range (70-150 minutes)			
• Mean Ventilatory support time (minutes)	620.5±117.86 ms range (4-72 hs)			
* Post-operative pulmonary complications	24(36.4%)			
* Sternal wound complications	19(14.4%)			
* Sternal wound mortality	1(0.76%)			
<b>Complicated sub groups</b>	<b>sub group 1</b>	<b>sub group 2</b>	<b>sub group 3</b>	<b>Total</b>
No & % with in study	4 ( 3.0 % )	7 ( 5.3 % )	8 ( 6.06 % )	19 ( 14.4 % )

Table (2) Intra and postoperative characteristics of the patients under

Preoperative characteristics	Patients without S.W.C. (n=113 patients)	Patients with S.W.C. (n=19 patients)	P value Significance
*Age	52.7±1.1	54.3±1.44	N.S.
Age ≥ 60 years	24 (21.2) %	6 (31.6) %	N.S.
*male Gender	95 (84.1%)	19 (100%)	N.S.
*Overweight & Obese (BMI>25Kg/m2)	35 (31.0%)	8 (42.1%)	N.S.
* Smokers	75 (66.4%)	17 (89.5%)	N.S.
*preoperative chest problems	15 (13.3%)	3 (15.8%)	N.S.
* Diabetics;			
-Diabetics on oral therapy	48 (42.5%)	13 (68.4%)	N.S.
-Diabetics on Insulin therapy	36 (31.9%)	6 (31.6%)	S.S.
* Cerebrovascular stroke	12 (10.6%)	7 (63.1%)	N.S.
* Renal impairment Creatinine > 2 gm/dl	7 (6.2%)	1 (5.3%)	N.S.
* Echocardiographic data E.F%	3 (2.7%)	1 (5.3%)	N.S.
*Angiographic data			
One vesseles dis.	57.32±1.16	56.87±1.4	N.S.
Two vessels dis.	29 (25.7%)	5 (26.3%)	N.S.
Three vessels dis.	28(27.4%)	7 (36.8%)	N.S.
	54 (47.8%)	6 (31.6%)	N.S.

Table (3) Preoperative characteristics of the complicated and non complicated patients:

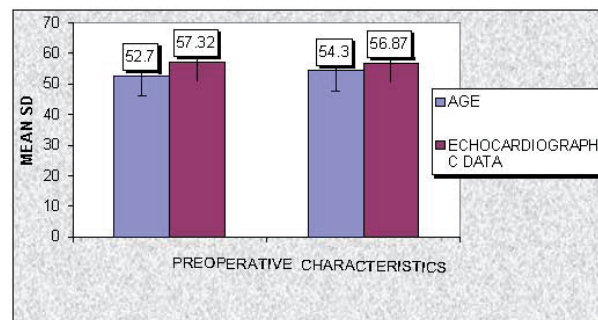


Fig (2) Preoperative characteristics of complicated and non complicated groups

• Culture and Sensitivity of complicated patients:-

Cultures were done for all complicated patients and revealed that:-

\*In subgroup 1, two patients were infected by Staphylococcus epidermis, one patient was infected by Staphylococcus aureus and one patient was infected by methicillin resistant Staphylococcus Aureus(MRSA).



\*In subgroup 2 all cultures were negatives.

\*In subgroup 3, 2 patients had pseudomonas infection, 3 patients had mixed infection by Staph.Aureus & Pseudomonas. One patient had klebisella infection, one patient was infected by candida and one patient culture revealed methicillin resistant Staphylococcus Aureus(MRSA).

Postoperative characteristics	Patients without S.W.C. (n=113 patients)	Patients with S.W.C. (n=19 patients)	P value Significance
*Ventilatorysupport time (minutes)	540.5±18.45	700.5±25.06	S.S.
*Postop. blood loss In ICU	689.87±28.74	854.02±37.21	S.S.
*Postop. blood transfusion	976.2±50.63	1467.87±87.18	S.S.
*Postop.Pulmonary complications	11(23.4%)	13(68.4%)	N.S.
*Laboratory data Hb (gm/dl)	10.63±0.15	9.31±0.23	S.S.
T.L.C	8570.21± 402.2	15241.5±578.1	S.S.
Creatinine (gm/dl)	1.2±0.07	2.47±0.17	S.S.
*ICU stay(days)	2.66±0.18	5.29±0.33	S.S.
*Hospital stay(days)	10.02±0.32	35.14±1.48	S.S.

**Table (4) Post-operative characteristics of the complicated and non complicated groups:**

So, the most common organism in this study was Staphylococcus aureus and Pseudomonas.

• Procedure done for sternal wound complications:

Subgroups	Procedures done
S.S.W.I. (4 patients)	Two patients were treated by trimming of the sternal incision curettage of the wounds & closure by secondary stitches and two patients were treated by simple dressing and local Antiseptics and antibiotics.
Sternal Dehiscence/ Instability (7patients)	3 patients were treated by chest belts & 4 patients were treated by sternal debridement & rewiring.
D.S.W.I. (8 patients)	7 patients were treated by sternal debridement & rewiring. One patients was treated by reconstructive surgery by pectoralis major flap & the other died before intervention due to generalized septicemia.

**Table (5) Procedures done for sternal wound complications**

## Discussion

The idea of using median sternotomy as an approach to thoracic organs was conceived in the late 1800s by Milton (11).

Nearly a century later, prevention and treatment of its infective complications remain a formidable challenge for cardiothoracic and plastic surgeons (loop et al., 1990) (9).

In our study, the incidence of the whole sternal complications was 14.4 %; superficial sternal wound infection (SSWI) represents 3.0%, aseptic sternal dehiscence/instability (SD/SI) represents 5.3% and deep sternal wound infection (DSWI) represents 6.06 %.

This incidence is higher than the incidences of sternal wound complications in other studies. In Zeitani et al., 2004 (12) the incidence of superficial wound infection was 5.75%, that of Aseptic sternal dehiscence was 2.75% and the incidence of deep sternal wound infection was 0.5%.

Our incidence is also higher than the incidence of sternal wound complications in Ridderstolpe et al., 2001 (13) study which noted that the incidence whole sternal wound complications was 9.7%; 6.4% for superficial wound infection, 1.6% for deep sternal wound infection and 1.7% for post-operative mediastinitis.

In Stahle et al., 1997 (14) , Borger et al., 1998 (15) , Losanoff et al., 2002 (8) and Abboud et al., 2004 (16) reported incidence of deep sternal wound infection after CABG was 1.7% ,0.8%, 2.6% and 0.5% respectively.

This high incidence of sternal wound complications in our study can be attributed partly to the high percentage of diabetics (50%), smokers (>70%), and overweight patients (>50%) and partly the less restrictive sterilizing programs performed. We noticed also that the incidence of deep sternal wound complication (12.1%) is higher than that of superficial wound infection (6.1%) and this may be due to that large number of patients with deep sternal wound infection were originally infected superficially and then the depth of infection increased later to be deep. Differences in the incidence between studies may be attributed to poor delineation of true depth and extent of infection, difference in surgical procedure done for complications and mode of follow up. So, these differences may result in combining deep serious infection and minor superficial wound infection.

In our study, the incidence of mortality due to post-sternotomy complications is 0.75%. This is slightly lower than that of Stahle et al., 1997 (14) study which was 2.8% and nearly equal to that of Ridderstolpe et al., 2001 (13) study which noted that the incidence of 30 days mortality due to sternal wound complications was 1%. In Losanoff et al., 2002 (8) study the incidence of

poststernotomy mediastinitis mortality was 2.5%

In our study, age was not a statistically significant risk factor for sternal wound complications after CABG and there is no definite age above which sternal wound complications could be suspected. This is in agreement with Borger et al., 1998 (15) study while Ridderstolpe et al., 2001, Ura et al., 2002 (18) study and Peivandi et al., 2003 (19) reported that age above 65 and 70 are risk factors.

As regards sex in our study, male gender isn't considered statistically significant risk factor for sternal wound complications (P value= 0.42) although male gender shows higher incidence of sternal wound complications than female. This may be due to the high percentage of male submitted in the study (87.9%) and females were not well represented in this study.

In contrast to this Stahle et al., 1997 (14) and Ura et al., 2002(18) studies in which female sex was one of the predictors of deep sternal wound infection

As regards body weight and smoking we found that obesity and smoking aren't a statistical significant risk factors for sternal wound complications in our study (P value = 0.25). but smokers have a high incidence of sternal wound complications and smoking is equally related to aseptic sternal dehiscences and deep sternal wound infection.

Regarding Diabetes Mellitus, diabetics on insulin therapy show more chance to develop sternal wound complications. In our study 68.4% of patients with sternal wound complications were diabetics. Moreover, 36.8% of patients with sternal wound complications were diabetics on insulin therapy. So, in our study 25% of diabetics on insulin therapy developed deep sternal wound infections.

Number of grafts and use of left internal mammary (LIMA) conduit does not contribute a significant risk factors for sternal wound complications.

In our study, prolonged operative time is a significant risk factor for sternal wound complications in comparison to the cross clamping time and cardio pulmonary-bypass time which are not.

In our study, postoperative mechanical ventilation is an extremely statistically significant risk factor for sternal wound complications (P value = 0.0002). This is

in agreement with Ridderstolpe et al., 2002 (13) study, Peivandi et al., 2003(19) and John CY et al., 2003 (20).

Both postoperative blood loss and postoperative blood transfusion are significant risk factors for sternal wound complications. Both factors are more related to deep sternal wound infection than its relation to superficial sternal wound infection. Abdullah and Farag 1996 (21) reported similar results.

Bacteriological investigations in our study revealed that staphylococcus epidermis was the most common pathogen in patient with superficial sternal wound infection (SWWI) and mixed infection by Staphylococcus aureus and Pseudomonas was the commonest in patient with deep sternal wound infection.

### Conclusion

The incidence of sternal wound complications either superficial or deep is distorted partly by poor delineation of true depth and extent of infection and partly by the difference in surgical procedure and mode of follow up. Often these differences result in mixing deep serious infection and minor superficial wound problems.

Identification of both patients related risk factors and procedures related risk factors for sternal wound infection is very beneficial. Patients related factors should be lessened as much as possible while procedures related factors should be eliminated to abort any chance for sternal wound complication.

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## PREOPERATIVE CLINICAL DETERMINANTS OF SHORT TERM MORBIDITY AND MORTALITY IN SURGICALLY MANAGED INFECTIVE ENDOCARDITIS PATIENTS

Mohamed Abul-dahab M.D.,  
Osama AbouelKasem M.D.,  
Tarek Salah M.D.,  
Tamer Farouk M.D. ,  
Tarek Eltawil M.D.

**Background:** Infective endocarditis is a diagnostic and therapeutic challenge that ultimately requires surgical intervention in 20% of all cases. Decisions regarding the indications for surgery, the timing, and the evaluation of the patient's ability to withstand the contemplated operation are complicated decisions requiring appropriate guidelines

**Methods:** In this study we followed 20 patients diagnosed with definite infective endocarditis according to the modified Duke's criteria and underwent cardiac surgery between June and December 2006. Clinical, laboratory and echocardiographic data were reported before surgery. Timing, type, indication for surgery and other intra-operative and post-operative variables were also reported.

**Results:** Rheumatic heart disease was the most common underlying cardiac risk factor (90% of patients), 75% of the patients had native valve endocarditis (NVE) and the remaining 25% had prosthetic valve endocarditis. The most common indications for surgical intervention were congestive heart failure (60%) and uncontrolled infection (60%). 90% of our patients were operated upon on elective basis. The most common post-operative complication was low cardiac output syndrome (15%) and new renal impairment. We had 6 mortalities (30%). The most common cause of in-hospital mortality was congestive heart failure and cardiogenic shock.

**Conclusion:** Preoperative renal impairment, abnormal white cell count, congestive heart failure and prosthetic valve endocarditis were associated with poor outcome. Further prospective studies with larger sample size are needed to study the actual prognostic value of other perioperative risk factors especially the benefit and optimal timing for surgical intervention.

Infective endocarditis is a very complex disease with a serious prognosis (Tornos, 2004 and Jassal et al., 2006). Despite improved preventive strategies the incidence of infective endocarditis remains high at 1.7-6.2 per 100,000 person years in the USA and Europe, with a one year mortality approaching 40% (Wallace et al., 2002 and Prendergast et al., 2004).

This lack of improvement in prognosis might be due to the fact that endocarditis is now occurring in old people, in patients unaware of having a cardiac disease, in patients with prosthetic valves, and is being caused by aggressive organisms such as staphylococci (Netzer et al., 2002 and Tornos, 2004).

The principal indications for cardiac surgery are heart failure, no control of infection, embolisms, large size of vegetations, severe valvar and perivalvar lesions, and infection caused by some microorganisms (Delahaye et al., 2004).

In developing countries, rheumatic heart disease, which occurs primarily among the young, remains the most frequent underlying cardiac condition predisposing patients to infective endocarditis (Choudhury et al., 1992 and Jalal

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Address reprint request to : Dr Mohamed Abul-dahab

Department of Cardio-thoracic Surgery,  
Kasr El-Ainy Hospital, Faculty of Medicine,  
Cairo University

Email : jegyptscts@gmail.com

Codex : 04 / cord / 56 / 0706

et al., 1998).

In recent series, staphylococci, particularly *Staph. aureus*, have surpassed viridans streptococci as the most common cause of infective endocarditis (Mylonakis et al., 2001).

The diagnosis of infective endocarditis requires the integration of clinical, laboratory, and echocardiographic data. Congestive heart failure and neurological events have the greatest influence on the prognosis of infective endocarditis (Mylonakis et al., 2001).

Surgery for IE is potentially life saving and required in 25–30% of cases during acute infection and in 20–40% during convalescence (Jault et al., 1997 and Olaison et al., 2002). Overall surgical mortality in active IE is 8–16%, with actual survival rates of 75% and 61% at five and 10 years, respectively (Alexiou et al., 2000).

The goals of surgical therapy are as follows: 1) to eradicate the infection; 2) to repair cardiac destruction related to the infection; 3) to prevent the development of complications and relapse of infection; and 4) to offer a survival advantage to medical therapy alone, when indicated (Delahaye et al., 2004).

Although no randomized trials have been conducted in this area, retrospective analyses have shown that the long-term outcome is similar in patients with IE who receive either mechanical, bioprosthetic, or homograft valve replacement (in the case of aortic valve IE) (Moon et al., 2001).

Indications for surgery and its timing are difficult decisions to reach. The patient must be followed up closely (Delahaye et al., 2004).

According to the recent European Guidelines; after manifestation of a cerebral embolism, cardiac surgery to prevent a recurrent episode is not contraindicated if performed early (best within 72 hours so that the blood–brain barrier can be expected not to be significantly disturbed) and cerebral hemorrhage has been excluded by cranial computed tomography immediately before the operation. If surgery is not performed early it is advisable to be postponed for 3–4 weeks (Horstkotte et al., 2004).

The development of a rocking prosthesis or a rapidly progressive paravalvular leak is urgent indications for valvular surgery (Olaison et al., 2002).

## Methods

Between June and December 2006, 20 patients diagnosed with definite infective endocarditis underwent cardiac surgery for either valve replacement or repair in the Department of Cardiothoracic Surgery, Kasr Al-Aini University Hospital, Cairo, Egypt.

### I. Selection Criteria:

In all cases diagnosis was based on strict case definition, in the presence of surgical confirmation or definite endocarditis by the Duke criteria:

Exclusion criteria: infective endocarditis in the pediatric age group.

Inclusion criteria include: All adult patients with IE with involvement of mitral, aortic, pulmonary or tricuspid valve, including NVE and PVE.

A written informed consent was obtained from each patient before surgery.

### II. Preoperative Assessment:

All patients of the study were assessed in the preoperative period by medical history taking and detailed clinical examination with emphasis on: fever, new or changing murmur, presence of co-morbidity (diabetes, age >75, immunosuppression), NYHA class, Full laboratory investigations including ESR and blood cultures added to the routine investigations, Transthoracic and transoesophageal echocardiography (TTE and TEE) with emphasis on presence, size, and mobility of vegetations, presence of abscesses, pseudoaneurysm, fistula or perivalvular leak in case of prosthetic valve endocarditis.

Emphasis is placed on assessment of preoperative risk factors e.g.: Age, Diabetes mellitus, Chronic lung disease, Peripheral vascular disease, Cerebrovascular accidents, Presence of pulmonary hypertension, Anaemia and leucocytosis, Elevated ESR, Renal failure, Reoperation.

### III. Operative Management:

The indications for surgery were congestive heart failure, uncontrolled infection, large vegetations, recurrent embolism, aortic root abscess, severe valve regurgitation, prosthetic valve dysfunction and one case of bartonella IE.

Routine intraoperative anesthetic technique was used in all patients.

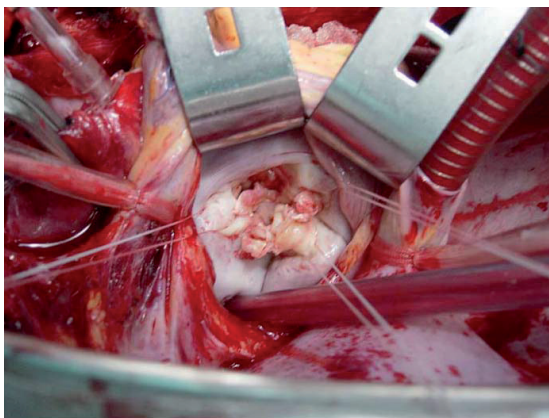
### Surgical technique:

Surgery consisted of valve replacement with mechanical prosthesis in 11 patients, valve repair in 5 patients combined valve replacement and repair in 4 patients.

In all cases, access to the heart was obtained through a median sternotomy. Cardiopulmonary bypass was instituted in a standard fashion. Myocardial protection was achieved by intermittent cold blood antegrade cardioplegia solution, keeping the myocardial temperature at 10–15°C, accompanied by systemic cooling at 25–28°C.

Fig. (4): A case of mitral valve endocarditis. Large vegetation were found attached to both anterior and posterior mitral leaflets.

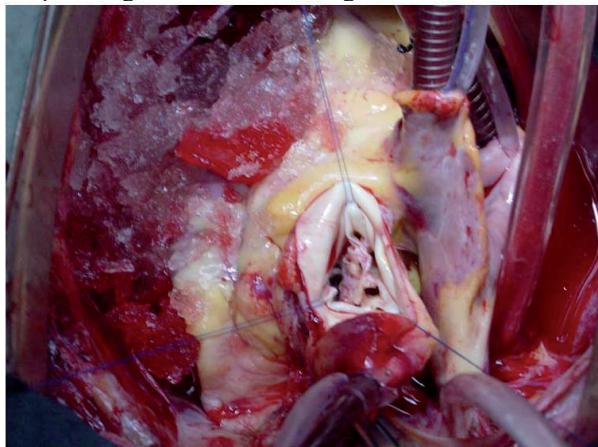




**Fig. (4): A case of mitral valve endocarditis.**

For mitral valve exposure the left atrial approach was the preferred technique. In the case of prosthetic valve endocarditis, the redo surgery was performed through redo sternotomy. In redo sternotomy the mitral valve was exposed transseptally or via a left atriotomy through the interatrial groove. Following valve exposure, an accurate valve analysis was performed to confirm the echocardiographic data and to assess the extent of lesions. Radical debridement with a 1 to 2 mm margin of healthy tissue to eradicate intracardiac foci of infection is the primary aim of surgery. Valve repair was performed when sufficient tissue remained to allow valvular reconstruction without excessive tension on the suture lines. Otherwise, valve replacement was performed using a mechanical prosthesis.

Intraoperative TEE was used to demonstrate any abscesses, fistulas, paravalvular leaks, and involvement of other valves. It was used also at the completion of the procedure to evaluate the quality of repair or assess prosthetic valve function. All excised tissues were sent for pathological and microbiological assessment.



**Fig. (6): A case of aortic valve endocarditis.**

**Operative data and parameters:**

**A record was made of the following:**

Timing of surgery (emergency, urgent or elective), Ischemic time (in minutes), Bypass time (in minutes), Total operative time (in minutes), Intraoperative findings with description of the pathological affection of the endocardium (site and nature of valvular affection-periannular extension-presence and size of vegetations), Surgical procedure performed (replacement or repair) and for which valve(s), Weaning from CPB and use of inotropes.

**IV. Postoperative assessment:**

All patients of the study were followed through their hospital stay by careful clinical assessment, routine laboratory workup, ECG, chest x-ray, transthoracic echocardiography.

**The following data were recorded:**

Period of mechanical ventilation (in hours), Inotropic support, Results of cultures for tissues excised intraoperative, postoperative fever and total leucocytic count, Results of postoperative transthoracic echocardiography, Duration of ICU stay, In-hospital mortality

**and incidence of major complications:**

Low cardiac output syndrome, reexploration for bleeding and the need for blood transfusion, neurologic dysfunction, new renal impairment, chest infection and respiratory failure.

Major end points were recurrence or relapse of IE, and death.

**Results:**

Patients demographics and co-morbid risk factors:

A total of 20 patients undergoing valve surgery for infective endocarditis were enrolled in this study.

The preoperative clinical, cardiologic characteristics as well as co-morbidities are shown in tables (5, 6, and 7).

	No. of patients (20)
Age	
Mean (±SD)	34.5±15.35
Range	15 to 69
Median	29 years
Sex	
Male	10 (50%)
Female	10 (50%)

**Table (5): Patients' age and sex**

Cardiac risk factors	
Acquired valvular heart disease:	19
- Rheumatic heart disease	18 (90%)
- Degenerative disease(calcific aortic valve).	1 (5%)
Congenital heart disease	1 (5%)

Table (6): Cardiac risk factors

Non-cardiac risk factors	
Diabetes mellitus	2 (10%)
Renal impairment	5 (25%)
Hepatic impairment	1 (5%)
History of cerebrovascular accident	6 (30%)
Cancer	1 (5%)
Immunosuppression	1 (5%)
Injection drug use	Nil

Table (7): Non-cardiac risk factors

### Clinical Findings:

These are listed in table (8).

Fever (at time of surgery)	13 (65%)
Congestive heart failure New York Heart Association (NYHA)Functional class III or IV (at the time of surgery)	15 (75%)
Embolic event (total):	8 (40%)
Cerebrovascular accident (total)	6 (75% of total embolic events)
Transient neurologic dysfunction	4
Permanent neurologic dysfunction	2
Limb ischaemia	2 (25% of total embolic events)

Table (8): Clinical findings

### Echocardiographic Findings:

Valve type:	
Native valve endocarditis	15 (75%)
Prosthetic valve endocarditis	5 (25%)
Vegetations:	
Visible vegetations	18 (90%)
Vegetation size >10 mm	10 (55%)
Free mobility	17 (94%)
Evidence of periannular extension of infection (para-valvular leak-dehiscence-aortic root abscess)	4 (20%)
Poor left ventricular function [ejection fraction (EF) <50%]	3 (15%)

Table (10) Echocardiographic findings

The offending microorganism was identified by pre-operative blood cultures, serological studies or surgical specimens in 12 patients (60%).

The remaining 8 patients (40%) had clinical and pathologic evidence of endocarditis but no microorganism could be cultured and they were treated as culture negative endocarditis.

### Indication(s) for Surgery:

The various indications are listed in table (13).

Indications for surgery	No. of patients	% patients	% total indications
Congestive heart failure	12	60%	18.5%
Uncontrolled infection	12	60%	18.5%
Large vegetation ( $\geq 10$ mm)	10	50%	15.3%
Recurrent embolism	3	15%	4.6%
Aortic root abscess (or other forms of periannular extension of infection)	5	25%	7.7%
Prosthetic valve dysfunction	1	5%	1.53%
Prosthetic valve endocarditis	5	25%	7.7%
Severe valve lesion	16	80%	24.6%
Others (Q fever endocarditis)	1	5%	1.53%

Table (13): Indications for surgery

### Operative Assessment:

The various surgical procedures performed are listed in table (14).

#### a-Timing of surgery:

Emergency (same day)	1 (5%)
Urgent (within 1-2 days)	1 (5%)
Elective	18 (90%)

b- Surgical procedure:	No. of patients	Native valve	Prosthetic valve
AVR	4	3	1
MVR	5	2	3
MV repair	2	2	
MV repair + CABG	1	1	
TV repair	1	1	
AVR + MV repair	3	6	
AV repair + MV repair	1	2	
AVR + MVR	2	3	1
AVR + MV repair + TV repair	1	3	

Table (14): Timing of surgery and surgical procedures

AVR, aortic valve replacement; MVR, mitral valve replacement;

MV repair, mitral valve repair; AV repair, aortic valve repair;

TV repair, tricuspid valve repair.

Cardiopulmonary bypass time and the ischemic time (aortic cross clamp time) are listed in table (15).

Ischaemic time (in min):	
Mean ( $\pm$ SD)	62.6 $\pm$ 25 min
Range	35-105 min
Cardiopulmonary bypass time:	
Mean ( $\pm$ SD) in min	83.25 $\pm$ 27.9 min
Range	50-135 min
Failed weaning from cardiopulmonary bypass (on first attempt)	1 (5%)
No. of patients who needed intra-operative inotropic support	17 (85%)

Table (15): Operative assessment

## Postoperative Assessment:

Period of mechanical ventilation:	
Mean ( $\pm$ SD)	22 $\pm$ 40 hours
Range	5-144 hours
Inotropic support (No. of patients)	15 (75%) patient
Duration of ICU stay (in hours)	76.6 $\pm$ 36 hours
Resolution of pre-operative fever	10 (76%)
Failure of resolution of fever	3 (23%)

**Table (16): Post-operative assessment**

Major Post-operative Complication and Morbidities:

The post-operative complications are listed in table (17).

Complications	Total population	Survived	Died
Low cardiac output syndrome	3 (15%)	Nil	3 (100%)
Reexploration for bleeding	Nil	Nil	Nil
New neurologic insult	2 (10%)	1 (50%)	1 (50%)
New renal impairment	3 (15%)	2 (66.6%)	1 (33.3%)
Chest infection and respiratory failure	1 (5%)	1 (100%)	Nil
Deep wound infection and mediastinitis	Nil	Nil	Nil
Embolization (other than CNS)	2 (10%)	2 (100%)	Nil
Conduction abnormality	1 (5%)	Nil	1 (5%)
Recurrent or relapsing infective endocarditis	1 (5%)	Nil	1 (5%)
Systemic sepsis	1 (5%)	Nil	1 (5%)

**Table (17): Major post-operative complications and morbidities**

## In-Hospital Mortality:

We had 6 mortalities in our study (30%). The direct causes of death are listed in table (18).

Mortality	Total	NVE	PVE
Total number of mortalities	6 (30%)	3 (20%)	3 (60%)
Direct cause(s) of death:			
Congestive heart failure/cardiogenic shock	2		2
Systemic sepsis	1	1	
Renal failure	1	1	
Cerebrovascular accident	1	1	
Others	1		1

**Table (18): Mortality**

NVE, native valve endocarditis; PVE, prosthetic valve endocarditis.

**Discussion**

Antibiotics contributed to an improvement in survival, but also changed the major cause of death from infection to congestive heart failure. Although antibiotics remain the first line treatment of bacterial endocarditis, it becomes insufficient when complications develop. Under these circumstances mortality rates are unacceptable with medical treatment alone (50-90%), when compared

to surgery (30%). (Dodge et al., 1995).

The results of surgery depend upon many factors. The general preoperative condition of the patient, antibiotic treatment, timing of surgery, perioperative management, surgical techniques (including choice of valve replacement versus repair, type of valve and methods of reconstruction), postoperative management and follow up are all important determinants of outcome. Preoperative New York Heart Association (NYHA) classification, age, and preoperative renal failure are common predictors of operative mortality (Olaison et al., 2002).

