Journal of the Egyptian Society of Cardio-thoracic Surgery

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Guidelines for Authors

Journal of The Egyptian Society of Cardio-Thoracic Surgery
(J. Egypt. Soc. Cardiothorac. Surg.)

Editorial Office
Please address all correspondence to:
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The Journal of the Egyptian Society of Cardio-Thoracic Surgery [ISSN 1110-578 X] is the official publication of the Egyptian Society of Cardio-thoracic Surgery. The journal is published every three months .

General Instructions

Every submission must include:
Cover letter, indicating the category of article , the Complete manuscript, including title page, abstract, text, tables, acknowledgments ,references and illustrations .

Required Disclosures;

A. Conditions for Publication Form which includes disclosures regarding freedom of investigation and conflicts of interest, signed by all authors. In single Author publication an additional Senior Consultant Signature is required.
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C. Written permission from unmasked patients appearing in photographs is also required.

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Revised manuscripts must be submitted in
three parts as Microsoft word-processing files : (1) cover letter with responses to reviewers' comments (2) revised, marked manuscript showing additions and deletions; (3) revised, unmarked manuscript.

General Information
Three copies of the Manuscripts should be sent preferably prepared in Microsoft Word , typed double-spaced throughout (including title page, abstract, text, references, tables and legends) with one (1) inch (2.5 cm) margins all around. Place Author name and page number in the upper right corner of each page.
Manuscripts written in 12 point Arial or Times New Roman fonts are preferred (Note: Do not submit your manuscript in PDF format it causes problems in processing your submission.)
Arrange manuscript as follows: (1) title page, (2) abstract, (3) text, (4) acknowledgments, (5) disclosures if required, (6) references, (7) tables and (8) legends. Number pages consecutively, beginning with the title page as page 1 and ending with the legend page.
If your manuscript contains illustrations, in addition to submitting them online, you must send two sets of original illustrations to the editorial office labeled with manuscript number, first author, and figure number on back.
Tables and figures should be provided separate from the text while there position in the text should be marked on the manuscript.

Word Limits by Category of Manuscript

Original articles should not exceed 4500 words including title page, abstract of 150-200 words, text, figure legends and references. The combined total of illustrations and tables should not exceed 10 and the number of references should not exceed 40.

Case reports and **"The way I do it"** articles are limited to a total of 1500 words including title page, abstract, text, references and figure legends. For each illustration subtract 100 words and for each table subtract 300 words from the word limit. References are limited to eight. A "how to do it" article should be a description of a useful surgical technique and contain descriptive, illustrative material.

Images in cardiothoracic surgery are limited to 350 words including title and text and to two, possibly three figures. The entire contribution must fit on one printed page .

Review articles are limited to 6500 words including title page, abstract, text, figure legends and all references. The total number of references should not exceed 80. Subtract 100

words for each illustration and 300 words for each table.

Our surgical heritage articles are limited to 2500 words including title page, abstract, text, figure legends and references. Subtract 100 words for each illustration and 300 words for each table.

Correspondence (Letters to the Editor) and commentaries are limited to 500 words. Subtract 100 words for each illustration and 300 words for each table.

Editorials are limited to 2500 words including references. Subtract 100 words for each illustration and 300 words for each table.

Manuscript Preparation

Title Page (first page)

The title is limited to 100 characters and spaces for original manuscripts and to 80 characters and spaces for all other categories of manuscripts. The title may not contain acronyms or abbreviations. All submissions, must have a title.

Running Head. Supply a short title of 40 characters and spaces.

Authors. List all authors by first name, all initials, family name and highest academic degree using "MD, PhD" for holders of both degrees (if more then 7 Authors justifie).

Institution and Affiliations. List the name and full address of all institutions where the work was done. List departmental affiliations of each author affiliated with that institution after each institutional address.

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Keywords. Provide up to 5 keywords selected from the appended list to describe the manuscript. Do not use any keywords that are not on the list.

Word Count. Provide the electronic total word count of the entire manuscript including title page, abstract,text,figure legends and entire reference list.

C**orresponding Author.** Provide the name, exact postal address with postal code, telephone number, fax number and e-mail address of the author to whom communications, proofs and requests for reprints should be sent.

Abstract Page (Second page)

Original articles
Provide a structured Abstract, no longer than 250 words, divided into four sections: Background or Objective, Methods, Results, Conclusions. Avoid abbreviations and acronyms. Indicate the abstract word count below the abstract.

Case reports, "the way i do it" articles, review articles and our surgical heritage articles. Provide an unstructured abstract of 100 words.

Images, correspondence, commentaries, editorials and updates. No abstract is required.

Text
Text should be organized as follows: Introduction, Material (or Patients) and Methods, Results, and Comment.Cite references,illustrations and tables in numeric order by order of mention in the text.

Avoid abbreviations. Consult the American Medical Association Manual of Style, 9th edition, for recommended abbreviations. Define abbreviations at first appearance in the text. If 8 or more abbreviations or acronyms are used, provide a separate table of abbreviations and acronyms.

Measurements and weights should be given in standard metric units.Statistical nomenclature and data analysis. Follow the "Guidelines for Data Reporting and Nomenclature" published in The Annals of Thoracic Surgery (1988;46:260-1). Footnotes. Type footnotes at the bottom of the manuscript page on which they are cited. Suppliers of drugs, equipment and other brand mentioned in the article within parentheses , giving company name, city and country .

Acknowledgments
Grants, financial support and technical or other assistance must be acknowledged at the end of the text before the references.

References
Identify references in the text using Arabic numerals in brackets on the line.
Type references double-spaced after text or acknowledgments beginning on a separate sheet. Number consecutively in the order in which they appear in the text. Journal references should provide inclusive page numbers; book references should cite specific page numbers. Journal abbreviations should conform to those used in Index Medicus. follow the formats outlined below:

Journal Article
Jones DR, Stiles BM, Denlinger CE, Antie P . Pulmonary segmentectomy: results and complications. Ann Thorac Surg 2000;76:343-9.(List all authors if 6 or fewer; otherwise list first 3 and add "et al.")

Chapter in Book
12. Vinten-Johansen J, Zhao Z-Q, Guyton RA. Cardiac surgical physiology. In: Cohn LH, Edmunds LH Jr, eds. Cardiac Surgery in the Adult. 2nd ed. New York, NY: McGraw-Hill; 2003:53-84.

Internet Address

3. 1996 NRC Guide for the Care and Use of Laboratory Animals. Available at: http://www.nap.edu/readingroom/books/labrats/contents.html. Accessed October 20, 2003.

Tables :

Tables should be typewritten double-spaced on separate sheets (one to each page). Do not use vertical lines. Each table should be numbered (Arabic) and have a title above. Legends and explanatory notes should be placed below the table. Abbreviations used in the table follow the legend in alphabetic order. Lower case letter superscripts beginning with "a" and following in alphabetic order are used for notations of within-group and between-group statistical probabilities.

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Figure Legends should be numbered (Arabic) and typed double-spaced in order of appearance beginning on a separate sheet. Identify (in alphabetical order) all abbreviations appearing in the illustrations at the end of each legend. Cite the source of previously published material in the legend and indicate permission has been obtained. Proof of permission must be surface mailed or faxed to the editor .

Illustrations :

You must send two sets of original illustrations to the editorial office labeled with manuscript number, first author, and figure number on back.

Images or figures are submitted online as one or more separate files that may contain one or more images. Within each file containing images, use the figure number (eg, Figure 1A) as the image filename. The system accepts Powerpoint (.ppt) files Most illustrations will be reproduced at a width of one column (8.25 cm; 3 1/4 inches). Black, white and widely crosshatched bars are preferable; do not use stippling, gray fill or thin lines.

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For figures submitted in electronic format, all images should be at least 5 inches wide. Graphics software such as Photoshop and Illustrator, should be used to create art.

Color images need to be at least 300 dpi.

Gray scale images should be at least 300 dpi .

Line art should be at least 1200 DPI .

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Include with the manuscript a cover letter that provides 1) the category of manuscript (e.g., original research, Brief Communication, Letter to the Editor); 2) statement that the material has not been previously published or submitted elsewhere for publication; 3) information about any personal conflicts of interest of any of the authors; and 4) names of sources of outside support for research, including funding, equipment, and drugs .You may also submit the name of one reviewer of your choice. You should include that individual's mailing address, telephone, fax and e-mail address.

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For Date of acceptance : letter is provided from the editor.

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□ Conflict of interest statement (if appropriate).
□ Sources of outside funding.
□ Signed Statistical Collaboration .

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□ Text (double-spaced).
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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.

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The following topics are offered to help guide the reviewer's assessment of an original scientific article.

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- '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, accurateand in proper format.

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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 se-

lective rather than inclusive.

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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".

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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

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**

■ 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 Exrracorporeal 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 Aiabia; telephone: (966-2) 667-7777, ext 2166; e-mail: fiaz_winner<§1 gmailxom 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, Addi-son, TX 75001, telephone: (972) 490-9495; fax: (972) 490-9499; e-mail: ishlt@ishlt.org; website: www.ishit, 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 Sinopis Str 11527, Athens, Greece; telephone: +30 210 7799261; fax: +30 210 7711768; e-mail: secretariat@wscts2OO8.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@prri. 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 Perf usion-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: continuinged@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@prri.com; website: www.westernthoracic.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.brighamandwomens. 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.

Editorial

DISTIRGUISHED MAN AND KNOWLEDGEABLE PROFESSOR

As winds of change are still blowing our journal chief in editor is leaving us being assigned to a more important post director of the new cardiothoracic center at Ain Shams university , Hoda Talaat Harb center .

Professer Ezz Eldin Mostafa has been always the leading drive in every position and responsibility he has under taken .

I was fourtunate to be his faithful student and follower throughout my carrer trying to find the right path with his continuous helps and assistance.

His abilites and skills as a professor of cardiothoracic surgery were all the time as excellent as it could be really wraped in a humble nice and always smiley attitude.he never turned anybody who seeked his help down and that despite his ultra busy schedule.

Professor Dr Ezz is the man of the job all the time very precise very simple doing any job as it must be done.

We as the board of the journal owe him a lot and would like to express our sincere gratitude and thanks to this greatman and professor who led us during the past four years.

We wish him all the suceess in his present post and tell him that he still our chief and consltant.

I would like as well to welcome to the board some distirguished professors and surgeous who will be sharing the responsibilities and carrying together the heavy tasks .

Dr Ahmed Deebis , Dr Ahmed Hassoura,Dr Ahmed El Kerdani and Dr Mohamed Nasr as coeditors.

This in addition to our new associate section editors Dr Ahmed el Nour,Dr Ashraf Bassiony,Dr Samir Keshk,Dr Samir Hossom and Dr Momdouh Sharawi.

Wishing them all the best

Yasser Hegazy MD,FRCS

Cardiovascular

OFF-PUMP VERSUS ON-PUMP FOR MULTIVESSEL CORONARY ARTERY BYPASS GRAFTING: COMPARATIVE STUDY OF OPERATIVE AND SHORT-TERM OUTCOMES

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Background: **patients undergoing multivessel coronary artery bypass grafting (CABG) are at increased risk of death, stroke, or myocardial infarction. Our objective was to compare the operative and short-term outcomes of multivessel CABG on the beating heart (OPCAP) versus conventional surgery with cardiopulmonary bypass (ONCAB) to determine which technique has the better early benefits and outcomes.**

Methods: **This prospective study included 150 consecutive patients who underwent elective isolated multivessel CABG which done either by OPCAB (68 patients) or ONCAB (82 patients) and followed up over a period of 40 months. All preoperative, intraoperative and postoperative data of all patients were collected, analyzed and compaired between OPCAB and ONCAB groups.**

Results: **The total operating time was significantly less in the OPCAB group ($p < 0.01$). Postoperatively, ventilation time, blood loss and blood and blood product transfusion requirements were significantly less in OPCAB group patients ($p < 0.01$). The major postoperative complications acknowledged as indicators for benefits did not result in any significant difference between the two groups. There was no significant statistical difference in overall mortality rate between the two groups. A significant early benefit in OPCAB surgery were the dramatic decrease in the length of intensive care unit (ICU) and hospital stay and the better postoperative biochemical profile of OPCAB group patients ($p < 0.05$). At follow-up, both groups had similar frequency for readmission and similar quality of life.**

Conclusions: **Both OPCAB and ONCAB is a safe and effective for patients with multivessel coronary artery disease with equal operative and short-term outcomes. There are overall early benefits in OPCAB surgery; patients have a better post-operative biochemical profile, dramatic decrease in the length of stay in the ICU and hospital with quicker mobilization of patients.**

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The development of cardiac surgery in the last 30 years is directly related to the improvement of the techniques of cardiopulmonary bypass (CPB). However, CPB utilization constitutes one of the primary causes of perioperative complications [1]. These complications relate to hypoperfusion, systemic inflammatory response, cardioplegia administration and interruption of normal blood flow to the aorta with potential complications to the brain and the kidneys [1-4]. In an attempt to avoid the above mentioned complications without jeopardizing the benefits, there was recently a renewal of interest in the performance of coronary artery bypass grafting (CABG) without using CPB (OPCAB). The technical improvements in OPCAB surgery such as the development of several stabilizers,

positioning devices and coronary occluder shunts have made OPCAB a more popular alternative to conventional surgery with CPB (ONCAB) for treating multivessel coronary artery disease [5-14].

Up to now, the access to deep areas that have to be revascularized remains problematic in OPCAB technique , as to bypass the circumflex system and the posterolateral branches of the right system the surgeon must expose the posterolateral aspect of the heart by displacing the heart vertically, which may compromise the hemodynamic stability and may induce dramatic hypoperfused state that may contribute to an increase in the incidence of complications or mortality[15].

Comparing multivessel CABG by OPCAB technique versus ONCAB technique was not well documented in literature [5]. For this purpose, our objective was to compare the operative and short-term outcomes of multivessel coronary revascularization by OPCAP versus ONCAB to determine which technique has the better early benefits and outcomes.

Patients and methods

This prospective study included all planned 150 consecutive patients who underwent elective isolated multivessel CABG for multivessel coronary artery disease which done either by OPCAB or ONCAB techniques and followed up between the periods of October 2004 to January 2008 (40 months) in Zagazig University Hospital. All procedures were performed by experienced surgeons and anaesthesia was exclusively managed by experienced anaesthesiologists.

The decision for a patient to undergo OPCAB or ONCAB techniques was made by the operating surgeon. All surgeons in our department perform OPCAB and ONCAB procedures with nearly equal distribution. Exclusion criteria included: 1) The presence of ≥ grad II mitral valve insufficiency, 2) Coronary endarterctomy, 3) Incomplete revascularization of the multivessel coronary disease due to severe calcification of the coronaries and 4) Redo surgery. Also, patients whose coronary revascularization was initially attempted without cardiopulmonary bypass and who required conversion to cardiopulmonary bypass (typically due to hemodynamic instability) were also excluded form the study. Such patients' potentially increased incidence of complications may disadvantage one method for revascularization in comparison with the other [1, 14].

Method of Anesthesia and hemodynamic monitoring:

The anesthesia protocol applied was the same for all patients. All patients received the same general anesthetic technique with standard hemodynamic monitoring including mean arterial and central venous pressures and electrocardiography. Oxygen saturation was continuously monitored with a pulse oximeter. After harvesting of conduits, Heparin was injected in a dose of 2 mg/kg in patients who underwent operation without CPB and 3 mg/kg in patients with CPB. Activated clotting time was measured initially and then every 30 minutes; it was maintained for more than 300 seconds in patients who underwent surgery off pump and more than 400 seconds in those who had their surgery on pump. Protamine sulfate was used in 1:1 ratio to reverse the heparin effect after the procedure.

Surgical technique for off-pump coronary artery bypass surgery

All patients underwent operation through a median sternotomy. The left internal mammary artery (LIMA) was harvested by standard technique using hemoclips. The other conduits (saphenous veins and radial artery) were harvested simultaneously.

Distal anastomoses were always constructed before proximal anastomoses. In most cases, the left anterior descending coronary artery was the first coronary artery to be grafted. The right coronary artery was always the second artery to be grafted. The vessels on the lateral and posterior wall were usually grafted last. However, the sequence of grafting was individualized for a particular patient, depending on the severity of the lesions in different coronary arteries and patient's hemodynamics.

Deep retracting sutures, the placement of a warm moist laparotomy sponge in the posterolateral aspect of the pericardial sac, Trendelenburg position, and right tilt were used to facilitate exposure of the lateral and posterior vessels of the heart. Octopus tissue suction stabilizer (Medtronic, Inc., Minneapolis, MN, USA) was used to stabilize the myocardium. During the construction of all anastomosis, target vessel hemostasis was obtained with proximal and distal silicone rubber (Silastic; Dow Corning, Midland, Mich) vessel loops as coronary snares and intracoronary shunts (Anastafloa, Research Medical, Midvale, UT, USA) were used for most of the anastomosis. The anastomoses were constructed with a single running stitch of 7-0 or 8-0 polypropylene (ProleneTM, Johnson & Johnson, New Brunswick, NJ, USA) and visualization was improved with use of a continuous air/saline blower.

Proximal anastomosis was performed with partial clamping of the ascending aorta using standard techniques. The proximal anastomosis was performed using a single running stitch of 6-0 Prolene suture.

Surgical technique for on-pump coronary artery bypass surgery

Conventional coronary artery bypass procedures were performed through a median sternotomy using standard CPB, which was established after full heparinization (at a dose of 3 mg/kg),using ascending aortic and two-stage venous cannulation with the use of membrane oxygenator and a roller pump. Arterial flow was adjusted to 2.2-2.4L/min/m^{-2}, and blood pressure was maintained between 50 and 70mmHg. Haematocrit level was kept at >22%. The patient was not actively cooled but temperature was allowed to drift was maintained at 34ºC. Intermittent Antegrade warm blood cardioplegia was used for myocardial protection. Cardioplegia was repeated after every distal anastomosis.

In both Surgical techniques, OPCAB and ONCAB, the total operative time was defined as time from skin incision to closure of the skin.

Postoperative clinical and biochemical parameters

To evaluate the in-hospital morbidity of both techniques, several clinical parameters were analyzed (e.g. the intubation time, the administration of inotropic drugs, the amount of blood transfusions, the incidence of perioperative myocardial infraction (MI), stroke (CVA), transient ischemic attack (TIA), atrial fibrillation (AF) and renal failure (RF), period of stay in intensive care unit (ICU) and hospital).

Blood loss was defined as total chest tube drainage until chest tubes were removed. Prolonged ventilation was defined as ventilation for more than 48 hours. The perioperative diagnosis of MI was based on the presence of two out of three standard criteria: a) development of a new pathological Q-wave or loss of R wave progression, new left bundle branch block, or new ST and T wave changes on postoperative electrocardiography, and b) increase of the creatine kinase (CK) level more than 40 U/L or increase of CK-MB value by more than 30% of the total value of CK. The development of a local or atypical precordium pain was not considered an MI criterion. Mediastinisis was defined as mediastinal collection with positive culture. Acute RF was defined as requirement of peritoneal or hemodialysis.

The biochemical markers that were included in the analysis were a) creatinine kinase myocardial fraction band (CK-MB) value, and b) serum creatinine value (Cr).

Follow-up:

At 6 months post-procedure, follow-up was done by a standardized questionnaire that focused on quality of life, lifestyle activities, recurrent angina, frequency and intensity of angina, and reporting rehospitalization for specific cardiac causes and follow-up mortality. Echocardiography was done for all patients at 6 months.