In this study 20 patients with infective endocarditis were followed and our aim was to identify the prognostic markers of a bad outcome in a group of patients diagnosed with definite infective endocarditis and surgical strategies in infective endocarditis and thus to identify patients for whom surgery may be beneficial in Kasr El-Aini Hospitals.

In developing countries, rheumatic heart disease remains the most frequent underlying cardiac condition predisposing patients to infective endocarditis (Choudhury et al., 1992 and Jalal et al., 1998).

This was eminent in our study we had 18 patients (90%) with underlying rheumatic heart disease, only one patient (5%) with calcific degenerative aortic stenosis and one patient (5%) with congenital valvular heart disease.

From our 20 patients, the majority of patients (75%) were diagnosed with native valve endocarditis (NVE) and only 25% had prosthetic valve endocarditis.

In Jassal study 85.7% of patients were diagnosed with NVE and the rest had PVE (Jassal et al., 2006).

In another study 62.3% of patients had NVE and 37.7% had PVE (d'Udekem et al., 1997).

One of the important predictors of post-operative mortality in our study was the presence of preoperative renal impairment. In this study we had 5 patients (25%) with preoperative renal impairment and the mortality in this group was 60% versus 20% in patients with normal preoperative renal function.

Wallace had a mortality of 29.8% in patients with renal impairment versus 13.7% in patients with normal renal functions (Wallace et al., 2002) and he found that high serum creatinine was strongly associated with mortality. Longer term prognosis was also influenced at six months with a mortality of 39% in the group with an increased creatinine, compared with 22% in those with normal creatinine concentrations (Wallace et al., 2002).

In another study, by univariate analysis, renal failure was associated with in-hospital mortality with P value of 0.05 (Habib et al, 2005).

Another preoperative risk factor was history of cere-

brovascular accident (CVA). We had 6 patients with history of CVAs, 2 of them died post-operative 33% versus 28% in the group without previous CNS insult.

In the study by Heiro et al., the patients treated surgically fared slightly better than those treated conservatively, with respective mortality rates of 9% and 15%. A similar tendency also was observed in the subset of patients with neurological complications. Although the surgical mortality rate in these patients was higher than in those without such complications, this finding probably reflects a more severe nature of infection in the former group, as indicated by the higher proportion of patients with *S. aureus* IE and involvement of both left-sided valves. (Heiro et al., 2000).

Collectively, these data strengthen the validity of the concept that a patient should not be denied cardiac surgery exclusively on the basis of a neurological event. In patients with IE and recent embolic CVA, it's better to postpone surgery for 2-3 weeks. Patients with intracranial haemorrhage secondary to embolic CVA can undergo valve surgery after 4 weeks. (Gillinov et al., 1996). It should also be noted that in patients with embolic CVA, valve surgery should be considered within the first 72 hours if they have severe heart failure (Angstwurm et al., 2004).

At the time of surgery we had 15 patients (75%) with NYHA functional class III or IV. Among these patients 6 died (40% mortality). This obviously shows that congestive heart failure was associated with poor outcome.

Many studies during past 3 decades have demonstrated that among the complications of IE, congestive heart failure has the greatest impact on prognosis (Baddour et al., 2005).

In two Swedish studies mortality rates for surgically treated versus non-surgically treated decompensated patients were 9% versus 20% and 10% versus 27% ( $P < 0.05$ ), respectively. The greatest benefit of early surgery was noted in patients with new heart failure at entry who underwent surgery on median treatment day 4 (Olaison et al., 1996 and Alestig et al., 2000).

Our results match with the above noted results that congestive heart failure is a powerful predictor of poor outcome with surgical therapy.

Our mortality is also slightly higher. This can be attributed to some delay in surgical intervention and other co-morbid factors and the large proportion of patients who underwent surgical intervention for two or more valves (7 patients i.e. 35% of the study population).

The delay in surgical intervention is mainly related to delay in diagnosis. As most of our patients presented first to other clinics or hospitals where they received empiric treatment and finally referred to our hospital as a

tertiary care centre.

We had 15 patients with leucocytosis ( $WCC > 11,000/mm^3$ ) and 4 patients with leucopenia ( $WCC < 4,000/mm^3$ ) with a mortality of 26% and 50% respectively. Actually all of our mortalities were associated with abnormal WCC.

Wallace et al., similarly found that WCC was strongly associated with mortality. Patients with WCC outside the normal range were at a significantly greater risk of death at both discharge and six months (Wallace et al., 2002).

In our 20 patients we had 15 patients with native valve endocarditis (NVE) with 20% mortality versus 5 patients with prosthetic valve endocarditis (PVE) with 60% mortality.

Despite improvements in medical treatment and surgery, prosthetic valve endocarditis carries a high mortality risk ranging from 20-80% of patients (Habib et al., 2005).

Yu and colleagues followed up 74 patients with PVE for one year and found higher mortality in medically than in surgically treated patients (56% versus 23%) (Yu et al., 1994).

The worse prognosis in patients with PVE can be attributed to several factors. PVE is frequently complicated by perivalvular invasive infection and in many of these cases; infection spreads behind the site of attachment of the valve prosthesis, resulting in valve ring abscess and valve dehiscence in most of cases. Patients with PVE require redo surgery which is associated with higher operative risk. These operations are very demanding technically (Olaison et al., 2002).

In our study, poor left ventricular function had no influence on outcome. We had 3 patient with poor left ventricular functions ( $EF < 50\%$ ) and no mortality was noted in these patients.

Similarly, Wallace et al., reported that poor left ventricular function as defined by echocardiography did not increase mortality at either discharge or six months (Wallace et al., 2002).

In our study the offending organism could be identified in 60% of cases. This was attributed to the nature of our hospital as a tertiary care centre. Most of our patients presented to other clinics or hospitals first where they received empiric antimicrobial therapy without withdrawal of blood cultures prior to their referral.

The mortality among patients with culture positive endocarditis was 37% and 25% among patients with culture negative endocarditis.

It's known that mortality rates are lower for patients who have culture-negative endocarditis and who had received antibiotics before blood cultures were obtained



and those who become a febrile during the initial week of antimicrobial treatment (Braunwald et al., 2005).

The indications for surgical intervention in our patients were congestive heart failure (60%), uncontrolled infection (60%), large vegetations ( $\geq 10$  mm) (50%), recurrent embolism (15%), aortic root abscess (25%), severe valve lesion (80%), prosthetic valve dysfunction (5%) and infection with bartonella (5%).

From these results we found that the most common findings leading to surgical treatment for both NVE and PVE were severe valvular regurgitation and intractable heart failure (80% and 60% respectively).

Jassal et al., reported similar results where severe valvular regurgitation with intractable heart failure was an indication for surgical intervention in 89% of patients (Jassal et al., 2006).

The majority of our patients (90%) received surgical intervention on elective basis (after 2 days from diagnosis).

Surgery is necessary in 25 to 30% of cases during the acute phase of infection, and in another 20% to 40% in later or secondary phases (Delahaye et al., 1995 and Jault et al., 1997).

In general, the prognosis is better after early surgery undertaken before the cardiac pathology and the general condition of the patient had deteriorated too severely (Olaison et al., 2002).

Actually we think that the poor outcome observed in our patients who received surgical treatment on emergency or urgent basis is due to a delay in diagnosis, a delay in reference to our surgical centre or other associated co-morbid risk factors.

Major post-operative complications in our patients included low cardiac output syndrome (15%) and all of them died, new neurological insult (10%) and 50% of them died and embolization to sites other than CNS (10%) and none of them died.

Jassal et al., reported new neurological insult in 5 patients (3.9%) and 3 of them died (60%). 22 patients (24.2%) needed post-operative insertion of permanent pacemakers and 31% of them died (Jassal et al., 2006).

In our study congestive heart failure and cardiogenic shock represented 33% of mortalities (2 patients).

Studies by Vlessis et al. and Olaison et al., showed an association between early surgery and improved survival over five years, although this was no longer significant after multivariate analysis in the latter study (Olaison et al., 1996 and Vlessis et al., 1996). For example, Olaison et al., reported 8% mortality for patients undergoing acute surgery versus 11% for those not undergoing surgery, and the adjusted 5-year survival rate of acute surgically treated patients was 91%, compared

with 69% for the medically treated patients (Olaison et al., 1996). Similarly, Vlessis et al., reported that long-term survival was significantly greater in patients treated with combined medical and surgical therapy than those treated with medical therapy alone (75% versus 54% at 5 years) (Vlessis et al., 1996).

Other studies found better long term survival after surgery in specific subgroups such as aortic and prosthetic valve disease. (Yu et al., 1994).

In our study we had a total in-hospital mortality of 30% with 20% mortality in patients within NVE (native valve endocarditis) and rises to 60% in patients with PVE (prosthetic valve endocarditis).

### Conclusion:

We found that preoperative congestive heart failure, pre-operative renal impairment, abnormal white cell count, severe valve regurge and periannular extension of infection were associated with higher in-hospital mortality.

The commonest indications for surgical intervention were congestive heart failure secondary to severe valve regurge and large vegetations.

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## FUNGAL ENDOCARDITIS AT AIN SHAMS UNIVERSITY HOSPITALS, CAIRO, EGYPT

Iman M. El-Kholy, MD,  
Sherif M. Zaki, MD,  
Ahmed Abdel-Aziz, MD,

**Objective :** of this study is to assess the prevalence of fungal endocarditis (FE) at Ain Shams University Hospitals and to determine the causative specific fungus of these infections.

**Methods :** Twenty patients were admitted to Ain Shams University Hospitals suspected to be infective endocarditis (IE) between May 2004 to May 2006. Surgical intervention was indicated in all cases. Blood samples and valve tissue, were used for culturing, and the separated sera were used for serological tests. Species identification determined by observation of their macro and microscopic characteristics complemented with sequencing of ITS1-5.8S-ITS2 rDNA region sequence.

**Results :** Fungal infections were detected in 12 (60%) cases out of 20 cases studied. *Aspergillus flavus* was detected in 6 cases (50%), *Aspergillus niger* in 2 cases only representing (16.6 %), while *Candida albicans* were detected in 4 cases representing (33.3%) of the positive cases for each while

**T**he infective endocarditis is defined as an endovascular microbial infection of the vascular structure (Bayer et al., 1998). Infective endocarditis is increasingly diagnosed in many patients as a nosocomial disease and its medical importance is increasing in most developed countries with growing proportion of elderly persons among population. IE is usually diagnosed based on the presence of vegetation on echocardiography and positive blood cultures (Brouqui and Raoult, 2001).

Fungal endocarditis was considered previously as an uncommon where it was reported in 1.3 to 6% of cases but recently it becomes an important infection associated with medical progress (Rubinstein and Lang, 1995 & Bayer and Scheld, 2000).

Advances in medical and surgical therapies, including reconstructive cardiovascular surgery, implantation of intracardiac prosthetic devices, prolonged use of IV catheters, exposure to multiple broad-spectrum antibiotics, and immunosuppression, have been implicated as causes of the perceived increase in the number of cases of fungemia and FE seen during the last 2 decades (Pierrotti and Baddour, 2002).

The most isolated fungal species were recorded as the cause factor of IE are *Aspergillus* spp., and *Candida* spp., (Rubinstein and Lang, 1995). Due to the importance of fungal endocarditis regarding the implicating and misleading proper treatment the fungal endocarditis was traced at Ain Shams University Hospitals.

### Methods:

During the period of May 2004 to May 2006 twenty patients were admitted at Ain Shams University Hospitals with query IE, 18 males and 2 female ranging from 18 to 54 years old with mean age (31.6 ± 9.9). The diagnosis

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Address reprint request to : Iman, M.  
El-Kholy Microbiology Department,  
fellow at Ain Shams University Special-  
ized Hospital, Cairo, Egypt.

Email : jegyptsets@gmail.com

Codex : 04 / cord / 57 / 0703

of IE depends on the clinical condition of the patient, echocardiographic findings and laboratory tests. Surgical intervention was indicated in all cases, according to, (table 1)

Indication of surgery	Number of patients
Heart failure	1
Sever valve destruction	6
Large vegetation more than 1 cm by Echo	5
Paravalvular abscess	1
Positive bacterial blood culture	7
Uncontrolled sepsis despite of medical treatment	3
Embolization	1

*Table 1 representing the indication of surgery in all patients*

The Principles of Surgical Management were aimed to minimal Cardiac manipulation before aortic cross-clamping to minimize the incidence of peripheral embolization of the vegetations. This was particularly important in patients with large, mobile, and friable vegetations. Following valve exposure, an accurate valve analysis were performed to confirm the echocardiographic data and to assess the extent of lesions (perivalvular abscess, and presence of intracardiac fistula. Radical resection of all infected and necrotic tissues was performed. Surgical instruments including suction tips were changed after debridement and excision of infected tissue. All the excised cardiac val and the infected tissues were sent for fungal culture. Replacements of damaged valves were performed, (table 2)

Type of operation	Number of cases
Mitral valve replacement	11
Aortic valve replacement	5
Double valve replacement	4
Para aortic root abscess repair	2

*Table 2 represents the type of the surgical procedures*

Isolation of the fungi: The excised valve and infected tissues were collected from each patient and transferred immediately to laboratory for mycological processing using Sabouraud's dextrose agar and brain heart infusion agar media supplemented with chloramphenicol (pH 5.5). The culture media were incubated at 28°C and 37°C for 4 weeks. Eight ml of blood samples were collected from each patient, divided into 2 parts (5 ml as EDTA blood for blood culture & 3 ml allowed to clot completely before centrifuge and separate into serum then stored in tightly closed tube at -20 c for serological test).

### Identification of the isolated fungal strains

The isolated fungi from the tissue culture were identified on the basis of macroscopic and microscopic morphology of each culture using the manual of (De-Hoog and Guarro, 1995).

### Serological Method

The tissue cultures which were reported to be positive for fungal infection were pointed and the sera of those patients were subjected for further serological tests. The sera collected from those patients were screened for fungal infection by detecting *Aspergillus* and *Candida* Galactomannan in their serum by using one-stage immunoenzymatic sandwich microplate assay Briefly, 300 µl of test serum was mixed with 100 µl of 4% EDTA acid solution (treatment solution), homogenize by shaking and boiled for 3 min. After centrifugation at 10,000 x g for 10 min, 50 µl of the supernatant was added to 50 µl of a conjugate (peroxidase-labelled anti-galactomannan monoclonal antibody EBA-2).

The 100- µl mixture was placed in the wells of a microtitration plate previously coated with the same anti-galactomannan monoclonal antibody EBA-2 and incubated at 37 °C. After 90 min of incubation, the plates were washed 5 times by prepared washed solution (TRIS-NaCl buffer (PH 7.4), 1%Tween 20), dry on to absorbent paper, then 200 µl of revelation solution (chromogen TMB solution diluted in substrate buffer) was placed in the wells .Then the plates were incubated for another 30 min in darkness at room temperature, followed by the addition of 100 µl of 1.5M sulfuric acid to stop the reaction. The optical density (OD) was read at 450 and 620 nm using a plate reader. Calibrators positive and negative controls were included in each assay.

The OD index for treated samples was calculated by dividing the OD value of each serum sample by the OD of a control serum at 1 ng of GM/ml (threshold positive control) according to(Platelia *Aspergillus* EIA; Bio-Rad laboratories, Marnes, France) as per the manufacturer's instructions.

The value is considered to be positive for presence of Galactomannan if index  $\geq 1.5$ , negative if value  $< 1.0$ , and if value between 1.0 and 1.5 the result was intermediate.

### Molecular typing techniques

#### Extraction of DNA

A small amount of mycelium grown on Sabouraud's dextrose agar was suspended in 200 µl of TE buffer (100mM Tris-HCl, pH 8.0, 1mM EDTA) in an Eppendorf tube (1.5ml). DNA extraction was carried out according to the procedure described by Sandhu et al.,

(1995). Briefly, 250 µl of GPT reagent (6M guanidine thiocyanate dissolved in 50 mM Tris [pH 8.3]) and 700 µl of phenol-buffered in Tris (pH 8.0) were added to a washed fungal inoculum in a screw-cap tube and boiled for 15 min; 250 µl of chloroform-isoamyl alcohol was then added, and the aqueous phase was separated by centrifugation at 14,000 x g, mixed with an equal amount of 100% isopropanol and 1/10 volume of 3 M ammonium acetate, and placed at 20 °C for 1h. Samples were centrifuged at 14,000 x g for 20 min, and the nucleic acid pellet was washed with ice-cold 70% ethanol, dried, and re-suspended in sterile TE-buffer at a concentration of 5 µg/ml.

**Oligonucleotides:**

The oligonucleotide primers used for amplification and sequencing of the ITS regions were those described by White et al., (1990). ITS5 (5'-GGAAGTAAAAGTC-GTAAACAAGG-3') and ITS4 (5'-TCCTCCGCTTATT-GATATGC-3') were made by Pharmacia Biotech CO., LTD. (Tokyo, Japan).

PCR and DNA sequencing of ITS1-5.8S-ITS2 region rRNA of fungal strains

Amplification reactions were performed in 25 µl of distilled water containing 2.5 µl of each primer (20 pm), 2.5 µl of genomic DNA (5 µg/ml) and one PCR bead. PCR was performed using the initial denaturation at 94 °C for 4 min, followed by 35 cycles at 94°C for 2 min, 55°C for 2 min and 72 °C for 2 min, and a final extension at 72 °C for 10 min. The PCR reaction products sequenced directly using a big Dye terminator reagent kit including Taq polymerase and the protocol recommended by the manufacturer (Model 3010 automated DNA sequencer, Perkin-Elmer/Applied Biosystems, Japan).

**Phylogenetic analysis**

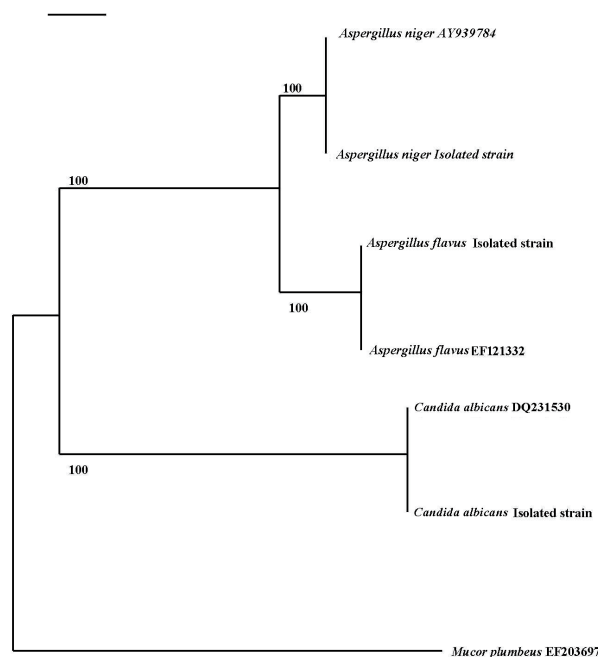
DNA sequences were aligned with Clustal W (Version 1.83) (Thompson et al., 1994) and the alignment was visually corrected. The phylogenetic tree was constructed by the neighbor-joining method that applied to DNA distance matrices calculated according to Kimura two-parameter model (Saito & Nei, 1987). The confidence values of branches were determined by a bootstrap analysis (Felsenstein, 1981).

**Results**

Although blood cultures in all cases gives negative results for fungal infection, the cardiac valve cultures for fungal infections give 12 cases (60%) of the total twenty cultures, with a variety of two genera *Aspergillus* (*A. flavus* 6 cases 50%, *A. niger* 2 cases 16.6%) and *Candida* (*C. albicans* 4 cases 33.3%). The positive results

were confirmed by the serological test in all cases where galactomannan test was > 1.5 in all cases .

Mycological and molecular typing of the isolated fungal pathogens:



**Figure 1. Phylogenetic tree based on ITS1-5.8S-ITS2 region sequences for three isolated strains with reference strains. Numbers at the respective nodes are percentage of 1000 bootstrap replicates. Bar indicates two base changes per 100-nucleotide position.**

The fungal strains were identified as three species belonging to 2 genera, *Candida albicans*, *Aspergillus niger*, and *Aspergillus flavus*. All the three strains yielded a unique PCR amplification. The sequences of the ITS1-5.8S-ITS2 rDNA region for the three strains were 440, 466, and 521 bp respectively. NCBI GenBank was accessed to identify the isolated species by using obtained ITS data. The ITS data of the isolated strains of *Aspergillus flavus*, *Aspergillus niger*, and *Candida albicans* are identical to the ITS data of *Aspergillus flavus* (GenBank Accession Number EF121332), *Aspergillus niger* (GenBank Accession Number AY939784), and *Candida albicans* (GenBank Accession Number DQ231530) respectively. Phylogenetic tree based on ITS1-5.8S-ITS2 region sequences for the three isolates with the reference strains was constructed (Figure 1). The tree shows the clear identity between the isolated strains and the reference strains (100% bootstrap support).

Cardiovascular

## Discussion

Fungal endocarditis has gained more attention in the recent investigations which expected an increasing number of fungal endocarditis cases due to the continued expansion of medical and surgical techniques (Pierrotti and Baddour 2002). A large number of organisms are responsible for fungal endocarditis, the most common are *Aspergillus* spp., *Candida* spp., and *Torulopsis glabrata*. Other fungal pathogens such as *Histoplasma*, *Cryptococcus*, *Fusarium*, and *Scopulariopsis* were also recorded as well (Rubinstein and Lang 1995). Due to the frequent negative blood cultures which characterizing fungal endocarditis, culturing of the embolus found in the arteries may provide the best and only clue for the presence of fungal endocarditis (Rubinstein and Lang 1995). Serological testing has been proven to be useful in the definition of infective endocarditis and in establishing the etiologic diagnosis of IE (Raoult, et al., 2005). In our study, a variety of techniques were used, to confirm the fungal infection of the presented cases at Ain Shams University Hospital, Cairo, Egypt. Using cardiac valve culture, the fungal pathogens could be isolated from 12 (60%) cases of the total cases studied. Moreover, serological testing was used to confirm the diagnosis. The identification of the etiologic agents was performed using both of the mycological typing and molecular typing and these methods have become more sensitive and trustful as used in previous studies (Makimura, 2001 and Zaki, et al., 2005). In this study the incidence is relatively high which was attributed to use mycological typing and molecular typing but others found low incidence of fungal infection in there study ranging from 1.3% to 6 % of the studied cases. All these results were confirmed by detection of galactomannan in the sera collected.

In conclusion, the study reports the fungal endocarditis and their etiology in Egypt which high light on the higher incidence in Egypt. As the fungal infection is a serious disease because of its higher incidence of embolization and higher incidence of mortality due to negative blood cultres obtained (Fernandez-Guerrero et al., 1995) (Rubinstein and Lang 1995). The managements of infective endocarditis patients should be aware to the presence of fungal infection. The control of fungal infection and its prevention is an important issue to avoid morbidity and mortality among patients with infected endocarditis..

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## PERI-OPERATIVE ASSESSMENT OF SERUM DIGOXIN LEVEL IN RHEUMATIC HEART PATIENTS.

MS AbdAllah, MD;  
M Al mosallum, MD;  
DD Fouda, MD.

**Background:** Digoxin is a popular drug in use for management of rheumatic heart patients. The current prospective study aimed to assess serum digoxin level peri-operatively for patients on oral doses of lanoxine (0.25 mg) in regular basis.

**Methods:** The study included 31 rheumatic heart patients with atrial fibrillation who underwent mitral valve replacement. They were 12 females (38.7%) and 19 males (61.3%). Their age ranged between 15 and 57 years old averages 31.48±13.22 years. Patients who had diseases or taking drugs that might interfere with the serum digoxin level were excluded. The oxygenator devices were Medtronic, Trillium® and Jostra. All patients' prime for the cardiopulmonary bypass was Ringer's lactate solution. The blood samples pre and post cardiopulmonary bypass were taken from the central venous line. The post bypass sample was taken once the cardiopulmonary bypass was terminated and before any external blood or fluids were given. The assessment was performed by an ELISA technique (Abbott AxSYM® system).

**Results:** There was a significant drop in serum digoxin level after cardiopulmonary bypass (P=0). Pearson's correlation showed a very strong relationship between serum digoxin level changes and bypass time (R = 0.89). However, there was no significant relationship between serum digoxin level changes and gender or age.

**Conclusion:** Revising serum digoxin level post cardiopulmonary bypass is recommended to get the required benefit of the drug's therapy. However, continue given digoxin soon post-operatively in uneventful circumstance is preferable.

**D**igoxin is a popular drug being used for management of rheumatic heart patients (RHP). Arrhythmias and heart failure are the common indications of using digoxin. Digitalis intoxication is among the most common serious adverse drug reaction in clinical medicine.

The disadvantageous aspects of digoxin therapy were not considered important until excess mortality was described in survivors of myocardial infarction who received digoxin (1). It has a narrow therapeutic index and large inter-individual variability in pharmacokinetics. Therapeutic and toxic digoxin serum levels (SDL) are still controversial due to inappropriate digoxin level monitoring (2). The aim of this study was to assess SDL before and after cardiopulmonary bypass (CPB) during open heart surgery for RHP as well as the possible reasons for the changes.

### Methods:

The study included 31 RHP with atrial fibrillation. All underwent surgical mitral valve replacement in Al-Azhar university hospitals and national heart

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Address reprint request to : Dr MS AbdAllah Department of Cardio-thoracic surgery, Al-Azhar University

Email : jegyptscts@gmail.com

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institute in 2 months' time. The studied patients were on a maintenance dose of daily one tablet of oral digoxin (lanoxine 0.25mg). They were 12 females (38.7%) and 19 males (61.3%). Their age ranged from 15 to 57 years old mean of 31.48 $\pm$ 13.22.

The study excluded patients who have diseases which interfere with SDL (renal failure, hepatic failure and thyroid malfunction), electrolyte disturbances (hypokalemia, hyperkalemia and hypomagnesaemia) and patients on drugs which interfere with the serum level (diltiazem, verapamil, diphenoxyllate, quinidine, spironolactone, rifampin and antacids). There was no discontinuation interval between digoxin dose and the operation. The last digoxin dose was given at least 8 hours before taking the samples.

The operation was performed using the CPB machine (Medtronic; Cobe Stockert® and Jostra; HL20®). The disposable tools used to run the CPB machine were oxygenators (Medtronic; Trillium® and Jostra; Quadrox® oxygenators) and plastic cannulae connected to tubing system. During the operations all disposable equipments, fluids and drugs were recorded. All patients were primed using Ringer's solution (U.S. P.XXV).

The data were used to assess digoxin serum concentration using a standard protocol, Slaughter, et al 1978; Canas, et al 1999 and Mordasini, et al 2002, (2,3,4). The blood samples pre and post CPB were taken from the central venous line. The pre bypass sample was taken shortly after insertion of the line. The post bypass sample was taken from the same line once the CPB was terminated and before any external blood or fluids were given. Each 5 ml of blood sample was collected into a heparinised tube and transferred to the laboratory for immediate plasma separation. After centrifuging, aliquot plasma was prepared and stored at approximately -20 °C ready for the test.