To compare the operative and short-term outcomes of multivessel coronary revascularization by OPCAP versus ONCAB, all preoperative, intraoperative and postoperative data of all patients were collected, analyzed and compaired between both groups.

Statistical analysis

The Values of variables data were presented as a mean value ± standard deviation (mean ± SD). Preoperative, intraoperative, and postoperative variables were analyzed and compared between these two groups using Student's *t* test and univariate analysis (chi-square test (χ^2), Fisher's exact test). Statistical significance was defined as a *p* value of less than 0.05($p<0.05$). Statistical analyses were performed using SPSS for Windows version 11.5 statistical package (SPSS, Inc, Chicago, Ill).

Results

The preoperative variables of the all patients of the two groups are shown in Table 1. There were no differences between the two groups as regards gender, age, severity of the coronary artery disease, ejection fraction and preoperative co-morbidities and risk factors, except that there were significantly more patients with hypercholesterolemia and history of CVA or TIA in the OPCAB Group ($p < 0.05$) (table 1).

***Table (1)**

There were more patients with aortic arteriosclerosis in the OPCAB Group, which was statistically significant ($p < 0.05$). The total number of grafts used in OPCAB group and ONCAB group were 2.6 ± 0.4 and 2.7 ± 0.5 respectively; hence such differences were not statistically significant. Venous grafts were used in all patients in both groups. LIMA was used in 96% and 95% patients in the OPCAB and ONCAB groups, respectively. Radial arterial grafts were use infrequently in both groups. Differences were not statistically significant between both groups as regard the types of grafts used. Intraoperatively, there were significantly more patients in the OPCAB group required inotropic drugs than those in the ONCAB group ($p < 0.01$). The total operating time was significantly less in the OPCAB group ($p < 0.01$) (table 2).

***Table (2)**

Table 3 summarizes the results regarding the postoperative outcome data for the two groups. During the stay in ICU, ventilation time, blood loss and blood and blood product transfusion requirements were significantly less in OPCAB group patients ($p < 0.01$). The major postoperative complications acknowledged as indicators for benefits did not result in any significant difference between the two groups (Table 3). The incidence of postoperative MI, stroke, renal dysfunction, pulmonary infection, new AF and sternal infection were comparable between the two groups (p = NS). Significant differences were observed in the biochemical markers of the study; OPCAB group patients have a better post-operative biochemical profile ($p < 0.05$) (Table 3). A significant early benefit in OPCAB surgery was the dramatic decrease in the length of stay in the ICU and hospital with quicker mobilization of OPCAB group patients ($p < 0.05$) (Table 3). There was no significant statistical difference in total 30-day postoperative mortality rate between the two groups (p = NS).

***Table (3)**

At the time of 6-months follow-up, both groups had improvement in LVEF by about 2-5% but with no significant statistical difference between both groups. Both OPCAB and ONCAB groups had nearly the same frequency for readmission to the hospital since discharge (4.4% vs 4.9% respectively; *p* = NS). Reasons for readmission focused on specific cardiac causes indications: recurrent angina (1.5% vs 2.4%), congestive heart failure (1.5% vs 1.2%), arrhythmias (1.5% vs 1.2%) for OPCAB Group and ONCAB Group, respectively; and all were non-significant (Table 4). Additionally, patient-reported quality of life and lifestyle activities were similar in both groups. There was no significant statistical difference in follow-up mortality rate between the two groups (*p* = NS).

The overall mortality rate for OPCAB Group and ONCAB Group were 2.9% and 3.7 % respectively, which was non statistically significant (*p* = NS).

***Table (4)**

Discussion

Multivessel cardiac disease patients present more frequently with multifactorial disease processes such as renal, pulmonary, neurologic, and peripheral vascular disease [5]. Accordingly, patients undergoing multivessel coronary artery bypass surgery are at increased risk of death, stroke, or MI compared with patients who need fewer diseased vessels [14]. ONCAB offers excellent symptomatic relief, carries a low operative mortality, and provides excellent long-term survival benefit. Despite these excellent results, the adverse effects of extracorporeal circulation and cardioplegic arrest may aggravate preexisting complications and disorders. CPB and cardioplegic arrest can cause myocardial dysfunction, negative central nervous system effects, neuropsychiatric phenomena, severe systemic inflammatory response, and coagulopathy associated with end-organ injury [5]. Accordingly, OPCAB has recently gained renewed interest as an alternative to ONCAB for multivessel revascularization to avoid CPB related complications [5- 14]. However, the role of OPCAB is still vaguely defined and is being critically evaluated. The main explanation for this difficulty in defining the role of off-pump procedures appears to be the lack of conclusive data and controversy with respect to the potential benefit (mortality, morbidity, graft patency and long-term outcome) of this approach compared with ONCAB [16].

Concerns regarding higher incidence of incomplete revascularization, recurrent angina, and early graft occlusion have prevented OPCAB from being universally adopted [5, 16]. There is no doubt that completion of the graft to coronary artery anastomosis is more difficult in the OPCAB procedure due to the cardiac motion and lack of a blood-free operative field, compared to conventional coronary artery bypass grafting on an arrested, flaccid heart [16]. Despite the availability of cardiac stabilizers and positioning devices, up to now, one of the main disadvantages of the technique is the difficulty of its application in bypassing the lateral and inferior wall vessels in triple vessel disease patients as the anastomosis is often performed in a vertical position [5, 15, 16]. This creates a parallax view with poor depth of vision for judging distance between stitches and contributes to the theoretical possibility of poor quality of the anastomosis and less anastomotic accuracy [16]. The coronaries undergo significant spasm when manipulated on a hemodynamically active heart. Also, the vertical displacement may compromise the hemodynamic stability and may induce dramatic hypoperfused state that may contribute to an increase in the incidence of complications or mortality [15, 16]. A recent meta-analysis of graft patency by Takagi et al. demonstrated a 27% increase in overall graft occlusion with OPCAB, especially a 28% increase in venous graft occlusion [17].

Current prospective data suggest that both techniques OPCAB and ONCAB have similar rates of mortality in patients with multivessel coronary artery disease [5- 14]. Our results showed that, the total 30-day post-operative mortality rate and the overall mortality rate did not differ

significantly between the two techniques (2.9% vs 2.4%, and 2.9% vs 3.7%, respectively).

As regard the morbidity in the postoperative period, perioperative bleeding and transfusion-related complications are among the major risks associated with open heart surgery. Avoidance of CPB has been reported to be beneficial in reducing blood product use [9, 18, 19]. In the present study, postoperative bleeding and transfusion requirements were significantly less with OPCAB technique (p <0.01). Also, OPCAB group patients clearly needed significantly less ventilation time after the operation (p <0.01), a finding that is consistent with that of other researchers [5, 9, 18, 19].

However, in this study, the differences in postoperative major complications acknowledged as indicators for benefits were non significant between the two groups which is consistent with that of other studies [5, 9, 18, 19]. The postoperative stroke rate in our study was comparable in the two groups, though there were more patients in the OPCAB group had arteriosclerosis of the aorta than those in the ONCAB group. After refinements in CPB techniques, especially use of membrane oxygenators and arterial line microfilters, a lowered incidence of postoperative neurologic dysfunction have been demonstrated [5]. Some studies [11, 14] suggest a decrease in stroke rates for OPCAB patients, but according to the most recent meta-analysis by Takagi and associates, randomized clinical trials of OPCAB versus ONCAB, postoperative 30-day stroke was not statistically significantly reduced in the OPCAB patients [20].

Also, in this study, we observed that incidence of postoperative TIA, MI, new RF, and AF were similar and statistically non-significant between the two groups, a finding that recent studies on multivessel coronary revascularization showed the same pattern [5, 9, 10, 14]. Also, the recent meta-analysis study by Cheng and associates [19] showed no significant differences in MI, stroke, renal dysfunction, intra-aortic balloon pump (IABP) support and wound infection between OPCAB and ONCAB techniques, meanwhile, OPCAB significantly decreased AF. However, results of neurocognitive function were inconclusive in this meta-analysis.

As regards the biochemical parameters, the pattern of perioperative enzyme release after either procedure is still contradictory [5, 12, 15, 18]. In this study, we observed significantly lower CK-MB values for patients operated by OPCAB technique (p <0.01). Although this finding is directly related to the number of perioperative MI, it seems that the cardioplegia administered to patients on whom CPB is used, greatly affects the post-operative increase of myocardial enzymes. Also, the difference in post-operative creatinine values of the patients of two groups was significant. Patients operated by OPCAB technique had significantly lower creatinine values (p <0.05). The renal function is a parameter that has been recently studied and the data to-date show a clear superiority of off-pump surgery on the beating heart versus CPB surgery with respect to maintenance of normal creatinine clearance values [2].

Nevertheless, both the mean stay in ICU and hospital were significantly less in OPCAB group patients (p <0.05) and this was important factor in quicker mobilization of patients in the postoperative period with early benefit in OPCAB patients. These findings are in accordance with the studies of Kshettry et al. [5] and Maharwal et al. [9] and the meta-analysis by Cheng and associates [19].

At follow up, the results presented here seem to indicate that both techniques provide similar rates of improvement of LVEF, quality of life, readmission rate and freedom from surgical reintervention. Selvanayagam et al. [21] used cine magnetic resonance imaging to assess left ventricular function and newly occurring irreversible myocardial damage in a consecutive series of 60 patients. Postoperative left ventricular function was significantly better in the OPCABG group. Interestingly, new irreversible myocardial damage does not differ between the two techniques. Kshettry et al. [5] showed that the rate of readmission, quality of life and freedom from surgical re-intervention were similar and statistically non significant between OPCAB and ONCAB patients.

OPCAB remains an emerging and developing surgical technique, and continued reevaluation is warranted. What remains to be confirmed are the quality of the anastomoses and the long-term patency of the grafts [5, 9, 15]. In conclusion, both OPCAB and ONCAB are safe and effective for patients with multivessel coronary artery disease with equal operative and short-term outcomes. Elimination of CPB did not significantly reduce postoperative morbidity. There are overall early benefits in OPCAB surgery; patients have a better post-operative biochemical profile, and dramatic decrease in the length of stay in the ICU and hospital with quicker mobilization of patients. However, prospective randomized studies with long-term results comparing these two techniques are required.

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THE USE OF OFF–PUMP CARDIOPULMONARY BYPASS IN EMERGENCY MYOCARDIAL REVASCULARIZATION

Cardiovascular

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Background: **Emergency coronary artery bypass grafting is associated with increased operative mortality. The use of off- pump coronary artery bypass is a well established technique for elective cases and is associated with low mortality rate even among high risk patients. The objective of this study is to evaluate the efficiency and safety of the use of off-pump surgery in emergency CABG and to compare the outcome with that of conventional CABG.**

Methods: **Seventy nine patients who underwent emergency isolated CABG between April 1999 to April 2005 were included in the study. The criteria for selection of these patients for emergency bypass were based on the guidelines of the Society of Thoracic Surgeons (1). 45 of these patients underwent off-pump cardiopulmonary bypass (OPCAB), while the rest (34 patients) had conventional cardiopulmonary bypass (CCAB). Their data was reviewed and evaluated. Patients were followed up to find midterm survival and control of symptoms.**

Results: **Patients undergoing OPCAB had a higher incidence of associated preoperative comorbidities. Their mean ejection fraction was 28±9 vs. 39 ± 10 in CCAB (P<0.001). Cardiogenic shock, acute myocardial infarction < 24 hours and post PTCA complications were seen more frequently in OPCAB patients, but the difference was not significant. Main stem disease was significantly more common in CCAB (P= 0.002). The mean number of grafts per patient was 1.8 ± 0.7 in OPCAB and 3.2 ± 0.8 in CCAB group (P <0.001). Subsequently, completeness of revascularization was greater in CCAB patients (79% vs. 51%; P = 0.01). Overall operative mortality was 11.4%. Patients who underwent CCAB had a higher mortality rate 14.7% vs. 8.9%; P=0.42. Major morbidity was more common among OPCAB patients, with a higher incidence of myocardial infarction, mediastinitis and reopening for extra grafting. Late follow up (15-82.8 months) was achieved in 96% of cases. Late mortality was similar among both groups. Patients operated on with CPB had lower rates of recurrent angina (16 vs. 34%; p = 0.08) and symptoms of congestive heart failure (20% vs. 51%; p = 0.04).**

The incidence of rehospitalization was more common among OPCAB patients. However, the percentage of cardiac reintervention was similar among both groups (8.6% vs. 8%; p = 0.94). Five – year survival (Kaplan Meier) of patients operated upon without CPB was better (90% vs. 83%), however the difference was not statistically significant (p = 0.94).

Conclusions: **Patients undergoing emergency CABG are at high risk. The use of either off-pump or conventional CABG is associated with high operative and late mortality. Off-pump coronary artery bypass can be performed safely among emergency cases. This technique did not show any significant superiority over conventional CABG except among patients with myocardial infarction less than 24 hours.**

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Off-Pump coronary artery bypass (OPCAB) is a well established technique used in myocardial revascularization. It has been shown to reduce both the mortality and morbidity which are associated with extra corporal circulation [2].

Initially, it was used in highly selected cases especially in young patients with single or double coronary artery disease. Indications have gradually expanded, especially with the advanced development of cardiac stabilizers. It is now routinely used in multi-vessel coronary disease. Recent studies have shown the importance of using off-pump technique among high risk patients with multiple comorbidities [3-5], and proved its superiority over conventional coronary artery bypass (CCAB) surgery [5, 6].

Mortality of patients undergoing emergency coronary revascularization whether after acute myocardial infarction (MI) or post angioplasty complications remains high [7, 8]. Avoiding the inflammatory reaction and ischemic injury caused by cardiopulmonary bypass (CPB) in these patients may be of great benefit. The objective of this study is to evaluate the efficiency and safety of the use of OPCAB in emergency coronary revascularization and to compare the outcome with CCAB.

Patients and Methods

Seventy nine patients who underwent emergency isolated coronary artery bypass surgery between April 1999 to April 2005 were included in this study. Those with combined procedures or with beating heart on pump were excluded. Patients were divided into two groups according to the technique used. Group I (OPCAB) included 45 patients who underwent off-pump operations and group II (CCAB) 34 patients who had conventional bypass. The emergency status of these patients was based on the guidelines of the Society of Thoracic Surgeons [1] which includes ongoing ischemia inspite of maximum medical therapy, acute evolving myocardial infarction and cardiogenic shock with or without support. The criteria used to select either technique were based on the hemodynamic status of the patients, the anatomy of the coronary vessels and associated risk factors. Patients with diffuse multi-vessel disease, poor quality vessels, evidence of coronary calcification and hemodynamic instability were considered for CCAB bypass. Those patients with associated co-morbidities, low ejection fraction (EF), suitable coronary anatomy (i.e. accessible vessels, no evidence of calcification and good vessel size), and acceptable hemodynamic state were considered candidates for OPCAB surgery.

Surgical technique

Hemodynamic stabilization was maintained either by using inotropic drugs or by an intra aortic balloon pump (IABP). Exposure of the heart was done using standard median sternotomy in all patients. After harvesting saphenous vein and left internal mammary artery, full heparinization was done keeping the activated clotting time more than 400 seconds in both groups. Standard cannulation of the aorta and right atrium was used in CCAB group. Myocardial protection was achieved by intermittent blood cardioplegia given antegradely and systemic hypothermia at 32oC.

In the OPCAB group, anterior vessels were simply exposed by elevation of the heart. Deep pericardial retraction sutures were used to expose circumflex and right coronary artery. The Starfish device (Medtronic, Inc, Minneapolis, MN) was used to expose the circumflex artery since early 2005. Stabilization of target vessels was accomplished by either pressure U-shaped foot stabilizer (Guidant, Indianapolis, IN) or suction stabilizer (Medtronic Octopus II and III). Intra coronary shunts (Medtronic Inc.) were used in constructing bypass grafts in all cases.

Different preoperative and postoperative variables were collected and analyzed. These variables are presented as mean ± standard deviation using student's t test. The data were expressed as percentage and comparison was made using the Fisher exact test. Postoperative survival was expressed by the Kaplan – Meier Method. Statistical significance was assumed if p value < 0.05 (2-tailed). Analyses were performed using SPSS 13 software (Chicago, IL).

Results

Preoperative patients' demography and risk factors among both groups are listed in (Table 1).

The majority of patients who underwent OPCAB had either single or double vessel disease (Table 2). The mean number of grafts per patient was 1.8 ± 0.7 and 3.2 ± 0.8 among OPCAB and CCAB respectively ($p < 0.001$). Grafting of obtuse marginal and posterior descending artery was much higher among CCAB ($P < 0.001$). Left internal mammary arteries was used in 71% of CCAB patients and in 67% of OPCAB ($p = 0.71$). Completeness of revascularization was achieved in 79 % of CCAB patients in comparison to 51% in OPCAB group ($p = 0.01$).

Operative mortality among both groups was seen in 9 patients (11.4 %), (Table 3). It was lower among the OPCAB group 4 patients (8.9%) than CCAB 5 patients (14.7%) $p = 0.42$. Patients who died among OPCAB group had a mean EF of 19 ± 6 vs. 33 ±13 in the CCAB

group ($p < 0.001$). All patients died of low cardiac output except two who died of uncontrolled arrhythmia. Only one patient who had CCAB died in theatre due to difficult weaning inspite of maximum support. Among the patients who died, five had preoperative MI < 24 hours; one had an old MI, while the rest showed no evidence of previous MI. Five patients who died had preoperative complicated PTCA.

Postoperative inotropic support was used in 53% of all patients. More patients among OPCAB received inotropic support ($p = 0.38$). However, the use of postoperative IABP was more common in conventional patients.

Intensive care unit stay was less in OPCAB (1.8 ± 1.5 days vs. 2.2 ± 2.2 days), but hospital stay was longer. These differences were not statistically significant.

Blood loss was greater in the conventional group. Only one patient was reopened for bleeding. The amount of blood transfused was 2.1 ±1.9 units vs. 1.5 ± 1.6 units in OPCAB.

Major postoperative complications were more common among OPCAB patients. They had a higher incidence of postoperative MI, mediastinitis and reopening for cardiac intervention, while among those in the CCAB group ventilation was more prolonged and there was a permanent stroke in one patient.

Late follow up (15 - 82.3 months) was achieved in 95.7 % of patients (Table 4). During that time seven patients (10.4%) died among both groups. Six were cardiac related and one was non cardiac among OPCAB patients. The statistical difference in late mortality was not significant $p = 0.42$. Patients operated on with CPB had lower rates of recurrent angina (16% vs. 34%; $p = 0.08$) and symptoms of heart failure (20% vs. 51%; $p = 0.04$). Nevertheless, the majority of symptomatic patients in OPCAB were in Class I or II according to NYHA and CCS classes.