The assessment of SDL in patient's samples was performed by an ELISA technique using the Abbott AxSYM® system. It is a fully automatic analyzer performing both random and continuous immunoassay using antibodies to alter the deflection of polarized light. AxSYM has three different techniques including Micro-particles enzyme immunoassay (MEIA), Fluorescent polarization immunoassay (FPIA) and Radiation energy attenuation (REA). AxSYM has very high sensitivity (99.69%) as well as high specificity (99.6 %). The Abbott AxSYM Digoxin II that was used in the study was a Micro-particles Enzyme Immunoassay (MEIA) and this method

was used for the quantitative measurement of digoxin in both serum and plasma.

Immunoassay for digoxin was obtained as a reagent kit (AxSYM Digoxin II) from Abbott Laboratories USA and used in accordance with the manufacturer's stated protocol. All patients' data were recorded in a collecting work sheet.

### Statistical analysis:

Statistical analysis was performed using SPSS version 13.0. Values were given as the mean  $\pm$  with standard deviation (SD). Correlations between SDL and the continuous variables age, sex, and time of bypass were calculated using Pearson's correlation coefficients.

The independent sample t- test was used to compare male and female pre and post bypass data. In addition, ANOVA was used to analyze the difference between two groups (female and male) with respect to SDL. The difference of the mean values between pre bypass SDL and post bypass SDL was calculated using paired sample t-test and box plots were used to study skewness of serum digoxin values. P values less than 0.05 (two-tailed) were considered to be significant.

### Results:

Thirty one patients had full information and laboratory results. The studied criteria were included constant and variable factors. There was a drop in SDL after CPB (Table 1, 2). Pre bypass level was ranged from 0.18 to 1.04 ng/ml, mean of 0.49 $\pm$ 0.22, post bypass was ranged from 0.0 to 0.69 ng/ml, mean of 0.33 $\pm$ 0.14.

Using paired sample t-test, the difference between pre and post bypass SDL was significant (P=0).

The box plot was used to study skewness characteristic which distinguish between the different distributions according to the level of concentration of frequencies for the different values of serum digoxin in pre and post CPB. The mean was lying in the middle of the box in pre and post bypass SDL; this confirming that cases values are symmetrical and not skewed figure (1).

Age, gender and time of bypass were analyzed as a variable values in correlation with the results of post bypass SDL.

Sample Number	Age ( y )	C P B time ( min )	Pre bypass SDL ( ng/ml)	Post bypass SDL ( ng/ml)	Change in SDL ( ng/ml)
01	30	145	0.49	0.21	0.28
02	45	85	0.43	0.37	0.06
03	18	100	0.18	0.00	0.18
04	33	85	0.40	0.36	0.04
05	20	125	0.46	0.35	0.11
06	15	195	0.57	0.26	0.31
07	20	150	0.73	0.52	0.21
08	23	130	0.52	0.29	0.23
09	57	135	0.74	0.50	0.24
10	52	65	0.32	0.31	0.01
11	28	190	1.04	0.69	0.35
12	22	190	0.79	0.41	0.38

*Table 1: Pre and post CPB, SDL (ng/ml) for female RHD patients underwent mitral valve replacement*

Sample Number	Age ( y )	C P B time ( min )	Pre bypass SDL ( ng/ml)	Post bypass SDL ( ng/ml)	Change in SDL ( ng/ml)
1	27	150	0.64	0.43	0.21
2	18	135	0.28	0.04	0.24
3	21	85	0.55	0.47	0.08
4	57	120	0.45	0.29	0.16
5	16	165	0.51	0.34	0.17
6	32	95	0.74	0.65	0.09
7	21	140	0.48	0.28	0.20
8	32	95	0.58	0.57	0.01
9	34	75	0.05	0.00	0.05
10	23	110	0.48	0.37	0.11
11	44	71	0.38	0.31	0.07
12	28	85	0.24	0.21	0.03
13	16	190	0.82	0.45	0.37
14	48	175	0.49	0.18	0.31
15	27	140	0.23	0.00	0.23
16	25	65	0.24	0.20	0.04
17	57	195	0.64	0.33	0.34
18	40	80	0.73	0.71	0.02
19	47	125	0.32	0.17	0.15

*Table 2: Pre and post CPB, SDL (ng/ml) for male RHD patients underwent mitral valve replacement.*

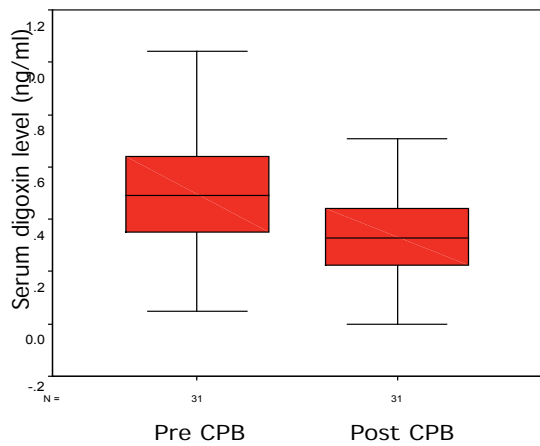


Figure 1: Box plot of SDL pre and post CPB

The studied patients have a broad range of age (15-57 years) from both males and females. The differences between them in SDL changes were analyzed. Using Pearson's correlation analysis a weak insignificant negative correlation was seen between SDL changes and age (P=0.45) (Figure 2,3).

The study classified patients into two groups, male and female. Independent-Samples T-Test was used to test the difference between male and female before exposed to CPB machine as well as after CPB. This was done initially to pool data for the final SDL changes analysis. There was no significant difference between groups as well as pre or post CPB; P-value was 0.26 and 0.59 respectively.

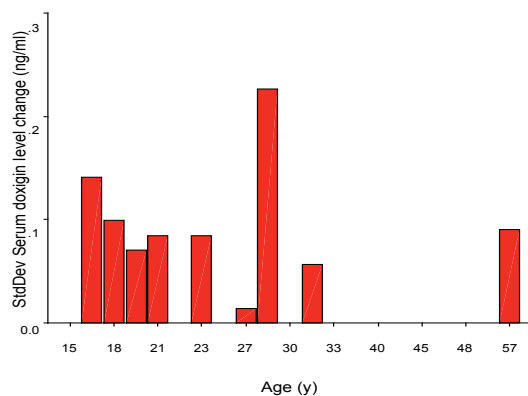


Figure 2: Difference in standard deviation of SDL change between studied patients.

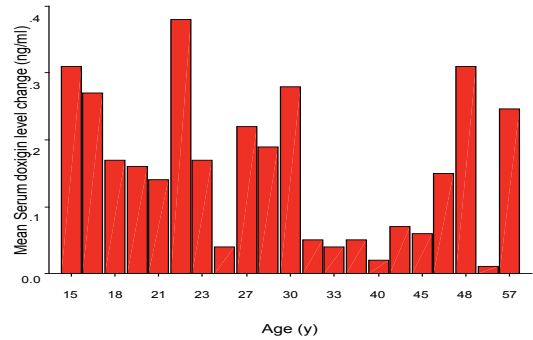


Figure 3: Difference in mean of SDL change between studied patients.

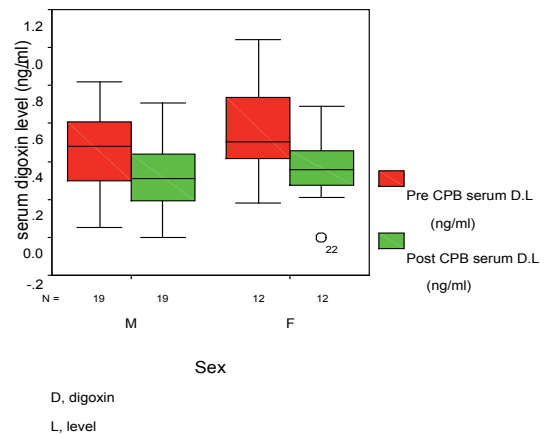


Figure 4: Box plot of pre and post CPB, SDL for both genders.

Using One-Way ANOVA method, there is also no significant difference in SDL change between male and female, P-value was 0.34. Using Pearson's correlation between male and female in SDL change was insignificant (r=0.177). The box plot was used to study skewness characteristic in pre and post CPB for both genders. The mean was lying in the middle of the box in post bypass SDL for male and female, this means that cases values will be symmetrical and not skewed (case number 22 extremely out of distribution). In pre bypass serum digoxin level, the mean was not lying in the middle of box thus means that cases value will not be symmetrical and skewed (Figure 4).

Pearson's correlation was showing a strong negative relation between SDL changes and CPB time (Table 3). In this case SDL goes down as the CPB time increases (R=0.89) (Figure 5).

		Serum doxigin level change (ng / ml )	CPB time (min )
Serum doxigin level change (ng / ml )	Pearson correlation	1.000	.946**
	Sig. ( 2-tailed )	.	.000
	N	31	31
CPB time ( min )	Pearson correlation	.946**	1.000
	Sig. ( 2-tailed )	.000	.
	N	31	31

\*\* . Correlation is significant at the 0.01 level ( 2 -tailed ) .

Table 3: Bivariate analysis to test the correlation between serum digoxin level change and CPB time

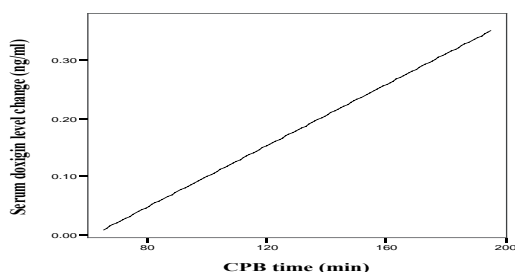


Figure 5: Dot/line diagram (mean) show the relation between SDL change and CPB time.

## Discussion:

The relative sample information from determination of SDL may give more than it could be an expected and its cost is part of clinical management (5). The value relates to the possibility of optimizing the individual pharmacotherapy as well as minimizing the risk of level dependant adverse drug reaction (6). Close clinical judgment for effectiveness and toxicity of digoxin is essential due to overlap of SDL between groups with and without toxicity especially in elderly (7).

This study was triggered by an obvious phenomenon in which the fibrillated rheumatic atrium returns to sinus rhythm on table after termination off bypass. The heart stays for 24-48 hours in sinus rhythm then flicks to unstable rhythm. The decision to continue digoxin or to re-initiate any other anti-arrhythmic drug therapy to keep the heart in sinus rhythm or to control the fibrillation that usually affects the hemodynamic stability in fragile post-operative patients would be late. Accordingly pre and post bypass SDL assessment would give a clue about the dose when to continue given digoxin post operatively and the relative required dose or other

anti-arrhythmic drugs.

Several studies were performed to assess the effect of CPB on the drug level pre and post CPB. Carruthers et al, 1975, reported slight fall in SDL concentration during CPB, with no significant differences were observed between plasma, atrial or skeletal muscle digoxin concentration before and at the end of CPB (8). Holley et al, 1982, found that the clearance of many drugs including digoxin may be reduced with using CPB. They added that the effect of CPB on pharmacokinetics of drugs are incompletely understood, and the subject merits further attention (9). In 1989 Buylaert et al, confirmed pharmacokinetic changes of drugs during CPB. They explained drug serum level drop was related to haemodilution and redistribution effect of the non pulsetile CPB (10). Anakar et al, 1996, reported significant drop of the SDL after CPB in 11 patients who were monitored for 24 hours post-operatively (11).

Most of published related articles had used various methods for assessment of SDL. However, their conclusion was quite similar. The current study has used more accurate method for assessment of quantitative analysis for SDL. The current protocol had also wide exclusion criteria for many patients and drugs to avoid factors which might affect the out come of SDL. The significant drop in SDL after CPB in this study denoted that even with recent technology of CPB consumables, there are considerable pharmacokinetic effects on SDL. This explained the indirect relation between the bypass time and the SDL. This phenomenon occurred among all studied patients. On the other hand, SDL drop after CPB was similar in both genders and all ages. This result has clarified the importance of how to keep SDL in the therapeutic range.

We would agree with Campbell J and McDonald S 2003 who reported that digoxin should be used as a first-line drug in patients with congestive heart failure who are in atrial fibrillation (12). In chronic rheumatic atrial fibrillation we use digoxin as a first line of treatment. The regimen consists of given loading dose of digoxin followed by maintenance dose of 250 ng/daily. The acceptable therapeutic SDL is between 0.5 and 0.8 ng/ml (13), however, this level has variation between nations. SDL above 1.0 ng/ml is associated with excess morbidity and mortality (12). In normal circumstances, anticoagulation is preceded digitalization. When diuretics are used for management of congestive heart failure, digoxin usually is omitted for a day of the week's 7 days. This regimen it has been found acceptable from the pre-operative SDL



assessment. In these circumstances continuing digoxin post-operatively is quite important once the patient starts oral feed. If oral feed in the first 24 hours post-operatively is not feasible for any reason, SDL is required and intravenous administration is an alternative. Toxicity or inadequate therapeutic level may arise if digoxin is given without accurate assessment of SDL particularly in post-operative patients.

Because of the lengthy duration of chronic rheumatic atrial fibrillation and the dilatation of the left atrium, maintaining sinus rhythm to some extent is difficult (14). We continue given digoxin post-operatively in patients who have been in digoxin and underwent one of those procedures for management of atrial fibrillation even if they went to sinus rhythm from the first attempt. It is not quite clear for how long post-operatively it should be continued as there is a great variation of response among rheumatic fibrillated atrium to therapeutic drugs (15,16).

### Conclusion:

Revising serum digoxin level post cardiopulmonary bypass is recommended to get the required benefit of the drug's therapy. However, continue given digoxin soon post-operatively in uneventful circumstance is preferable.

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## CARDIAC SURGERY IN DIALYSIS-DEPENDENT PATIENTS WITH END-STAGE RENAL DISEASE: EARLY RESULTS

Mohamed Sewielam, M.D,  
Yasser El-Messeery, M.D,  
Ahmed Mukhtar, M.D,

**Background:** Patients on dialysis for end-stage renal disease (ESRD) are undergoing cardiac surgery with increasing frequency. Furthermore, ESRD is known to be an important risk factor for mortality and morbidity after cardiac operations performed with cardiopulmonary bypass. The aim of this study was to evaluate the short-term outcome of dialysis-dependant patients undergoing cardiac surgery.

**Methods:** A retrospective analysis was performed on eighteen consecutive patients with ESRD dependant upon maintenance hemodialysis who underwent cardiac surgery in the period from January 2003 to October 2007 at Kasr Al-Aini hospitals Cairo University. Surgery included isolated coronary artery bypass grafting in twelve patients (66%), isolated valve surgery in four cases (22%), and combined procedures in two cases (11%).

**Results:** The hospital mortality was 11% (two cases). The most important and serious complication was bleeding requiring re-exploration in two patients (11%), wound infections in three patients (16%), stroke in one patient (5.5%) ,perioperative myocardial infarction in one case (5.5%), atrial fibrillation in three cases (16.5%),pleural and pericardial effusion in three patients (16.5%).

**Conclusion:** Cardiac surgery in patients with ESRD could be performed with an increased but acceptable risk for mortality and morbidity; however we believe that ESRD should not be regarded as an absolute contraindication to cardiac surgery and cardiopulmonary bypass. Accurate patient selection and adequate perioperative management is advisable.

Chronic kidney disease or end-stage renal disease (ESRD) is a worldwide public health problem. Myocardial infarction and other cardiac events are the leading causes of mortality in the population of patients who are on maintenance dialysis due to end-stage renal disease [1]. Both for functional and for vital reasons a cardiac operation is often considered necessary to improve life quality and prolong life expectancy, especially in patients suffering from coronary artery disease [1– 6], valvular stenosis [6, 7] or acute endocarditis (3,8)

The mortality due cardiovascular disease is 10–30 times higher in dialysis patients than in the general population (9) Myocardial infarction and other cardiac disorders such as pericarditis or bacterial endocarditis remain the leading causes of death in patients treated for end stage renal disease (ESRD) [10-12]. It is reported [13] that between 30% and 53% of deaths among long-term dialysis patients are due to coronary artery disease. In this patient population cardiac death is higher because of the presence of hypertension, hyperlipidemia, and abnormal carbohydrate metabolism leading to accelerated atherosclerosis [14-16].

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Address reprint request to : Dr

Mohamed Sewielam Department of Cardio-thoracic surgery, Cairo University

Email : jegyptscts@gmail.com

Codex : 04 / cord / 58 / 0709

Coronary artery bypass grafting (CABG) has become the standard of care for dialysis patients with cardiac disease that is uncontrollable with medical therapy. This becomes increasingly important as more patients go on dialysis, and the dialysis population becomes older. Chronic uremia, hypertension, volume overload, dyslipidemia, and anemia—all associated with ESRD—predispose patients to cardiac valvular abnormalities. Secondary hyperparathyroidism and the resultant increased calcium phosphate product accelerate calcification of cardiac valves and specialized conduction tissue [17]. Calcific degenerative cardiac valve disease predisposes to bacterial endocarditis in the presence of frequent vascular access-related bacteremia and compromised immunity associated with chronic renal failure [18].

As a consequence, ESRD is known to be an important risk factor complex for patients undergoing a cardiac operation on cardiopulmonary bypass (CPB). Specifically, CPB-associated problems such as fluid and electrolyte balance, hemoglobin concentration, and hemostasis necessitate optimal perioperative management of patients with ESRD.

The aim of this retrospective study was to review our management policies, to identify the intra operative and postoperative complications of cardiac surgery in patients with ESRD and to investigate the short-term outcome and survival among this group of patients.

### Methods:

Between January 2003 and October 2007, eighteen consecutive patients with chronic renal failure on maintenance hemo-dialysis required cardiac surgical procedure with cardiopulmonary bypass (CPB) at Kasr Al Aini Hospitals-Cairo University. We retrospectively reviewed all these patients' demographic and clinical data, including risk factors, preoperative cardiac and angiographic profile, operative data, postoperative complications and results. Patients who underwent emergent CABG, concomitant surgery of the ascending aorta or patients on peritoneal dialysis or acute renal failure patients were excluded from the study. The patients' demographic data are summarized in table 1. The surgical procedures done are shown in table 2.

### Peri-Operative Management:

#### Anesthetic precautions and management:

Anesthesia was induced with fentanyl, 10 µg/kg and midazolam, 0.1 mg/kg. Pancuronium 0.15 mg/kg was administered to facilitate endotracheal intubation and was repeated intraoperative as required to maintain

muscle relaxation. Anesthesia was maintained using isoflurane 0.3%–1.5% in oxygen-air mixture (1:1 ratio). The concentration of isoflurane was titrated to maintain mean arterial pressure (MAP) and heart rate (HR) in the range of 80%–120% of baseline values. Mechanical ventilation was provided by Narkomed anesthesia machine (North American Dräger, US) using a tidal volume of 10 ml/kg with the respiratory rate adjusted according to age, aiming to maintain PaCO<sub>2</sub> between 30 and 35 mm Hg. Nitrous oxide was not used throughout surgery. Potassium-free crystalloid was infused in all patients before CPB, minimizing the fluid intake to a minimum. Monitoring consisted of electrocardiography, pulse oximetry, capnography, catheterization of radial artery, and monitoring of pharyngeal temperature.

Variable	Value
Number of patients	18
Age (years)	56.7±15.0 (range: 15-72)
Gender	
Male	14 (77%)
Female	4 (22%)
Cardiac profile	
Isolated CAD	12 (66%)
CAD + valve disease	2 (11%)
Isolated valve disease	4 (22%)
Ejection fraction (%)	51.16±9.12 (range 38-72)
NYHA class	2.77±0.73 (range 1-4)
CCS class	2.83±0.81 (range 1-4)
Angiographic profile:	
Left main disease	3/14 (21.5%)
One vessel disease	2/14 (14.2%)
Two vessel disease	3/14 (21.5%)
Three vessel disease	6/14 (42.8%)
Renal profile and relevant labs:	
Cause of renal failure:	
Diabetes mellitus	7/18 (38.8%)
Chronic glomerulonephritis	6/18 (33.3%)
Other	5/18 (27.7%)
Duration of dialysis (months)	44.4±30.4 (range 6-120)
Preoperative creatinine (mg/dl)	6.22±1.92 (range 3-10)
Preoperative hemoglobin level (g/dl)	9.41±1.66 (range 7-12)
Risk factors and co morbidities	
Diabetes mellitus	9/18 (50%)
Hypertension	7/18 (39%)
Dyslipidemia	8/18 (44%)
Smoking history	9/18 (50%)
Family history for CAD	5/14 (36%)
COPD	6/18 (33%)
Peripheral vascular disease	2/18 (11%)
Previous cerebro-vascular accident	2/18 (11%)
Calcified ascending aorta	2/18 (11%)

**Table (1): Patients' demographics and preoperative variables:**

Operative procedures	Value
Isolated CABG	12 patients (66%)
CABG+AVR	1 patient (5.5%)
CABG+ MVR	1 patient (5.5%)
MVR	1 patient (5.5%)
MVR+Tricuspid valve repair	1 patient (5.5%)
Tricuspid valve replacement	1 patient (5.5%)

**Table (2): Surgical procedures**  
**CABG, coronary artery bypass grafting; AVR, aortic valve replacement; MVR, mitral valve replacement.**

### CPB and myocardial preservation:

Standard CPB using membrane oxygenator and roller pump was used in all patients. During CPB the hematocrit level was maintained between 20 and 25 % and flow rates between 2.0 and 2.5 l/min/sq.m, and mean arterial pressure about 70mmHg. Human albumin and fresh frozen plasma are added routinely on the priming solution and blood if needed.

Our protocol for myocardial preservation differs according to the procedure. Patients undergoing isolated CABG underwent CPB at mild hypothermia (32-34) and involved intermittent, antegrade tepid blood-potassium cardioplegia. For patients performing valve surgery or combined CABG and valve surgery we used moderate hypothermia (26-28), cold ante grade blood-crystalloid cardioplegia, and topical ice cooling.

### Perioperative dialysis:

Preoperative dialysis was performed in accordance with the patients' previous routine. The final dialysis was performed 12-24 hours before surgery in an attempt to optimize their hemodynamic and hydroelectrolytic situation. Intra operative ultra filtration was performed in all of our patients during CPB.

Post operatively; patients underwent their usual hemodialysis on the second postoperative day, with minimal intermittent heparinization. None of our patients required dialysis on the first postoperative day.

### Surgical procedures:

All operations were performed through a mid line sternotomy by using CPB. In patients undergoing CABG procedure (14/18), Left internal thoracic artery (LITA) was used in 10 patients (71%) to revascularize the left anterior descending artery. All other grafts were constructed using the long saphenous vein

Only mechanical valves (bileaflet) were implanted in the patients with valve disease except one patient with tricuspid valve endocarditis, where a bioprosthesis was implanted in the tricuspid position.

## STATISTICAL ANALYSIS

Descriptive statistics were used to describe the patients' characteristics and outcomes. Normally distributed continuous data are expressed as mean  $\pm$  standard deviation (SD) or median with range when appropriate. Categorical variables were expressed as real numbers and percentages. All data analysis was performed using Statistical Package for the Social Sciences (SPSS 11.0, Inc., Chicago, IL)

### Results:

#### Operative and early results

The characteristics of 18 dialysis dependant patients are listed in table (1). Twelve patients (66%) underwent isolated coronary artery bypass grafting, with a mean of  $2.92 \pm 0.8$  distal anastomoses (range, one to four anastomoses). Four patients (22%) had replacement or reconstruction of one or two valves, and two patients (11%) underwent CABG and valve replacement. In the patients having CABG procedure, the left internal mammary artery was used in ten patients (10/14-71%) to bypass Left anterior descending artery lesion. The right internal mammary artery was not used in any patient. Since most of the patients had an upper extremity arterio-venous fistula, and a future fistula may be required in the other extremity, harvest of the radial artery was avoided intentionally. The rest of the anastomoses were constructed using long saphenous vein.

Variable	Time in minutes (mean $\pm$ SD)
Pump time (min)	74 $\pm$ 26.5
Aortic clamp time (min)	51.6 $\pm$ 22.5
Total operation time (min)	218 $\pm$ 49

**Table (3): Operative data**

Postoperative duration of mechanical ventilation was  $12.3 \pm 9.1$  hours (range 4-41 h), the mean postoperative drainage for 24 hours was  $790 \pm 642$  ml (range 290-2300 ml). All the patients (100%) required blood transfusion, and the total blood units administered during the operation or within 24 hours after the operation was  $3.72 \pm 2.1$  units (range 2-9 units). Only one patient (5%) needed mechanical support during weaning from the CPB, and an intra-aortic balloon pump was inserted in the operating theatre. Six patients (33%) needed postoperative inotropic support (epinephrine and/or norepinephrine) for a variable period of time ( $19.4 \pm 8.22$  hours).

The mean interval between the end of surgery and the commencement of hemodialysis was  $29.2 \pm 5.74$  (range 19-40 h). Fifteen patients could be extubated before resuming hemodialysis (83 %) and only three (17%) could not be weaned from mechanical ventilation, two of them



could not be weaned due to re-exploration for bleeding, and the third patient had an extensive cerebrovascular accident.

The total number of ICU days after the operation was  $3.5 \pm 0.98$  days (range 2-6 days) and the total hospital stay was  $12.5 \pm 3.4$  days (range 8-22 days).

### Hospital Mortality

Hospital mortality, defined as 30 days mortality, was 11% (two cases). One 70 years old woman, with previous history of cerebro-vascular accident, impaired left ventricular functions (E.F 38%), underwent CABG (three vessel disease), the ascending aorta was found calcified during the procedure. The patient needed insertion of an Intra-aortic balloon in the operating theatre, and she did not regain her conscious level in the ICU, a CT scan and neurological examination confirmed the presence of a recent extensive cerebral infarction, and the patient died on day 4 postoperative. The other patient was a 68 years man, who underwent CABG (two vessel disease)+mitral valve replacement for rheumatic mitral valve disease, died in the surgical ward on the sixth postoperative day for unknown reason.

### Hospital Morbidity

Peri-operative complications are shown in table 4. The main complications were postoperative hemorrhage caused by coagulation disturbances (11%) that necessitates re-exploration. Peri-operative myocardial infarction occurred in one patient (5.5%) Three patients (16.6%) had infections: one had superficial wound infection that was treated conservatively, another CABG patient had a leg wound infection, and the most serious infection was deep sternal wound infection and mediastinitis that was successfully treated by debridement and omental flap closure.

Variable	Value (expressed as percentage)
Mortality	2 (11%)
Morbidity	
Intra-aortic balloon insertion	1 (5.5%)
Re-exploration for bleeding	2 (11%)
Perioperative myocardial infarction	1 (5.5%)
Atrial fibrillation	3 (16.5%)
Stroke	1 (5.5%)
Mediastinitis	1 (5.5%)
Superficial wounds infection	2 (11%)
Pleural effusion	2 (11%)
Pericardial effusion	1 (5.5%)

**Table 4. Perioperative complications**

Three patients (15.5%) experienced post-operative atrial fibrillation that responded to antiarrhythmic therapy.

Two patients (11%) had neurological complication one of them had an extensive cerebral infarction, and the other had a temporary neurological complication of disorientation and delirium.

Two patients (11%) had pleural effusion that required aspiration, and one patient (5.5%) had moderate pericardial effusion that was treated conservatively.

### Discussion:

The first report of valve replacement in patients with ESRD was by Lansing and coworkers in 1968 [19], while the first report of CABG in a patient with ESRD, was published by Menzoian and coworkers in 1974 [20]; since then, numerous reports have documented the feasibility of CABG [6, 21] and valvular operations in patients on dialysis [22, 23].