The majority of patients who were hospitalized belonged to the OPCAB group. More patients operated on

Variables	Total [79]	OPCAB [45]	CCAB [34]	p Value
Age, year	55.6 ± 9	54.2 ± 9	57.4 ± 7	0.10
Females	17 (21.5%)	8 (17.7%)	9 (26.5%)	0.24
Hypertension	40 (51.9%)	19 (43.2%)	21 (63.6%)	0.08
Diabetes	29 (36.7%)	17 (37.8%)	12 (35.3%)	0.82
Dyslipidemia	41 (51.9%)	21 (46.7%)	20 (58.8%)	0.28
Smoking	48 (60.8%)	31 (68.9%)	17 (50.0%)	0.09
COPD	19 (24.1%)	13 (28.9%)	6 (17.6%)	0.25
Chronic Kidney Disease	7 (8.9%)	5 (11.1%)	2 (5.9%)	0.42
Cerebrovascular Disease	3 (3.8%)	2 (4.4%)	1 (2.9%)	0.73
Peripheral Vascular Disease	6 (7.6%)	5 (11.1%)	1 (2.9%)	0.18
Redo CABG	3 (3.8%)	2 (4.4%)	1 (2.9%)	0.73
Post PTCA Complication	31 (39.2%)	20 (44.4%)	11 (32.4%)	0.28
Cardiogenic Shock	16 (20.3%)	9 (20.0%)	7 (20.6%)	0.95
Intra Aortic Balloon Bump	18 (22.8%)	10 (22.2%)	8 (23.5%)	0.71
Preoperative Cardiac Arrest	24 (30.4%)	13 (28.9%)	11 (32.4%)	0.74
Acute Infarction < 24 hours	30 (38.0%)	19 (42.2%)	11 (32.4%)	0.21
Ejection Fraction	33 ± 11	28 ± 9	39 ± 10	< 0.001
Left Main Stem Disease	17 (21.5%)	4 (8.9%)	13 (38.2%)	0.002
Number of Involved Vessels				
• Single Vessel Disease	8 (10.1%)	8 (17.7%)	0 (0.0%)	0.03
• Double Vessel Disease	22 (27.8%)	16 (35.6%)	6 (17.6%)	0.09
• Triple Vessel Disease	43 (54.4%)	21 (46.7%)	22 (64.6%)	0.19
• Quadruple Vessel Disease	6 (7.6%)	1 (2.2%)	5 (14.7%)	0.04
NYHA Class				
• Class 0	7 (8.9%)	2 (4.4%)	5 (14.7%)	0.11
• Class I	15 (19.0%)	7 (15.6%)	8 (23.5%)	0.37
• Class II	19 (24.1%)	12 (26.7%)	7 (20.6%)	0.53
• Class III	24 (30.4%)	15 (33.3%)	9 (26.5%)	0.51
• Class IV	14 (17.7%)	9 (20.0%)	5 (14.7%0	0.54
CCS Class				
• Class I	5 (6.3%)	3 (6.7%)	2 (5.9%)	0.89
• Class II	14 (17.7%)	9 (20.0%)	5 (14.7%)	0.54
• Class III	28 (35.5%)	18 (40.0%)	10 (29.4%)	0.33
• Class IV	32 (40.5%)	15 (33.3%)	17 (50.0%)	0.14

Table 1: Preoperative Patient Profile and Causes of Emergency

with CPB underwent cardiac catheterization, but the incidence of angioplasty was more in OPCAB. No patient in either group had redo CABG.

Five-year survival excluding operative mortality was 90% in OPCAB patients in comparison to 83% among CCAB group.COX regression analysis showed no significant difference between both groups(p = 0.94),(Fig 1).

CCAB: Conventional Coronary Artery Bypass. CCS: Canadian Cardiovascular Society, COPD: Chronic Obstructive Pulmonary Disease, NYHA: New York Heart Association, OPCAB: Off-Pump Coronary Artery Bypass.

Variables	Total [79]	OPCAB [45]	CCAB [34]	p Value
Number of Grafts	2.4 ± 1.0	1.8 ± 0.7	3.2 ± 0.8	< 0.001
• LAD Graft	75 (94.9%)	44 (97.8%)	31 (91.2%)	0.19
• RCA Graft	12 (15.2%)	7 (15.6%)	5 (14.7%)	0.92
• Cx Graft	4 (5.1%)	1 (2.2%)	3 (8.8%)	0.19
• D1 Graft	16 (20.3%)	7 (15.6%)	9 (26.5%)	0.23
• D2 Graft	26 (32.9%)	13 (28.9%)	13 (38.2%)	0.38
• OM1 Graft	23 (29.1%)	3 (6.7%)	20 (58.8%)	< 0.001
• OM2 Graft	2 (2.5%)	0 (0.0%)	2 (5.9%)	0.10
• PDA Graft	21 (26.6%)	5 (11.1%)	16 (47.1%)	< 0.001
LIMA	54 (68.4%)	30 (66.7%)	24 (70.6%)	0.71
Complete Revascularization	50 (63.3%)	23 (51.1%)	27 (79.4%)	0.01

Table 2: Operative Data
Cx: Circumflex Artery, D1: First Diagonal, D2: Second Diagonal, LIMA: Left Internal Mammary Artery, OM1: First Obtuse Marginal, OM2: Second Obtuse Marginal, PDA: Posterior Descending Artery.

Variables	Total [79]	OPCAB [45]	CCAB [34]	p Value
Mortality	9 (11.4%)	4 (8.9%)	5 (14.7%)	0.42
ICU Stay, days	1.9 ± 1.8	1.8 ± 1.5	2.0 ± 2.2	0.64
Hospital Stay, days	8.5 ± 4.2	8.6 ± 4.7	8.3 ± 3.6	0.82
Estimated Blood Loss, ml	540 ± 290	490 ± 250	575 ± 320	0.38
Blood Transfusion, Units	1.8 ± 1.7	1.5 ± 1.6	2.1 ± 1.9	0.15
FFP Transfusion	5 (6.3%)	3 (6.7%)	2 (5.9%)	0.92
Platelet Transfusion	1 (1.3%)	1 (2.2%)	0 (0.0%)	0.39
Inotropic Support	42 (53.2%)	22 (48.9%)	20 (58.8%)	0.38
Major Morbidity				
• Post Operative Infarction	8 (10.1%)	5 (11.1%)	3 (8.8%)	0.74
• Post Operative Stroke	2 (2.5%)	1 (2.2%)	1 (2.9%)	0.84
• Prolonged Ventilation	3 (3.8%)	1 (2.2%)	2 (5.9%)	0.40
• Acute Renal Failure	4 (5.1%)	2 (4.4%)	2 (5.9%)	0.77
• Mediastinitis	1 (1.3%)	1 (2.2%)	0 (0.0%)	0.38
• Reopening for Extra Grafting	1 (1.3%)	1 (2.2%)	0 (0.0%)	0.38
• Malignant Ventricular Arrhythmias	6 (7.6%)	4 (8.9%)	2 (5.9%)	0.62
Other Morbidity				
• Atrial Fibrillation	7 (8.9%)	5 (11.1%)	2 (5.9%)	0.42
• Reopening for Bleeding	1 (1.3%)	0 (0.0%)	1 (2.9%)	0.25
• Superficial wound Infection	3 (3.8%)	0 (0.0%)	3 (8.8%)	0.12
• Left Atrial Thrombus	1 (1.3%)	1 (2.2%)	0 (0.0%)	0.38
• Femoral Embolectomy	1 (1.3%)	1 (2.2%)	0 (0.0%)	0.38

Table 3: Early Post Operative Outcome
FFP: Fresh Frozen Plasma, ICU: Intensive Care Unit.

Variables	Total [67]	OPCAB [39]	CCAB [28]	p Value
Missed Patients	3 (4.3%)	2 (5.1%)	1 (3.6%)	0.56
Mortality	7 (10.4%)	4 (10.3%)	3 (10.7%)	0.95
CCS Class				
• Class 0	44 (73.3%)	23 (65.7%)	21 (84.0%)	0.08
• Class 1	7 (11.7%)	5 (14.3%)	2 (8.0%)	0.63
• Class 2	7 (11.7%)	7 (20.0%)	0 (0.0%)	0.09
• Class 3	2 (3.3%)	0 (0.0%)	2 (8.0%)	0.46
• Class 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.00
NYHA Class				
• Class 0	39 (58.2%)	19 (48.7%)	20 (80%)	0.04
• Class 1	7 (11.9%)	5 (14.3%)	2 (8.0%)	0.63
• Class 2	8 (13.6%)	6 (15.4%)	2 (8.0%)	0.14
• Class 3	6 (9.0%)	5 (14.3%)	1 (4.0%)	0.43
• Class 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.00
Hospitalization	16 (26.7%)	12 (34.3%)	4 (16.0%)	0.11
Angiography	8 (13.3%)	4 (11.4%)	4 (16.1%)	0.61
PCI	5 (8.3%)	3 (8.6%)	2 (8.0%)	0.94
Redo CABG	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.00

Table 4: Midterm Outcome
CABG: Coronary Artery Bypass Grafting, PCI: Percutaneous Coronary Intervention

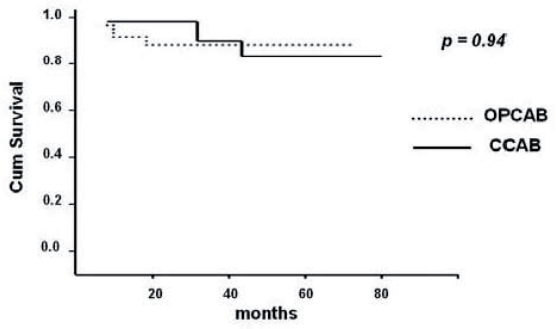

Figure 1: Kaplan Meier survival curve for both groups excluding operative mortality.

Discussion

The use of the off-pump technique in emergency myocardial revascularization is still debatable. When this technique was first used, emergency cases were considered an absolute contraindication [9, 10], and these patients were treated by conventional CPB believing that they may benefit more from the protective effect of cardioplegic arrest [11, 12].

However, operative mortality remained high, which is believed to be due to multi-factorial reasons, among which is the intense inflammatory response which is associated with extracorporal circulation. These inflammatory mediators cause temporary dysfunction of nearly every organ [13]. The effect is usually minor and reversible in the majority of patients. However, in high risk patients the effect can be irreversible and fatal [14]. In spite of major advances in myocardial protection offered by cardioplegia, some degree of myocardial stunning still occurs [15], this was clearly shown by the high level of serum Troponins and Creatine Kinase MB fraction when compared to patients undergoing off – pump bypass. Also the use of aortic cross clamping during bypass may precipitate hemodynamic failure among patients who already have an impaired left ventricle [16].

Perrault and colleagues [16] in their study using a beating heart on pump, found less damage to the myocardium than when using aortic cross clamping. However the use of cardiopulmonary bypass without cross clamping is still associated with an inflammatory response capable of causing myocardial damage when

compared with off-pump technique [17].

Clinical applications of off-pump bypass in emergency CABG is limited [7, 8, 10, 18 – 21]. Most of the studies showed that off-pump surgery can be applied effectively with low risk inspite of the compromised hemodynamic state of these patients. Operative mortality varies from 0 to 5 % [19, 20], depending on various factors. Worse prognosis is associated with preoperative use of IABP, non use of LIMA to LAD and less than three grafts used during operation, also patients undergoing cardiopulmonary resuscitation on their way to theater have a higher operative risk [7,19].

Operative mortality among our off-pump patients was 8.9%. The majority of these patients had MI less than 24 hours prior to surgery, low EF and complication of angioplasty. Similar to the observation of Locker and colleagues [7], we found that 60% of these patients had no LIMA used, and less than three grafts have been applied. These factors contributed to the high early mortality.

The mortality rate among our patients is in accordance with the results found by Locker and colleagues [20], but was higher than the recent study by Kerendi and coworkers [19], who had a 0% early mortality. This is directly attributed to the preoperative hemodynamic state of their patients. In the Kerendi study, the mean EF was 47 ± 2.3 % in comparison to 28 ± 9 % among our patients. Similarly, the incidence of cardiogenic shock and MI was much lower than in our patients.

Late mortality among both of our groups was the same. Patients in the OPCAB group died early after operation, within 1-2 years, in contrast to conventional patients who died after three years. Control of symptoms whether angina or heart failure was better among CCAB patients, subsequently hospitalization and reintervention was less frequent. These results were related to completeness of myocardial revascularization and the preoperative hemodynamic condition among both groups.

Previous studies [7, 20] had a higher late mortality among their patients who were subjected to OPCAB. It varied from 19 % [7], to 23% [20]. Similarly, control of symptoms was less among their patients.

The difference in mortality from our study is due to the fact that all their patients had myocardial infarction within one week before surgery. It seems that the timing of performing surgery is crucial and affects both early and late mortality. In Locker and colleagues' study [20], their patients had infarction within 48 hours; subsequently they had a higher early and late mortality in comparison to their more recent study [7] whom their patients had infarction within 7 days.

The timing and technique of surgery used among patients with acute myocardial infarction remains controversial. Previous studies [22, 23] showed that mortality is related to the time of intervention. Patients operated upon after 48 hours of infarction had a better result than those who were operated on earlier [22].

A similar observation was noticed in our recent work. Fifty percent of our patients who died either early or late had acute MI less than 24 hours before surgery. Beside the timing of intervention, the technique used whether off-pump or conventional is also important. The application of off-pump among patients with recent MI has been studied [7, 19 – 21] and confirmed the superiority of off-pump surgery in comparison to conventional bypass in these patients

Evaluating early and late mortality among our patients who had infarction less than 24 hours before surgery, we noticed that the majority of these patients underwent conventional bypass. This emphasized the importance of using off-pump among patients with early acute myocardial infarction.

The relationship between preoperative hemodynamic state, completeness of myocardial revascularization and late control of symptoms was clearly seen in previous studies [7, 20], and our recent work. We noticed that the control of symptoms whether angina or heart failure was better among patients who underwent conventional bypass. They had a better preoperative hemodynamic state in relation to EF, cardiogenic shock and angioplasty complications. Also the number of grafts used per patient was significantly higher among these patients.

Similarly, in the early work by Locker and colleagues (20), the control of symptoms among their off-pump patients during follow up was less than conventional patients. More of their patients referred to off-pump had PTCA complications. This reflects the hemodynamic instability among their off-pump patients. Also, the mean number of grafts used was less than the conventional bypass group. In their recent study [7], their off-pump patients had better results whether late mortality or control of symptoms. This is due to the fact that preoperative hemodynamic state of their patients was much better than their previous study.

In conclusion, we believe that the use of either off-pump or conventional emergency CABG is associated with high operative and late mortality. Patients associated with preoperative cardiogenic shock, low EF, acute MI less than 24 hours and angioplasty complication carry the highest risk. Off-pump bypass can be used in emergency myocardial revascularization .Although, it is associated with lower rate of early and late mortality, it did not show any significant superiority over conven-

tional CABG except for patients with myocardial infarction less than 24 hours.

Limitations of the Study

Our study has some limitations. It is an observational retrospective trial. It contained a relatively small number of patients with preoperative inequality of left ventricle function which may represents a potential source of bias of choosing the surgical approach. But, the surgeon's preference and the general agreement that OPCAB surgery represent a safe approach for patients of severely compromised left ventricle may ameliorate this bias. Of course, the nature of the study precluded the investigators from being blinded to the procedure.

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RISK FACTORS OF CEREBRO-VASCULAR ACCIDENTS AFTER ONPUMP ISOLATED CORONARY ARTERY SURGERY

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Background: **Cerebrovascular accidents (CVAs) after surgical myocardial revascularization is one of the most hazardous complication. Its - related mortality remains high and patients who experienc*e this event have lower long-term survival than patients who do not . Many reports focus on the relationship between the degree of atherosclerotic affection of the ascending aorta ; degree of manipulation and postoperative CVAs . Different surgical strategies for myocardial revascularization with the least manipulation to the aorta of these patients were described in the literatures. Other independent predictors of cerebrovascular accidents (CVAs) following onpump isolated CABG(s) include Extracoronary Vasculopathy ,Low output syndrome ,Low EF. and others Identification of other risk factors allows preoperative risk stratification and may facilitate improved patient selection and contribute to reduce the risk of a stroke by providing an opportunity for adequate medical and surgical intervention.**
Objective: **Identification of the independent predictors of cerebrovascular accidents (CVAs) following onpump isolated CABG(s).**
Methods: **A retrospective study on a total of (1192) isolated coronary patients whom were operated upon ONPUMP at the Department of Cardiology and Cardiac Surgery, "G. D'Annunzio" University, Chieti, Italy , From January 1991 to December 2001. The patients who survived less than 24 hours and who had aortic cannulation without cross-clamping were excluded.Univariate and multivariate analyses were applied to identify independent predictors of higher incidence of CVAs.**
Results: **Our study demonstrated that (23) patients out of the total number (1192) patients had experienced CVAs with an incidence of (1.93%) . Univariate analysis of risk factors in patients with and without a CVAs showed that there are seven independent factors: Low Output Syndrome (LOS) (p .000) & Simultaneous (CEA) (p .000) & LV dysfunction (EF<0.35)(p .003) & Previous CVAs (p.034) ECV(Extra Coronary Vasculopathy)(p .024) & CVD (Carotid Vascular Disease) (p.042) & COPD (p.047). In all of them p<.05. Stepwise Logistic Regression analysis for CVAs confirmed five of them (p<0.05) Low Output Syndrome (LOS) (p .0002) & LV dysfunction (EF<0.35) (p .0096) & Simultaneous carotid endarterectomy (CEA) (p .0063) & Extra Coronary Vasculopathy(ECV) (p .0315) & COPD (p.0489) In all of them p<.05**
Conclusions: **Aortic manipulation must be avoided in patients with atherosclerotic changes of the ascending aorta. Maintenance of a good hemodynamic status is crucial for any patient to reduce CVAs incidence. Patients with low EF. ; Simultaneous carotid endarterectomy ; extracoronary vasculopathy or COPD are at higher risk, and a correct surgical strategy should be tailored for each case.**

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Cerebrovascular accidents (CVAs) after surgical myocardial revascularization remain a complication that, despite the increased quality of treatment, still has an incidence that ranges from (1.0% to 3.1%) . Cerebrovascular accident-related mortality remains high. The outcome of patients with a postoperative CVA is still poor, both in the early and in the late period. Its incidence is not high, but it is relatively stable and patients who experience this event have lower long-term survival than patients who do not. (1- 11)

The pathophysiology of this severe complication is complex and multifactorial, Different authors found different risk factors, most of it focused upon arteriosclerosis of the ascending aorta .2 , 3 , 7 , 8, 12 , 13 , 14 , previous CVA 2 , 5 , 7 ,8 , 9, 10 , 15, 16, 17 , peripheral vascular disease 3 , 5 , 8 , ,10 , 17 , Carotid occlusion was a risk factor for some authors 3, but not for others 11 . Unstable angina 2 , low ejection fraction 10 and LOS 7, are logic factors and were also reported but to a less extent.

Atrial fibrillation was a risk factor in some reports 7, 21 , 22 and CPB time in others 4, 7 , 8 , 15 , 17 Calafiore et al 23 found no correlation between postoperative atrial fibrillation and CVAs incidence was found (7 CVAs in 526 patients who experienced postoperative atrial fibrillation, 1.2%, and 43 in 4,297 patients who did not, 1.0%). None of the 68 patients with preoperative atrial fibrillation had any CVA.

Other risk factors, such as age, were constantly present in the great majority of the studies 2, 3 , 4 , 5 ,8, 9 , 10 , 15 , 16 , 17, , Diabetes 2 , 5 , 8 , 10 , 16 , 17 , hypertension 2 , female sex 7, smoking 8, chronic renal failure 4, 5 , 8

Normothermic perfusion, identified as a risk factor by some studies 17, 18 but excluded by others 19 , was considered by Gaudino and associates 6 to be responsible for a superior extension of cerebral d**am**age, but this finding was not confirmed by other reports 20. Calafiore et al 23 concluded that hypothermic perfusion was related to a higher CVA rate (2.4% versus 1.2%; p = 0.023); multivariate analysis confirmed this finding.