Although dialysis prolongs the lifespan and life quality of patients with ESRD, people who undergo dialysis still have only an overall 5-year survival rate of 55% to 60%. Cardiovascular complications are the leading cause of death in patients with ESRD; these account for 47% to 54% of deaths in patients who are on maintenance dialysis [24,25] The higher incidence of coronary artery disease in this patient population can be attributed to the presence of co morbid conditions that include hypertension, hyperlipidemia, renal anemia, fluid overload by arteriovenous shunt, heterotopic calcification due to secondary hyperparathyroidism, and abnormal carbohydrate metabolism that leads to accelerated atherosclerosis [26-28]. Also, valvular calcification may be accelerated in patients with chronic renal failure [22] and septic events with endocarditis may be regarded as typical complication from long-term hemodialysis procedures [3, 6].

So far, the optimal treatment of heart disease in ESRD patients is unknown. There are no randomized controlled trials that specifically address this question. It is known that cardiac medication is used relatively infrequently for patients on dialysis [31] and that the number of coronary artery bypass grafting (CABG) and valve procedures is lower among them than among the general population, but relatively constant [29]. In contrast, the number of percutaneous coronary interventions (PCI) is increasing [29] despite evidence for better long-term outcome in ESRD patients after CABG as compared with conservative management or PCI [30].

This reluctance to refer dialysis-dependent patients to the cardiac surgeon may largely be due to "dialysis" having been identified as a very strong indicator of increased perioperative risk. Operative mortality is in-



versely related to the preoperative renal function, and perioperative mortality is highest among patients on dialysis [32, 33]. Although dialysis-dependent patients are undoubtedly at increased risk after cardiac surgery as compared with nondialysis patients [32, 33], there are not many publications that specifically deal with the prognosis of patients on dialysis who undergo cardiac surgery. Most of these studies are small (fewer than 100 patients). Therefore, uncertainty prevails regarding risk stratification in ESRD patients who are candidates for cardiac surgery and the factors that influence prognosis after surgery.

Patients data in this study were similar to those previously published [1, 5, 6, 23, 26, 34-37] in particular those concerning age, comorbidities, cause of renal failure, duration of dialysis and functional status of the patients.

Recently, larger series of successful cardiac operations have been published [23,38-43]. The operative mortality of patients with chronic dialysis undergoing cardiovascular surgery is reported to range from 2.6 to 14.6% [4, 38-45]. Dacey [43] underwent a prospective regional cohort study in isolated 15 574 CABG patients in Northern New England from 1992 to 1997. Overall, 283 (1.8%) of the patients were on dialysis and their hospital mortality was 12.1%. Ko et al. [23] reviewed an early postoperative mortality of 9% in 296 cases. Recently, Horst and colleagues [44] summarized the result for 863 patients over 30 years by overview of the available literature including KO's overview. That shows an overall perioperative mortality rate of 12.5%. In KO's study, the perioperative mortality rate for isolated CABG, isolated cardiac valve operation, and combined procedures, was 8.9%, 19.3%, and 39.5% respectively. In our series, the operative mortality was 11%, which is comparable with those in the widely variable range of these previous reports. The rate is reported to be better in elective cases. Therefore, to improve the results of surgery in dialysis patients, elective surgery is recommended before the condition deteriorates [44].

Several factors possibly contribute to this high mortality. In addition, factors associated with ESRD can mask clinical symptoms [46,]. Specifically, it has been reported that even in the presence of substantial coronary artery disease, patients with ESRD have little or no anginal pain, which is probably the result of diabetic or uremic polyneuropathy or both [48]. Hassler and colleagues [47] reported that in 100 patients with ESRD undergoing coronary angiography, the coronary artery disease would not have been detected in 48% of the patients had angina pectoris been the sole criterion. Even a coronary stenosis of greater than 90% would have been

overlooked in 30% of these patients. Potential underestimation of cardiac valve disease is even more evident in patients with ESRD. Renal anemia, arterial hypertension, volume overload, or the presence of an arteriovenous shunt can lead to intravascular sound phenomena that can mask cardiac valve disease [46]. In addition, typical symptoms of progressive valve disease such as congestion and effusions can be concealed by dialysis, thus making timely diagnosis of potential cardiac decompensation more difficult [47]. Further, Hassler and associates [47] found that cardiac valve disease as determined by valve calcification progresses with the duration of dialysis; this is thought to be due mainly to secondary hyperparathyroidism [46]. These data suggest that both indications and referral for operation can be delayed in patients with ESRD who have coronary artery disease, valve disease, or both and that this may contribute to the high perioperative mortality in these patients.

The incidence of postoperative complications is reported to range from 7.4 to 75% [1, 39, 40, 42]. By Franga, 73% of CABG in dialysis patients experienced some type of complication [42]. He recognized that postoperative bleeding has been a common problem after CABG in dialysis patients and reported their rate of 7% in 44 patients.. Our rate of 11% is in line with previous reports: Blakeman and associates [34], 8%; Batiuk and coworkers [5], 5%; Opsahl and colleagues [4], 3%; Marshall and associates [2], 0%; and Jahangiri and coworkers [21], 11%. Interestingly, our 2 patients with postoperative bleeding occurred in our first 9 patients and before 2004. We have routinely used tranexamic acid prophylactically in recent years, with a recent reoperation for bleeding rate of 0 %. With use of tranexamic acid or possibly aprotinin in these patients, postoperative bleeding rates should approach usual CABG rates. Considering the incidence of postoperative bleeding, the high blood transfusion rate in patients with renal failure seems not to be due to not only preoperative anemia but also hemorrhagic tendency from platelet dysfunction. In our study, perioperative blood transfusion rate was high and all of our patients required blood transfusion.

Additionally, infections are more common because of a decreased chemotaxis, lymphopenia, decreased cell mediated immunity, reduction of interferon and monocyte function [15]. In our series, infection was the one of the most important complication

The cerebrovascular accident rate of 5.5% was similar to other reported series of dialysis patients: Kaul and coworkers [6], 11%; Marshall and associates [2], 8%; Christiansen and colleagues [50], 6%; and Blum and associates [35], 8%. Cerebrovascular accident is a frequent

cause of death in dialysis patients, falling only behind cardiovascular disease and sepsis as a cause of death in dialysis patients [51]. It is unclear whether the strokes in these CABG patients were caused by embolism, lower perfusion pressures on cardiopulmonary bypass, or carotid vascular obstructive disease. Reasonable steps to improve these results might include more liberal use of aortic ultrasound examination before cross clamping, increased perfusion pressure on bypass, and routine noninvasive carotid artery screen before operation.

In patients with CRF the preoperative, intraoperative, and postoperative care are important. In our practice, and according to other authors [2,6,37] all patients with dialysis-dependent renal insufficiency underwent preoperative hemodialysis within 24 hours of the operation, the second day after the operation, and then according to their preoperative routine or as dictated by the nephrologist. We have no experience of postoperative peritoneal dialysis, which is advocated by Ko et al. [23] and others [1,26]. For them, its advantages would be to start immediately after

surgery, not to require a specialized team, to avoid bleeding due to anticoagulation, to control electrolytic disorders, to lessen the risk of infective endocarditis and especially to avoid hemodynamic instability [23]. However, this technique needs an intra-peritoneal catheter in those patients prone to infection, and to postoperative gastrointestinal complications [23], and is known to have disadvantages as protein loss, respiratory disturbances, and pericardial or pleural effusion due to diaphragmatic leakage [26]. Moreover, in the event of postoperative bleeding, hemodialysis can be achieved with low-molecular-weight-heparin or even without heparin [52]. Some researchers recommend dialysis more than 24 hours before the cardiopulmonary bypass procedure [49], but we believe that it is best to dialyze as close to the procedure as possible. Although some investigators advocate the use of intraoperative hemodialysis [53], we chose intraoperative hemofiltration for reasons of simplicity in achieving control of water and electrolyte (mainly K<sup>+</sup>) balance until maintenance hemodialysis was resumed on the first postoperative day. This was possible in all patients, and did not generate any untoward hemodynamic sequelae.

Recently, off-pump CABG has been advocated for patients on chronic hemodialysis to avoid the possible deleterious effects of CPB [54,55]. The coronary arteries of patients with chronic renal disease are often diffusely diseased or calcified, and many of these patients have significant left ventricular hypertrophy, making off-pump surgery technically difficult. In most previous

studies investigating the efficacy of OPCAB in patients with renal dysfunction, the number of grafts in OPCAB was significantly less than that of conventional CABG [56,57]. One concern regarding off-pump surgery has been adequacy of revascularization owing to the difficulty of exposing the circumflex artery and its branches with this technique.[58] A fairly consistent pattern of fewer distal anastomoses being performed with the off-pump technique is present in the existing literature. This is somewhat concerning given the 26% reduction in mortality that has been shown with complete versus incomplete revascularization after CABG surgery [59]

In our study, radial artery was not used because of future use of the radial artery for blood access of dialysis. LITA was frequently used in addition to venous grafts. Internal mammary artery patency has been found superior to saphenous vein in patients with ESRD owing to its resistance to atherosclerotic changes [60]

Recent isolated reports have raised concerns about the use of the left ITA as a pedicled graft

in ESRD receiving hemodialysis through a left upper extremity arteriovenous fistula [61,62]. Rahbar et al in his study concluded that arterio-venous fistula placement in the ipsilateral upper limb and its usage for hemodialysis have modest hemodynamic effect on the insitu internal thoracic artery.[63]

Given the overwhelming evidence that the ITA has significantly better patency rates than vein grafts, the first association is not surprising. However, there is also good evidence that two ITA grafts are better than one [64, 65]. Whether this also holds true for ESRD patients has not been

studied. Surgeons are often reluctant to perform bilateral ITA grafting in ESRD patients because excessive blood loss and mediastinitis are feared. The two reports that specifically deal with this question, however, indicate that both ITAs can be used without a significant increase of the perioperative risk [38, 66]. Randomized studies may be inevitable to assess the potential risks and benefits of bilateral ITA grafting in ESRD patients.

Regarding patients with valvular disease, some authors recommend biological prosthesis in order to avoid oral anticoagulation [67] but, because of the early calcification and dysfunction of these in renal patients, we, like other authors, prefer metallic valve prostheses to avoid this problem [68].

### Conclusion:

Patients on chronic dialysis who require cardiac surgery constitute a surgical challenge, for their condition is still associated with increase but acceptable risk of mortality and morbidity following cardiac surgery; however

we believe that ESRD should not be regarded as an absolute contraindication to cardiac surgery or cardiopulmonary bypass.

We believe that patients with ESRD require screening at short-term intervals using noninvasive techniques such as Doppler ultrasonography and echocardiography to detect cardiac deterioration prior to decompensation. This could result in earlier referral for cardiac surgical intervention and might reduce perioperative mortality and morbidity.

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## APOPTOSIS IN RHEUMATIC AND DEGENERATIVE AORTIC VALVE STENOSIS. A PROGRESS TOWARD UNDERSTANDING

Amro R. Serag, MD.  
Eman M. Saied, MD.  
Amany R. Serag, MD.

**Background:** Although cardiologists and cardiac surgeons encounter aortic valve stenosis on a frequent basis, the molecular biology of cuspal calcification is poorly understood. Now, there is compelling histopathologic data suggesting that apoptosis is involved in calcification of degenerative stenotic aortic valves. Little is known about its contribution to calcification of rheumatic valves.

The aim of this study was to investigate the possible role of apoptosis in cuspal calcification in both rheumatic and degenerative aortic valve stenosis.

**Methods:** The study population included 20 patients undergoing aortic valve replacement for aortic valve stenosis. Ten cases were rheumatic (age  $28 \pm 8.6$  years) and ten cases were degenerative (age  $65.3 \pm 7.4$  years). The severity of aortic valve disease was determined preoperatively by echocardiography. We performed histological, histochemical and immunohistochemical studies on formalin-fixed, paraffin-embedded stenotic aortic valve leaflets removed during aortic valve replacement. Masson trichrome stain was performed to highlight fibrotic changes. Immunohistochemical studies were performed according to avidin-biotin-peroxidase complex (ABC) method using polyclonal rabbit antihuman Bax antibody. An immunoreactive score (IRS) was calculated by multiplying the grade of percentage of positive cells by the grade of intensity of Bax immunostaining.

**Results:** All the studied valves showed positive Bax immunostaining that was predominantly detected in the cytoplasm of interstitial fibroblasts “especially in areas adjacent to calcification” as well as the endothelial cells of the new-capillary sprouts present in the valvular interstitium. A differentiating feature was the positive Bax immunostaining, detected only in the cytoplasm of the valvular surface endothelial cells of rheumatic cases. Also, areas of neovascularization were more abundant in degenerative aortic valves and in the vicinity of calcification of these valves. The IRS was higher in degenerative aortic valve stenosis compared to rheumatic valves.

**Conclusions:** Our data attest that apoptosis contributes to calcification of stenotic aortic valve cusps. However, the interplay of endothelial cells and fibroblasts apoptosis in the pathogenesis of rheumatic and degenerative aortic stenosis seems to be different. Understanding the role of apoptosis and angiogenesis in the pathogenesis of both rheumatic and degenerative aortic stenosis offers the potential to develop targeted therapeutic regimens.

Rheumatic heart disease is the most common cause of valvular heart disease in developing countries including Egypt. Despite the high prevalence, increased morbidity, and well-described histopathological findings of this disease, little is known about the cellular mechanisms responsible for calcifica-

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Address reprint request to : Dr Amro R.

Serag

Department of Cardiothoracic surgery,

Faculty of Medicine, Tanta University,

Egypt

Email : amroserag@yahoo.com

Codex : 04 / cord / 60 / 0707

tion in these valves. Until recently, this has been thought to be due to a passive accumulation of calcium along the surface of the valve leaflet. (1)

On the other hand, calcific aortic valve disease is a slowly progressive disorder more common in the elderly and is the most common acquired valvular disorder found in developed countries. (2) It represents a disease spectrum that spans aortic sclerosis (mild valve thickening without obstruction of blood flow) to aortic stenosis (severe calcification with impaired leaflet motion and obstruction to left ventricular outflow). (3)

There has been a long-held notion that this disease was “degenerative”, because of time-dependent wear-and-tear of the leaflets with passive calcium deposition and therefore unmodifiable, condition. (4)

Now, there is compelling histopathologic data suggesting that calcification in either rheumatic or non-rheumatic aortic valve stenosis is an active regulated disease process. (1, 5) In degenerative aortic stenosis, it includes the apparent early involvement of apoptotic vesicles (6) and apatite nucleation of these sites with calcification of devitalized cells. (5) In rheumatic aortic stenosis, the data on involvement of apoptosis in calcification of rheumatic valves are scarce.

Apoptosis means programmed cell death which describes the orchestrated collapse of a cell. (7) Apoptotic cell death plays an important role in maintenance of the normal physiological state and in the pathogenesis of different diseases in the body. (8)

Proteins of the Bcl-2 family are key regulators of apoptosis. Certain members promote cell survival (e.g. Bcl-2, Bcl-xL, Bcl-w and A1/Bfl-1) while others promote cell death (e.g. Bax, Bak, Bad and Bim), and their relative abundance in any cell may determine its fate. (9)

The aim of this study was to investigate the possible role of apoptosis in cuspal calcification in both rheumatic and degenerative aortic valve stenosis.

## Methods:

**Tissue:** Twenty stenotic aortic valves represent the material of this study. The etiology of aortic stenosis was rheumatic in 10 cases and degenerative in 10 cases. The ten patients with degenerative aortic stenosis had no past history of rheumatic fever or infective endocarditis showing only isolated aortic valvular stenosis. The stenotic aortic valves were collected from patients undergoing aortic valve replacement and they were fixed immediately in the operating room in 10% formalin.

The mean age of our patients in the rheumatic group was (28 ± 8.6 years) with male to female ratio of 3:2. On the other hand, the mean age of the patients in the

degenerative group was (65.3 ± 7.4 years) with male to female ratio of 2.33:1

## Echocardiography:

Pre-operatively all patients were subjected to complete echocardiographic study using commercially available machines. The studies were recorded on videotapes for revision off-line.

M-mode and 2D were done in standard parasternal long axis, short axis and apical four and five chamber views. The aortic valve morphology was assessed with characterization of the severity and extent of the pathological process in patients with aortic valve disease. The anatomic abnormalities of the stenotic aortic valve were determined as thickening, calcification, fusion of the commissures and restriction of the leaflet motion. The left ventricular internal dimensions, wall thickness, FS and EF were measured according to the recommendations of the American Society of echocardiography. (10) Color Doppler examination was done to assess the degree of aortic stenosis :( 11)

Indicator	Mild	Moderate	Severe
Jet Velocity m/s	Less than 3	3 -4	>4
Mean Gradient (mm Hg)	<25	25-40	>40

Aortic regurgitation was assessed by color Doppler echocardiography and graded to mild, moderate and severe according to the following parameters:

Jet area/LVOT area (12)

<20%→mild, 20-40%→moderate, 40-60%→moderate to severe, >60%→severe.

## Tissue processing and staining:

All explanted valve specimens were fixed in 10% formalin, subsequently; the valves were embedded in paraffin. Paraffin-embedded sections were subjected to: 1-Haematoxylin and Eosin (H&E) staining for routine microscopy.

2-Masson's trichrome staining to highlight fibrotic changes. The procedure of Masson's trichrome staining was performed according to Bancroft and Gamble (2002). (13)

## 3-Immunohistochemistry:

Immunohistochemistry was performed on paraffin-embedded 3-5µ sections according to avidin-biotin-peroxidase complex (ABC) method. (14) Briefly, sections were deparaffinized with xylene and rehydrated with graded alcohol series. Antigen retrieval was done by immersing the sections in 10 m mol /L citrate buffer (pH 6.0) for 10 minutes at 100° C in microwave. Endogenous

peroxidase activity was blocked with H<sub>2</sub>O<sub>2</sub> (0.6% in methanol). After thorough washing of the sections with phosphate buffered saline, incubation was done for 30 minutes with non-specific blocking reagent “normal goat serum” to prevent non-specific binding. Subsequently, an overnight incubation of the sections with polyclonal rabbit antihuman Bax antibody (Bax-A3533 polyclonal rabbit antihuman-Dako) was done at a dilution 1:1000 at room temperature in a humidity chamber. The sections were then washed with PBS and the following steps were performed:

1. Incubation with biotinylated secondary antibody for 30 minutes.
2. Incubation with avidin-biotin-peroxidase complex solution for 30 minutes.
3. The reaction products were visualized using 3,3'-diamino-benzidine-tetra-hydrochloride (chromogen).
4. Sections were then counterstained with Mayer's haematoxylin, dehydrated in alcohol and mounted in DPX.

The germinal centers of a reactive lymph node were used as positive controls. Negative controls were prepared by omission of the primary antibody.

Immunohistochemical analysis of Bax immunostaining:

Bax positivity was indicated by cellular brownish cytoplasmic staining. A semiquantitative immunostaining analysis was done in which the percentage of cells positive for Bax was determined and graded as follows: 0: 0%–5%, 1: 6%–25%, 2: 26%–50%, 3: 51%–75%, and 4: 76%–100%, and the intensity of Bax staining was graded as follows: 0: None, 1: Weak, 2: Moderate, and 3: Intense staining. An immunoreactive score (IRS) (15) was calculated by multiplying the grade of percentage of positive cells by the grade of intensity of staining. In cases of heterogeneous staining intensities within a sample, each component was scored independently and the results were summed. The cases were categorized according to their IRS into the following groups:

Group I: IRS 1 - <3, group II: IRS 3 - <6, Group III: IRS 6 - <9, and group VI: IRS 9-12. The mean and the standard error of the mean of the scores of each of the degenerative group and the rheumatic group were calculated and the data were expressed as mean± standard error of the mean.

## Results:

### Pathological findings:

#### Macroscopic findings:

Inspection of the aortic valves during surgical excision indicated that all the stenotic valves were obviously thickened and irregular. Rheumatic valves were tricuspid with variable degree of commissural fusion and calcifi-

cation. Heavy calcification was noticed in 3 cases (30%). On the other hand, 9 cases (90%) of the degenerative valves were tricuspid with no commissural fusion while only one patient (10%) had fusion of one commissure. Heavy calcification was observed in 8 cases (80%).

### Histopathological findings:

Histopathological examination of the studied cases revealed that both rheumatic and degenerative stenotic aortic valves displayed the same histopathological picture in the form of subendothelial thickening, abundant interstitial fibrosis (Fig. 1A), infiltration by inflammatory cells mainly lymphocytes and macrophages (Fig. 1B), and foci of dystrophic calcification ranging from minute foci to extensively calcified nodules (Fig. 1B&2A).

The only differentiating point on the histopathological level was the presence of numerous newly formed capillary-like sprouts (neovascularization) with irregularly-sized lumens within the cusps of the degenerative stenotic aortic valves which were more evident close to the areas of calcification (Fig. 2A). These new capillary sprouts were observed in 8 cases (80% of cases) of degenerative aortic stenosis while they were not frequently observed in the studied rheumatic stenotic aortic valves as they were observed only in 2 cases (20% of cases).

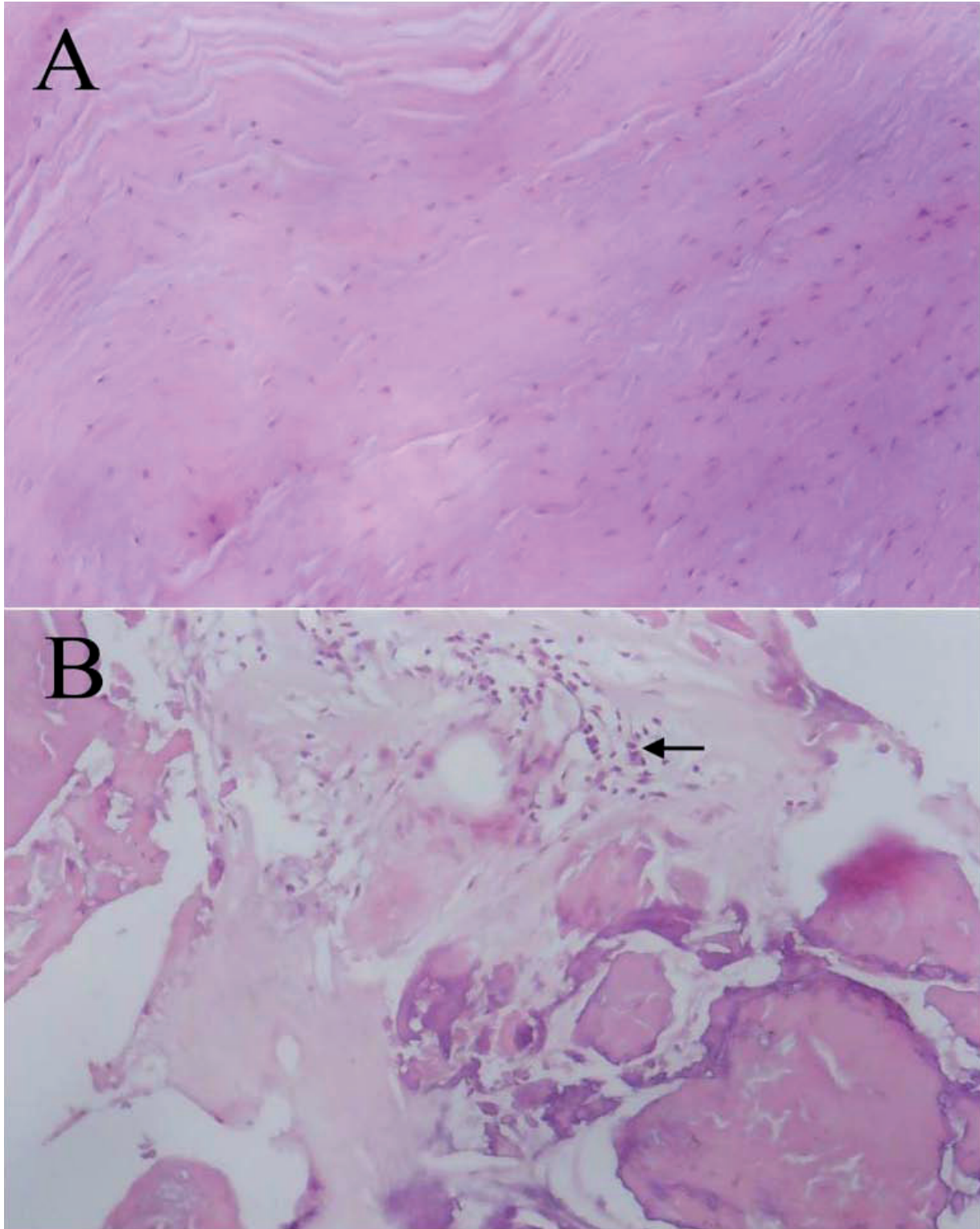
Fibrosis within the studied valves was highlighted by the Masson's trichrome stain, the collagen fibers showed green color (Fig. 2B).

Immunohistochemical analysis of Bax immunostaining in cases of degenerative aortic valve stenosis:

Bax immunohistochemistry studies of specimens of degenerative aortic valve stenosis revealed that all the studied valves showed positive Bax immunostaining, which was predominantly detected in the cytoplasm of the interstitial fibroblasts “especially in areas adjacent to calcification” (Fig. 3A) as well as the endothelial cells of the new capillary sprouts present in the valvular interstitium and the perivascular cells (Fig. 3”B&C”).

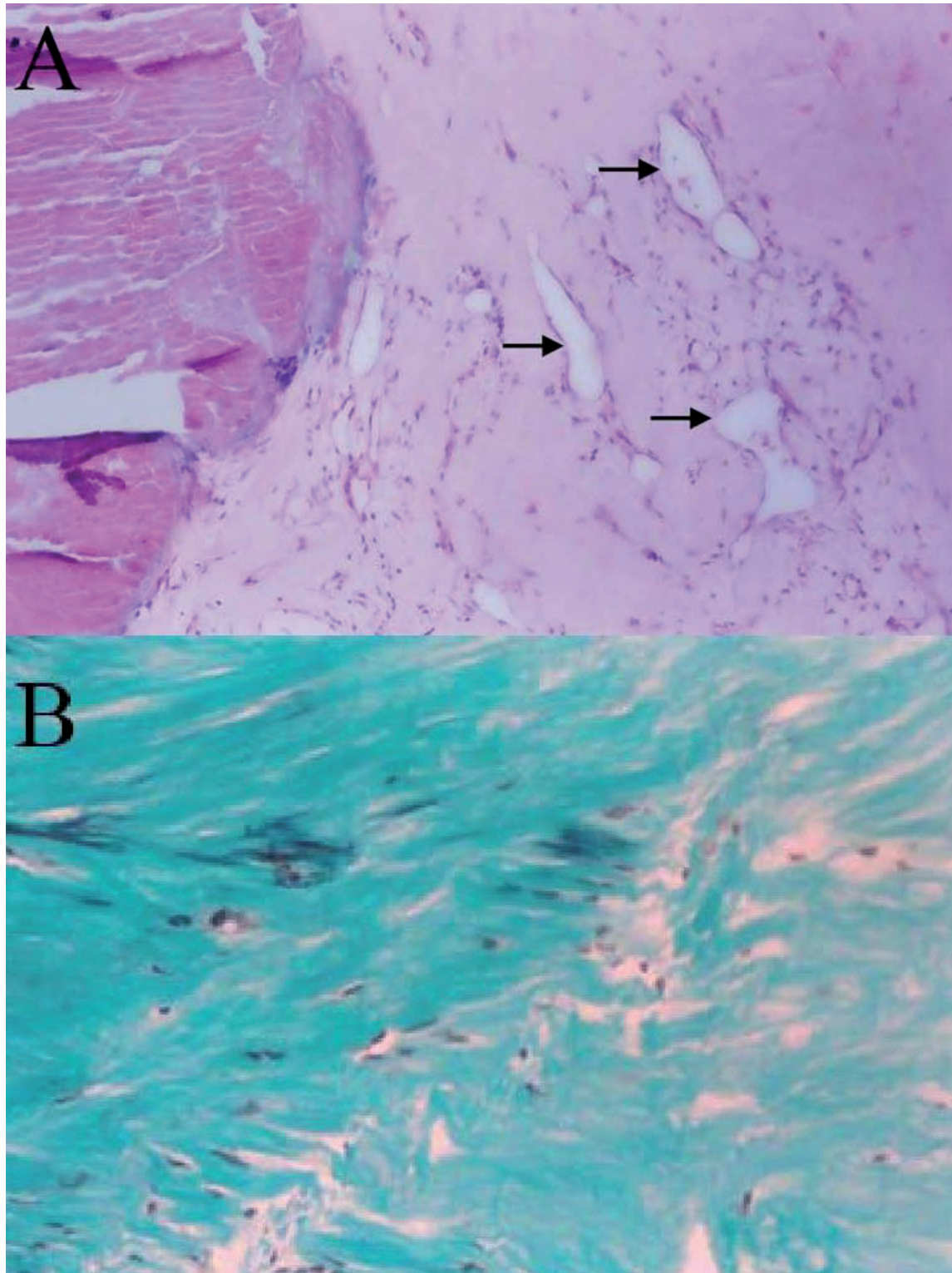
Eight cases (80% of cases) showed Bax positivity in both sites (interstitial fibroblasts and endothelial cells), while two cases (20% of cases) showed Bax positivity only in the interstitial fibroblasts. No difference in the staining intensity was observed between fibroblasts and new-capillary vascular endothelial cells. None of the studied cases showed Bax positivity in the valvular surface endothelium (Fig. 3D).