In the last 13 years different surgical strategies for myocardial revascularization were used in our institution for patients with atherosclerotic changes. In almost all of these procedures the ascending aorta was either not touched or touched only to a limited extent and the role became revascularization with the least manipulation to the aorta of these patients.

Material and methods

Patient population

From January 1991 to December 2001, 1,192 patients underwent isolated onpump coronary artery bypass grafting (CABG). Two hundred seventy five (275) were females(23%) and nine hundred seventeen (917) were males (77%) .All the patients who died in the operating room and in the first 24 hours after operation were excluded.

Preoperative data

Patient data were taken from our database, which was assembled from the medical records. Prior CVA was documented on the basis of previous medical records and reviewing the computed tomographic scan or nuclear magnetic resonance images related to the episode. All variables included in the study are listed in the Appendix.

Perioperative data

After median sternotomy,and pericardiotomy, The quality of the aorta was assessed by the surgeon using his fingers. Disease of the ascending aorta was suspected preoperatively from the angiography or the echocardiog**am**, and, in selected cases, confirmed by computed tomographic scan. Intraoperatively, no routine epicardial scanning was performed. The operative technique has been described in detail elsewhere with nothing special in the technique,3mg \kg of heparin was administered to the patients,after preparing the conduits, Myocardial protection was achieved with Intermittent Antegrade Warm Blood Cardioplegia; Blood is taken directly from the oxygenator by means of ¼ inch tubing and a roller pump and is infused in the aortic root. The tubing is connected to a Syringe pump that deliver potassium(K) In the concentration of 2 mEq./ ml. After the first infusion of cardioplegia (600 ml of blood and 10 mEq. K In 2 min) , Reinfusions are administered every 15 min. of ischaemia(400 ml of blood and 4 mEq. K in 2 min. The body temprature is maintained at 37°c . The distal and proximal anastomoses were performed during aortic crossclamoing (Single Clamp Technique " SCT "). The left system vascularization was routinely with arterial conduits, mostly Y grafting to the anterior and lateral walls , and Vein graft to the inferior wall. Anastomosis was fashioned with 8/0 polypropylene . At the end of the grafting procedure,Transit time Flowmetry (Butterfly Flowmeter Version 111) evaluation to all grafts was done as a routine. Finally ,protamine was injected to reverse the effect of heparin.

Postoperative data

Cerebrovascular accident was defined as global or focal neurologic deficit, lasting less (transient ischemic

attack) or more (stroke) than 24 hours, that could be evident after emergence from anesthesia (early CVA) or after first awaking without any neurologic deficits (delayed CVA). Cerebrovascular accident was diagnosed by a neurologist and confirmed by a brain computed tomographic scan or nuclear magnetic resonance image. Stroke was defined as a focal or global cerebral dysfunction of presumed vascular origin lasting more than 24 hours. Transient ischemic attack was defined as a focal cerebral dysfunction of presumed vascular origin that resolved completely within 24 hours.

Statistical analysis

Results are expressed as mean value ± standard deviation unless otherwise indicated. Statistical analysis comparing two groups was performed with unpaired two-tailed Student's t test for the means or x2 test for categorical variables. All variables included in the study are listed in the Appendix. Univariate analysis of risk factors in patients with and without a CVA was performed. Stepwise logistic regression was used to select the independent variables that could predict postoperative CVAs,. For any independent predictor odds ratio (OR), 95% confidence limit when necessary, and probability value are indicated. All the multivariate analyses included univariate variables with $p < 0.2$; the final significance level for univariate and multivariate analyses was at p less than 0.05. SPSS software (Chicago, IL) was used for all the analyses in this study.

Results

Risk factors	CVA (n=23)	Non-CVA (n=1169)	P-value
Age (years)	70.5±3.7	70.8±4.4	ns
Female sex	5 (21.7%)	270 (23.1%)	ns
Diabetes mellitus	7 (30.4%)	285 (24.4%)	ns
Hypertension	14 (60.9%)	557 (47.6)	ns
Dyslipidemia	6 (26.1%)	372 (31.8%)	ns
Smoking	8 (34.8%)	364 (31.2%)	ns
COPD	4 (17.4%)	64 (5.5%)	.047
ECV(Extra Coronary Vasculopathy)	12 (52.2%)	332 (28.4%)	.024
PVD (Peripheral Vascular Disease)	4 (17.4%)	139 (11.9%)	ns
CVD (Carotid Vascular Disease)	8 (34.8%)	193 (16.5%)	.042
Left Main Coronary Artery Disease	7 (30.4%)	192 (16.4%)	.088
Previous CVAs	4 (17.4%)	62 (5.3%)	.034
Non-elective surgery	8 (34.8%)	234 (28.6%)	ns
Unstable angina	11 (47.8%)	414 (35.4%)	ns
Intraaortic Ballon Pump(IABP)	0	4 (0.3%)	ns
LV dysfunction (EF<0.35)	6 (26.1%)	75 (6.4%)	.003
Simultaneous (CEA)	4 (17.4%)	33 (2.9%)	.000
Mean CPB time (min)	65.6±30.2	65.6±23.8	ns
Mean CXC time (min)	47.3±15.2	54.2±20.7	ns
Need for Inotropic Support	1 (4.3%)	6 (0.5%)	ns
Low Output Syndrome (LOS)	6 (26.1%)	43 (3.7%)	.000
Postoperative Atrial Fibrillation (AF)	0	28(2.4%)	ns

Table 1. Univariate analysis of risk factors in patients with and without a CVAs:

CVA, cerebrovascular accident; CEA, Carotid Endarterectomy; COPD, chronic obstructive pulmonary disease; LV, left ventricle; EF, ejection fraction; CPB, cardiopulmonary bypass.

Risk Factors	OR	p
Low Output Syndrome (LOS)	6.4 (2.4-17.1)	.0002
LV dysfunction (EF<0.35)	3.8 (1.4-10.5)	.0096
Simultaneous carotid endarterectomy (CEA)	4.7 (2.1-12.3)	.0063
Extra Coronary Vasculopathy (ECV)	3.1(1.2-8.6)	.0315
COPD	2.6 (1.0-7.0)	.0489
Left Main coronary artery disease	**1.9 (0.7-4.8)**	**.1868**

Table 2. Stepwise Logistic Regression analysis for CVAs

CVA, Cerebrovascular accident ; COPD, chronic obstructive pulmonary disease; LV, left ventricle; EF, ejection fraction.

****Cerebrovascular accident incidence**: Our study demonstrated that Twenty three (23) patients had experienced CVAs out of the total number (1192) patients with an incidence of (1.93%) . Univariate analysis of risk factors in patients with and without CVAs showed that seven variables were independent risk factors for higher incidence of perioperative or postoperative CVAs. Stepwise Logistic Regression for Cerebrovascular Accident Incidence confirmed five of them. P Value was considered significant when <0.05 in both.

**Univariate analysis of risk factors in patients with and without a CVAs showed that there are seven independent factors: Low Output Syndrome (LOS) (p .000) & Simultaneous (CEA) (p .000) & LV dysfunction (EF<0.35)(p .003) & Previous CVAs (p.034) ECV(Extra Coronary Vasculopathy)(p .024) & CVD (Carotid Vascular Disease) (p.042) & COPD (p.047). In all of them p<.05

**Stepwise Logistic Regression analysis for CVAs confirmed five of them (p<0.05) Low Output Syndrome (LOS) (p .0002) & LV dysfunction (EF<0.35) (p .0096) & Simultaneous carotid endarterectomy (CEA) (p .0063) & Extra Coronary Vasculopathy (ECV) (p .0315) & COPD (p.0489) In all of them p<.05

Left Main coronary artery disease can be considered as a weak predictive value in this study regarding p Value (p.1868) p< 0.2

Comment

Poor neurologic outcomes, specifically stroke, after coronary artery bypass grafting (CABG) have been extensively reported in the past. There have been many attempts to identify patients at higher risk, as well as to identify intraoperative variables that may contribute to poor outcomes 24

Identification of risk factors allows preoperative risk stratification and may facilitate improved patient selection. Additionally, this information may contribute to reduce the risk of a stroke by providing an opportunity for adequate medical and surgical intervention. Although many reports on postoperative stroke after CABG have been published,A lot of these reports focus on the relationship between the arteriosclerosis of the ascending aorta and postoperative CVAs 2 , 3 ,4, 7 , 8, 12 , 13 , 14 .

Aortic manipulation is a very strong risk factor for increased incidence of CVA, both early and delayed. When the ascending aorta is manipulated, cerebral embolization can be the consequence. Cl**am**p removal was demonstrated to be the major source of emboli. 25

Aortic cannulation gave the s**am**e incidence of microemboli as cl**am**p application , lower than uncl**am**ping. Importance of perfusionist intervention in causing microemboli was also emphasized. 26

Anytime a vessel is manipulated, the possibility of plaque rupture, local intimal d**am**age, and thrombotic phenomena related to coagulation changes during and after the procedure has to be considered. This can cause both early and delayed strokes. Moreover, Ura and colleagues 14 demonstrated that new lesions can be identified by ultrasonography after decannulation, related mainly to cannulation itself or to aortic cross-cl**am**ping or side-cl**am**ping. Some of these lesions were located opposite from the aortic cannula, suggesting that the probable cause could be the aortic cannula jet. Thus, aortic manipulation can not only act on preexisting lesions, but also cause new ones by itself.

The impact of aortic manipulation in patients with ECV was studied by Calafiore et al. 23 concluding that Aortic manipulation was a CVA predictor in patients with ECV. However, In patients who had no ECV ; the multivariate analysis failed to confirm that in patients without ECV, aortic manipulation is a risk factor, very likely because of the small number of events.

If the different degrees of aortic manipulation are separately evaluated, each of them shows the s**am**e effects, higher for cannulation and cross-cl**am**ping, and lower for side-cl**am**ping. Side-cl**am**ping is confirmed as a CVA predictor, mainly for the delayed ones; however, this was evident only when CPB was not used 23. Other authors already advocated the elimination of side-cl**am**ping, but only for technical reasons 27; In one earlier study, Aranki and coworkers 28 also reported that SCT patients had more favorable outcomes, such as fewer strokes. Recently Kim and associates29 reported that in patients operated on with CPB, single-cl**am**p technique is not protective against CVA in coro-

nary operation, demonstrating that the topic is still controversial. Calafiore et al. 23 support these conclusions, as in patients operated on with CPB, side-cl**am**ping did not add any further risk to CVA incidence. It was an independent predictor only when CPB was not used. This means that CPB, per se, is not related to higher incidence of CVA, but the maneuvers necessary to institute it are. Conversely, myocardial revascularization without CPB does not reduce CVA incidence per se, as previously demonstrated 30, but only when any aortic manipulation is avoided.

In the last 13 years different surgical strategies for myocardial revascularization were used in our institution. In some of these procedures the ascending aorta was either not touched or touched only to a limited extent. Disease of the ascending aorta can, by itself, be an important risk factor 2 ,3 ,7 ,8 , but its detection forces the surgeon to consider possible strategies to avoid aortic manipulation 12 ,13 ,23 such as operation without CPB or arterial cannulation in peripheral sites (eg, femoral or subclavian artery) without cross-cl**am**ping. Use of arterial revascularization or proximal anastomosis of veins in nonaortic sites limits the effects of aortic disease on early outcome.

In patients whom operated upon using CPB; "SCT" Single Clamp Technique was the routine of our work aiming for minimization of the degree of manipulation of the aorta although not proved to be a risk factor in this group of patients. Safety of the cardioplegic regimen used in our center in myocardial protection was discussed in previous literatures31 and reflected on the routine "SCT" Single Clamp Technique in these patients

Our study specifically addresses the other inepenent risk factors other than dealing with the atheromatous aorta with its different degees.

Stepwise Logistic Regression analysis for CVAs confirmed five of the independent risk factors shown by the univariate analysis ($p<0.05$)

Extra Coronary Vasculopathy (ECV) showed to be a significant inepenent risk factor for CVAs in the univariate analysis (p .024) and was confimed with the multivariate analysis (p .0315) . Although It is the sumption of both the PVD and CVD , the PVD showed insignificant values in both. So, we can say that the risk become more if the Vasculopathy is Cerebral.It was shown to be significant in the univariate analysis (p .042) but not confimed in the multivariate regression analysis.

The presence of left main coronary artery disease could be considered as a risk factor as shown in the results of Stepwise Logistic Regression analysis for CVAs if P Value was considered significant when < 0.2(not in our study) . Left main coronary artery disease is related to higher incidence of ECV. It is likely that even if ECV is not diagnosed, the presence of left main coronary artery disease can be an indirect sign of some degree of vasculopathy not clinically evident, at the basis of a CVA in particular situations such as during myocardial revascularization.

A history of prior stroke or ITA is a strong predictor of recurrent stroke, and this variable is present in the great majority of the risk models . Such a history denotes the existence of pathologic conditions within the **cerebrovascular** system. 32 ,33

Univariate analysis showed that the pesence of Previous CVAs (p.034)is an inepenent risk factor .A history of neurologic disease suggests existing pathologic cerebrovascular conditions, such as impaired cerebral blood flow and autoregulation or inadequate collateral vessels, which may predispose patients to a cerebral complication after CABG surgery 34

Multivariate regression analysis in our stuy showed that Simultaneous carotid endarterectomy (CEA) is a stong inepenent factor (p .0063) for CVAs.

In our study Single Carotid endarterectomy (CEA) was performed simultaneously with CABG if the patient had unstable angina or was considered at risk for a cardiac-related event, such as left main coronary artery disease; it was performed before CABG if the patient was stable. If the patient needed bilateral CEA, the carotid artery with the most dangerous lesion was operated on before CABG and the second lesion at the s**am**e operation as CABG.

Calafiore et al. 23 analyzed more deeply the risk factor carotid disease, which was divided into carotid disease without and with CEA. The latter was the strongest one; however, the presence of carotid disease, even if without any necessity of operation, remains related to higher incidence of CVA. Whereas carotid disease can be a sign of diffuse cerebral vasculopathy, CEA of this artery can cause, both immediately and hours after operation, local clotting (perioperative and postoperative changes from hypocoagulation to hypercoagulation can be a predisposing cause) followed by cerebral embolization. These results were also shown by others 35

However, other authors 11 , in a group of patients smaller than ours, found that extracranial carotid stenosis was a risk factor for postoperative CVA, but contemporary CEA was protective. These authors advised prophylactic CEA also in patients with asymptomatic carotid stenosis of at least 75%.

Multivarient regression analysis confirmed that Low Output Syndrome (LOS) was a powerful risk factor (p .0002) At the end of the procedure,it was identified as a need for intraaortic balloon pump or inotropic agents

(epinephrine or norepinephrine, any dose; dop**am**ine > 10 µg · kg-1 · min-1; or dobut**am**ine > 5 µg · kg-1 · min-1).

Critical cerebral perfusion enhances the possibility of focal ischemia and can be at the basis of a postoperative CVA. However, a significant number of these patients had ECV, a direct expression of diffuse vascular disease, with an incidence higher than in the remaining patients. Multivariate analysis in patients with LOS showed that presence of ECV was the only risk factor for CVA. Indeed, maintenance of a satisfying hemodyn**am**ic status is crucial for brain integrity. The impact of LOS is constant in total, early, and delayed CVAs, but is higher in early CVAs, likely because of the direct effects of reduced cerebral perfusion. Other more general risk factors, such as peripheral vasculopathy or carotid disease without need of CEA, acted more on early CVA because of expression of a diffuse vasculopathy, more sensitive to any perioperative hypotension or early hypercoagulability.

Multivarient regression analysis confirmed that LV dysfunction (EF<0.35) was a powerful risk factor in t(p .0096) Several other studies have identified the same risk factors for stroke during CABG. Most probably, the mechanism related to the higher rate of CVA in patients with LV dysfunction observed in this series is related to the increased incidence of left side intracardiac thrombi as a direct cause or indirect cause through LOS affecting the brain blood supply. 32, 33, 36, 37

Surprisingly, a well-known risk factor, age, was not found to be an independent CVA predictor. Mean age was 70.5±3.7 years in patients with and 70.8±4.4 years in patients without CVA (ns).

A less common inepenent factors like Chronic Obsstructive Pulmonary Disease COPD was found significant in univariate analysis(p.047) and confirmed to be significant (p.0489) with the multivarient regression analysis. Pulmonary disease (emphysema, chronic bronchitis, restrictive lung disease, or asthma), was previously reported as a risk factor in CVAs. 34, 38

Patients with pulmonary disease probably retained carbon dioxide (thus affecting cerebral vasoreactivity) or required prolonged mechanical ventilation (thus affecting the degree of cerebral perfusion and oxygenation). 39, 40, 41

Conclusion

Postoperative CVAs are a dangerous event after myocardial revascularization, related to higher early and late mortality. Its prevention is a critical feature of coronary operation. Our study reports that preventing LOS is crucial in reducing CVA incidence in any patient, with or without ECV.

Avoiding any aortic manipulation is another goal, not always easy to fulfill, but it is valid mainly for patients with ECV. In patients with ECV any of the general risk factors increases CVA incidence. Maintaining hemodyn**am**ic stability and avoiding any aortic manipulation is crucial in this cohort of patients at high risk for postoperative CVA.

Limitations of the study

is that it is a retrospective study that considers 11 years of activity. During this time, surgical strategies changed and could influence directly CVA incidence. No preoperative screening of disease of the ascending aorta was made. Even if some patients had transesophageal echocardiography, epicardial scanning was never used. However, this reflects the reality of the great majority of the operating theaters and, for this reason, the conclusions of this study can be used by the great majority of surgical te**am**s.

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OUTCOMES OF REDO CORONARY ARTERY SURGERY

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Objective: **To assess early and midterm results of redo CABG procedures performed .**

Methods: **Between 2004 and 2007 twenty five patients underwent redo-CAGB in Cairo University hospitals and National Heart institute. History of myocardial infarction (MI) was present in 19 (76 %) patients, reduced (<50%) left ventricular ejection fraction in 10 (40 %) patients.. Coronary angiography revealed left main disease in 4 (16%) patients, three-vessel disease in 17 (68%) patients, and graft occlusion in 21 (84%) patients.**

Results: **The redoCABG procedures included 25 operations with the use of cardiopulmonary bypass, performed through median sternotomy. One intra-operative death occurred. In the postoperative period 5 (20%) patients developed peri-operative MI, 3 (12%) - renal failure, and 7 (28%) - heart failure. Four (16%) patients required prolonged intubation. There were three deaths. Thus, in hospital mortality rate was 12% (3 patients). Twelve patients remained free from anginal symptoms, 8 were in CCS class I, 2 - in CCS class II, and there were no patients in CCS class III or IV.**

Conclusions: **RedoCABG can be performed successfully in most cases but in-hospital mortality and morbidity are higher compared with primary CABG. Patients are older had longer time between bypass operations during which underwent more MI . survival is good with improved quality of life and reduction of anginal symptoms.**

Between 2004 and 2007 twenty five patients underwent redo-CABG.

Fifteen (62%) patients had a history of myocardial infarction (MI). Ten (40%) patients had reduced (<50%) left ventricular ejection fraction (LVEF). Clinical data are presented in Table I.

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	n (%)
Males n (%)	19 (76 %)
Females n (%)	6 (24 %)
Age (years) < 60 > 60	 9 (36 %) 16 (64 %)
Myocardial infarction	15 (60 %)
Ejection fraction <50%	10 (40 %)
Hypertension	12 (48 %)
Hyperlipidemia Ch>250 TGS >200 TCS	 22 (88 %)
Congestive heart failure	4 (16 %)
lung disease	3 (12 %)
History of PTCA	6 (24 %)
Insulin-dependent diabetes	13 (52 %)
History of cerebrovascular accident	2 (8 %)

Table I. Clinical characteristics

During primary CABG. The types of implanted grafts are listed in Table II

Coronary artery	LAD	MO	DIAG	RCA	PLCX
Number of grafts	25	18	7	11	2

Table II. Type of graft performed during primary CABG

Clinical indications for redoCABG (Table III)

Coronary artery disease	Total
CCS class II	3 12%
CCS class 111	8 32%
CCS class IV	14 56%
Total	

Table III. Clinical indications for redoCABG

In all patients the decision to perform a repeated surgery was based on the clinical presentation. The recurrence of angina took place from 3 to 12 months, prior to the redoCABG. Persistence of anginal symptoms in spite of pharmacotherapy was an indication for coronary angiography and subsequent redoCABG. Based on the patient's history, 15 (60 %) had unstable angina whereas 10 (40 %) - stable angina.

Coronary angiography findings

The majority of patients (24 patients - 92.3%) had a multi-vessel disease are presented in Table IV .

	n (%)
Multi –vessel disease	24 (68 %)
Left main stenosis TCS	4 (16 %)
Graft occlusion	21 (84 %)

	<5 years (n=1 1)n (%)	> 5 years (n=15) n (%)	Total (n=26) n (%)
Progression of coronary atherosclerosis	6 (24)	7 (28)	13 (52)
Graft occlusion	3 (12)	9 (36)	12 (48)

Table V. Factors causing angina recurrence during follow-up in respect to the time from primary CABG to redoCABG

The chest was opened through sternotomy as in the first procedure. After partial heart dissection from adhesions and administration of heparin, extracorporeal circulation (ECC) was started in the typical manner (cannulation of aorta and right atrial appendage). Next, the remaining part of the heart was liberated from adhesions. In cases with easily accessible coronary vessels or contraindications to ECC, the procedure was performed on a beating heart (OPCABG). After coronary arteries were identified, new grafts were implanted. In order to minimise the number of grafts, left and right internal mammary arteries (LIMA and RIMA) were used whenever possible. Radial artery or saphenous vein were used for other grafts. Drains left in the mediastinum, pericardium and, if necessary, in the pleural cavity.

Results

Early results were assessed by analysing intra-operative and peri-operative data, taking into account complications, early mortality and the extent of revascularisation procedure.

The mean time of follow-up was 16.4 months. Postoperative adhesions in the anterior mediastinum or pericardium which were present in all patients.

Identification of coronary arteries, located on the epicardial surface which was covered by fibrin, was difficult in all patients. Altogether, in 25 patients 62 grafts were implanted (a mean of 2.48 grafts per patient). In 16 (64%) patients arterial grafts were used, including 6

RIMA grafts and 10 radial artery grafts. In 22 (88%) patients venous grafts were implanted. ECC was completed without any problems in 8 (32%) patients whereas 14 (56%) patients required administration of inotropic support and in 3 (12%) patients additional reperfusion, high doses of inotropic agents and intraaortic balloon pumping were needed to terminate the ECC successfully in two of them a failure of one due to (LCO). The total duration of ECC was quite long and ranged from 90 to 256 min (mean 120.3 min) which was mainly due to the prolonged initial part of the procedure when the heart had to be liberated from adhesions. Duration of stay in the post-operative unit ranged from 12 hours to 10 days (mean 4 days). The intubation time ranged from 8 to 60 hours (mean 10.5 hours). Postoperative complications are listed in Table VI. During the post-operative period two patients died. One death was due to peri-operative infarction. The second patient died due to ventricular fibrillation with subsequent electro-mechanical dissociation. Thus, including one intra-operative death, the total in-hospital mortality was 12 %.

Complication	n (%)
Prolonged intubation (>24 hours)	4(16)
Left ventricular failure	7(28)
- with intra-aortic balloon pumping	2(8)
Peri-operative infarction	5(20)
Renal failure	3(12)
Wound infection	1 (4)
Increased pleural drainage (>1000 ml during the first day after surgery) Exploration	6(24) 2 (8) (4)
Blood transfusion	19(76)
Atrial fibrillation	4(16)
Ventricular fibrillation	3(12)
Atrio-ventricular block	2 (8)

Table VI. Complications following redoCABG

Mid-term results

The (22) patients were followed up in outpatient clinic. The duration of follow-up ranged from 3 to 24 months (mean 16.4 months). Anginal symptoms were present in 10 (45%) patients, however, there were mild or moderate, being in CCS class I in 8 patients and in CCS class II in 2 patients. Because of transient aggravation of angina, 3 (14.3%) patients were hospitalised; in two of these patients PTCA was performed. The remaining 12 (48%) patients remained free from angina. 15 (68%) patients developed mild heart failure symptoms (NYHA class I), and 3 (13.6%) patients - moderate heart failure symptoms (NYHA class II).

DISCUSSION

For many reasons, redoCABG is a more difficult and dangerous procedure than standard primary CABG. Postoperative adhesions in the mediastinum or pericardium may be the cause of cardiac injury during sternotomy. The need for heart preparation increases the duration of bypass, causes a danger of destruction of already existing grafts. Thickened epicardium makes visualisation of coronary arteries difficult. In many cases grafts can not be implanted because coronary artery can not be identified. Taking into account the very high proportion of patients with a multi-vessel disease (68% in our study)..

Difficulties during redo CABG may be also due to the limited access for grafts. According to literature, peri-operative mortality in redoCABG is higher than following primary CABG and ranges from 3.7% to 12.5% (1-6), and in urgent procedures may reach even 13 to 40% (3, 5). The post-operative complication rate is also higher; in particular, peri-operative infarctions are frequent, occurring in 6.3-16% of patients (2, 5).

Indications for redoCABG are often difficult to establish because of the high risk of this procedure. Data from literature show that long-term mortality rate following surgical treatment of patients with early (<5 years) dysfunction of grafts is similar to conservative therapy, even in cases when graft to LAD is occluded. However, the quality of life is much better following redoCABG than in patients who remained on pharmacological therapy because the symptoms of angina are significantly reduced (9, 10). According to Christenson et al. perioperative mortality is higher when redoCABG is performed within one year of the primary procedure (2). The prognosis in patients with late (>5 years) graft dysfunction in whom progression of coronary artery atherosclerosis is significant, is different from that in patients with early graft dysfunction. It has been shown that in this population of patients the long-term mortality is significantly higher in patients treated conservatively than in patients who undergo redoCABG, particularly in those with LV dysfunction, left main stenosis or multivessel disease (9, 10). To conclude, a patient should be selected for redoCABG when anginal symptoms are increasing and the time since the primary procedure is long enough. Indications for surgery should be mainly based on clinical symptoms which was apparent in our study - of 25 patients as many as 22 were in CCS class III or IV. It seems unjustified to expose a patient to all

the risks of redoCABG only on the basis of the results of coronary angiography. Overall, the 5-year survival rate following redoCABG is satisfactory and according to literature ranges between 75 and 90.1% (2, 4, 7).

Dysfunction of grafts and progression of atherosclerosis in coronary arteries, are the main causes of angina recurrence. According to our findings, the contribution of these factors in symptom recurrence depends on the time passed from the primary CABG. During the first five years, problems with progression of coronary atherosclerosis are dominant, whereas in the later stages of follow-up graft patency becomes more important. Various factors cause graft malfunction. Histological changes in vein grafts may be observed as early as 2 to 3 months following surgery. Narrow microlesions with thrombus may be seen in the endothelium (11-13). Early thrombosis in vein graft, occurring up to 4-5 years after surgery, is usually caused by an inadequate blood flow through the vessel due to graft occlusion following technical surgical error or low blood uptake in case of poor distal run off. The effects of risk factors as smoking have also to be taken into account (11-13). Intimal proliferation which is the first step of atherosclerosis, are observed in vein grafts shortly after surgery (within a few months). These extensive, concentric and progressive changes cause graft narrowing and finally, closure. Graft dysfunction due to atheromatous changes may be enhanced by thrombus formation which is a frequent finding in this place (11, 12). Intra-graft thrombus may be also a source of thrombosis of distal coronary arteries which is an important issue during redoCABG because of the possibility of mechanical dislodgement of thrombi. After 10 years, the proportion of closed vein grafts is high, reaching 30%, whereas a further 30% of these grafts show significant narrowing (13).

Atherosclerotic changes in arterial grafts develop much slower compared with vein grafts. They remain patent for many years. It has been shown that the first and most frequently performed anastomosis - LIMA to LAD, shows a high patency rate even 20 years after surgery (13). Because LAD is the most important vessel for a systolic function of the LV, arterial grafting of this vessel decreases mortality and the need for redoCABG during long-term follow-up. These results prompted the use of other arteries for grafting such as radial artery. However, the duration of follow-up is not as long as that concerning the use of mammary arteries.

The course of atherosclerotic changes in arterial grafts is different than in native coronary arteries. The changes mainly develop in segments proximal to anastomosis and adversely effect graft function. This cause obstruction of the graft and may diminish blood uptake from the graft with subsequent graft thrombosis when they develop in a distal part of the coronary artery.

CONCLUSIONS

Our data suggest that surgery can be performed and give expectation for success in early results. Progression of atherosclerosis in coronary arteries and graft dysfunction are the two main causes of angina recurrences following CABG. Reoperative coronary grafting is currently being performed in patients with greater incremental risk. Indications for redoCABG are mainly based on clinical presentation (CCS class III or IV), particularly when the time from primary procedure is long. Peri-operative mortality and peri-operative infarction rate are higher after redoCABG than primary procedure which is in line with data from literature.

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ROUTINE USE OF TRANEXAMIC ACID PREOPERATIVELY IN CORONARY ARTERY BYPASS SURGERY

Cardiovascular

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Background: **Our objective in this study was to study the effect of low-dose tranexamic acid on postoperative bleeding after coronary artery bypass operation done on-pump.**
Methods: **200 patients undergoing primary coronary artery bypass were divided into two groups. One group composed of 100 patients received 2g tranexamic acid with induction of anesthesia. The other group also composed of 100 patients received placebo. Data measured included blood loss, blood transfusion or its products and reoperation.**
Results: **All demographic data were the same between the two groups. Postoperative bleeding was less in the tranexamic acid group (184±115 mL versus 528±218 mL, p, 0.001), also blood transfusion was higher in the placebo group (all the patients in placebo group received blood transfusion when only 32 patients in tranexamic acid group received blood transfusion.). The number of packed red blood cells received is also less in tranexamic acid group. Platelet number was reduced equally in both groups by cardiopulmonary bypass. Other test results were not statistically different between groups.**
Conclusion: **The use of low-dose tranexamic acid after induction of anesthesia in coronary artery bypass significantly reduced the coagulopathy-induced postoperative bleeding and allogenic blood products requirements.**

Bleeding as a result of coagulopathy caused cardiopulmonary bypass (CPB) is an important factor affecting the morbidity and mortality in patients undergoing cardiac operation(1). The coagulopathy is multi-factorial with platelet dysfunction and plasmin-induced fibrinolytic activity represents the major contributors to the process (2). Postoperative bleeding may lead to allogenic blood transfusion and/or reoperation, which are independently associated with a number of adverse outcomes (3). This caused a renewed interest in the pharmacological reduction of bleeding (4).

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Pharmacological agents to reduce bleeding have recently gained much interest, since they are readily available, easy to administer, can be used prophylactically, do not require the use of costly equipment, and appear to be very safe and efficacious. The perioperative use of tranexamic acid have gained acceptance around the world for the prophylactic reduction of allogenic blood transfusions in cardiac operation patients.

Tranexamic acid is a synthetic lysine analogue antifibrinolytic. It competitively inhibits the activation of plasminogen to plasmin, and is also a weak noncompetitive inhibitor of plasmin, blocking its action on fibrin. Thus, tranexamic acid is thought to act by preventing the premature dissolution of the normal fibrin clot. It is also possible that tranexamic acid may help to pre-

serve platelet function, by reducing the effect of plasmin on platelet membrane receptors (5).

Kojima and his colleagues studied the effects of tranexamic acid on fibrinolysis and bleeding during and after cardiopulmonary bypass surgery and concluded that it can inhibit fibrinolytic activity during CPB by reducing tissue plasminogen activator activity and by blocking plasmin activity measured as D-dimer. In contrast, tranexamic acid has no influence on the release of plasminogen activator inhibitor-1 from endothelium and neutralization of plasmin by α2-antiplasmin. These results suggest that the antifibrinolytic effects of tranexamic acid can bring the reduction of blood loss in patients undergoing CPB surgery (6).

Fortunately, the incidence of complications, such as graft thrombosis leading to myocardial infarction, stroke, renal dysfunction and allergic reaction is low (4). The results of Ruel on 221 patients underwent primary CABG with end-arterectomy suggest that the clinical effectiveness of tranexamic acid in reducing postoperative blood loss in patients undergoing coronary end-arterectomy is not associated with a higher incidence of myocardial ischemia-related complications (7).

We speculated whether preoperative use of tranexamic acid as a routine, would have any major significant clinical haemostatic effects in a group of patients with low risk of postoperative bleeding in our hospital.

Patients and Methods

Between October 2006 and October 2007, 200 patients scheduled for elective or urgent CABG were enrolled in the study. Patients were randomly assigned to one of two groups: Group "A" (100 patients), to receive tranexamic acid (TA) immediately after induction of anesthesia, and group" B "(100 patients), who received equal volume of placebo.

I. Selection Criteria:

Exclusion criteria:

1) Patients with a history of abnormal bleeding or abnormal coagulation profile.
2) Patients had recent (< 7 days) acetylsalicylic acid ingestion, thrombolytic therapy (streptokinase) or anticoagulant therapy (heparin < 4 hours or warfarin < 3 days).

Inclusion criteria:

All adult patients with ischemic heart disease subjected to CABG procedure.

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 a special emphasis on any coagulation problems, full laboratory investigations with special emphasis on hemoglobin, hematocrit, platelet number, international randomized ratio (INR) and transthoracic echocardiography.

III. Operative Management:

Anesthetic technique:

Routine anesthetic procedures were employed. All patients were premedicated with an intramuscular injection with morphine half an hour preoperatively. Induction of anesthesia with a bolus of midazolam and fentanyl. Muscle relaxation was achieved and maintained with pancuronium. Anesthesia was maintained with isoflurane (pre-cardiopulmonary bypass) and propofol infusion during CPB.

Drug administration:

Tranexamic acid was administered as an intravenous bolus dose of 2g after induction of anesthesia and before skin incision.

Surgical technique:

In all cases, access to the heart was obtained through a median sternotomy. The left internal mammary artery was harvested in all patients. Saphenous veins were used as routine grafts for coronary anastomoses other than left anterior descending. Anticoagulation was achieved using 300 IU/kg of heparin before cannulation. Cardiopulmonary bypass was instituted in a standard fashion.

Myocardial protection was achieved by intermittent warm blood antegrade cardioplegia solution with repeated doses every 20 minutes. The heparin effect was reversed by protamine administration (3mg/kg). Before closure of the chest, mediastinal and pleural tubes were positioned in the mediastinum and left pleura separately (the left pleura was routinely opened). A chest tube was positioned on right chest only when the right pleuron was opened.

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), number of grafts, Weaning from CPB and use of inotropes. All distal anastomoses were performed first and proximal anastomoses were performed after declamping but on total bypass.

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, Duration of ICU stay and In-hospital mortality, postoperative blood loss, the number of patients requiring blood transfusion, and the need for surgical re-exploration within 24 hours.

Bleeding was monitored as chest tube output at hourly intervals in the ICU until the next morning. The type of allogenic transfusions (packed red blood cells, platelets and FFP) during and after the operation was registered. Secondary outcome measures were development of perioperative myocardial infarction (by ECG and troponin level), acute renal insufficiency (creatinine value twice the baseline or need for dialysis), transient ischemic attacks or stroke, mediastinal infection within 30 days.

Indication for postoperative transfusion of allogenic red blood cells was a hematocrit below 25%. Indication for fresh frozen plasma (FFP) and platelets is excessive chest tube drainage with no signs of clot formation. Indication for re-exploration is chest tube drainage by a rate of 3 to 5 ml/kg/hour for three successive hours or drainage affecting haemodynamics.

Results

Preoperative data are presented in tables (1) and (2). Preoperative Hb values were not significantly different between groups which were the same also for platelet count and coagulation profile as shown in table (3). No difference was observed with regard to type of graft used, number of grafts per patient, CPB time, or cross clamp time as shown in table (5). By 24 hours postoperatively Hb in the control group was higher. Also as a result o more platelet transfusions, platelet count in the control group increased compared with that of the study group as shown in table (6).

		Group A	Group B	p value
Age (y)		65.6±9	65±13	0.86
Sex	Male	80(80)	72(72)	0.78
	Female	20(20)	28(28)	0.74

Table (1): Patients' age and sex

The amount of mediastinal bleeding during the first 24 hours after the operation was significantly less in the TA group compared with the control group(184±115mL versus 528±218mL, p <0.001). More units of packed red blood cells were administered in the first 24 hours after the operation to the control group table (7). The percentage of patients exposed to blood products was 100% in the control group compared with 32% in the TA group (p<0.001).

	Group A	Group B	p value
Diabetes mellitus	20	28	0.74
Hypertension	60	44	0.39
Smoking	74	58	0.39

Table (2): Risk factors

7 patients, 1 in the group A and 6 in the group B were reopened due to excessive bleeding. Surgically correctable bleeding was found in 5 patients and non-surgically correctable cause was present in the remaining 2 patients all of them were in the group B. There were 4 mortalities, 2 of them due to repeated arrhythmias the other 2 patients had unexplained hypotension and they died after discharge from the ICU. None experienced postoperative Myocardial infarction, mediastinal infection or stroke within 30 days.

	Group A	Group B	p value
Hemoglobin	12.3±0.9	12±0.9	0.39
Hematocrit	36.9±0.04	36±3.1	0.73
Platelet count	245±58	209±103	0.47
INR	1.1±0.1	1.1±0.1	0.73

Table (3): Preoperative laboratory Results

	Group A	Group B	p value
Urgent	20	16	0.61
Elective	80	84	0.76

Table (4): Timing of surgery

	Group A	Group B	p value
CPB time(min)	125±40	133±43	0.41
Cross clamp time(min)	66±23	78±27	0.08
Number of grafts	2.6±1.3	2.7±1.4	0.64

Table (5): Operative assessment

	Group A	Group B	p value
Hemoglobin	8.9±3.2	9.6±0.4	0.08
Hematocrit	26.9±3.2	28.7±2	0.05
Platelet count	128±27	145±42	0.16
INR	1.4±0.1	1.4±0.1	0.99

Table (6): Postoperative laboratory Results

	Group A	Group B	p value
Bleeding (ml)	184±115	528±218	<0.001
Number of patients receiving transfusion	32	100	<0.001
Packed cells	0-4	1-6	<0.001

Table (7): Mediastinal bleeding and patients receiving transfusion in the first 24 hours

Discussion

Prophylactic use of TA has been shown to reduce perioperative blood loss following primary elective heart operations including primary myocardial revascularization in several randomized, placebo-controlled studies and meta-analyses (8). Meta-analysis of multiple studies has shown aprotinin and anti-fibrinolytics to reduce mediastinal chest tube drainage by 30% versus placebo. Although delivery protocols were uniform for aprotinin, they still vary widely for TA (9).