Bax-positive cases of degenerative aortic valve stenosis were categorized according to the Bax immunoreactive score (IRS) as shown in Table 1.



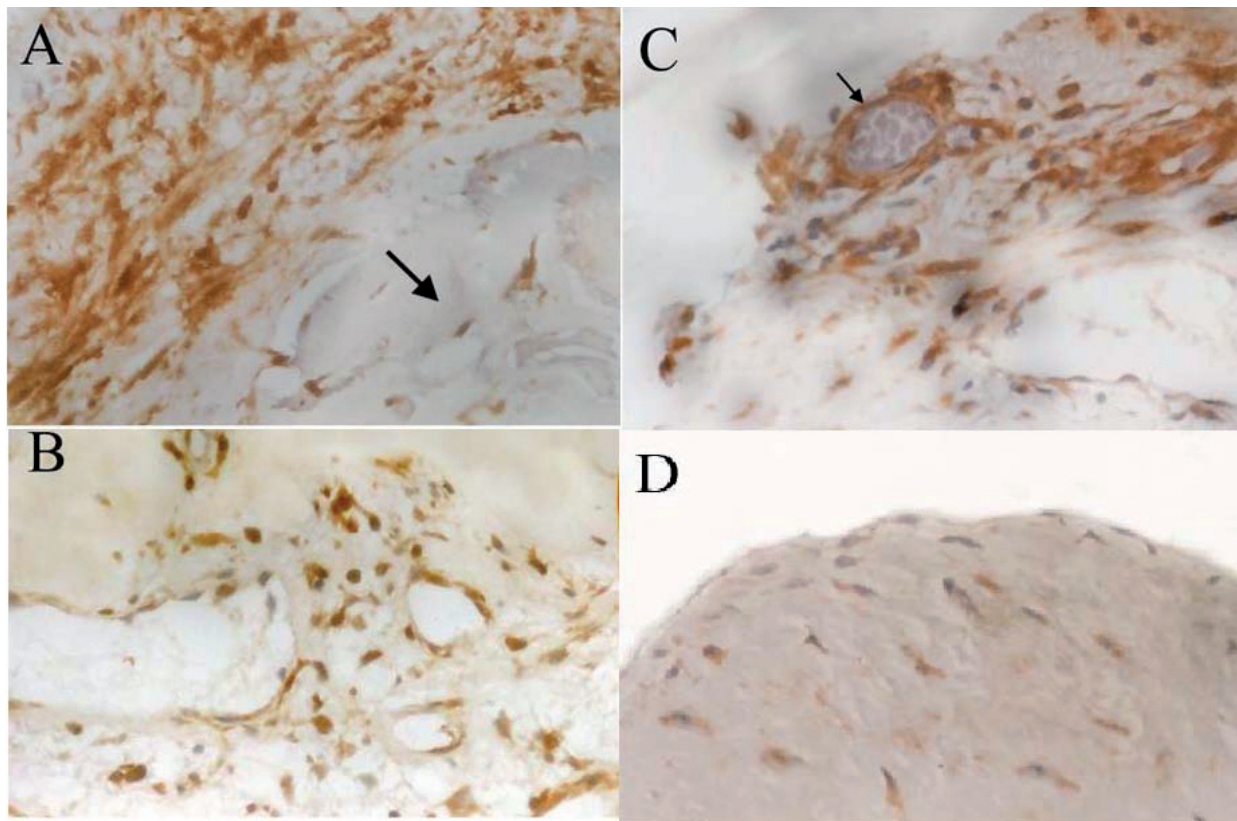
*Fig. (1): Rheumatic aortic valve stenosis showing: (A) Abundant interstitial fibrosis formed of collagen bundles with interspersed fibroblasts (H&E X 100), (B) Variable-sized and shaped foci of dystrophic calcification and interstitial infiltration by inflammatory cells "arrow" (H&E X 200)*





*Fig. (2): Degenerative aortic valve stenosis showing: (A) Numerous newly-formed capillary-like sprouts (neovascularization) with irregularly-sized lumens “arrows” close to an area of dystrophic calcification (H&E X 100), (B) Abundant interstitial fibrosis in which the collagen fibres are highlighted by the green color of the Masson’s trichrome stain (Masson’s trichrome X 200).*





**Fig.(3): Degenerative aortic valve stenosis showing: (A) Positive Bax immunostaining (Bax IRS 8) detected in interstitial fibroblasts; near which an area of dystrophic calcification “arrow” is seen (Immunoperoxidase X 400), (B) Positive Bax immunostaining (Bax IRS 3) detected in the new-capillary vascular endothelial cells and interstitial fibroblasts (Immunoperoxidase X 400), (C) Positive Bax immunostaining (Bax IRS 4) detected in the new-capillary vascular endothelial cells and perivascular cells “arrow” as well as in interstitial fibroblasts (Immunoperoxidase X 400), (D) Negativity of the valvular surface endothelial cells for Bax, while some interstitial fibroblasts show positive Bax immunostaining (Immunoperoxidase X 400).**

Immunohistochemical analysis of Bax immunostaining in cases of rheumatic aortic valve stenosis:

Bax immunohistochemistry studies of specimens of rheumatic aortic valve stenosis revealed that all the studied valves showed positive Bax immunostaining, which was predominantly detected in the cytoplasm of the valvular surface endothelial cells “8 cases, 80%” (Fig. 4A), interstitial fibroblasts “7 cases, 70%” (Fig. 4A&B), and the new-capillary vascular endothelial cells “2 cases, 20%” (Fig. 4C).

The intensity of staining was higher in the valvular surface endothelial cells lining the valve leaflets than both the interstitial fibroblasts (Fig. 4A) and the new-capillary endothelial cells.

Bax-positive cytoplasmic remnants of fragmented fibroblasts were seen adjacent to the calcified areas (Fig. 4D).

Bax-positive cases of rheumatic aortic valve stenosis were categorized according to the Bax immunoreactive score (IRS) as shown in Table 1.

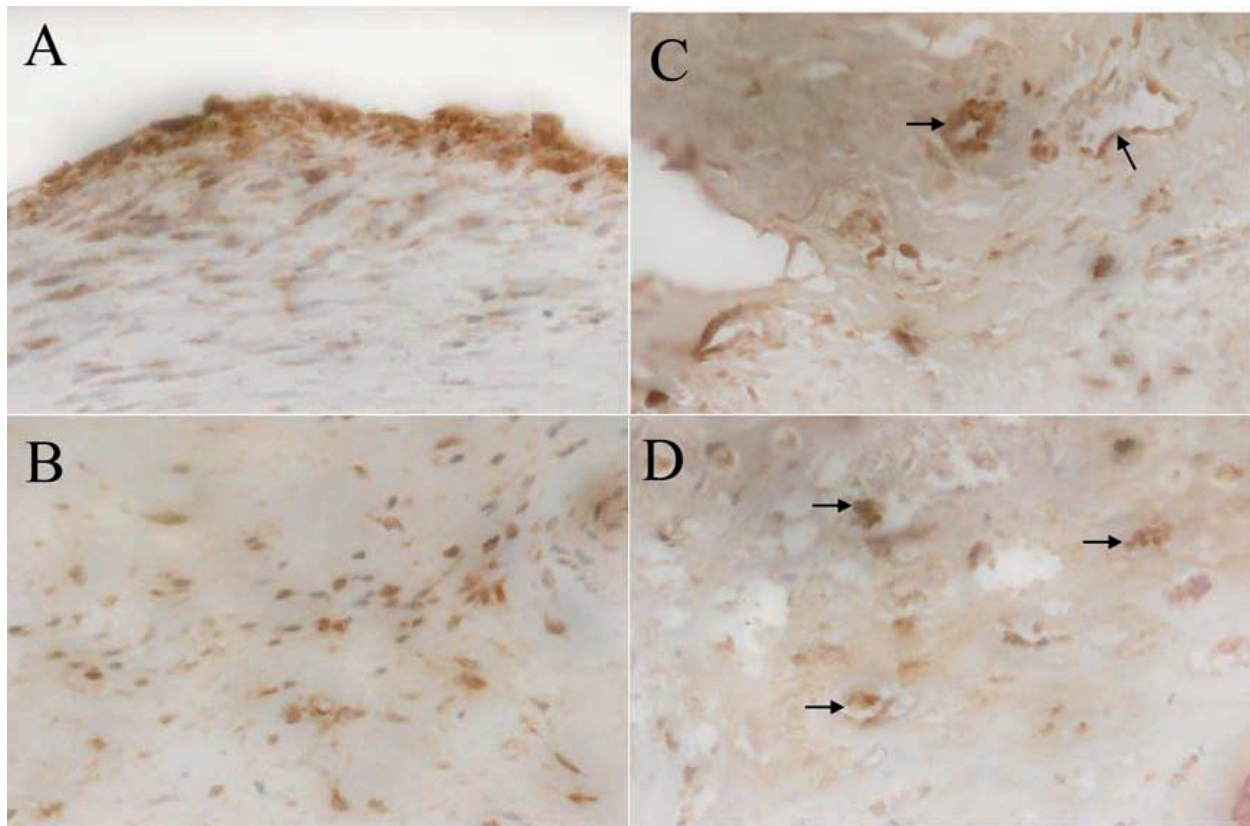
Bax immunoreactive score (IRS)	Degenerative valves n=10		Rheumatic valves n=10	
	n	%	n	%
Group I (IRS 1 - <3)	3	30	6	60
Group II (IRS 3 - <6)	4	40	4	40
Group III (IRS 6 - <9)	2	20	-	-
Group IV (IRS 9 - <12)	1	10	-	-
Mean±SE	5.3±0.94		3.2±0.49	

**Table 1: Bax immunoreactive score (IRS) in both degenerative and rheumatic aortic valve stenosis.**

### Clinical and echocardiographic findings:

#### Diagnosis:

The diagnosis of the 20 patients who underwent aortic valve replacement is illustrated in Table 2.



**Fig. (4):** Rheumatic aortic valve stenosis showing: (A) Positive Bax immunostaining (Bax IRS 4) detected in the valvular surface endothelial cells and in interstitial fibroblasts, with higher intensity of staining in the valvular surface endothelial cells (Immunoperoxidase X 400), (B) Positive Bax immunostaining (Bax IRS 2) detected in interstitial fibroblasts (Immunoperoxidase X 400), (C) Positive Bax immunostaining (Bax IRS 2) detected in the new-capillary vascular endothelial cells “arrows” and in interstitial fibroblasts (Immunoperoxidase X 400), (D) Bax-positive cytoplasmic remnants of fragmented fibroblasts “arrows” (Immunoperoxidase X 400).

Diagnosis/ Echocardiography	Degenerative valves n=10	Rheumatic valves n=10
Severe AS	10	6
Severe AS+ mild AR	-	4
Mean transvalvular gradient ± SE (mmHg)	67.8±5	66.3±2.4 (mmHg)

**Table 2: Echocardiographic diagnosis of the study population**

Relation between echocardiographic parameters and pathological findings:

It was observed that echocardiographic examination underestimated the degree of fibrosis and calcification in the excised aortic valves. However, there was a general trend of matching between the two different methods i.e. patients with higher jet velocity and mean transvalvular gradient showed higher degree of fibrosis, calcification and vascularization.

**Discussion:**

Many studies to date have concentrated on elucidating the similarities between rheumatic and non-rheumatic aortic valve stenosis, while explanatory studies explaining the observed discrepancies are lacking. We believe that continuous study of the disease process in aortic stenosis will provide important information on the treatment of valvular heart disease.

**Calcification:**

In addition to fibrosis, calcification is a defining feature of aortic valve lesions. Aortic valve stenosis characteristically progresses due to cuspal calcification, often necessitating valve replacement surgery. For nearly a century, the mechanical failure of calcified heart valves was attributed to a passive process. But now, it has been shown unequivocally to be an active, rather than a passive, process. Valvular calcium deposits contain both calcium and phosphate as hydroxyapatite, (16) the form of calcium-phosphate mineral present in both calcified

arterial tissue (17) and bone.

In stenotic aortic valves, we have shown a positive immunoreactivity to a pro-apoptotic marker (Bax) in both endothelial cells and valve fibroblasts. Calcific deposits were frequently observed in association with the apoptotic fibroblasts. These findings reiterate the results of previous investigators who demonstrated that, initiation of apoptosis of valvular interstitial cells was a mechanistic event in cuspal calcification. They showed that TGF- $\beta$ 1 was involved in this process. (18)

However, a major difference between rheumatic and degenerative valves was evident. Positive Bax immunoreactivity was demonstrated only in surface endothelial cells of the rheumatic valves while fibroblasts in both rheumatic and non-rheumatic valves were positive. This paradox suggests that the underlying disease processes determine which type of cells predominantly undergoes apoptotic changes.

Based on the above finding, our results provide circumstantial evidence that apoptosis in rheumatic valves may play an important role in the alterations of endothelial integrity. It is possible that this will lead to increased filtration of calcium into the deeper layers of the valve tissues. Then, the cellular degradation products and organelles extruded from the apoptotic interstitial cells provide the substrates for calcium binding with progressive development of calcification in the valve tissue.

Interestingly, this observation may explain a common macroscopic and echocardiographic finding, i.e. early commissural fusion in rheumatic valves and sparing the commissures in degenerative stenotic aortic valves. The involvement of surface endothelium and stronger staining intensity in these cells compared to the interstitial fibroblasts indicate a more active disease process along the rheumatic valve surface. This may elicit an intense inflammatory response and initiate the development of calcific deposits in a coaptation pattern (along the line of cusp coaptation) leading to early commissural fusion in rheumatic valves.

### Angiogenesis:

Another finding in this study was the presence of areas of neovascularization in 80% of cases of degenerative aortic valve stenosis compared to 20% of cases in rheumatic valves. Such areas have previously been described in both rheumatic and degenerative heart valves. (1, 4)

The process of angiogenesis is thought to involve a

stereotypical cascade of events, based mainly on study of development, pathologies and on extensive literature studying *in vitro* systems. (19) It is generally believed that new vessels are derived from the invasion of tissues by new capillary beds made of the proliferation of adjacent capillary and venular endothelium. (20) It is assumed, but has not been established, that this cascade holds true for physiological angiogenesis. In addition, there is evidence that different patterns of angiogenesis can occur *in vivo* when the mechanical environment, both inside and outside vessels, is changing. (21) It has also been suggested that the recruitment of interstitial fibroblasts may also participate in angiogenesis. (22)

The role of angiogenesis in the pathogenesis of aortic stenosis remains under investigation. It is possible that these areas of neovascularization are a response of tissue to injury as they are known to be associated with wound healing in general (23) or they result from autoimmune process. Rheumatoid arthritis, an autoimmune disease, is known to have such areas (24) and rheumatic heart disease is considered to have an autoimmune etiology. (25) In addition, Olsson et al 1994, (26) postulated that immune response plays an important role in the progression of degenerative aortic stenosis.

Previous investigators suggested that mineralization of rheumatic cardiac valve tissue is similar to skeletal bone formation that is associated with neoangiogenesis. (1) Mohler et al 2001 (27) demonstrated the association of angiogenesis to ossification occurring in degenerative aortic valves.

Of note, our results showed the presence of neovessels in the vicinity of calcified areas in degenerative stenotic aortic valves that are similar to those distributed in relation to an atherosclerotic plaque. However, studies supporting similarities between calcific aortic valve disease and atherosclerosis have produced, at best, circumstantial evidence without providing clear evidence of a direct causative pathway. Barger et al 1984 (28) supposed that neovessels are essential for growth of atherosclerotic lesion and may be contributing to the morbidity and complications of the disease process. The hypothesis of Barger was buttressed in a paper published by the group of Folkman. They showed that inhibition of angiogenesis by endostatin caused a reduction of atherosclerotic plaque growth, suggesting a direct role of angiogenesis in the progression of atherosclerotic plaque. (29) Similar implications could be made for the role of angiogenesis in the pathogenesis of degenerative aortic stenosis.



Our study showed that the newly-formed vessels in aortic valves are abnormal with irregularly-sized lumens and multi-layered in some sections especially in degenerative aortic valves. Such abnormalities have been previously described in tumors and these vessels were highly permeable. (30) We postulate that an increased permeability of those abnormal vessels could result in exposing a calcific deposit or valvular tissue to many cytokines and growth factors that normally are confined to the plasma, and through this indirect mechanism stimulate fibrosis and calcification or increase the size of calcific lesions.

### Survival of vascular endothelium:

Once new vessels have assembled, the endothelial cells become remarkably resistant to exogenous factors, and are quiescent, with survival measured in years. Diminished endothelial survival or endothelial apoptosis is characterized by vascular regression. (31) The list of factors identified that regulate endothelial apoptosis is extensive, (32) and these vary considerably according to the development time point, the specific site, function and type of vessel, in addition to surrounding physiological and/or pathological stimuli.

Molecular mechanisms implicated in mediating cell cycle arrest and survival of vascular endothelial cells include several factors involved in regulation of cell cycle and apoptosis such as p53, p21 and Bax. (33)

In this study, positive pro-apoptotic Bax immunoreactivity was detected in the cytoplasm of endothelial cells of the new-capillary sprouts present in the valvular interstitium and the perivascular cells.

Although the endothelium has received the most attention in angiogenesis research, the surrounding periendothelial cell layers are critical for ongoing structural and functional support of the vascular network. Vascular smooth muscle cells stabilize nascent vessels by inhibiting endothelial migration and proliferation. Indeed vessels regress more easily when not covered by smooth muscle cells in case angiogenic stimuli become limiting. (34) A similar phenomenon of neovascularization and subsequent regression of newly formed vessels has been observed in tumor vessels. (35)

We think that apoptosis of endothelial cells of single layered vessels and/or apoptosis of perivascular cells will interfere with integrity and increase the permeability of these new vessels and ultimately lead to vessel regression. This will lead to inclusion of a new area of the valve in the pathologic process (fibrosis and/or calcification). This seems to be predominant in degenerative aortic stenosis rather in rheumatic aortic stenosis.

### Clinical implications:

As results from studies on the pathogenesis and progression of aortic valve stenosis emerge, targeted pharmacotherapeutic regimens to interfere with the disease pathways to either slow or halt the disease process are being proposed. Clinical implementation of pharmacological regimens will require rigorous validation in experimental models and prospective intervention trials, as well as from retrospective databases.

Retrospective studies have demonstrated strong associations between statin use and decreased risk of progression of aortic valve calcification. (36) In addition, Thompson 1995 (37) suggested that members of the Bcl-2 family involved in apoptosis, could provide ideal targets for therapeutic intervention. Promising results were obtained using several agents in a variety of cardiovascular apoptotic models. (38) Also, the therapeutic goal, that is to mitigate against angiogenesis during pathological processes, has become realizable at the clinical level. (39)

Our data provide new insights into the mechanisms of rheumatic valvular disorders and open new perspectives for prevention of progression and treatment of rheumatic aortic stenosis.

Until benefits of potential pharmacological therapies are well established, conventional treatment of aortic valve stenosis should be guided by conventional recommendations. These include diligent clinical follow-up to monitor for symptoms onset, with surgical valve replacement as the preferred option of treatment.

### Conclusions:

Our results confirm that apoptosis contributes to calcification of stenotic aortic valve cusps. However, the interplay of endothelial cells and fibroblasts apoptosis in the pathogenesis of rheumatic and degenerative aortic stenosis seems to be different. Further studies are mandatory in order to clarify the mechanism for the initiation of apoptotic process in the endothelial cells and fibroblasts.

Understanding the role of apoptosis and angiogenesis in the pathogenesis of both rheumatic and degenerative aortic stenosis offers the potential to develop targeted therapeutic regimens.

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## PREDICTABILITY OF THE NEED FOR DELAYING THE STERNAL CLOSURE AFTER NEONATAL OPEN HEART SURGERY

Khaled Samir MD,  
Ayman Ammar MD,  
Tamer El Ghobary MD,  
Hossam Ashor MD,  
Ahmed Elkardny MD.

**Objectives:** The pseudosternal tamponad syndrome after open-heart procedures in neonates renders delayed sternal closure (DSC) a life-saving measure. The goal of this study is to determine and evaluate the risk factors that may predict the need for DSC.

**Methods:** Between January 1995 and November 2005, 396 open-heart procedures in neonates (226 males, 170 females) were studied retrospectively. Median age was 10.6 days (range 1–30 days) and weight 3.49 kg (range 1.7–4.65 kg). The major pathologies were transposition of the great arteries (n=185), interruption of the aortic arch (IAA) (n=39), total anomalous pulmonary venous drainage (TAPVD) (n=31) and single ventricle (n=31). Profound hypothermia with circulatory arrest was used in 248 and 158 normothermic cardiopulmonary bypass (CPB), 204 had crystalloid cardioplegia and 192 had blood cardioplegia. Continuous ultrafiltration was used in 321 and 59 had a modified ultrafiltration. The criteria for DSC were hemodynamic instability, deterioration of the central venous saturation, metabolic status and/or high ventilatory pressures.

**Results:** DSC was used in 137 (34.6%). Median CPB time was 139 min (range 35–289 min) and aortic clamping 61.6 min (range 0–164 min). Twenty-two patients (8.8%) needed reopening in the intensive care unit (ICU) during the first 24 h. Among the studied factors, the age below 7 days, the diagnosis of IAA and TAPVD, CPB duration over 179 min, clamping time over 97 min and central venous saturation below 51% were statistically significant risk factors. All the patients who had more than 106 min of clamping, more than 198 min of cardiopulmonary bypass or less than 47% of central venous saturation were either left opened or reopened in the ICU.

**Conclusions:** Many of the factors thought to be associated with the need for delaying the sternal closure had no statistical significance as risk factors. On the other hand, the diagnosis of IAA or TAPVD, an age less than 7 days, aortic clamping more than 97 min, CPB time more than 179 min and a post-bypass central venous saturation less than 51% were statistically significant risk factors that could be used in predicting the need for delaying the sternal closure.

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Address reprint request to : Dr Khaled Samir

Departement of cardiothoracic surgery  
Ain Shams university.

Email : jegyptsets@gmail.com

Codex : 04 / cord / 61 / 0705

**T**he decision to close the chest of a newborn after performing an open-heart procedure can be sometimes a critical one. Several techniques were suggested in the mid-1970s starting with sternal suspension and ending with delaying the sternal closure, many surgeons had become either for or against the idea [1,2].

Despite all the suggested methods the problem of the decision-making persisted as in all these methods it was built on subjective data.

All pediatric cardiac surgeons know that many neonates at the end of the procedure and despite being stable at the time of closure and even in the immediate post-operative period, some of them occasionally need to be reopened on an emergency basis and sometimes in a catastrophic condition. It is also very easy to recognize the increased morbidity and mortality of this particular group of patients when compared with those in whom the sternal closure was delayed. The application of the technique of delaying the sternal closure varies among different centers to the degree that while a few centers delay the sternal closure almost routinely in all neonates or for certain pathologies, others never apply the technique except after repetitive failed trials to close the sternum. We can also see that after all the advances in postoperative management; the technique of delaying the chest closure carries no or negligible additional risk to the patient [3].

From all of this, after more than 25 years of the introduction of the technique and after our previous publications that gained a lot of interest in the pediatric cardiac community; we find ourselves obliged to continue our work to have statistically significant proofs to our suggestions and to try to end by building up an objective risk score in order to be able to predict, at the end of the operation, the need for delaying the sternal closure and the potential risk of closure.

#### Aim of the work:

To conform the value of the parameters that can be used to render the decision of sternal closure more objective and the need for delaying the sternal closure objectively more or less predictable.

#### To achieve this aim we had two goals:

1. To continue studying the factors thought to be associated with the need for delaying the sternal closure in neonates after open-heart procedures and to verify the actual objective risk factors.
2. The establishment of objective criteria that might help in the decision making for sternal closure.

#### Methods:

Between January 1995 and November 2006, 396 neonates underwent open-heart operations were included in our study, 312 were studied retrospectively and 84 prospectively. The patients' characteristics and the studied variables are listed in table 1.

Variable	value
Age (days)	14 – 30 days, median 10.6
Body weight (kg)	1.7 – 4.65 kg, mean 3.49
Sex	170 females, 226 males
Diagnosis	
TGA	185 (47%)
IAA	39 (9.8%)
Single ventricle physiology	33 (8.3%)
TAPVD	29 (7.3%)
VSD	17 (4.3%)
AS	16 (4%)
CA-VC	11 (2.8%)
VSD+ coarctation	10 (2.5%)
Fallot tetralogy and DORV	14 (3.5%)
Fallot tetralogy/absent valve	5 (1.1%)
P. atresia + VSD	11 (2.8%)
P. atresia /intact septum	5 (1.1%)
Truncus arteriosus	7 (1.8%)
Anomalous coronary artery	6 (105%)
Others	8 (2%)
History of prematurity	102 (25.8%)
History of mechanical ventilation	156 (39.4%)
History of prostaglandin perfusion	256 (64.6%)
Preoperative mean peripheral saturation	81% (59-100%)
History of preoperative inotropic support	36 (9%)
CPB time in minutes, median (range)	139 min (35–289 min)
Hypothermic circulatory arrest	248 (62.6%)
Aortic clamping time, median (range)	61.6 min (0–164 min).
Use of ultrafiltration	
Continuous	321 (81%)
modified (at the end of bypass)	59 (14.9%)
Central venous saturation postbypass	
Type of cardioplegia	
Blood	204
crystalloid	192

**Table 1, patients' characteristics and studied variables**

TGA: transposition of the great arteries, TAPVD: total anomalous pulmonary venous connection, VSD: ventricular septal defect, IAA: interrupted aortic arch, DORV: double outlet right ventricle, CAVC: complete A-V canal, PSC: primary sternal closure; DSC: delayed sternal closure, SDSC: secondary delayed sternal closure.

The criteria for DSC were haemodynamic instability, deterioration of the central venous saturation, metabolic status and/or high ventilatory pressures.