Tranexamic acid has been shown as effective as aprotinin in reducing coagulopathy-caused bleeding after CPB and cheaper than aprotinin (10). As TA is presently is the available drug of choice to reduce coagulopathy-caused bleeding, we designed our study to gain knowledge about the benefit of using low-dose TA in terms of reducing blood loss and allogenic transfusion.

In the preoperative data of our patients, in both groups, there was no statistically significant difference as regard to the age and sex. The age was slightly high as all our patients were ischemic cardiac patients subjected for CABG procedure with predominance of males due to the nature of the disease, more affecting males.

As regard preoperative risk factors for ischemic heart disease, there were no statistical differences between both groups and there were high percentage of smoking and systemic hypertension. In preoperative laboratory data there were no abnormalities in the platelet counts of the patients or their coagulation profiles preoperatively. There was slight anemia preoperatively in our patients which are common figures in this community, keeping in consideration doing the research in a public hospital.

In a low-risk patient population, TA was shown to decrease mediastinal bleeding after cardiac operation as early as 1990 (8). A similar result was found in studies by Karski and associates. The first significant study of a uniform patient population undergoing coronary operation was reported by Rousou and colleagues. They retrospectively studied 415 patients undergoing CABG excluding emergency and redo operations. The first 209 patients were operated on without TA and the subsequent 206 with a 2g bolus of TA followed by 8g during the procedure. Chest tube drainage in the control group was 1114mL versus 803mL in the study group (8).

A double-blind randomized placebo-controlled study was reported from Brook Army Medical Center on patients undergoing primary coronary artery operation. The dose of TA was 15 mg/kg before CPB and 1 mg/kg continued for 5 hours. The bleeding was reduced from 1202mL in the control group versus 1020mL in the TA group. Since then, multiple studies have shown the efficacy of TA in prospective studies comparing patients receiving TA to groups receiving aprotinin or ε-aminocaproic acid (EACA) (2).

In all previously mentioned studies the authors used high doses of TA. The aim of this study is to answer the question of whether the addition of low-dose TA as given in our study will be beneficial. In our study although control patients only bled 528mL in 24 hours, the use o TA significantly reduced this even further to 184mL. The low amount of bleeding in the TA group is compatible with recently published reports.

The increased platelet transfusions in the control group most probably represent more oozing in the control group whereas the lower percentage of platelet transfusion in the study group is probably not related to any effect of TA on platelet number and function. This increased platelet transfusion in the control group explains the high platelet count in the control group at 24 hours after the operation.

Extracorporeal circulation causes fibrinolysis by plasmin activation (11). Tranexamic acid is a competitive inhibitor of plasminogen and, at higher doses, acts as a noncompetitive inhibitor of plasmin (2). The timing of TA administration to reduce postoperative blood loss is unclear. It is both logical and established that TA should be given before CPB as an initial dose (2). Whether to continue the TA after the operation is controversial. Tranexamic acid has been used effectively when given up to 12 hours after an operation and when only given during the operation. They postulated that because the half-life of TA is 80 minutes, a second bolus would prevent fibrinolysis after the operation. A recent study failed to prove the efficacy of postoperative administration of TA (12).

Andreasen and Nielsen concluded in their study that an anti-fibrinolytic effect following prophylactic use of tranexamic acid in elective, primary CABG among patients with a low risk of postoperative bleeding did not result in any significant decrease in postoperative bleeding compared to placebo group (13). This was not in concordance with many other studies findings, which could be attributed to the act that they give additional heparin dose to the patients in the study group than the control group which led to significant increase in APTT (activated partial thromboplastin time) in the treatment group next morning. Another factor may contribute to their result was their exclusion of the reopened cases for bleeding from the study which were more in the control group.

Ruel and his colleagues studied giving prophylactic TA in cases of coronary endarterectomy. They said intra-operative use of TA in patients undergoing coronary endarterectomy is safe and effective in reducing postoperative blood loss (7). We concluded that administering a low dose of 2g of tranexamic acid with induction of anesthesia is associated with decreased fibrinolysis during CPB. This effect has positive clinical results in terms of bleeding and blood transfusion in patients undergoing primary CABG.

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CAN LOCAL APPLICATION OF TRANEXAMIC ACID REDUCE POST- CABG BLOOD LOSS?

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Introduction: **Diffuse microvascular bleeding remains a common problem after cardiac procedures.**
Systemic use of antifibrinolytic (tranexamic acid) reduces the postoperative blood loss.
The purpose of this study was to examine the effectiveness of local application of tranexamic acid to reduce blood loss after coronary artery bypass grafting (CABG).
Methods: **Thirty eight patients scheduled for primary isolated coronary artery bypass grafting were included in this double blind, prospective, randomized, placebo controlled study.**
Group (I) included 19 patients who received 1 gram of tranexamic acid diluted in 100 ml normal saline. Group (II) included 19 patients who received 100ml of normal saline only as placebo. The solution was purred in the pericardial and mediastinal cavities. Postoperative blood loss and blood product transfusion were compared between the two groups.
Results: **Both groups were comparable with respect to baseline demographic data and surgical characteristics. During the first 24 hours postoperatively, cumulative blood loss was significantly less in TA group (691.1 + 377.3 ml) compared to Placebo group (1094.1 + 672.1 ml) (P =0.03). There was no significant difference in the post-op Packed RBCs transfusion between both groups (1.53 + 1.47 units vs. 1.95 + 2.12 units, respectively)**
(P = 0.5). Significant less platelets transfusion required in TA group (0.47 + 0.84 units) than in placebo group (1.57 + 1.87 units) (P= 0.02). Apart from re-exploration for surgical excessive bleeding in one patient in the TA group, no difference was found in morbidity or mortality between the two groups.
Conclusion: **Topical application of tranexamic acid solution in patients undergoing primary coronary artery bypass grafting led to a significant reduction in postoperative blood loss without adding extra risk to the patient. Consequently tranexamic acid could be advocated for routine use topically in patients undergoing coronary artery bypass grafting.**

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Coagulopathy remains a common problem after coronary artery bypass Grafting (CABG) using cardiopulmonary bypass (CPB). It results from many factors like thrombocytopenia, acquired platelet dysfunction, clotting factors loss, free heparin, and increased fibrinolysis (1-3). Lemmer and Colleagues4 found that extracorporeal circulation results in significant fibrinolysis, as reflected by increased concentrations of plasmin and fibrin degradation products (FDP), both of which have deleterious effects on platelet function. Re-exploration for bleeding following cardiac surgery with CPB was reported to be in the range of 2-7%. Of these, 50-80% was found to be medical rather than surgi-

cal bleeding5. Fibrinolysis was found to be responsible for 25-45% of significant postbypass bleeding6. Many antifibrinolytic agents have been used to diminish postbypass bleeding. These include ε aminocaproic acid5, aprotinin7, and tranexamic acid (TA)8. Tranexamic acid has been found to bind to lysine binding sites of plasmin and plasminogen. Saturation of these sites displaces plasminogen from the fibrin surface thus inhibiting fibrinolysis9. TA has been used both systemically and topically. Intravenous TA administration increased the risk of thromoembolic complications and consequently early graft closure in coronary artery bypass grafting10. When used topically, TA was found effective in controlling bleeding in patients with hemorrhagic diathesis and in patients who were being treated with anticoagulants pre-operatively. Topical TA has also been successfully used in controlling bleeding in bladder, gynaecologic, oral, and otolaryngeal surgeries11-13.

This prospective, double-blind, randomized, placebo-controlled study was designed to investigate the effect of topical TA in reducing postoperative blood loss after coronary artery bypass Grafting.

Methods

With institutional ethics committee approval, all patients scheduled for primary isolated elective CABG between March 2004 and November 2005 were eligible for enrolment. Our exclusions criteria included patients who had combined procedure; redo surgery, bleeding diathesis (Haemophilia or platelet count < 100 X 109 L-1), renal failure (Creatinine > 160 mg/dl), known allergy to TA, recent (<7days before surgery) intake of anti-platelets (e.g. Aspirin, non-steroidal anti-inflammatory drugs) or Heparin administration within 48 hours of operation.

Thirty eight patients met the requirements for inclusion, and informed consent was obtained from all of them. The patients were randomly allocated into one of the two groups. Group I (TA group) included 19 patients who received 1 gm of TA diluted in 100 ml normal saline. Group II (Placebo group) included 19 patients who received 100 ml normal saline as placebo. The solution was purred in the pericardial and mediastinal cavities before closure of the strenotomy while clamping the chest tubes. These clamps were released once the closure of the strenotomy was completed.

The study was carried out as a prospective randomized, double blind investigation. Randomization was carried out with random-number tables by a research pharmacist who prepared the two solutions in two identical bottles and delivered to the operating theatre. Neither the surgeon, assistant, anaesthetist, scrub nurse nor the perfusionist knew the composition of the solution administered. Only two cardiac surgeons were responsible for the surgical hemostasis.

The anaesthetic management and conduct of CPB were standardized. The patients were premedicated using nitrozepam 0.1 mg/kg tablet the night of the operation, and morphine 0.15 mg/kg intramuscular half an hour before operation. Induction was done using Fentanyl 2-5 ug/kg, Propofol 1-2mg/kg, and Pancronium 0.1mg/kg. Anesthesia was maintained by using Sevoflurane 0.5-1%, Pancronium 0.06 mg/kg, Fentanyl 1-2ug/kg during cardiopulmonary bypass time. All patients received Heparin 300 units/Kg before CPB to achieve target activated clotting time (ACT) of > 480 seconds. During CPB, extra heparin was given as needed to maintain the target ACT. After separation from CPB, heparin was reversed using protamine sulphate in the dose of 1 mg/100 units of heparin to achieve target ACT 80-120 seconds.

After the patient was transferred to the intensive care unit (ICU), continuous low grade suction (10-15 cm H2O) was applied .together with periodic milking of the drains. Haemoglobin level (Hb), Hematocrite value (Hct %), Platelet count, International Normalized Ratio (INR), Partial Thromboplastin time (PTT), and Fibrinogen level were measured before the operation and when the patients arrived at the intensive care unit. The drainage of the chest tubes was measured hourly and were removed when the total drainage volume of 80-100 ml over the previous12 hours and of serous color. Uniform transfusion protocol was applied to all patients. Blood and blood components were administered only when the hemocrite level < 24% or the haemoglobin level < 8.0gm/dL in the postoperative period. Shed mediastinal blood was not transfused into any patient during this study.

Beside patients' demographics, the numbers of grafts, left internal mammary artery (LIMA) use, cross-clamp time, duration of CPB, incidence of reoperation for bleeding, ICU stay and the length of hospital stay (LOS) were recorded for all patients.

Statistical Analysis

Data were expressed as mean ± standard deviation. Differences between the two groups were analysed using 2- tailed unpaired student t test. Values of p less than 0.05 were considered significant. Statistical analyses were made by using Excel for windows.

Results

Both groups were comparable with respect to baseline demographic data and there was no statistically significant difference in the prevalence of risk factors between both groups as shown in Table 1.

	TA (n=19)	Placebo (n=19)	*P*-Value
Age (y)	55 ± 11	60 ± 7	0.17
M/F	18/1	18/1	1.0
Wt. (Kg)	73 ± 15	71 ± 14	0.74
BMI	27 ± 4	27 ± 4	1.0
Smoking	6 (31.5%)	6 (31.5%)	1.0
Diabetes	7 (37%)	10 (53%)	0.42
Hypertension	7 (37%)	12 (63%)	0.17
Hyperchol	3 (16%)	0 (0%)	0.08
COPD	1 (5%)	1 (5%)	1.0
RF	0 (0%)	1 (5%)	0.33
PVD	3 (16%)	0 (0%)	0.08
Previous MI	4 (21%)	6 (31.5%)	0.42
LVEF	48 ± 10	46 ± 10	0.49
Euroscore	2.3 ± 1.7	2.5 ± 1.6	0.58

Table 1. Patients' Demographics.
Values are means + SD where shown.M/F: Male/Female Wt.: Weight BMI: Body Mass Index COPD: Chronic Obstructive Pulmonary Disease RF: Renal Failure PVD: Peripheral Vascular Disease MI: Myocardial Infarction LVEF: Left Ventricular Ejection Fraction

The two groups were matched with regard to intra-operative data; use of left internal mammary artery, average number of distal ananstmoses, cross clamp time, cardiopulmonary bypass (CPB) time and duration of the operation (Table 2).

	TA	Placebo	*P*-Value
Graft/pt	2.8 ± 1.1	2.9 ± 1.0	0.64
LIMA	100%	100%	1.0
CX time (min)	72 ± 17	75 ± 20	0.09
TBT (min)	100 ± 28	97 ± 28	0.07

Table 2. Intra-operative Data.
Values are means + SD where shown.
LIMA: Left Internal Mammary Artery. CX Time: Cross Clamp time. TBT: Total Bypass time.

There was no bias in the distribution of the anaesthesiologist and surgeons between the two groups. Pre and postoperative haemoglobin concentrations, hematocrit concentrations, platelet counts, international normalized ratio, partial thromboplastin times and fibrinogen level were not significantly different between the two groups (Tables 3&4). Chest tube drainage in the first 24 hours was significantly less in TA group (651 + 398 ml) in the placebo group (1032 + 693 ml) (p=0.04). This represented about 37% decrease in the blood loss. Total post-operative chest tube drainage was 732 + 430 (range 248- 2105 ml) in TA group and 1080 + 726 ml (range 210-3010 ml) in the placebo group, which represents 32% reduction in total bleeding (Figures 1 &2).

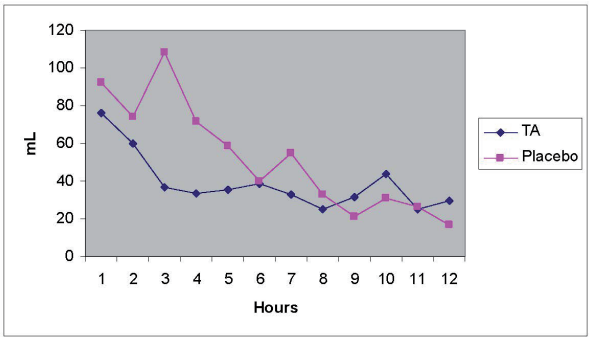

Figure 1. Post-op Blood Loss /Hour

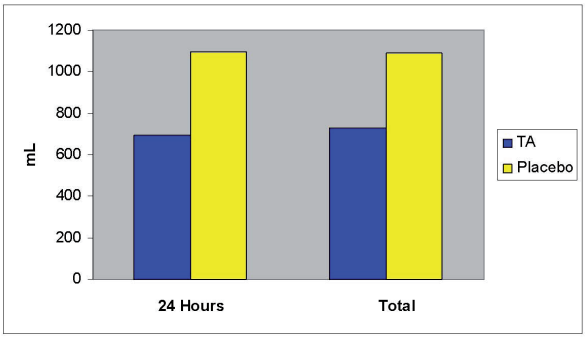

Figure 2. Post-op Blood Loss

There was no significant difference in the post-op Packed RBCs transfusion between both groups (1.53 + 1.47 units vs. 1.95 + 2.12 units, respectively) (P = 0.5). Also there was no significant difference in regard Fresh Frozen Plasma (FFP) transfusion between both groups (1.2 + 1.6 units vs. 1.3 + 1.2 units, respectively) (P = 0.7). Significant more platelets transfusion required in the Placebo group (1.57 + 1.87 units) than in TA group (0.47 + 0.84 units) (P= 0.02) (Figure 3). Tropo-

nin I level recorded a lower level in TA group (2.4 + 3.8) than Placebo group (4.7 + 2.0) (p= 0.68). There was no post-op myocardial infarction encountered in either group. Although there was no difference in intubation time between both groups, Placebo group patients stayed significantly longer in ICU (49 + 20 Hrs) than the TA patients (29 + 26) (p=0.02). Total length of Hospital stay was comparable in both groups (Table 5).

	TA	Placebo	*P*-Value
Platelets	265 ± 119	156 ± 71	0.77
Hb (gm/dl)	14 ± 1.0	14 ± 1.3	0.08
Hct (%)	39 ± 2.8	41 ± 3.7	0.15
INR	1.1 ± 0.3	1.0 ± 0.2	0.23
PTT	31.2 ± 4.8	33.6 ± 3.5	0.34
Fibrinogen	362 ± 163	438 ± 158	0.46

Table 3. Pre-operative Hematologic Profile
Values are means + SD where shown. Hb: Hemoglobin. Hct: Hematocrite Value.INR: International Normalized Ratio. PTT: Partial Thromoplastin Time

	TA	Placebo	*P*-Value
Platelets	192 ± 64	196 ± 68	0.86
Hb (gm/dl)	10 ± 1.3	10 ± 1.3	0.39
Hct (%)	29 ± 3.8	30 ± 3.9	0.39
INR	1.3 ± 0.3	1.2 ± 0.4	0.18
PTT	41.2 ± 5.4	45.6 ± 7.4	0.22
Fibrinogen	239 ± 49	359 ± 202	0.15

Table 4. Post-operative Hematologic Profile
Values are means + SD where shown. Hb: Hemoglobin. Hct: Hematocrite Value. INR: International Normalized Ratio. PTT: Partial Thromoplastin Time

	TA	Placebo	*P*-Value
Trponion I (mmol/L)	2.4 ± 3.8	4.7 ± 2.0	0.68
Intub (Hrs)	14 ± 7	17 ± 12	0.52
ICU (Hrs)	29 ± 26	49 ± 20	0.02*
LOS (Days)	7.5 ± 3	7.8 ± 2.0	0.68

Table 5. Post –operative data
Values are means + SD where shown. Intub: Intubation time. ICU: Intensive Care Unit. LOS: Length of Hospital Stay

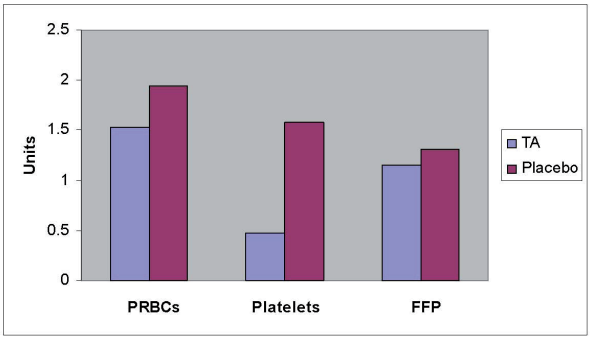

Figure 3. Post-op Blood Products Transfusion

Apart from re-exploration for excessive surgical bleeding in one patient in the TA group (due to leaking one of the grafts that has been fixed by adding extra stitch), no difference was found in morbidity or mortality between the two groups. There were no deaths in either group.

Discussion

Despite being effective in decreasing post-operative bleeding in both primary and redo coronary artery bypass grafting, intravenous use of Aprtonin and Tranexamic acid increases the incidence of early graft occlusion and post-operative myocardial infarction8&14.

In the large International Multi-center Aprotinin Graft Patency Experience (IMAGE) study, no statistically significant difference in graft occlusion could be found between patients given aprotinin and controls when the results were adjusted for risk factors known to be associated with graft failure15.Therefore, the benefit of antifibrinolytic agents must be always weighted against a possible increases risk of thrombo-embolic complications that might lead to early graft closure. Moreover, these patients are at increase risk of cerebral, pulmonary, mesenteric and retinal thrombosis.

Following the success of systemic use of aprotinin and tranexamic acid in controlling post-CABG bleeding, trials for topical use were initiated by Tarter et al16 in 1993, who reported reduced post-operative blood loss and the need for transfusion after topical aprotinin use in CABG patients. Similar results were described by O'Regan and his colleagues17 and Khalil et al18. This encouraged De Bonis group19 in 2000 to start topical use of TA. They conducted a prospective randomized, double blinded study on 40 patients who had primary CABG. They reported blood loss significantly diminished by 36% during the first 3 hours but not during

the following 21 hours after operation compared to the placebo group. Our study demonstrates that pouring of one gram of TA into the pericardial cavity after CABG, significantly reduced post-operative blood loss in the first 24 hours after surgery (37%) with the maximum reduction at the 3rd hour (66%). Abdul Azem and his colleagues20 in 2006 described similar results in 100 patients underwent various open heart procedures. In contradictory to our findings, Yasim and his group21 did not find a statistically significant reduction in post-operative bleeding after topical application of aprotinin and tranexamic acid.

In our study the overall post-operative bleeding was modest in both groups and this could be explained by the tight inclusion criteria, meticulous surgical hemostasis, normothermic CPB and the use of LIMA alone as a pedicle graft in all patients. Therefore, despite the significant reduction of post-operative bleeding in TA group, the effect of its topical use might be masked by those factors. A greater effect of topical TA in reducing blood loss could be possibly evident in more prolonged and complex procedures with a higher risk of bleeding.

The use of blood products was not significantly different between both De Bonis' groups19, while we had a significant reduction only in platelet transfusion and Abdul Azm20 had a significant reduction only in packed cells use in TA group. This difference in reports might be explained by the difference in number of patients, type of operations and transfusion protocols used in each study.

Limitation of the study

We did not measure the level of TA in the serum or in the pericardial cavity. The number of the patients was relatively small and the inclusion criteria with strictly tight. Larger multi-center prospective control trials using larger dose of TA are needed to address its topical effect in procedures with higher risk of bleeding.

Conclusion:

Topical use of Tranexamic acid into the pericardial cavity in patients undergoing primary coronary artery bypass grafting significantly reduces postoperative bleeding and platelet transfusion.

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A RANDOMIZED TRIAL OF APROTININ ON BLEEDING, BLOOD PRODUCTS REQUIREMENT AND MYOCARDIAL INFRACTION IN PATIENTS TREATED WITH CLOPIDOGREL BEFORE CORONARY ARTERY BYPASS GRA

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Background: **An increased proportion of patients undergoing urgent coronary artery bypass graft surgery (CABG) is being treated with clopidogrel, an irreversible platelet inhibitor. Clopidogrel in combination with aspirin is known to augment bleeding, transfusion requirements, and reoperation rates after CABG. Aprotinin, a protease inhibitor, is approved for use in cardiac surgery to reduce bleeding.**
Aim of the work: To investigate whether or not intraoperative use of aprotinin decreases bleeding and number of transfusions after CABG in patients treated with clopidogrel less than 5 days before surgery.
Methods: **Patients admitted with acute coronary syndrome requiring urgent CABG with cardiopulmonary bypass surgery were considered for inclusion. All patients were first time cardiac surgery candidates. All patients were initially loaded with 300 mg of clopidogrel followed by a daily intake of 75 mg. All patients were received aspirin 150 mg. The patients were divided into 2 equal groups, to compare of two strategies for the management of antiplatelets therapy during urgent surgery. The treatment group (T) continued clopidogrel and aspirin therapy until surgery, mean duration of treatment before surgery was 17±4 days. The control group (C) had both antiplatelets drugs discontinued at least 5 days before surgery. All patients continued to receive intravenous heparin which was discontinued 30 minutes before surgery. The treatment group received aprotinin (Trasylol; Bayer AG, Leverkusen, Germany) 2 million KIU before start of surgery, 500 000 KIU/h during surgery, with an additional 2 million KIU in the CPB prime. None of the patients continued with aprotinin after completion of surgery**
Results: **The two groups were comparable with respect to baseline characteristics and operative data. There was a highly significant reduction in the blood loss in the treatment group compared with control group at time of removal of chest tube (811.7 ± 234.7 vs 2096 ± 238.6) respectively (table IV). The duration of chest tube drainage was greater in the control group with (p value 0.0001). The need for red blood cell transfusion was reduced from 3.333 ± 0.8841 units in the control group to 0.5667 ± 0.6261 units in the treatment group (p = 0.0001). Similarly, there was a highly significant reduction in the need for coagulation products in the treatment group: Fresh Frozen Plasma and platelets transfusion was (0.5667 ± 0.7279 vs 2.200 ± 1.3235) (1.30 ± 2.18 vs 8.00 ± 5.75) in the treatment group and control group respectively. One patient (3.3%) in each group underwent surgical re-exploration for bleeding. CI, RVSWI, and LVSWI were significantly higher in the treatment group as compared to the control group at the end of the surgery. CTnI, duration of post-operative mechanical ventilation, LOS-ICU, and postoperative myocardial infraction were comparable in the 2 groups.**
Conclusion: **Aprotinin reduces bleeding, transfusion requirements of**

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packed red blood cells, platelets, and total blood units in patients on clopidogrel undergoing urgent CABG with no statistically significant increase in the prevalence of myocardial infraction in patients treated with aprotinin.

Coronary artery bypass graft (CABG) surgery has become a commonly performed operation, with more than 800,000 patirnts undergoing this procedure worldwide each year [1]. Clopidogrel is currently used to reduce ischemic events in patients with history of myocardial infarction [2]. More recently, there has been a trend toward extending the use of clopidogrel to patients presenting with acute coronary syndrome and non-ST-elevation myocardial infraction [3]. Recent studies have indeed shown the clopidogrel treatment in combination with aspirin before CABG is associated with increased postoperative bleeding, transfusion, and re-exploration rates [4].

The main causes of bleeding include incomplete surgical hemostasis, defective coagulation, and platelet dysfunction after cardiac surgery (may be due to the effect of cardiopulmonary bypass (CPB) or preoperative antiplatelet medications) [5].

Re-exploration due to bleeding may not only lengthen the hospital stay, but has also been associated with an increase in mortality. Since clopidogrel is often given before angiography and percutaneous coronary interventions, the patient may later be reffered to surgery with the additional handicap of an irreversible platelet inhibition that lasts about 5 days. Thus, the surgical team is facing the question whether the patient should have surgery delayed for 5 days at the risk of acute ischemic events, or should be operated upon earlier at the risk of increased bleeding and morbidity [6].

Several studies have demonstrated that aprotinin, an inhibitor of certain serine proteinases administered during coronary surgery, significantly reduce postoperative blood loss and the need for allogenic blood transfusion [7-10]. The major concern over the routine use of aprotinin is, however, an increased risk of graft occlusion and perioperative myocardial infraction through prothrombotic mechanisms [7,8 &11].

The aim of this work is to compare of two strategies for the management of antiplatelets therapy during urgent coronary artery bypass graft surgery and the potential adverse effect of aprotinin which could be postoperative graft occlusion. This has been studied indirectly by electrocardiography (ECG) and by measuring enzyme levels in patients undergoing primary coronary artery bypass grafting.

Patients and methods

After approval of the study design by the Hospital Ethics Committee, this prospective randomized study was conducted on 60 adult patients of both sexes, scheduled for first elective coronary artery bypass graft (CABG) surgery with cardiopulmonary bypass (CPB).

Patients admitted with acute coronary syndrome requiring urgent CABG with cardiopulmonary bypass surgery were considered for inclusion. Acute coronary syndrome was defined as patients with unstable angina or non-ST-segment elevation myocardial infraction. All patients were first time cardiac surgery candidates. The exclusion criteria were patients in whom CABG was performed less than 5 days of the decision to operate, impaired renal function, severe left ventricular dysfunction (ejection fraction $\leq$ 40%), previous history of stroke, peripheral vascular diseases, warfarin therapy, and other coagulopathies. Also patients need more than three grafts. All patients were initially loaded with 300 mg of clopidogrel followed by a daily intake of 75 mg. All patients were received aspirin 150 mg. The patients were divided into 2 equal groups, to compare of two strategies for the management of antiplatelets therapy during urgent surgery. The treatment group (T) continued clopidogrel and aspirin therapy until surgery, mean duration of treatment before surgery was 17±4 days. The control group (C) had both antiplatelets drugs discontinued at least 5 days before surgery. All patients continued to receive intravenous heparin which was discontinued 30 minutes before surgery.

On the night prior to surgery, the patients were visited where a thorough medical examination was performed and all the preoperative investigations were checked. All the cardiac medications were continued till the time of surgery.

On the day of surgery, the patient was premedicated with intramuscular morphine sulphate 0.1 mg/kg (max. 10 mg) 60-90 minutes before surgery and then was brought to the preoperative holding area where a 16-G cannula was inserted into a peripheral vein and Ringer's infusion was started. ECG, Blood Pressure, and Pulse Oximeter monitors were connected to the patient and base-line values were recorded. After intravenous sedation with 2-5 mg midazolam, a radial artery catheter and an internal jugular vein triple lumen catheter were inserted under local anesthesia with lidocaine 2%. After induction of general anesthesia, a pulmonary artery

catheter was inserted through the right internal jugular vein.

General anesthesia was induced with Fentanyl 5-10 µg/kg and propofol in a dose of 10 mg bolus every 10 s until loss of consciousness. Orotracheal intubation was facilitated with Pancuronium bromide 0.1 mg/kg IV. Anesthesia was maintained using boluses of Fentanyl 1-3 µg/kg, Pancuronium 1-2 mg, and Isofluorane 0.5-2% in an oxygen/air mixture. Controlled ventilation was adjusted to maintain end-tidal carbon dioxide at 35-40 mmHg.

Activated clotting time (ACT) was performed with a Kaolin-activated hemotec device to monitor anticoagulation during CBP. Heparin (3-4 mg/kg) IV was injected 3-5 minutes before cannulation and every 30 minutes during CBP to ensure an ACT ≥ 400 seconds. Anesthesia during CBP was maintained by Isofluorane (a vaporizer built-in the CBP machine) and increments of Fentanyl and Pancuronium.

The heart-lung machine used in this study was SIII STOCKERT-Germany. CBP was instituted through cannulation of the right atrium and ascending aorta. A membrane oxygenator was used (Jostra Quadrox hollow fiber membrane oxygenator, Germany). Non-pulsatile flow was used (2.4 L.m-2 .min-1). Systemic temperature was kept between 34oC and 36oC. Myocardial protection was achieved by using intermittent anterograde hyperkalemic warm blood cardioplegia.

At completion of CPB, heparin was reversed by protamine sulfate given in 1:1.3 ratio. After this dose, a further dose of 100 mg protamine was administered if the ACT remained above 140 seconds. The treatment group received aprotinin (Trasylol; Bayer AG, Leverkusen, Germany) 2 million KIU before start of surgery, 500 000 KIU/h during surgery, with an additional 2 million KIU in the CPB prime. None of the patients continued with aprotinin after completion of surgery.

Patients were transferred to the intensive care unit (ICU), on arrival in the ICU, all patients underwent a routine coagulation screening. Elevation of activated clotting time (ACT) of longer than 30 seconds when compared with baseline was treated with an additional 25 mg dose of protamine. Values of prothrombin time, activated partial thromboplastin time, and International Normalized Ratio (INR) of more than 1.5 times control, suggesting factor deficiency, were corrected by infusion of fresh frozen plasma. A platelet count of less than 80,000/µL was an indication for platelet transfusion. A hematocrit of less than 24% was corrected by transfusion of red blood cells. The total blood loss was measured starting immediately after closure of the chest in the operating theatre until the chest drains were removed, providing the drainage was less than 20 mL/h for 3 consecutive hours. Indications for reopening were a blood loss greater than 500 mL over the first hour, more than 300 mL for 2 consecutive hours, more than 200 mL for 3 consecutive hours, or more than 1 L over the first 8 hours.

Patients were extubated as soon as they met the following criteria: hemodynamic stability, no excessive bleeding (<80 mL/h), normothermia, and consciousness with pain control. Aspirin 300 mg daily was started on the first postoperative day. Clinical diagnostic criteria for preoperative and postoperative myocardial infraction were new Q waves of greater than 0.04 ms or a reduction in R waves greater than 25%, or both, in at least two leads.

The diagnosis of possible myocardial infraction was made when the cardiac enzymes profiles were: Cardiac troponin (CTnI) > 2.5 µg/L at 24 hours, as determined by Mair and colleagues [12].

The following data were collected:

I- Data collected in the operating room (OR) included:

- CBP time and aortic cross-clamp time.
- Pulmonary artery catheter measurements of cardiac index (CI), pulmonary capillary wedge pressure (PCWP), right ventricular stroke index (RVSWI), and left ventricular stroke work index (LVSWI); were performed following induction anesthesia, at the end of surgery, and 6 hours post-extubation in the ICU.
- Rate of spontaneous defibrillation following CPB.
- Need for inotropes or intra-aortic balloon pump (IABP) following CPB-weaning.

II- ICU data included:

- ECG (12 lead) at 2 and 24 hours after admission to ICU. ECG diagnosis criteria for perioperative myocardial infraction (MI) were new "Q" waves of greater than 0.04 ms and/or a reduction in R waves of greater than 25% at least 2 leads.
- Duration of mechanical ventilation.
- Length of stay in the ICU (LOS-ICU).
- The post-operative blood loss which was defined as total chest tube drainage.
- The amounts of allogenic whole blood, RBCs, fresh frozen plasma, platelets transfused were noted.

- Patients with focal neurologic deficits (motor weakness, dysphasia, aphasia, cognitive deficits, seizures, or coma) were evaluated by staff intensivists. A computed tomography scan was performed in these patients as soon as the clinical condition allowed.
- Renal complications included acute renal failure as defined by (creatine mg/dl).
- Finally, infective complications were defined by positive culture and requirement for antibiotic therapy.

Results

The preoperative characteristics of the patients in the two groups were comparable including: age, sex, body surface area, incidence of previous myocardial infraction, ratio of stable/unstable angina, use of intravenous nitrates, ejection fraction, incidence of left main coronary artery stenosis, and the number of diseased vessels (table I).

	Control group (n = 30)	Treatment group (n = 30)	p value
Age (years)*	57.6 ± 8.1	59.4 ± 9.9	> 0.05
Sex (M/F)†	22/8	20/10	> 0.05
Body surface area (m2)*	1.77 ± 0.17	1.76 ± 0.14	> 0.05
Previous MI †	3 (10%)	5 (16.7%)	> 0.05
Stable/unstable angina †	27/3	25/5	> 0.05
Intravenous nitrates †	8/30	9/30	> 0.05
Ejection fraction *	49.87 ± 4.27	51.63 ± 3.48	> 0.05
Left main stenosis †	3 (10%)	4 (13.3%)	> 0.05
Three vessel disease †	21 (70%)	23 (76.7%)	> 0.05
Two vessel disease †	7 (23.3%)	6 (20%)	> 0.05
One vessel disease †	2 (6.7%)	1 (3.3%)	> 0.05

Table I: Preoperative patients' characteristics
**** Data expressed as mean ± standard deviation***
† Data presented as number and percentage of patients

Operative data (table II) showed a comparable CPB time and aortic cross clamp time in the 2 groups. The rate of spontaneous defibrillation was significantly higher in the treatment group than in the control group. The number of patients who required positive inotropic support while coming-off CPB was significantly higher in the control group (10/30) than in the treatment group (3/30). Only one patient in the control group and no patients in the treatment group needed IABP.

	Treatment group(n = 30)	Control group(n = 30)	P value
CPB time (min)*	72.5 ± 19.6	77.1 ± 24.2	> 0.05
Aortic cross-clamp time (min)*	51.8 ± 13.8	57.5 ± 19.5	> 0.05
Spontaneous defibrillation †	28 (93.3%)	17 (56.7%)	> 0.05
Inotropic support †	3 (10%)	10 (33.3%)	> 0.05
Use of IABP †	0	1 (3.3%)	> 0.05

Table II: Operative data
**** Data expressed as mean ± standard deviation***
† Data presented as number and percentage of patients

The hemodynamic data measured by the pulmonary artery catheter showed no significant differences in the PCWP between the two groups at all the measurement times. The CI, RVSWI, and LVSWI were comparable in the 2 groups after induction of anesthesia, and in the ICU. The CI, RVSWI, and LVSWI were significantly higher in the treatment group as compared to the control group at the end of surgery (table III).

	After Induction	End of Surgery	After Extubation
PCWP			
§ Control	8.9 ± 2.9	10.6 ± 3.2	10.4 ± 3.1
§ Treatment	9.1 ± 2.7	9.8 ± 2.5	9.5 ± 2.4
CI			
§ Control	2.3 ± 0.4	2.6 ± 0.8	2.8 ± 0.9
§ Treatment	2.4 ± 0.6	3.1 ± 0.9*	3.1 ± 1.0
RVSWI			
§ Control	11.4 ± 4.1	13.7 ± 3.5	14.1 ± 4.3
§ Treatment	12.6 ± 3.9	17.4 ± 6.1*	16.7 ± 5.6
LVSWI			
§ Control	51.6 ± 23	57.8 ± 23	58.9 ± 24
§ Treatment	52.2 ± 23	63.1 ± 26*	60.1 ± 23

Table III: Hemodynamic Data
**** p < 0.05 (statistically significant difference between the two groups)***
PCWP: Pulmonary Capillary Wedge Pressure (mmHg)
CI: Cardiac Index (L/min/m2)
RVSWI: Right Ventricular Stroke Work Index (g-m/m2/beat)
LVSWI: Left Ventricular Stroke Work Index (g-m/m2/beat)

There was a highly significant reduction in the blood loss in the treatment group compared with control group at time of removal of chest tube (811.7 ± 234.7 vs 2096 ± 238.6) respectively (table IV) & (figure 1). The duration of chest tube drainage was greater in the control group with (p value 0.0001). The need for red blood cell transfusion was reduced from 3.333 ± 0.8841 units in the control group to 0.5667 ± 0.6261 units in the treatment group (p = 0.0001). Similarly, there was a highly significant reduction in the need for coagulation products in the treatment group: Fresh Frozen Plasma and platelets transfusion was (0.5667 ± 0.7279 vs 2.200 ± 1.3235) (1.30 ± 2.18 vs 8.00 ± 5.75) in the treatment group and control group respectively (figure 1). One patient (3.3%) in each group underwent surgical re-exploration for bleeding.

The duration of postoperative mechanical ventilation and the length of stay in the ICU were comparable in the two groups (table V). Postoperative myocardial

infraction developed in 2 patients in the control group and 1 patient in the treatment group. One patient in the control group died postoperatively from cerebral stroke. No mortality was recorded in the treatment group.