#### Definitions of terms:

Primary sternal closure (PSC) is the closure of the patient's sternum at the end of the operation.

Delayed sternal closure (DSC) is leaving the chest opened for some time by delaying the closure of the sternum, **and we can distinguish two types of DSC:**

1. Primary delayed sternal closure (PDSC) is delaying the sternal closure either as a principal method or after failure of one or several trials of closure at the end

of the operation

2. Secondary delayed sternal closure (SDSC) is the closure of the sternum that was primarily closed at the end of the operation and was reopened during the early postoperative period.

The analyzed variables we thought were the factors most suspected to be associated with the need for DSC.

### Conduct of cardiopulmonary bypass and myocardial protection:

During the period of the study many of the techniques used, either surgical or parasurgical (cardiopulmonary bypass, cardioplegia, ultrafiltration, anesthesia and ventilation) changed sometimes even more than once. The CPB was performed with a basic flow of 2.5 l/min per m<sup>2</sup>. Total circulatory arrest with profound hypothermia at 18 °C was used in most of the cases before May 1998 and in selected cases afterwards. Myocardial preservation was performed by surface cooling (by intermittent irrigation of 4 °C cold saline) and antegrade cardioplegic solution. Crystalloid cold cardioplegia was routinely used before 1999 afterwards blood cardioplegia was the rule except for a few selected cases.

The average interval between the cardioplegic doses was about 20 min. The ultrafiltration was used in all cases. It was conducted throughout the cardiopulmonary bypass except between March 1994 and March 1996, where it was conducted only postbypass (the technique of modified ultrafiltration of great Ormond street).[3] The aim and the conduction of ultrafiltration depended on the type of CPB. In cases of deep hypothermia and circulatory arrest ultrafiltration was used during the re-warming period, aiming at achieving a haematocrit of 25% or more at the end of the cardiopulmonary bypass while in normothermic CPB the goal was a haematocrit above 28%. On the other hand when modified ultrafiltration was used it was conducted as long as was necessary to raise the haematocrit above 30% and/or to empty the extra corporeal circuit sometimes at zero fluid balance post CPB.

### Methods and decision-making:

PDSC was decided even with out performing a trial of closure in cases of: 1. The presence of important bleeding of nonsurgical cause. 2. Massive increase of the cardiac volume due to myocardial edema or dilatation or after the implantation of a homograft. 3. need of high ventilatory pressures to maintain acceptable oxygen saturation.

In all other cases at least a trial of closure was performed. In the trials the following parameters were considered as indicators of the possibility of PSC: 1. The

arterial blood gases and metabolic status, 2. The hemodynamic parameters including the heart rate, the systemic arterial pressure, central venous pressure, pulmonary artery pressure, and left atrial pressure, 3. The central venous saturation, and 4. The ventilatory pressures.

After marking all of the above parameters, the chest retractor was gently removed and then the sternal borders were approximated without using any instrument that might express any additional pressure on the chest. The patient was closely monitored for 15 min; during this period all the parameters were noted every 5 min and the data were compared to those taken before the approximation of the sternal borders. The trial was considered a failure if there was one or more of

the following results:

1. A drop in the heart rate, arterial blood oxygen saturation, central venous saturation and/or systemic arterial pressure.
2. An increase in the heart rate, left atrial pressure, central venous pressure, pulmonary artery pressure and/or airway pressure.
3. The appearance of arterial blood acidosis.

In case of failure of the trial the chest retractor was reused and the patient was stabilized. Any correctable factor was managed before performing another trial, otherwise a stint (usually a rigid plastic tube) was fixed in place to keep the chest widely opened and an airtight synthetic transparent patch was used to cover the sternal gap (being fixed to the skin and recently to the subcutaneous tissue to have a more cosmetically acceptable scar later on). An antiseptic ointment was put all around the plaque to close the portal entry of infection as well as the needle holes, to keep the closure airtight.

In the case of a successful trial the sternum was closed with nonabsorbable sutures, the deep subcutaneous tissue with absorbable suture and the skin were closed with widely separated interrupted mattress non-absorbable sutures.

Our routine antibiotic prophylaxis was in the form of Cefamandole (a second-generation cephalosporine) 50 mg/ kg at the induction of anesthesia, 25 mg/kg on the bypass, then switching to Vancomycin 10 mg/kg per 8 h in case of DSC until the removal of drains.

### Statistical analysis

The data were compared with a two-tailed paired t-test. Comparisons between groups of unequal populations were achieved with use of a two-tailed unpaired t-test assuming unequal variances or the Wilcoxon rank sum test, or with both tests. Univariate analysis and multivariate logistical regression were used to determine predictors for delayed sternal closure (DSC). A value of  $P > 0.05$  was considered

significant.

### Results:

DSC was used in 159 patients (40.2%). The decision to delay the sternal closure was taken intraoperatively in 137 patients (34.6%) due to one or more of the above-mentioned indications as mentioned in table 2. Twenty-two patients (8.8%) showed severe hemodynamic instability in the immediate postoperative period (first 24 hours) and needed to be reopened in the ICU. Table 3 shows the distribution of the studied patients between the 3 groups: PSC, PDSC and SDSC.

Indication	DSC	PDSC	SDSC
Failure of closure	113 (71%)	113 (71%)	1 (5%)
After trials	45 (40%)	45 (40%)	21 (95%)
Without closure trials	68 (60%)	68 (60%)	
Nonsurgical bleeding	17 (11%)	16 (12%)	21 (100%)
Post closure instability	29 (18%)	8 (17%)	
In the OR	8 (28%)	8 (100%)	
In the ICU	21 (72%)		
Total	159	137	22

**Table 2: Indications of DSC.**

Pathology	No.	DSC	PDSC	SDSC
TGA	185(47%)	78(42%)	69(89%)	9(11.5%)
IAA	39(9.8%)	25 (64%)	21(54%)	4(10.3%)
Single ventricle physiology	33(8.3%)	11 (33%)	8(73%)	3(17%)
TAPVD	29(7.3%)	22 (76%)	19(86%)	3(14%)
VSD	17(4.3%)	4 (24%)	4(100%)	0
AS	16(4%)	3 (1.8%)	3(100%)	0
CA-VC	11(2.8%)	1 (9%)	1(100%)	0
VSD+ coarctation	10(2.5%)	1 (10%)	1(100%)	0
Fallot tetralogy and DORV	14 (3.5%)	1 (7%)	0	1(100%)
Fallot tetralogy/absent valve	5 (1.1%)	2 (40%)	1(50%)	1(50%)
P. atresia + VSD	11(2.8%)	2 (18%)	2(100%)	0
P. atresia /intact septum	5 (1.1%)	2 (40%)	2(100%)	0
Truncus arteriosus	7 (1.8%)	3 (43%)	3(100%)	0
Anomalous coronary artery	6 (105%)	3 (50%)	2(67%)	1(33%)
Others	8 (2%)	1 (13%)	1(100%)	0
	396	159(40%)	137(86%)	22(14%)

**Table 3: Types of DSC and the distribution of patients on the two groups (fractions in the percentages approximated)**

Using statistical regression; an age less than 7 days, a cardiopulmonary bypass duration exceeding 179 minutes, aortic clamping time exceeding 97 minutes and a central venous saturation at the end of the cardiopulmonary were recognized as a risk factor ( $P < 0.05$ ).

On the other hand; the patient weight, sex, preoperative arterial oxygen saturation, history of prematurity, preoperative inotropic treatment, history of assisted ventilation, use of total circulatory arrest with profound hypothermia, type of used cardioplegia and prostaglandin E2 infusions had no statistical risk significance ( $P > 0.05$ ). The statistically significant studied variables are listed in table 4.

Variable	P value
Age >7 days	0.021
Diagnosis	0.043
IAA	0.047
TAPVD	0.016
CPB time > 179minutes	0.038
Aortic clamping time > 97	0.029
venous saturation < 51%	0.009

**Table 4: The statistically significant variables for DSC**

We have also found that all patients who had CPB time > 198 minutes needed to be either left opened in the theater or reopened in the early postoperative period. We had also found that all patients with a clamping time more than 108 min had either DSC or SDSC.

The central venous saturation at the end of the cardiopulmonary bypass with the chest retractor in place was a sensitive marker for the liability of closure. All patients who had a central venous saturation less than 47% needed either a PDSC or SDSC.

In the 84 patients studied prospectively we applied our former results as objective parameters for the need for DSC. From This group of patients only one needed SDSC due to persistent nonsurgical bleeding with and incidence of 1.2% compared with no mortality to and incidence of 6.7% in the retrospective group with 38% mortality.

### Discussion:

The importance of sternal closure as a cause of cardiac compression after cardiac operations was first emphasized in 1975 by Riahi and colleagues and they suggested the external traction as a method of relieving this compression [2]. Jögi and Werner by measuring the detrimental hemodynamic have confirmed the effects of chest closure after complex cardiac operations for congenital disease. They related the intolerance to closure to a fall in the transmural left and right ventricular



end-diastolic pressures; in other words, due to impaired filling rather than to a change in contractility [5].

Gielchinsky and associates reported the first series of 29 adult patients with DSC in 1981 [6]. In the same year Gangahar et al. reported relief of tamponade conditions after postoperative sternal reopening in an infant [7]. In 1982, Shore et al. reported a significant decrease in central venous pressure as well as significant increases in blood pressure and urine output after postoperative sternal reopening done because of low output state [8].

Edema, unstable hemodynamic conditions or non-surgical bleeding can make the decision of sternal closure very difficult and raises the need for DSC after complex operations for congenital heart disease. In addition to all the above it can also be used electively to improve the hemodynamic and respiratory stability in the initial postoperative period [9].

Kay and coworkers studied the involvement of sternal closure in the postoperative haemodynamics of pediatric patients was by using pericardial catheters to measure directly the rise in pericardial pressure after cardiac operations for congenital disease [10]. They found that pericardial pressure climbed significantly after transventricular repair of tetralogy of Fallot or homograft repair of truncus arteriosus. There was a negligible rise in pressure in patients who underwent closed cardiac procedures or transatrial open cardiac operations. More recently, DSC has been described in a few series after pediatric cardiac operations with no or an acceptable additional morbidity compared with PSC [3,11–21].

Unfortunately neither those studies nor in the other main publications concerning this technique discussed the indications of DSC thoroughly, as they concentrated on the evaluation of the technique without suggesting clear indications or limitations [3,11–21]. It should be also remarked that the feedback of the decision of PSC might be also a determining factor for the postoperative outcome. We continued in this study to concentrate in this study on the probable indications that we call risk factors for DSC to support our published primary results. On the other hand, we studied prospectively the decision making guided our primary results and the results showed a decrease in the incidence of SDSC and hence the overall mortality.

During the time period covered by the retrospective part of our study, several changes have been noted in the operative (and probably even pre- and postoperative) management of the patients. This is on one hand a limitation of the power of this part of the study although the fact that the overall incidence of DSC did not change over this time period gives a relative value to the actual significance of the statistical results. It must be kept in

mind that it may reflect also that, despite an increasing number of more complex cases and more severe preoperative status, those changes did not significantly change the incidence of DSC.

Since the report of Fanning and his associates considering DSC as a life-saving measure in certain patients after open-heart operations [13], the technique has become more popular. At the beginning many closed the skin leaving the sternum opened, but this method was not very satisfactory because the sternum with not retracted enough to give the heart the needed space. In 1990 Majid came up with the idea

of the plastic struts to keep the sternal edges retracted to the required distance [22]. The skin gap is closed using a transparent synthetic airtight patch that protects against infection and at the same time allows one to see accumulating effusion or clots that can be easily evacuated. For a few years now we have started to fix the skin patch to the superficial part of the subcutaneous tissue, thus avoiding skin necrosis that results in an ugly scar after DSC.

Our study showed that among all the claimed risk factors studied we found that having less than 7 days of age, a diagnosis of either IAA or TAPVD, aortic clamping time exceeding 97 minutes, cardiopulmonary bypass time longer than 179 minutes or a central venous saturation postbypass with the chest retractor in place lower than 51%, were statistically significant ( $P < 0.05$ ) as effective risk factors. Many of the factors we previously thought to be undoubtedly risk factors for DSC such as low body weight, prematurity, preoperative assisted ventilation, preoperative inotropic support, prostaglandin infusion, the use of total circulatory arrest with profound hypothermia, and the type and mode of myocardial protection and ultrafiltration had no statistical risk significance. It is also interesting that the pathologies associated with a statistically significant risk to DSC are those associated with increased pulmonary vascular resistance, either due to preoperative pulmonary venous stasis in TAPVD or preoperative plethora in IAA. This may be due to the increase in the intrathoracic pressures in these patients causing more myocardial compression.

The mortality in our DSC group (not related to the DSC procedure itself and mainly due to multiorgan failure, DIC or infection) was acceptable (18%; 15% in the PDSC group and 34% in the SDSC group) compared with the range of mortality reported for the DSC in the literature (11–36%, keeping in mind that this range was given in heterogeneous groups with an older pediatric population and without including the SDSC population) [10–16]. The mortality rate in the SDSC group (34%) was markedly higher than that in the PDSC group

(15%), and this gives more value to our trial to predict the need of delaying the sternal closure even in cases of temporary hemodynamic stability and a successful trial of closure. We have to remark also that this mortality was not related to the technique in any of our patients. In the prospective group only one patient had SDSC due to nonsurgical postoperative bleeding with no mortality, which means that applying our guidelines for the sternal closure decision making effectively and considerably decreased the incidence of SDSC and hence the overall mortality which was the main aim of our study. We have built up a scoring system for the risk factors that was applied in the prospective part of the study and helped us to avoid the need for SDSC with its high mortality rate. The scoring system is being tested by a prospective randomized trial to evaluate its importance objectively.

### Conclusion

The technique of delayed sternal closure is a simple, safe and very useful technique that helps to overcome the problem of pseudo-tamponade after open-heart procedures in neonates. Many of the supposed risk factors associated with the need for delayed sternal closure such as the body weight, prematurity, preoperative inotropic support, preoperative assisted ventilation, profound hypothermia, circulatory arrest, type of cardioplegia and the use of ultrafiltration were not statistically significant as risk factors. On the other hand the age of less than 7 days, increased pulmonary vascular resistance as in TAPVD and IAA, aortic clamping time longer than 98 min, cardiopulmonary bypass time longer than 179 min and a central venous saturation in postbypass less than 51% were statistically significant risk factors for DSC. The mortality in the SDSC group is significantly higher than that of the PDSC group (34 versus 15%). The prediction of the need of PDSC is possible (bearing in mind these risk factors even in cases of temporary apparent hemodynamic stability) and is important in order to avoid the higher mortality associated with SDSC. A scoring system for these risk factors was built up and being objectively tested for its application value.

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**Invited commentary****Predictability of the need for delaying the sternal closure after neonatal open heart surgery**

The published article is an extremely interesting topic in pediatric cardiac surgery. The number of patients is important. The authors did not precise the centers where such patients were done. The first author from Ain Shams University worked in Marseille in France with Professor METRAS , then in Canada then in Saudi Arabia . The four mentioned centers have different surgical strategies and different experience. In such an aspect the paper is interesting as a multi-center study. Nevertheless , the different centers should be mentioned.

The different factors mentioned in the conclusion stated that the IAA , TAPVD, age below 7 days, aortic clamping more than 97 min and CPB more than 179 min. and a post-bypass central venous saturation less than 51% were statistically significant risk factors that could be use in predicting the need for delaying sternal closure. The research work did not take in consideration the difference between cold crystalloid cardioplegia , total circulatory arrest under deep general body hypothermia and normothermic total blood cardioplegia as method of myocardial protection used during surgery of the series of patients.

Apart from such critics this paper is an excellent research work .

Mohamed AHMED-NASR  
Professor of Cardiac Surgery  
National Heart Institute

## PULMONARY ARTERY BANDING IN INFANTS AND CHILDREN WITH CONGENITAL HEART DEFECTS

Ayman Shoeb, MD.  
 sherif azzab , MD.  
 Ahmed Shamy ,M.D.  
 Waleed Ismail Kamel , MD.

**Background:** Pulmonary artery Banding (P.A.B) is one such palliative procedure which has been supplanted largely by early primary repair, performed in 1st year of life. (1) .But still has a role in management of patients with V.S.D, C.A.V.S.D, or single ventricle and tricuspid atresia with increased pulmonary Blood flow. Who generally are not amenable to early primary repair or had a high risk for primary repair.

**Methods:** this study included A series of 250 (Two hundred fifty patients) who underwent P.A.B between 1998 and 2007 were analyzed to determine the current results for this procedure. A retrospective analysis of hospital echo, CXR, CATH were analyzed together with indications of P.A.B, operative and postoperative data to determine the current results of this procedure.

**Results:** 250 patients from ain shams university hospitals from 1998 to 2007, age was from 3.5 to 28 months,there body weight is from 3.5 to 15 kg. 92 % received good band ,6 % loose band ,2% failed band due to fixed p++,intraop PAP 60-90 (mean 66.25 +- 12.890), preband ,PAP 30-63 (mean 42+ \_ 12.63) on FIO2 50% postband .total 9.2 %(23/250) mortality,6% early mortality operative,3.2% late mortality operative .Risks factors for early mortality is down syndrome .old age ,more than 1 year ,mean PAP more than 75 mmhg,cardiac cachexia ,poor chest condition ,low cardiac output ,prolonged ventilation .Risk factors for late mortality included loose band or inadequate band .91.8%(227/250) showed who survived, 85% showed clinical improvement .15% didn't show much reduction in PAP or a noticeable improvement in the clinical condition.

**Conclusion:** PAB can be performed on complex congenital heart at relatively low risk of death and is recommended for symptomatic infants with TA or single ventricle with increased pulmonary blood flow ,it is also the preferred method for management of infants with DORV ,TGA +VSD.If primary repair is not feasible and carries a high risk due to small body weight ,cardiac cachexia or poor chest condition ,PAB should be the second option at the time of surgery ,and if the decision is made to do a band ,every effort should be made to have adequate banding to prevent progression of p++ and to have good prognosis on the second operation (debanding and repair).

**M**uller and Dammann [1] introduced pulmonary artery (PA) banding in clinical practice in 1951. Since then, this operation has been used as a palliative procedure for small infants with congenital heart defects, to be followed by definitive repair at an older age. The technical difficulty involved in primary repair and concerns regarding the use of cardiopulmonary bypass in small infants led many institutions to favor this staged approach. However, the perioperative morbidity and mortality of early primary repair has significantly

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Address reprint request to : Dr Ayman

Shoeb Departement of cardiothoracic  
 surgery Ain Shams university.

Email : jegyptscts@gmail.com

Codex : 04 / cord /62 /0709



improved in recent years. Many neonates and infants are now treated by primary repair with good results, and PA banding is selected as the initial operative procedure in fewer patients. However, this operation still remains the procedure of choice for a specific diagnostic subset of patients. The mortality of PA banding improved dramatically in the 1980s. The reported mortality rate decreased from approximately 30% before 1980 to approximately 10% during the 1980s [2–6]. With advances in cardiac operations, the results of PA banding should have improved further in the 1990s. However, there are no data to support such an assumption, partly because PA banding has a smaller role now in the surgical treatment of congenital cardiac defects. Banding is a technically simple procedure, performed with out by pass, banding reduces pulmonary blood flow. Thus preventing pulmonary vascular disease.

In this series we will review our results in diagnosis and surgical management in 250 patients with multiple congenital anomalies who underwent PAB at Ain Shams University from 1998 to 2007

### Methods:

Two hundred fifty patients (250pt) underwent P.A.B were performed at the university of Ain Shams between Feb. 1998 and Feb. 2007.

P.A.B was placed to alleviate the symptoms of increased pulmonary blood flow or congestive heart failure.

Their age ranged from 3 month and 28 months and the mean age was 9 months.

While the body weight ranged from 3.5 kgs to 15 kgs and the mean weight was 8.5 kgs.

The type of cardiac defects are listed in table 1.

Preoperatively, all patients were subjected to fully clinical examination, chest x. ray, complete laboratory investigation and Echocardiography.

The P.A.B. was preferred to be done through. Median sternotomy rather than through Lt. Thoracotomy.

		No
<b>Group I</b>	V.S.D	150
<b>Group II</b>	CA.V.SD	70
<b>Group III</b>	Single ventricle	30
Total		250

**Table 1: show the different clinical diagnosis of the patients underwent P.A.B:**

Legend: (V.S.D., ventricular septal defect (S.V.), single ventricle.

(A.V.S.D) (Common atrio – ventricular canal)

Indication for PAB in addition to severe P++ were CHF with failure of medical treatment ,repeated chest infections ,failure to thrive ,cardiac cachexia and poor general condition .

### Surgical technique of pulmonary artery banding :

we start our technique by dissection and taping the ascending Aorta, dissection of main pulmonary artery, dissection and ligations of P.D.A .using a big right angle clamp, the same tape around the ascending aorta is passed around pulmonary artery taking care of left atrial appendage and circumflex coronary artery.

An appropriate position of P.A.B. is 15 mm distal to P.A valve.

With routine fixation of the band to the adventitia of the pulmonary artery using ethibond 4/0 stitches to avoid migration of the Band. Toward Bifurcation to fix the nylon tape.

A different surgical methods for applying the Bond were used in this study including:

- we started the Band by applying trusler,s formula, (20 mm +1mm for every kg body weight ) our object was to decrease systolic pulmonary artery pressure to normal (25 to 30 mm hg). Or less than half of systemic arterial blood pressure without producing Brady cardia or desaturation (O2 saturation less than 90%) and by direct and continuous monitoring of distal pulmonary artery pressure. (P.A.P).

If distal P.A.P still high more stitches in the band were taken to make the band tight.

Or adjustable band was used using nylon tape and snugger around the pulmonary artery. Band and then by applying two or three large or medium size mega clip on the tape below the snugger. Which was removed after that.

The band can be easily loosened or tightened intra-operatively and past operatively depending on the

Haemodynamic situation making the band more tight without producing hypotension or Bradycardia or hypoxia. Taking into consideration that these measure were taken on.

FI O2 50% and not on 100% oxygen, also 10mg doubutamine was started before applying the P.A.B as a routine.

If the patients homodynamic cannot tolerate Band a loose band can be applied or removed completely and the patients considered inoperable or unfit for P.A.B

Due to severe fixed pulmonary hypertensions

Intraoperatively all pts were subjected to the following measurement before and after the banding

ABP (S-D-M)

PAP (S-D-M)

O2 SATURATION on fio2 50 and 100 %

Any intraoperative events :bradycardia,desaturation, low C.O.P and hypotension

Postoperatively :systolic bl pr ,o2 saturation ,arrhythmias, low C.O.P PH crisis.

Echo before discharge ,2 months and 4 months

Echo describes the site ,distance from valve ,migration ,obstruction

Pressure gradient ,direction of flow across the vsd

Followup for signs of CHF and p++

The indications for P.A.B in these study were:

In group I, II, the indication of Bonding in these patients were, small body weight ( less than 50% expected for age age and sex). with C.H.F, failure to thrive, repeated chest infection major G.T.T problem with very bad general condition. Multiple V.SDS, or associated lesion as coarctation of the Aorta.

### In group III:

The indication for P.A.B in pts with single ventricle with unprotected pulmonary circulation with C.H.F with failure of medical treatment and as a step for preparation for Glenn's shunt then fontan procedure later an: Echo cardiography was performed for every patient before discharge from the hospital, after two month then every 6 months until the time of second surgical intervention for (V.S.D closure & debanding) or Glenn's operation in case of single ventricle.

Echo cardiographic examination was directed at:Site of Band, distance from pulmonary valve any migration or obstruction to pulmonary artery Branches, pressure gradient across the Band and direction of blood flow across the V.S.D.The patients who survived the procedure were followed up at our patient clinic for evaluation for signs of congestive heart failure, pulmonary hypertension in addition to follow up by serial Echo cardiography.

indication	Number	percent of patients
1 SEVER P++	210	84%
2 CHF	190	76%
3 REPEATED CHEST INFECTION	123	49%
4 CACHEIXA ,FAILURE TO THRIVE	105	42%
5 POOR GENERAL CONDITION	95	38%

**Table II :indication and preoperative ECHO evaluation of the patients**

### Preoperative echo readings :

	Preoperative echo readings	Pressure measurement	Mean value	Standard deviation
1	RV PR	55-95	69.50	12.69
2	PA PR	52-90	67.68	10.55
3	DELTA PR VSD	5-30	20.35	6.22

### Results:

This study was carried out on 250 patients who underwent P.A.B as an initial palliative procedure before definitive surgical repair.

Age of patients ranged from 3 months to 15 months with a mean of 9 months

While their body weight ranged from 3.5 kgs to 15 Kgs with a mean of 8.5 Kgs

They are divided into three group's:

Group I: (Patients with V.S.D, Big, V.S.D or multiple V.S.Ds ) with or without associated anomalies as coarctation of Aorta

Group II: (patients with complete atrio ventricular septal defect (C.A.V.S.D)

Group III:

( patients with single ventricle with unprotected pulmonary circulation )

In group III:

Patients with single ventricle with unprotected pulmonary circulation.Because if the patients were left to age of 6 months or one year,the pulmonary vascular resistance will increase and severe pulmonary hypertension will result . So we should band them as soon as possible before the age of 6 months.

In groupI:

Out of 150 cases ,there were a mortality of nine cases . Due to severe low cardiac out put. Or chest inflection or persistent failure . Debanding was done and inotropic support was added but without improvement .debanding was done based either on basis of the clinical deterioration in the general condition and cardiac function or on basis of transthoracic ECHO finding of a tight band (gradient more than 80 mmhg ).usually the debanding was in the ICU without transfer to the OR.the chest is opened and the band is released ,the chest is left open until clinical improvement .the debanding was done in 6 cases out of the nine mortalities .

In group II:

Out of 70 cases there were a mortality of 12 cases .

In group III:

Out of 30 cases there were a mortality of 2 cases .

in our series we had 23 mortalities among 250 cases as shown in table II

Group	Table number of cases	Mortality	%
Group I	150	9	6%
II	70	12	17%
III	30	2	6%
	250	23	9.2%

Table II

Postoperative Echocardiograph was done immediately before discharge, 2 months postoperatively and every 6 months during follow up. Till the time of definitive repair.

In Group I

it revealed satisfactory decrease in pulmonary artery pressure, gradient across the pulmonary artery ranged from 40 – 65 mm Hg in 130 patients

But it show loose Band in 15 cases ,2 of them underwent early V.S.D closure and debanding .

One case showed migration of the Band with RT pulmonary artery stenosis.

in 5 cases the band was found to be very tight ,these patients suffered low C.O.P and there clinical condition deteriorated

The general condition improved in 110 patients with no signs of congestive heart failure or chest infection And the patients started to gain weight very nicely according to their own age.

Cardiac catheterization and angiography was performed in 90 patients after definitive prolonged P.A.B before definitive repair for confirmation of the diagnosis and to diagnose any pulmonary artery distortion, and bifurcational stenosis by the band. In all of these 90 patients the cath showed no pulmonary artery problems and the band was situated in an optimal position.

Only 50 patients underwent pulmonary artery Debanding and V.S.D closure with 4 cases operative mortality. The period between P.A.B and P.A.D depending and V.S.D closure ranged from 12 months. To 24 months with a mean of 12 Months.

In Group III

Out of 30 patients 20 underwent glenn's operation with 2 cases mortality. The two patients died late postoperatively due to heart failure ,severe chest infection, and or severe pulmonary hypertension.usually the glenn was made in a period ranging from 20 -35 months with a mean of 30 months .

In group II :

Most of these patients went on low cardiac output and had a vey stormy postoperative period ,these group of patients had the highest mortality among the groups ,probably because the banding increased the av valve

regurgitation .

## Discussion

PA banding was once indicated in most patients with congenital heart defects with excessive pulmonary blood flow, and it contributed to improved outcome of various cardiac anomalies. However, the diagnostic subset of patients with excessive pulmonary blood flow has recently been treated by a one-stage operation, with satisfactory results [8]. Primary repair is expected to replace staged operation, because the latter is associated with risks and there is a high probability of death in the interval before subsequent repair. The complications of banding include erosion of the band into the pulmonary arterial lumen, distal migration with obstruction of the right or left pulmonary arteries, and pulmonary insufficiency secondary to dilation of the pulmonary annulus. Another concern in neonate patients with double-inlet left ventricle with minimal or no obstruction of the bulboventricular foramen and unrestricted pulmonary blood flow, is that PA banding may hasten the development of subaortic obstruction by reducing the ventricular volume and inducing progressive ventricular hypertrophy [9]. Currently, early primary repair is the treatment of first choice for congenital cardiac defects. Palliative operations play a smaller role and are indicated in fewer patients. Isolated ventricular septal defect has been treated by primary repair with a very low operative mortality rate. However, we still prefer to perform PA banding for patients with multiple or apical muscular ventricular septal defects, and also for patients with ventricular septal defect with complex extra cardiac congenital anomalies. Some groups advocate early primary correction of atrioventricular septal defects [10]. Gu<sup>n</sup>ther and colleagues [11] reported that the operative mortality in patients who underwent primary repair decreased from 17.6% (during 1974 to 1979) to 5.0% (during 1990 to 1995), despite an increase in the number of patients younger than 6 months. However, they also identified patients who were younger than 6 months old as an incremental risk factor. The mortality among these young patients was 18.2%. Although survivors of banding still have an increased risk of death in the interval before subsequent repair, we believe that PA banding has some advantages for these diagnostic groups of patients, especially in those with very low weight, atrioventricular valve abnormality, and unbalanced ventricles. The particular problem of aortic coarctation associated with ventricular septal defect has been dealt with differently in recent years. It has been proposed that the coarctation alone be repaired without PA banding, and that the ventricular septal defect be closed in a second operation or

be allowed to close spontaneously [12]. Even one-stage repair has been advocated recently [13]. Haas and colleagues [13] documented their results of primary repair of aortic arch obstruction with ventricular septal defect in pre-term and low birth weight infants concluded that early repair was associated with good results. The overall hospital mortality rate was 14% (3 of 21). Most of the deaths were related to residual obstructive lesions of the left ventricular outflow tract or the aorta, which led to congestive heart failure. The present approach in specialized centers is to perform complete repair during infancy for patients with such anomalies as transposition of the great arteries with ventricular septal defect, double-outlet right ventricle with subaortic ventricular septal defect, or truncus arteriosus [14]. However, other groups have not had similar success [15–16]. The majority of patients with single ventricle physiology with excessive pulmonary blood flow, who are eventually candidates for a Fontan-type operation, should be initially treated by PA banding. Another important indication for this operation is morphologic left ventricular retraining in patients with transposition of the great arteries, in patients with prior atrial switch operation with transposition of the great arteries, and in patients with congenitally collected transposition of the great arteries. This is a relatively new indication that has recently become the focus of our attention [17]. Most deaths were related to sepsis or congestive heart failure. Some of the deaths could be attributed to concomitant extracardiac anomalies or chromosomal abnormalities. However, the rest of the deaths were related to the procedure itself. The congestive heart failure may have been caused by residual obstructive lesions in the left ventricle or the aorta, or by inadequate tightness of the band. To decrease the mortality, we need careful management of extracardiac anomalies in the patients, complete repair of obstructive lesions in the left heart system, and modification of the procedure. The circumference of the band was mainly determined using the modified Trusler and Mustard's [7] formula, and it was adjusted according to the pulmonary artery pressure as previously described. However, measurements of the pulmonary artery pressure were carried out in an anesthetized and mechanically ventilated patient with an open chest, and the physiology was clearly quite different from that in an awake and spontaneously breathing child. In fact, the intraoperative PA pressure decreased to approximately a third of the systemic pressure in most patients. Some modification, such as the development of an adjustable band, would be needed to achieve appropriate tightness of the band [18–19].

In this series, the main bulk of the work was in pa-

tients having V.S.D and A.V.S.D lesion which is quite different with what is been written in literature nowadays. In most of the recent published series, the indication for P.A.B in V.S.D or A.V.S.D patients were limited only to patients with multiple muscular V.S.D.S, patients with V.S.D and severe aortic coronation or in patients with associated general anomalies or diaphragmatic hernia or G.I.T anomalies. (2), apart from these indications.

The V.S.D closure and A.V.S.D repair is the treatment of choice now in the majority of pediatric cardiac center all over the world. yet in Egypt as in third world countries, We are faced with a group of V.S.D and A.V.S.D patients referred to surgical consultation in a very bad shape, severe cachexia, severe chest infection and severe malnourishment, and we found that open heart surgery and primary V.S.D or A.V.S.D repair carries a very high mortality in such kids which can reach up to 50%. for these local Egyptian reasons and unsolved problem, we preferred to modify these indication for P.A.B to include some children with severe pulmonary hypertension who are at a high risk for primary repair.

- In the present series, we operated upon a small body weight kids with severe cachexia starting from 3-6 kgs and we found that recovery of these kids were remarkable especially if a good Band is applied and by following up of these kids. After the banding we found that the body weight curve after the Band was encouraging.

Our study had some limitations. First it was a retrospective study, whereas, a prospective study comparing primary repair and staged repair using PA banding would be ideal. Second, because many patients in groups 1 and 2 were lost to follow-up after the banding operation, the long-term morbidity and mortality could not be addressed. In conclusion, despite the recent advances in cardiac operations, we found no improvement in the early mortality of PA banding. PA banding as a measure for left ventricular retraining is the procedure of choice for a selected subset of patients. As for conventional indications, early primary repair may be more beneficial. However, PA banding could be performed even in small neonates with an early mortality rate around 10%. We believe that PA banding still has some role in the treatment of congenital cardiac anomalies.

Currently most if not all patients with isolated VSD are receiving primary repair if they are more than 4 kg body weight or 3 to 4 months old at Ain Shams University hospitals .



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## AORTIC ROOT REPLACEMENT WITH A PULMONARY AUTOGRAFT IN INFANTS AND CHILDREN

K.Samir,MD.,  
A.Ammar,MD.,  
T.El-Ghobary,MD.,  
H.Ashor,MD.,  
D.Metras,MD.

**Background:** The choice of a valve to replace a diseased aortic valve can be a difficult decision that vary according to factors related either to valve pathology and configuration or the patient characteristics. The use of allografts for aortic valve replacements in young patients was popular but limited by its short durability in this age group. The Aim of this work is to determine and evaluate the mid and long term results of the aortic root replacement by a pulmonary autograft in infants and children.

**Methods:** Between 1996 to 2005, 32 patients had aortic root replacement with a pulmonary autograft, The operation was an emergency in 2 patients (6.3%) due to aortic valve endocarditis. we used the usual surgical technique reported by Ross. The largest implantable allograft was always chosen. All patients had trans-oesophageal echocardiographic examination before discharge, trans-thoracic examination every 3 months in the first year then annually afterwards.

**Results:** There was no hospital mortality. The mean aortic clamping time was 124 minutes (97-157), the mean cardiopulmonary bypass duration was 146.8 minutes (139-183), the mean hospital stay duration was 11.8 days (7-23). The allograft diameter used in the RVOT position ranged from 17 to 25 mm. The average follow up time was 43 months (8-96). All the patients are in good hemodynamic condition: 27 (84.4%) in NYHA class I and 5 (15.6%) in class II. The last echocardiographic follow up findings, neo-aortic valve function as well as the changes in the homografts inserted in the pulmonary position shows no AS and minimal gradient. The follow up echocardiographic examinations showed gradual increase in the transannular diameter of the autograft .

**Conclusion:** The replacement of the aortic valve with the pulmonary autograft is a safe technique in infants and children. The Ross technique provides the possibility of growth of the autograft with no need for anticoagulation. The mid and long term follow up shows good neo-aortic valve and left ventricular functions. Using the largest possible diameter can minimize the effect of degeneration of the allograft inserted on the RVOT.

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Address reprint request to : Dr Khaled Samir

Departement of cardiothoracic surgery  
Ain Shams university.

Email : jegyptscts@gmail.com

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**T**he choice of a valve to replace a diseased aortic valve can be a difficult decision that may vary according to factors related either to the valve pathology and configuration or the patient characteristics as regard the age, sex, body mass, activity and others. The use of allografts for aortic valve replacements in young patients was popular but limited by its short durability in this age group. Donald Ross introduced the replacement of the aortic root by a pulmonary autograft in the year 1967. (1)

The international community of cardiac surgery only started to recognize

the value of the technique 20 years later after the publication of its long term follow up result.(2)

The prosthetic valves remain the most commonly used for aortic valve replacement in the young especially in the developing countries despite its disadvantages including its size in relation to body growth, the possibility of endocarditis and the need for anticoagulation.

The Ross operation has many advantages compared to the other options: No need for anticoagulation, Possibility of growth of the autograft, less incidence of endocarditis, Durability of the autograft and Near normal hamodynamics.

#### Aim of the work:

To determine and evaluate the mid and long term results of the aortic root replacement by a pulmonary autograft in infants and children.

#### Methods:

From 1996 to 2005, 32 patients had aortic root replacement with a pulmonary autograft in the children's hospital - university of Marseille- France. The patients' characteristics are listed in table 1.

The operation was an emergency in 2 patients (6.3%) due to aortic valve endocarditis.

The surgical technique: All patients had conventional sternotomy, normothermic or light hypothermic cardiopulmonary bypass, antegrade intermittent warm blood cardioplegia (every 20 minutes), the pulmonary autograft was harvested and preserved in patient's blood, pulmonary allograft preparation, cardioplegic arrest, removal of the aortic root with preservation of the coronary buttons, implantation of the autograft, reimplantation of the coronaries and finally implantation of the pulmonary allograft in the pulmonary position.

The technique of implantation of the autograft was by multiple short continuous nonabsorbable monofilament sutures proximally and a single continuous suture distally while continuous sutures were used for the allograft implantation. The largest implantable allograft was always chosen.

All patients had trans-oesophageal echographic examination before discharge, trans-thoracic examination every 3 months in the first year then annually afterwards.

Variable	value
Age (month)	2.5 – 180 months, mean 73.2, 5 patients<12 months
Body weight (kg)	4.9 - 63 kg, mean 26.7, 5 patients < 10 kg
Sex	8 females, 24 males
Diagnosis	Congenital AS: 24 patients (75%) Rheumatic AVD: 3 (9.5%). Aortic valve endocarditis: 3(9.5%) Congenital AR: 2(6%)
Associated anomalies	subaortic stenosis in 7. neonatal aortic coarctation in 2. MR in 2. VSD in 1. Sinus of Valsalva aneurysm in 1. Para aortic false aneurysm in 1.
Previous operations	Aortic commissurotomy in 11. Balloon valvotomy in 4. Subaortic membrane resection 2. AVR by homograft in 2. VSD repair with aortic repair in 1.

**Table 1: patient characteristics**

#### Results:

There was no hospital mortality. The mean aortic clamping time was 124 minutes (97-157), the mean cardiopulmonary bypass duration was 146.8 minutes (139-183), the mean hospital stay duration was 11.8 days (7-23). The allograft diameter used in the RVOT position ranged from 17 to 25 mm. The average follow up time was 43 months (8-96). Associated surgical maneuvers are listed in table 2.

Associated maneuvers	No. of patients
LVOT enlargement (Konno)	4
Mitral valve repair	2
Subaortic membrane resection	1
Supramitral membrane excision	1
Repair of aorto-mitral disruption	1
Total	9

**Table 2 associated surgical maneuvers**

There was 2 reopenings: one for immediate postoperative bleeding and a pacemaker insertion for complete postoperative heart block in a patient with recurrent subaortic stenosis. There was 2 late reoperations; the first for recurrent subaortic stenosis (recurrence for the 3rd time) where a transinfandibular approach was used to create a longitudinal subaortic VSD that was repaired by a patch to enlarge the LVOT and the second for pseudo-

aneurysm of the proximal anastomosis of the autograft 8 months postoperatively. All the patients are in good hemodynamic condition: 27 (84.4%) in NYHA class I and 5 (15.6%) in class II. The last echocardiographic follow up findings, neo-aortic valve function as well as the changes in the homografts inserted in the pulmonary position are listed in table 3. the follow up echocardiographic examinations showed gradual increase in the transannular diameter of the autograft that was comparable with the expected diameter for age and body surface area shown in the Great Ormond Street normalized diameters; 28 (87.5%) patients have transannular diameters exceeding the expected for there body surface area and only 4 (12.5) had diameters less than the expected. The gradient on the allograft is also shown in table 3 and its relation with the allograft diameter is clearly expressed by diagram 1.

focus	Echocardiographic finding	No.
Neo-aortic valve	Aortic stenosis	0
	Competent valve	25 (78.1%)
	Grade I insufficiency	7 (11.9%)
	Grade II, III, IV	0
	Transannular diameter (mean)	14-29mm(22)
Allograft	Gradient <20 mmHg	29 (90.6%)
	Gradient 25-35 mmHg	3 (9.4%)
	Gradient > 35 mmHg	0

Table 3: Echocardiographic findings

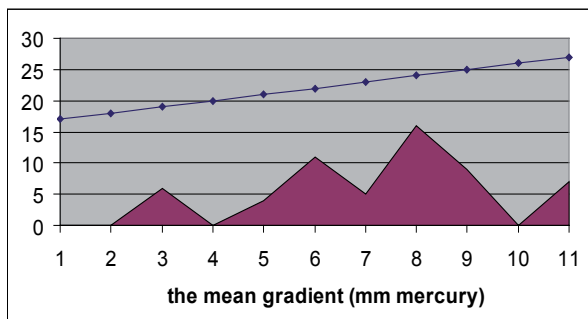


Diagram 1: the relation between the mean gradient and the diameter of the allograft on the RVOT

### Discussion:

The results of the replacement of the aortic root by a pulmonary autograft were studied by different work groups. Stienbruchel and his colleagues have studied the blood speed and turbulence at the level of the pulmonary autograft in the aortic position compared to those who had aortic valve replacement using a metallic valve and the found that the turbulence energy on the autograft is much less if compared to the metallic valve. (3) Santini and associates presented a comparative prospective

study of 70 patients: 37 had aortic root replacement by a pulmonary autograft and 33 had replacement by an aortic allograft. The mean follow up time was 16 months and their conclusion was in favor of the Ross procedures despite its technical difficulty with cautious follow up for the degeneration of the allograft used in the pulmonary position. (4) Long term results in adult patients shows the durability of a competent well functioning pulmonary autograft in the aortic position for more than 20 years. (2) The long-term exposure of the pulmonary autograft to the relatively systemic pressure doesn't lead to tissue necrosis or aortic insufficiency that if happens is usually due to annular dilatation or intraoperative microscopic injuries and perforations of the valve cusps due to technical deficiency or latent effect of endocarditis rather than valve malfunction as suggested by Joyce and associates. (5) Our results showing an increase in the transannular diameter of the autograft and suggesting

its growth, are supported by the study of Kreitmann and colleagues who proved by histological examination the growth of an autograft implanted in an infrarenal aortic position in the rabbits. (6) The change in the neo-aortic diameter was studied by Hokken and colleagues showing a clear increase in both the transannular diameter and the sinotubular diameter starting as early as the 10th postoperative day and progress rapidly for a few months before slowing down without causing neo-aortic incompetence. (7) Rubay and Hokken independently studied and concluded the improvement of the left ventricular function in most of the patients having the Ross operation. (8) Dore and his team were the first to report the safety of pregnancy and labour in females after being subjected to the Ross operation. (9) Al-Halees and associates published excellent results for 78 patients of the same age group with more percentage of rheumatic pathology. (10) Very promising research projects in the last few years came with the possibility to create autografts using tissue culture and the results of its implantation in animals was first reported by Shinoka and associates with promising results. (11)

### Conclusion:

The replacement of the aortic valve with the pulmonary autograft is a safe technique in infants and children. The Ross technique provides the possibility of growth of the autograft with no need for anticoagulation. The mid and long term follow up shows good neo-aortic valve and left ventricular functions. Using the largest possible diameter can minimize the effect of degeneration of the allograft inserted on the RVOT.

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## PREDICTORS OF MORTALITY IN THORACIC TRAUMA

Amro R. Serag, MD.

***Background:*** Thoracic injury directly accounts for 25% of all trauma-related deaths and plays a major contributing role in another 25% of trauma deaths. Identification of patients at risk may lead to a better quality of care. The aim of this study was to identify the independent risk factors of mortality in patients with chest trauma admitted into a thoracic surgical unit of a teaching university hospital.

***Methods:*** Two hundred and fifty patients with a primary diagnosis of chest trauma consecutively admitted to Cardio-thoracic Surgery Department-Tanta University Hospital were candidates for the study. The recorded data of the study subjects included age, gender, type of trauma, outcome (survival or death), intrathoracic injuries, associated extrathoracic injuries, hemodynamic status on admission, need for mechanical ventilation, management, length of hospital stay (LOS) and injury severity score (ISS).

***Results:*** The male to female ratio was 7:1. One hundred and sixty eight patients (67.2%) sustained blunt trauma and 82 patients (32.8%) sustained penetrating trauma. The incidence of mortality was 11.6%. Univariate analysis identified type of trauma, ISS, isolated fracture ribs, associated head and neck injuries and need for mechanical ventilation as predictors of mortality in chest trauma. However, ISS and need for mechanical ventilation were independently associated with mortality on multivariate analysis

***Conclusions:*** Changes in the care of patients with chest trauma based on review of complications and identification of independent risk factors of mortality may ultimately lead to focusing research, education, and resource allocation in a more targeted manner to reduce trauma death.

**T**rauma is a major health problem and a leading cause of mortality with an incidence of traumatic death ranging from 10-40 %.(1) Thoracic injury is often a component of major multisystem injuries. It directly accounts for 25% of all trauma-related deaths and plays a major contributing role in another 25% of trauma deaths.(2,3)

Because the degree of thoracic injuries range from brief, uneventful complications to critical conditions, early accurate assessment of the patient's condition and prediction of mortality is often difficult. While much of the mortality in patients sustaining serious thoracic injuries is a direct result of trauma itself, several other factors contribute to death in chest trauma. Outcome predictors of patients with thoracic injury have been described, which included advanced age,(4) the presence of co-morbidities,(5) numbers of units of blood transfused, oxygenation ratio (PaO<sub>2</sub>/FIO<sub>2</sub>) on admission,(6) pulmonary con-

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Address reprint request to : Dr Amro R.

Serag

Department of Cardiothoracic surgery,

Faculty of Medicine, Tanta University,

Egypt

Email : amroserag@yahoo.com

Codex : 05 / other / 10 / 0707



tusion,(7) Glasgow Coma Scale (GCS),(8) need for mechanical ventilation,(7) trauma score (1,6) and Injury Severity Score (ISS).(1,8) However, for effective therapeutic management, independent risk factors of mortality must be identified.

The aim of this study was to identify the independent risk factors of mortality in patients with chest trauma admitted into a thoracic surgical unit of a teaching university hospital.

### Methods:

Two hundred and fifty patients with a primary diagnosis of chest trauma consecutively admitted into the cardiothoracic surgery department –Tanta University Hospital between January 2003 and December 2005 were candidates for the study. This group of patients comprised 219 males (87.6%) and 31 females (12.4%) with a mean age of  $28.6 \pm 17$  years (range 1.5-75 years).

The recorded data of the study subjects included age, gender, type of trauma (blunt or penetrating), outcome (survival or death), intrathoracic injuries (pneumothorax, hemothorax, hemopneumothorax, fracture ribs and sternum), associated extrathoracic injuries (head and neck, abdominal, pelvic or extremity fractures), hemodynamic status on admission (shock was defined as a systolic blood pressure below 90 mmHg), need for mechanical ventilation, management, length of hospital stay (LOS) and ISS.(9)

ISS was defined as the sum of the squares of the highest Abbreviated Injury Scale (AIS) (10) grade in each of the three most severely injured areas.(11)

Plain chest radiographs were available for all patients so that a diagnosis of pleural and pulmonary parenchyma involvement could be established. Computed tomography (CT) of the chest was not available for all patients. Complementary tests were ordered during a patient's hospital stay as needed based on clinical course.

### Statistical analysis:

The continuous data in this study were expressed as mean  $\pm$  standard deviation and categorical data were expressed as frequency and percentage. By univariate analysis, the in-between group differences in patients who survived or died were assessed by the unpaired Student's t-test for continuous variables and Chi-square test for categorical variables.

Independent variables: (age, type of trauma, intrathoracic injuries, associated injuries, ISS, presence of shock on admission, need for mechanical ventilation and need for emergency surgery) with  $p < 0.1$  in univariate analysis were put into a forward stepwise multivariate logistic regression analysis with death as the dependent

variable. The goal was to determine which variables were independently associated with mortality in chest trauma.

All statistical tests were two-tailed and statistical significance was defined as  $p < 0.05$ .

### Results:

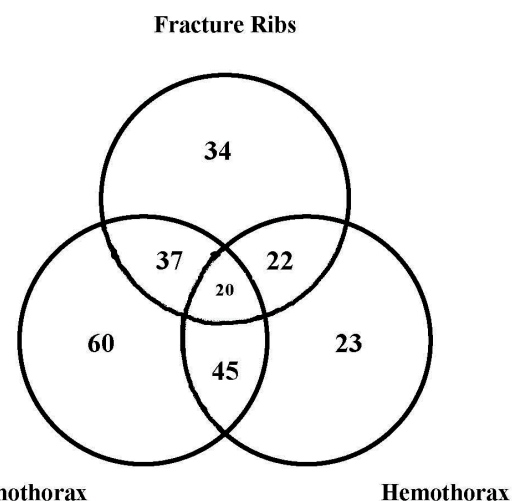
One hundred and sixty eight (168/250 – 67.2%) were the result of blunt injuries. Eighty two (82/250 – 32.8%) were due to penetrating injuries.

The mean age in patients with blunt trauma was  $31.8 \pm 19.2$  years while it was  $22.1 \pm 8.1$  years in patients with penetrating chest trauma.

### Chest injuries:

Rib fractures were present in 113/168 (67.2%) of patients with blunt trauma and the incidence of isolated rib fractures was 20.2% (34/168). Significant intra-thoracic injuries occurred without rib fracture in 55/168 (32.8%) of patients with blunt trauma.

Considering the whole group of patients, the most frequent isolated injury was pneumothorax (60/250) with an incidence of 24% followed by fracture ribs that occurred in 34/250 (13.6%) of cases. Hemothorax was least common as a solitary injury (23/250 – 9.2%). The previous injuries occurred also in groups of two or more lesions in a single patient in 124/250 (49.6%) cases and this is well illustrated in (Fig.1).



**Figure 1:** Venn diagram showing distribution of intra-thoracic injuries

### Associated injuries:

The distribution of associated injuries among the

whole group is illustrated in figure 2. They occurred in 118/250 (47%) of patients. Head injury alone (occurring in 32/118) accounted for 27.1% of associated injuries, abdominal injury accounted for 36.4% (43/118) and orthopedic injuries for 24.5% (29/118) while affection of more than one extra-thoracic system occurred in 13 cases (11%). The mean ISS for the group with associated injuries was  $26.5 \pm 8.9$  compared to ISS of patients with isolated thoracic injuries ( $10.2 \pm 2.8$ ) ( $p < 0.0001$ ). Associated head, abdominal or orthopedic injuries almost tripled the ISS and resulted in 12 fold increase in hospital mortality compared to patients with isolated chest injuries.

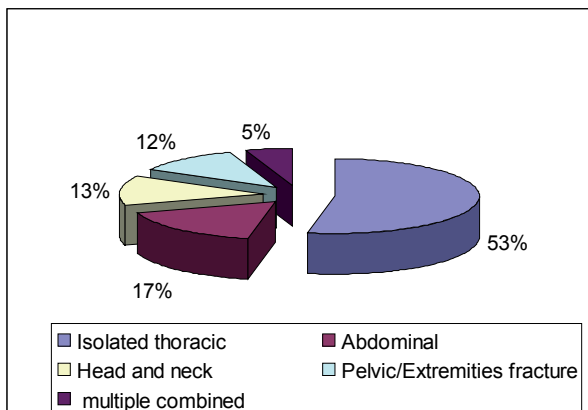


Figure 2: Distribution of isolated thoracic and thoracic associated with extra-thoracic injuries

### Management:

Thirteen patients/250 (5.2%) were managed conservatively. Intercostal drains were inserted in 228/250 patients (91.2%) and it was bilateral in 11/228 (4.8%) patients. Only 9/250 (3.6%) patients required emergency thoracotomy for chest trauma, in 5 with penetrating injuries and in 4 with blunt injuries. The reasons for interference were significant hemo-pericardium in 4 patients and massive hemothorax in one patient with penetrating trauma, massive hemothorax in one patient, repair of rupture diaphragm in 2 and repair of bronchial injury in one after diagnosis by bronchoscopy in cases of blunt trauma. Eight cases underwent delayed thoracotomy for decortication in 7 and repair of rupture diaphragm in another one.

Thirty three patients had laparotomy, in 3 of them, it was combined with thoracotomy.

Nineteen cases received endotracheal intubation and ventilatory support with an overall incidence of mechanical ventilation of 7.6% (19/250). Of all 32 patients with

head injury, 14 were intubated (43.7%) compared to 2 of 132 (1.5%) patients who had isolated chest injury and one of 43 (2.3%) who had associated abdominal injuries. Two patients/13 (15.4%) with multiple associated injuries required mechanical ventilation.

### Mortality:

Twenty six patients from the study group died, 25 with blunt trauma, and one with penetrating injury yielding a mortality rate of 11.6%.

Table 1 shows comparison between survivors and non-survivors. Univariate analysis of variables in both groups identified type of trauma, ISS, isolated rib fractures, associated head injury and need for mechanical ventilation as predictors of mortality in chest trauma in our cohort of patients. However, multivariate analysis identified ISS and need for mechanical ventilation as independent predictors of mortality (Table 2).

	All patients (n=250)	Survivors (n=224)	Non survivors (n=26)	p
Gender M/F	219/31	198/26	21/5	0.26
Age (yr)	28.6±17	28.3±16.4	31.4±21.7	0.38
Type of trauma (Blunt/Penetrating)	168/82	143/81	25/1	0.001*
ISS	17.9±10.4	16±8.5	34±10.9	0.001*
Intra-thoracic injuries n(%)				
Isolated pneumothorax	60 (24)	55 (24.5)	5 (19.2)	0.5
Isolated fracture ribs	34 (13.6)	25 (11.2)	9 (34.6)	<0.001*
Isolated hemothorax	23 (9.2)	21 (9.4)	2 (7.7)	0.7
Combined	124 (49.6)	115 (51.3)	9 (34.6)	0.1
Extra-thoracic injuries n(%)				
Abdominal	43 (17.2)	40 (17.8)	3 (11.5)	0.41
Head and neck	32 (12.8)	17 (7.6)	15 (57.7)	<0.0001*
Pelvic/extremities fracture	29 (11.6)	27 (12.1)	2 (7.7)	0.5
Multiple	13 (5.2)	9 (4)	4 (15.4)	0.18
Shock n(%)	54 (21.6)	45 (20.1)	9 (34.6)	0.08
Mechanical ventilation n(%)	19 (7.6)	4 (1.8)	15 (57.7)	0.001*
Emergency Surgery n(%)	52 (20.8)	46 (20.5)	6 (23.1)	0.76
LOS (days)	13.7±11.9	13.5±12	12.9±12.7	0.79
Outcome				
Mortality n(%)	26 (11.6)			

Table 1: Univariate analysis of variables between survivors and non-survivors

\* Significant

Variable	Wald X2	P
Type of trauma	1.093	0.24
ISS	7.325	0.007*
Fracture ribs	0.972	0.65
Associated head and neck injuries	1.265	0.16
Mechanical ventilation	24.923	0.001*

**Table 2: Multivariate analysis of variables associated with mortality in chest trauma**

\* Significant

## Discussion

In this study, we identified ISS and need for mechanical ventilation as independent risk factors of patient mortality in chest trauma compared with other variables. These findings are in agreement with previous studies.(1,7,8,12)

Severity scales to characterize the nature and extent of injury are important adjuncts to trauma care systems, trauma research and many of the elements of a complete public health approach to injury.(13) However, there is mounting confusion as to which anatomic scoring systems can be used to adequately control for trauma case mix when predicting patient survival.(14)

In our study we used the ISS that was significantly different between survivors and non-survivors. The ISS in our mortality cases was  $34 \pm 10$  that is similar to previous reports, which were  $35 \pm 10$  and  $32 \pm 10$ , respectively.(6,8) ISS has been reported to be associated with prognosis in patients with chest trauma, (1,12) and it was a major determinant of mortality in our study.

When compared with Kollmorgen et al (6) report, our study had a lower intubation rate (7.6 % vs. 42%). The cause of mortality in patients requiring mechanical ventilation is debated. Crude mortality rates approximating 20% have been reported for trauma patients with ventilator associated pneumonia (VAP) that is a common infection among patients in trauma ICU.(15) It has been suggested by different investigators that VAP is an indicator of injury severity and not necessarily associated with mortality. Most studies have involved the most severely injured patients, making it difficult to determine the relative contribution of either VAP or injury severity to death. However, there is a need for effective diagnostic techniques of VAP so that adequate therapy may be initiated. (16)

Univariate analysis of our results indicated that type of trauma (blunt), diagnosis of rib fractures and associated head and neck injuries were predictors of mortality in chest trauma.

Review of literature revealed conflicting results regarding which type of thoracic trauma (blunt vs. penetrating) that determine mortality. This study showed that the presence of blunt trauma adversely affect mortality after thoracic injuries. In addition, it is necessary to investigate the causes and patterns of injuries resulting from blunt trauma for effective prevention.

Combined intra-thoracic injuries were the most common injuries encountered. Isolated fracture ribs came third in rank as it was as likely to occur in 13.6% of cases. For those patients admitted to hospital with identified rib fractures, there is a trend towards higher mortality and morbidity.(17) The risk of complications increases with age and cardiopulmonary disease.(5) This results in readmission to the hospital and intensive care unit and prolonged length of hospitalization. Also, there is an apparent increased risk of death with more fractured ribs and therefore several investigators adopted a standardized surgical management plan for ribs fixation aiming to reduce the risk of death in this patient group.(18) Considering all patients with rib fractures in this study, the incidence of fracture ribs was 45.2% (113/250) that reached 69.2% (18/26) in non-survivors and subsequently it was found as a predictor of mortality in our patients with chest trauma.

Of note, previous investigators (17, 19) showed that association of fracture ribs and morbidity and mortality is better predicted by age and ISS.

There was a significant difference of head and neck injuries between survivors and non-survivors. Head injuries caused most deaths in this study, an observation also, noted by others.(20) This supports the view that the main determinants of prognosis in chest trauma are the presence of associated injuries, not chest injuries alone.(21)

Successful treatment of chest trauma largely depends on the accurate and rapid diagnostic work-up, as well as the adequate surgical management. According to our results, most patients with chest injury can be treated conservatively with close observation and tube thoracostomy. However, 16.8% (42/250) of cases required definitive emergency surgery. In fact, emergen-

cy laparotomy rather than thoracotomy was the major surgical procedure for our patients. Thoracic operations are indicated only for specific circumstances. When patients require both thoracotomy and laparotomy, a surgical decision must be made as to which problem area should be dealt with first. There are no easy or rigid guidelines in this situation. However, prompt intervention is required to reduce morbidity and mortality and ensure optimal outcome.

### Conclusions:

ISS and need for mechanical ventilation independently predict mortality in our patients with chest trauma. Changes in the care of patients with chest trauma based on review of complications and deaths may ultimately lead to focusing research, education, and resource allocation in a more targeted manner to reduce trauma death.

### Acknowledgement:

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## A COMPARISON OF TREATMENT OPTIONS IN PEDIATRIC EMPYEMA

Ibrahim B. M. MD,  
Attia A.MD,  
Wahby E.MD,

**Background:** The optimal management of empyema in children remains controversial and currently there is insufficient evidence to give clear guidance on therapy.

**Methods:** This study was conducted on 47 patients who needed surgical consultation for empyema thoracic in the cardiothoracic surgery department, Tanta university hospitals.

**Results:** The age incidence ranged from 0.42 – 18 years with 34 male and 13 female. The patients were divided into 4 groups depending on the treatment received: The most common presentations of the patients were fever, cough, dyspnea, tachypnea and chest pain. The formal decortication was associated with statistically significant decrease in the length of the stay, the postoperative febrile period and the ICT duration.

**Conclusion:** Open thoracotomy remains an excellent option for management of multiloculated empyema in children, when open thoracotomy is performed in a timely manner there is low morbidity and it provides rapid resolution of symptoms with a short hospital stay.

Despite continued improvement in medical therapy, pediatric empyema remains a challenging problem for the surgeon.

Multiple treatment options are available, however, the optimal therapeutic management has not been elucidated. (Cemal O, Refik ü, Serdar O, Zerrin O, Ilhan I and Omer S., 2005) (1)

As outlined by Mayo P, Saha S and McElvein R., 1982 (2) the goals of treatment in patients with pediatric empyema are to (1) save life, (2) eliminate the empyema, (3) reexpand the trapped lung, (4) restore mobility of the chest wall and diaphragm, (5) return respiratory function to normal, (6) eliminate complications or chronicity, and (7) reduce the duration of hospital stay.

Available treatment options include thoracentesis, tube thoracostomy, image directed pleural catheters, intrapleural fibrinolytics, thoracoscopic drainage, and thoracotomy with decortication (Eren N, özçelik C, Ener B, özgen G, Solak H, Balcı A, and Ta S, 1995) (3)

Treatment measures are often used in a stepwise manner. The role of primary operative therapy has yet to be determined. (Jeffrey R, Bryan G, Robert S, and David R, 2004) (4)

Streptokinase (SK) and Urokinase (UK) are used as thrombolytics. SK is a streptococcal exotoxin. It becomes plasmin activator after combining with plasminogen. When inactive plasminogen is cleaved, plasmin is generated. Plasmin hydrolyzes fibrin leading to hydrolysis of fibrin coagulum. (Himeiman R. et al., 1986) (5)

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Address reprint request to : Dr Ibrahim  
B.M.

Department of cardiothoracic surgery  
Faculty of Medicine Tanta University

Email : jegyptscts@gmail.com

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The use of fibrinolysis has been studied extensively as a way to treat fibrinopurulent or organized empyema without resorting to decortication. (Wells R and Havens P., 2003) (6)

The goal of fibrinolysis is to degrade fibrin, blood clots and pleural loculi to allow more complete drainage of the pleural space, effectively converting a fibrinopurulent or organized empyema into an exudate and forestalling development of pleural peel, thereby allowing antibiotics and chest tube drainage to work more effectively. (Rosen H, Nadkarni V and Theroux M., 1993). (7)

Thoracotomy has been used in the treatment of empyema for more than a century. Thoracotomy with decortication is a thoracic surgical procedure in which pus is evacuated from the empyema cavity and the pleural peel is resected or stripped of all fibrous tissue. For many years, surgeons considered open thoracotomy and decortication the definitive treatment for empyema. (Li E, Langer J and Dillon P., 2002) (8)

VATD is a less invasive means of decortication, involving placement of 2 or 3 trocars (one for video equipment and another for surgical tools) figure through small incisions in the thoracic wall and debridement of the pleura through the ports. (Grewal H, Jackson R and Wagner C., 1999) (9)

The prognosis in children with empyema is usually very good. (Gocmen A, Kiper N and Toppare M., 1993) (10)

Satish B, Bunker M and Seddon P., 2003(11) have shown that, despite the heterogeneity of treatment approaches, the majority of children make a complete recovery and their lung function returns to normal.

Sarihan H, Cay A and Aynaci M., 1998(12) reported minor abnormalities in lung function of both a restrictive and obstructive nature.

but the children were still symptomatic with normal exercise tolerance. (McLaughlin F, et al., 1984) (13)

The chest radiograph returns to normal in the majority of children (60–83%) by 3 months, in over 90% by 6 months, and in all by 18 months. (Chan P, Crawford O and Wallis C., 2000) (14)

This study aimed to assess the outcome of different management options of empyema thoracis in children

## METHODS

This study was conducted on 47 patients who needed surgical consultation for empyema during the period of study from June 2005 to January 2007, in cardiothoracic

surgery department - Tanta university hospitals.

Diagnosis of empyema was established based on a combination of physical examination, chest X-rays, and pleural fluid chemical and culture analysis. This study included all cases of parapneumonic effusion which needed surgical consultation for drainage. Cases of post-traumatic empyema or tuberculous empyema were excluded.

**On admission; Patients were subjected to the following:-**

(A) History taking:-

(B) Examination:-

- 1- General examination:
- 2- Chest examination:

(C) Investigations:-

- 1-Routine laboratory investigation
- 2-pleural fluid samples: were investigated for Gram stain, cultures and biochemical examination.

(D) Imaging study:

- 1- Chest x-ray:
- 2- Chest Ultrasoundography:

All patients underwent chest ultrasound evaluation by commercially available equipment (Hewlett-Packard Unit SONOS 5500/ USA) with imaging transducer 3.5MHZ and 7 MHZ.

- 3- CT chest study:

**Management options:**

**1- Tube thoracostomy:**

Closed tube thoracostomy is employed as a primary surgical maneuver when drainage is indicated  
Indication for drainage:

- 1-pleural fluid pH below 7.2.
- 2-pleural fluid glucose below 50mg /dl .
- 3- identification of bacteria using Gram's stain or culture.
- 4- presence of frank pus. (Light R.1995) (15)

**2-Intrapleural fibrinolytics:**

Fibrinolytic therapy was instituted when there was :

- 1- persistent radiographic evidence of effusion after 24-48 hours of ICT insertion.
- 2- a lower than expected tube output (based on previous imaging) despite appropriate positioned patent chest tube.
- 3- septated pleural fluid as appeared by ultrasoundography. or complicated-appearing fluid (debris or loculations ) on ultrasound scan.

Streptokinase 25,000 IU/kg in 100 ml saline was instilled intrapleurally via the chest tube and clamped for 4-6 h, The streptokinase was allowed to dwell in the pleural space for 4-6hour before re-attaching to suction. a total dose of 250,000 IU per instillation was never exceeded. and the amount of fluid drained was recorded every 12h, radiographic evaluation every 24 hours were followed. (Gülen E, Bekir H, Selami S, Aye T and Ufuk E. ,2004)

**3- decortication :**

Follow up:

Follow up of the patient was done before discharging from hospital. the time to a febrile period ,duration of the ICT and LOH was noticed.

The patients followed up clinically and radiologically every 2 weeks in the outclinic.

Patients could be categorized into four treatment groups:

Group I: chest tube drainage alone

Group II: chest tube drainage with intrapleural fibrinolytic therapy

Group III: chest tube drainage and surgery.

Group IV: primary operative management without chest tube drainage.

**Statistics:**

- values were expressed as mean ± SD. Comparison between groups and the results were analysed for significance utilizing the chi-square , a nova test and student t-test with statistical significance defined as p value <0.05.

**RESULTS**

This study was conducted on 47 patient who were categorized into 4 groups according to treatment modalities :

Group I : include patients who managed by intercostals tube drainage alone, they were 28 cases(59.57%).

Group II : include patients who managed by intercostal tube drainage plus fibrinolytic therapy, they were 9 cases(19.155%).

Group III : include patients who managed by intercostal tube drainage plus fibrinolytics treatment then decortecation was done, they they 3 cases(6.38%).

Group IV : include patients who managed by formal decortication, they were 7 cases (14.89%).

Two patients in group IV subjected to lobectomies, One had upper lobectomy and the other had lower lobectomy.

		Group I	Group II	Group III	Group IV	Total	Chi-square X2	P-value	
Sex	Female	N	7	1	1	4	13		
		%	25.00	11.11	33.33	57.14	27.66		
	Male	N	21	8	2	3	34	4.420	0.220
		%	75.00	88.89	66.67	42.86	72.34		
	Total	N	28	9	3	7	47		
		%	59.57	19.15	6.38	14.89	100.00		
Side	Rt	N	13	5	2	3	23		
		%	46.43	55.56	66.67	42.86	48.94		
	Lt	N	15	4	1	4	24	0.709	0.871
		%	53.57	44.44	33.33	57.14	51.06		
	Total	N	28	9	3	7	47		
		%	59.57	19.15	6.38	14.89	100.00		
Age	Range	0.42-13	2-5	5-9	1.42-18		F	2.451	
	Mean ±SD	2.44±2.93	3.58±1.05	5.33±2.30	6.84±6.69		ANOVA P-value	0.078	

Table 1: Summarize the demographic data in each treatment group.

		Group I	Group II	Group III	Group IV	Total	Chi-square X2	P-value	
echogenicity	Echogenic	N	13	7	3	7	30		
		%	46.43	77.78	100.00	100.00	63.83		
	not echogenic	N	15	2	0	0	17	10.907	0.018*
		%	53.57	22.22	0.00	0.00	36.17		
	Total	N	28	9	3	7	47		
		%	100.00	100.00	100.00	100.00	100.00		
Plural Fluid characters (U/S)	free	N	28	2	0	0	30		
		%	100.00	22.22	0.00	0.00	63.83		
	septated	N	0	7	1	0	8	75.026	<0.001*
		%	0.00	77.78	33.33	0.00	17.02		
	loculated	N	0	0	2	7	9		
		%	0.00	0.00	66.67	100.00	19.15		
Total	N	28	9	3	7	47			
	%	100.00	100.00	100.00	100.00	100.00			
pleural thickning	no pleural thickning	N	24	7	1	0	32		
		%	85.71	77.78	33.33	0.00	68.09		
	pleural thickning	N	0	0	1	4	5	28.185	<0.001*
		%	0.00	0.00	33.33	57.14	10.64		
	Total	N	24	7	2	4	37		
		%	51	14.8	4.2	8.5	78.7		

Table 2: Summerize the results of ultrasound finding revealed in each group..

**Management Options:**

A therapeutic procedure was performed in 47 patients which were categorized into 4 groups according to treatment option:

group I included 28 cases (59.57%), group II 9 cases (19.155%), group III 3 cases (6.38%) ,group IV 7 cases (14.89%)

An intercostal tube alone was placed in 28 patients (59.57%), chest tube with fibrinolytics in 12 (19.155%) patients and 3 (6.38%) patients had failed fibrinolytic treatment and needed thoracotomy ,formal decortication was performed in 7 patients (14.89%).

A comparison between patient who had fibrinolytic treatment( group II,III) was done by student t-test. ICT initial drainage ,pre instillation drained amount ( on the previous 24 hours of first time instillation ),post instillation amount ( within 24 hours) , the number of doses was compared and the results are shown in Table 11.

	Group I	Group II	Group III	Group IV	ANOVA	
					f	P-value
LOH	Range	5.0	9.0	14.0	8.0	6.752 <0.001*
		14.0	14.0	16.0	11.0	
	Mean	11.250	11.333	15.000	9.429	
	SD	1.974	1.732	1.000	1.134	
	Tukey>s test	I & II	I & III	I & IV	II & III	
	0.999	0.007*	0.093	0.019*	0.169	<0.001*
post oper febrile days	Range	1.0	4.0	4.0	2.0	2.962 0.043*
		8.0	8.0	7.0	6.0	
	Mean	4.411	6.111	5.667	3.714	
	SD	2.069	1.269	1.528	1.380	
	Tukey>s test	I & II	I & III	I & IV	II & III	
	0.088	0.675	0.805	0.983	0.060	0.421
ICT duration	Range	6	8	11	2	35.145 <0.001*
		11	13	19	6	
	Mean	9.03	9.66	14.33	3.85	
	SD	1.29	1.58	4.16	1.34	
	Tukey>s test	I & II	I & III	I & IV	II & III	
	0.735	<0.001*	<0.001*	<0.001*	0.00*	<0.001*

Table 3: Summarise treatment outcomes in each group

The results of our study showed no significant difference in the initial drainage and pre instillation amount of drainage between group II,III (p value 0.277 , 0.115 respectively) although the initial and pre-instilled amount

was higher in group II.

There was a significant increase in post instillation amount of drainage (P value 0.003 ) especially in group II which had mean amount 278.88 ml (range 180-400 ml /24 hours ) and group III mean amount 113.33 ml (range 90-150 ml/24h)

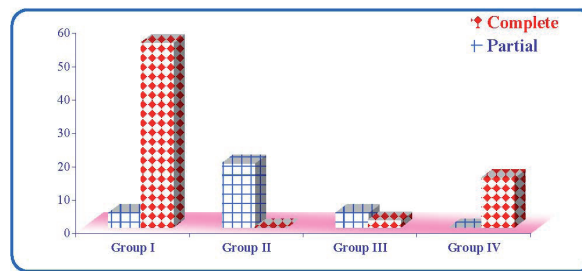


Figure 1: response to treatment in different groups.

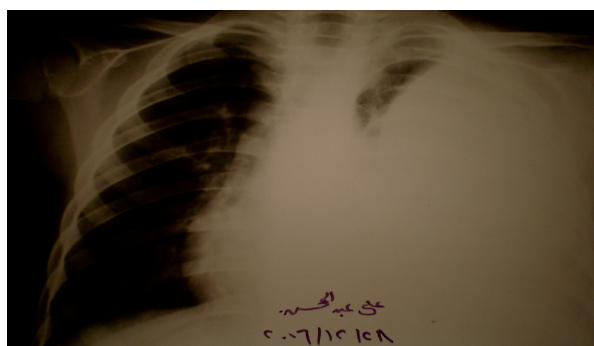


Fig 2 : PA-CXR on admission for a child in group III which demonstrate encysted effusion on the left side



Fig 3 : Chest Ultrasonography of The same patient in fig 2 showed multiloculated empyema .

Thoracic

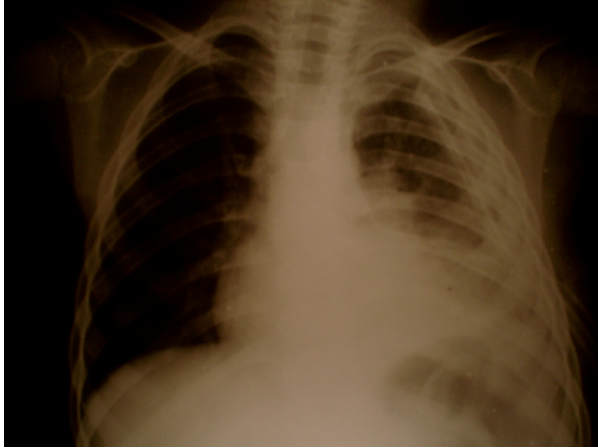


fig 4 : PA-CXR of the same child in fig 3 after streptokinase instillation

## DISCUSSION

The optimal management of parapneumonic effusions and empyema in children remains controversial and currently there is insufficient evidence to give clear guidance on therapy. The immediate objectives in the treatment of empyema are to eradicate persistent fever, to evacuate pleural contents, and to fully re-expand the lung. The long term objective is to prevent chronic lung damage. Gagliardini R , Martino A , Fabrizzi G , Pagni R, and De Benedictis F,2004. (16)

In our study, Closed tube thoracostomy is employed as a primary surgical maneuver when drainage is indicated in 40/47(85.11%) patients .

ICT drainage was sufficient treatment for empyema in 28 /47(59.57%) of the total cases and 28/40 (70%) of patients who had ICT drainage .

Meier et al., 2000(17) found that chest tubes placed in children with parapneumonic effusions resulted in the least morbidity and most cost-effective treatment.

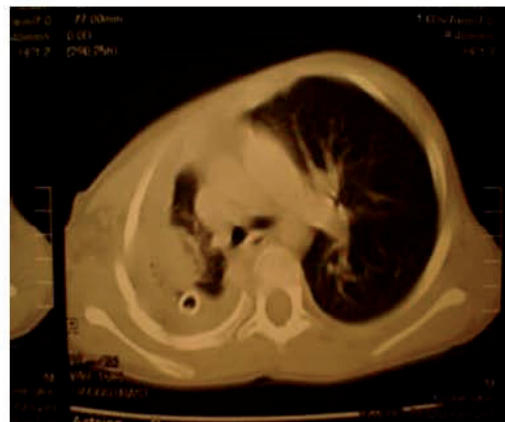
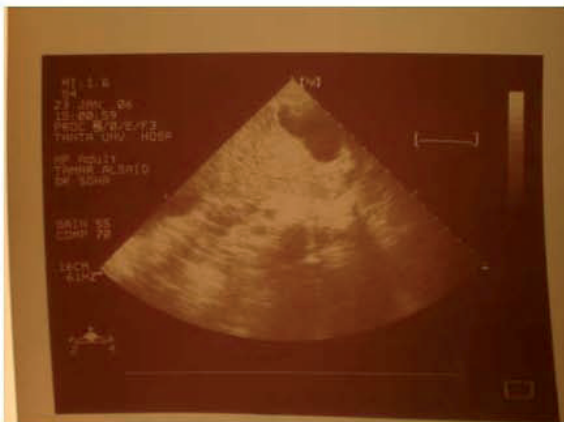


Fig 5 : A child aged 5 years (from group III) presented by fever ,chest pain,tachpnea and dysnea, ICT drainage was done , no improvment was noted neither clinically nor radiologically after ICT insertion , Streptokinase was tried for 4 doses after that no improvement was noted , Axial chest CT scan was done which revealed encyeted empyema and underlying lung collapse with pleural thickening.



Furthermore, Satish B and Seddon P., 1998(18) found that chest tube drainage and antibiotics alone were sufficient treatment for all 14 patients in their study; even those patients with pleural peel were clinically well after approximately 2 weeks of treatment. In our study, mean duration of chest tube in group I was 9.3 days (6-11 days)

One of the major criticisms of all-inclusive surgical approach we met in our study is that children who may otherwise respond to less-invasive therapies and how can you stratify these patients.

If persistent radiographic evidence of effusion after 24-48 hours of ICT insertion, a lower than expected tube output (based on previous imaging) despite appropriate positioned, patent chest tube, septated pleural fluid as appeared by ultrasonography, or complicated-appearing fluid (debris or loculations) on ultrasound scan, fibrinolytic therapy was instituted.

When we combined group II and III, 9 of 12 patients resolved with adjuvant fibrinolytics. In patients not improving with 48 hours, patient went for operative decortication. Using this approach, the overall surgery rate in our group of patients was 10/47, including those children who were thought to be operative candidates at the onset. This is the same work done by Robert G, et al 1997(19) who used the criteria listed above beside In our study, Of the 12 patients (12/47) who failed ICT alone, 9 patients (75%) managed successfully with fibrinolytic treatment.

failure rate was 25% (3 patients of 12). In failure group the ultrasound finding was revised retrospectively which revealed multiloculated empyema in 2 and one had, in addition, thickened pleura.

the suboptimal clinical response, to institute fibrinolytics.

This in agreement with Hilliard T, Henderson A and Langton H., 2003(20) who found that further fibrinolytics isn't warranted if no response within 48 hours. However, Cemal O, et al., 2005(1) reported that fibrinolytics may be used for 2-10 times.

Success rates of fibrinolytics in Jerjes C, Ramirez A and Elizalde J, 1996(21) study varied from 60 to 90%, this wide range explained in their study as outcome measures differ widely from length of stay to improved radiographic appearance.

Our results were supported by de Souza A, Offner P and Moore E, 2000(22) study who found those patients, who failed fibrinolytic therapy, at surgery had pleural peel in addition to multiloculated fluid collections. So they concluded that the presence of pleural peel is a contraindication to fibrinolytic therapy and an indication for proceeding directly to decortication.

In their study this finding was operative finding, but in our study the multiloculated and thickened pleura was ultrasonographic and/or CT findings.

We have found that one of the best predictors of success with fibrinolytic therapy is a "gush" of pleural fluid after the initial instillation of streptokinase. In Group II, mean amount of postinstillation drainage was 278.88 ml (180-400 ml) in the first 24 hours post instillation period.

But in Group III, mean amount of postinstillation drainage was 113.33 ml (90-150 ml).

On the contrary of our study as regards multiloculated empyema, Robinson L, Moulton A and Fleming W, 1994(23) have found that fibrinolytics instilled through chest tubes over the course of several days will clear loculated fluid collections and shorten hospital stays, often avoiding the need for further surgery.

From our results, inappropriate fibrinolysis should be avoided in multiloculated empyema and surgical intervention should not be delayed.

This is in agreement with Cemal O, et al., 2005(1) who reported that no role for delaying or avoiding open decortication when progression of the disease has occurred.

In their study they depend on the American Thoracic Society stages of empyema thoracis as a staging system and conclude that when late stage II is reached, multiloculations, decortication is the treatment of choice.

Open surgery should be undertaken in the confidence that meticulous technique results in early drain removal, rapid recovery, prompt hospital discharge, and complete resolution.

Our study was supported by Raveenthiran V. 2005(24) recommended early decortication in empyema thoracis even in asymptomatic patients as in such patients will silently suffer restrictive lung disease and abnormal spirometry.

In our study LOH, ICT duration and time to afebrile period was significantly shorter in patients had formal decortication in comparison with other modality of treatment. The mean LOH in Group IV was (9.42) days compared with Group I

(11.25) days, group II (11.33) and Group III (15) days.

The mean duration of ICT in group IV was (3.85) days which had significant decrease in duration between other groups.

In group IV the patients had the least time to afebrile period 3.7 days (range 2 – 6 days). Meier A, Smith B and Raghavan A, 2000(17) agreed with our study when compared with other modalities in treatment of



multiloculated empyema, decortication resulted in best outcome.

In our study we found that in the partial responders (complete clinical improvement with minimal residual space radiologically), follow up for 3 months is recommended as all partial responders in our study had complete response after that.

This is in agreement with Chan P, Crawford O and Wallis C, 2000(13) who reported that The chest radiograph returns to normal in the majority of children (60–83%) by 3 months.

### Conclusion

**From this study we can conclude that :**

Open thoracotomy remains an excellent option for management of multiloculated empyema in children, when open thoracotomy is performed in a timely manner there is low morbidity and it provides rapid resolution of symptoms with a short hospital stay.

Multiloculations on chest ultrasound scanning plus markedly decreased level of pleural glucose suggested to be a predictors for early decortication in cases of pediatric thoracic empyema

Intrapleural fibrinolytic treatment with streptokinase should be attempted in any child who has persistent PPE inresponsive to simple chest tube drainage as it found increasing drainage.

Further study is needed to assess the role of VATS in the management of empyema thoracis in children.

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