	Treatment group	Control group	p value
Drain Loss*	811.7±234.8	2069±238.6	< 0.001
Blood transfusion (units)*	0.566±0.626	3.33±0.884	< 0.001
Platelets (units)*	1.3±2.18	8.00±5.75	< 0.001
FFP (units)*	0.566±0.727	2.200±1.323	< 0.001
Re-exploration†	1 (3.3%)	1 (3.3%)	> 0.05
Chest tube duration (hours)*	20.13±2.28	29.97±2.846	< 0.001

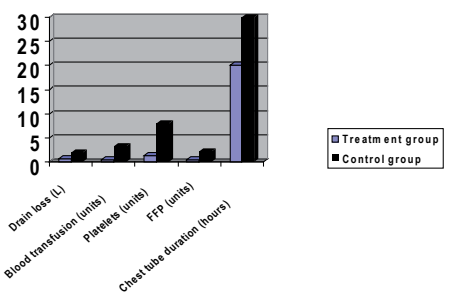
Table IV: Bleeding and transfusion
**** Data expressed as mean ± standard deviation***
† Data presented as number and percentage of patients

Serum creatinine one day in both groups was presented. Overall, there was no significant difference between the 2 groups. Although there were no significant differences in neurological complications between both groups, there were 2 patients in the control group complicated with stroke (table V).

	Treatment group	Control group	p value
Duration of MV (hours)*	4.6 ± 3.1	5.2 ± 2.7	> 0.05
LOS-ICU (hours)*	26 ± 7	31 ±9	> 0.05
Postoperative MI†	1 (3.3%)	2 (6.7%)	> 0.05
Cardiac troponin*	1.33±0.23	1.21±0.19	> 0.05
Ejection fraction*	51.63±3.48	49.87±4.272	> 0.05
Cerebral stroke †	1 (3.3%)	2 (6.7%)	
Creatinine*	0.786±0.19	0.716±0.172	> 0.05
Mortality†	0	1 (3.3%)	> 0.05

Table V: Postoperative Data
**** Data expressed as mean ± standard deviation***
† Data presented as number and percentage of patients
MV: mechanical ventilation
LOS-ICU: length of stay in ICU
MI: myocardial infraction

Figure 1:Bleeding and transfusion



Discussion

Aspirin is the main antiplatelet medication used in patients with coronary artery disease, but there is growing evidence that the use of the more potent antipletlet clopidogrel, on its own or in combination with aspirin, has superior outcomes in both chronic and acute settings [13 & 14].

Clopidogrel and ticlopidine are thienopyridines. They are prodrugs that are noncompetitive antagonists of the platelet adenosine diphosphate receptor, P2Y12. clopidogrel is an acetate derivative of ticlopidine and has several advantages, including more rapid onset of action, more potent antiplatelet effect, and lower incidence of severe neutropenia and thrombotic thrombocytopenic purpura [15]. The antiplatelet effect of clopidogrel is time and dose dependent. Maximal inhibition of platelet aggregation of 50% to 60% can be achieved with a dose of 75 mg daily (without loading dose) within 4 to 7 days, or more rapidly with a loading dose of 300 to 600 mg within 4 to 24 hours [16]. This level of platelet inhibition caused a twofold increase in the bleeding time of healthy human volunteers. Platelet function recovered completely 7 days after stopping clopidogrel in healthy volunteers [17].

Several large randomized studies have demonstrated the superior antiplatelet action of clopidogrel in combination with aspirin in patients with acute coronary syndrome without ST-segment elevation [18].

Also several studies have demonstrated that clopidogrel treatment within 4 days of CABG significantly increases blood loss, requires more re-operations for bleeding, and has greater transfusion requirements for red blood cells (6 to11 times), plasma (2 to 4 times), and platelets (2 to 45 times) [3,4,19&20].

Furthermore, the usual combination of aspirin and clopidogrel has synergistic antiplatelet effects, because each agent affects platelets aggregation by different mechanisms [21]. Clopidogrel acts by inhibiting adenosine diphosphate-dependent platelet activation and aspirin acts by inhibiting thromboxane-dependant platelet activation. It has been postulated that the combination of clopidogrel and aspirin produces a synergestic effect on platelet inhibition [3] that increases bleeding postoperatively. The addition of clopidogrel to aspirin preoperatively has been reported to significantly increase the risk of postoperative bleeding and blood transfusion [4].

Yende and Wunderink [3] found that the re-opera-

tion rate in patients undergoing CABG increased from 2.3% to 10.4% when the patients were treated with aspirin only and with the combination aspirin/clopidogrel, respectively. In comparison, their re-operation rate was 0% for patients who received neither aspirin nor clopidogrel.

Ascione and colleagues [22] investigated the independent effect of preoperative exposure to, aspirin, heparin, and clopidogrel on early clinical outcomes of in-hospital referral patients undergoing first time coronary artery bypass graft surgery. On average, patients prescribed clopidogrel lost 37% more blood than those not prescribed the drug (95% CI: +3% to +82%, $p = 0.033$) after adjustment for demographic, comorbid, cardiac and operative differences between patients. Clopidogrel patients were also more likely to need a re-operation for bleeding/tamponade ($p < 0.001$). Conversely, heparin and aspirin were not associated with increased blood loss, or re-operation for bleeding/tamponade ($p \geq 0.58$ for all comparisons). Platelets and fresh frozen plasma transfusion rates increased > 4-fold ($p \leq 0.015$ for both outcomes) when clopidogrel was used but no association with aspirin or heparin use was found ($p \geq 0.26$ for all comparisons). The pattern for red blood cells usage was somewhat different; the data suggest that the combination of clopidogrel and aspirin was associated with an increased risk of a red cell transfusion, but when either drug was given alone (or with heparin) the risk was not significantly different to when the drug was not prescribed. In contrast, patients prescribed clopidogrel or heparin stayed in hospital significantly longer than other patients ($p = 0.019$ clopidogrel and $p < 0.001$ heparin), while aspirin was associated with a shorter stay ($p = 0.041$).

In another study, clopidogrel therapy within 7 days of elective CABG resulted in increased blood loss, use of blood products, and a 10-fold increase in re-exploration rates. These patients had received no intraoperative aprotonin [4].

This finding was also supported by the paper by Englberger and associates [23] who reported increased bleeding and platelet and fresh frozen plasma transfusion in patients receiving clopidogrel within 3 days of surgery. Interestingly, all patients received low-dose aprotinin treatment. However, Karabulut and Toraman [24] showed no increase in bleeding and transfusion requirements after preoperative use of clopidogrel.

Aprotinin, a serine protease inhibitor with anrifibrinolytic activity, has successfully been used in cardiac surgery to reduce overall bleeding and transfusion requirements in patients exposed to aspirin [25]. Aprotinin is appealing as it not only reduces overall bleeding in cardiac surgery but also appears to preserve platelet function during cardiopulmonary bypass (CPB) [5]. Moreover, in animals, aprotinin has been shown to shorten prolonged bleeding induced by clopidogrel [26].

Lindvall and colleagues [27] indicate that a significant reduction of clopidogrel-induced bleeding and transfusion requirements can be achieved with full-dose aprotinin treatment. They retrospectively reviewed the medical records of all consecutive patients, with preoperative clopidogrel exposure less than 5 days before surgery, who underwent urgent CABG at their institution during 1 year ($n = 33$). Eighteen patients received a full-dose aprotinin regime intraoperatively whereas 15 patients not receiving aprotinin served as a control group. Mean postoperative bleeding was 710 ml (95% confidence interval [CI] 560 to 860) in the aprotinin group versus 1210 ml (95% CI 860 to 1550) in the control group ($p = 0.004$). The aprotinin group received fewer transfusions of packed red blood cells (0.9 U, 95% CI: 0.1 to 1.7, versus 2.7 U, 95% CI: 1-4 to 4.1; $p = 0.01$), platelets (0.1 U, 95% CI: 0 to 0.3, versus 0.6 U, 0.2 to 0.9; $p = 0.02$), and fewer blood product units (1.1 U, 95% CI: 0.1 to 2.0, versus 3.7 U, 95% CI: 2.1 to 5.4; $p = 0.002$).

The results of the current study showed that postoperative blood loss and at the time of chest drain removal was greater in the control group compared with the treatment group who also received less blood components transfusion.

From June 2002 to July 2003, patients underwent urgent coronary artery bypass graft surgery for acute coronary syndrome were studied by Akowuah and his colleagues [28]. They concluded that the strategy of continuation of aspirin and clopidogrel therapy before surgery, coupled with intraoperative use of aprotinin, may adopted. In view of the deaths due to embolism, further investigation in a larger trial is warranted. Nevertheless, this strategy leads to a reduction in postoperative bleeding and blood transfusion, prevents delay to surgical treatment, and may prevent major adverse cardiac events before surgery.

The results of the current study showed a significantly higher rate of spontaneous defibrillation and a significantly lower need for inotropic support in the treatment

group than in the control group. The CI, RVSWI, and the LVSWI were significantly higher in the treatment group as compared to the control group at the end of surgery. The duration of postoperative mechanical ventilation, the length of stay in the ICU, the incidence of postoperative myocardial infraction, and mortality were comparable in the two groups.

When aprotinin administered to patients undergoing CPB surgery, aprotonin is consistently associated with decreased fibrinolysis and reduced bleeding in the perioperative period. However, reduction in fibrinolysis could potentially increase the risk of thrombus formation and perioperative myocardial infraction. Double blinded, randomized study was undertaken in a sufficiently large number of subjects, using blinded readings at a core laboratory, and applying uniform entry and interpretation criteria to evaluate the safety of aprotinin in terms of its effect on graft patency, prevalence of myocardial infraction, and blood loss in patients undergoing primary coronary surgery with cardiopulmonary bypass. Patients from 13 international sites were randomized to receive intraoperative aprotinin (n = 436) or placebo (n = 434). Graft angiography was obtained a mean of 10.8 days after the operation. Electrocardiograms, cardiac enzymes, and blood loss and replacement were evaluated. In 796 assessable patients, aprotinin reduced thoracic drainage volume by 43% ($p < 0.0001$) and requirement for red blood cell administration by 49% ($p < 0.0001$). Among 703 patients with assessable saphenous vein grafts, occlusions occurred in 15.4% of aprotinin-treated patients and 10.9% of patients receiving placebo ($p = 0.03$). After they had adjusted for risk factors associated with vein graft occlusion, the aprotonin versus placebo risk ratio decreased from 1.7 to 1.05 (90% CI, 0.6 to 1.8). These factors included female gender, lack of prior aspirin therapy, small and poor distal vessel quality, and possibly use of aprotinin-treated blood as excised vein perfusate. At United States sites, patients had characteristics more favorable for graft patency, and occlusions occurred in 9.4% of the aprotinin group and 9.5% of the placebo group ($p = 0.72$). At Danish and Israeli sites, where patients had more adverse characteristics, occlusions occurred in 23% of aprotinin- and 12.4% of placebo-treated patients ($p = 0.01$). Aprotinin did not affect the occurrence of myocardial infraction (aprotinin: 2.9%; placebo: 3.8%) or mortality (aprotinin: 1.4%; placebo: 1.6%). So in this study, the probability of early vein graft occlusion was increased by aprotinin, but this outcome was promoted by multiple risk factors for graft occlusion [29].

The previous results were in agreement with our results which showed no difference in the incidence of perioperative MI or need for IABP support between the 2 groups. Also the results of the current study showed a higher level of CTnI in the control group than the treatment group (24 hours), but the difference was not significant.

Troponin I is a myofibrillar protein regulating the interaction of actin and myosin without calcium. Heart muscle isoform (cardiac troponin I, CTnI) has been shown to be a sensitive and specific marker of myocardial injury during open heart operations. The plasma concentration of CTnI is also unaffected by renal failure or skeletal muscle disease [30]. The specificity of CTnI is particularly beneficial for patients undergoing cardiac operation because the value of measurements of serum creatine kinase and lactate dehydrogenase is limited by enzyme release from non-cardiac tissues [31].

Mair and colleagues [12] in a study concerning patients undergoing CABG concluded that a wide range of myocardial damage even in the absence of postoperative myocardial infraction is common and not always indicated by creatine kinase isoenzyme MB mass or activity. They reported that CTnI measurements can detect these small difference in myocardial tissue damage.

Lindvall and colleagues [27] observed lower troponin-T values postoperatively in the aprotinin group, which is in accordance with the study by Taggart and coworkers [32]. These findings may be explained by the antithrombotic and anti-inflammatory mechanisms of action of aprotinin [33].

In our study postoperative complications including, stroke, incidence of mediastinitis, renal failure, and hospital death were not different.

The published meta-analysis of 35 randomized controlled trials revealed no increased risk of mortality, myocardial infraction, or renal failure in patients undergoing CABG who received aprotinin [34]. This is consistent with the trial by Schweizer and colleagues [35], who randomized 57 patients undergoing cardiac surgery with CPB to high-dose aprotinin and placebo and detected no difference in several sophisticated parameter of renal function between the groups. Also the trial of Taggart and coworkers [32] did not show any adverse effects of aprotinin on renal functions as judged by serial serum creatinine levels. It should be noted, however, that 4 patients in the aprotinin group and 2 patients in

control group had postoperative creatinine levels exceeding 2 mg/L on day 5. In the control group, 1 patient had a hypovolemic cardiac arrest requiring emergency thoracotomy to control bleeding, and other patient had no obvious explanation for the precipitous increase in creatinine. Of the 4 patients in the aprotinin group, 3 had elevated preoperative creatinine levels, and 4 had other complications that may have contributed to postoperative renal impairment. It is therefore uncertain whether it was the elevated preoperative creatinine level or a perioperative complication that contributed most to the postoperative elevation, but it would seem sensible to use aprotinin cautiously in those with preoperative renal impairment.

Conclusion

Aprotinin reduces bleeding, transfusion requirements of packed red blood cells, platelets, and total blood units in patients on clopidogrel undergoing urgent CABG with no statistically significant increase in the prevalence of myocardial infraction in patients treated with aprotinin.

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MODERATE ISCHEMIC MITRAL REGURGITATION: EVALUATION OF FACTORS AFFECTING ITS DEGREE AFTER ISOLATED CORONARY ARTERY BYPASS GRAFTING

Tamer Farouk MD.

Background: **Ischemic mitral regurgitation (IMR) is not infrequently (3-7%) seen in patients with coronary artery disease (CAD). However, surgical management of moderate (2+) IMR in such patients is controversial. Our aim is to study the factors affecting the fate of moderate IMR following isolated coronary artery bypass grafting (CABG).**

Methods: **The study group included 35 patients with moderate IMR associated with CAD undergoing isolated CABG. Different variables were studied to evaluate their effect on the degree of regurgitation postoperatively.**

Results: **Mean age of the patients was 62.0 ± 4.39 years, and there were 25 males (71.4%).CABG alone reduced the degree of IMR in 20 (58.9%) patients, did not improve it in 11 (32.3%) patients and increased its degree to 3-4+ in 3 (8.8 %) patients at follow up echocardiography. However, there were 5 variables that showed a role in the progression of IMR. These were: the number of preoperative infarctions, LVEDD, LVESD, preoperative EF %, and ungrafting of the occluded right coronary system.**

Conclusion: **Moderate IMR progresses to more severe grades in only a minority of patients (8.8 %) in the early follow up. Number of preoperative infarctions, a larger LV dimensions, lower ejection fraction, and failure to graft the right coronary system can all lead to progression of moderate IMR.**

Mitral regurgitation (MR) is not infrequent in patients with coronary artery disease (CAD) and those undergoing coronary artery bypass grafting (CABG) (1). Moderately severe and severe MR has been shown to regress after CABG due to reduction in left ventricular (LV) size (2). Ischemic mitral regurgitation (IMR) depends on LV size and geometry, which may progress in a patient with CAD even after CABG. The natural history of milder degrees of MR following CABG is not known despite the potential impact on prognosis. Different descriptions have resulted in heterogeneous patient groups, which in turn complicate comparisons between studies (3).

In chronic IMR, the leaflets and subvalvular apparatus appear normal. Chronic IMR is therefore not a disease of the valve per se, but rather a disease of the ventricle (4). Patients with organic mitral valve (MV) leaflet pathology (myxomatous, rheumatic, or other) and incidental CAD should not be classified as having chronic IMR. This is an important distinction because patients with organic MR and concomitant CAD have a much better long-term prognosis than patients with chronic IMR (5). IMR may present acutely secondary to papillary muscle (PM) infarction and rupture, a condition known as acute IMR. Surgical therapy usually consists of MV replacement. Intermittent MR is completely attributable to transient ischemia. It is an infrequent condition (4). As a result of the confounding terminology Borger and colleagues adopted a

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more precise definition and defined chronic IMR as MR occurring more than 1 week after myocardial infarction (MI) with: (1) one or more LV segmental wall motion abnormalities; (2) significant CAD in the territory supplying the wall motion abnormality; and (3) structurally normal MV leaflets and chordae tendinae. The third criterion is particularly important as it excludes patients with organic MR and associated CAD. Adoption of this definition should ensure homogeneity of patient populations and facilitate comparison between studies (3).

Decrease of IMR has been reported in certain patients who underwent coronary reperfusion at the acute phase of myocardial infarction or later on. IMR persisted in more than 50% of them at six months. Therefore, coronary reperfusion does not avoid the development of ischaemic mitral regurgitation after myocardial infarction (6).

Many studies proved that IMR is associated with reduced survival. In a study that used quantitative echocardiographic study in nonsurgical patients, Grigioni and colleagues demonstrated that IMR was associated with excess mortality independent of the degree of LV dysfunction (7). Mortality risk was directly related to the degree of IMR; those with more severe MR had the greatest reduction in survival. Trichon and colleagues also demonstrated a graded effect of MR on survival (8). Ellis and colleagues noted similar decreased survival in patients with IMR early after percutaneous coronary intervention. This effect was particularly pronounced in patients with an ejection fraction (EF) of less than 40 % (9) .

Till now the decision to correct moderate IMR is left solely to the surgeon and is institution dependent. Many factors (variables) may play a role in the regression or progression of un-attacked moderate IMR in the ischemic heart disease (IHD) patients undergoing CABG surgery. These factors (when known) might help the decision.

Methods

In this study 35 patients with moderate (4-8 cm2 regurgitant jet area) IMR associated with multivessel CAD comprise the study group. Patients were admitted to 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. The following patient characteristics were collected : patient demographics (age and gender), non cardiac co-morbidities (diabetes mellitus, hypertension, smoking, dyslipidaemia, chronic obstructive pulmonary disease [COPD], peripheral vascular disease [PVD]) , cardiac co-morbidities (extent of CAD regarding the number of vessels with more than 50 % occlusion on coronary angiography, site and number of preoperative MI) and medications used prior to surgery (B blockers, ACE inhibitors and diuretics). The following echocardiographic data were collected preoperatively: LV size (Left ventricular end-systolic dimension –LVESD- and Left ventricular end-diastolic dimension –LVEDD-), left atrial (LA) dimension, MR grade, mitral regurgitation jet area and EF.

The following patients were excluded from the study; Patients with mild or severe degrees of IMR, papillary muscle rupture, cardiogenic shock, other valvular pathologies requiring intervention, associated left ventricular aneurysm or ischaemic VSD, severe associated co-morbidities as severe hepatic or renal impairment and patients with CABG reoperations.

Intaoperative evaluation

In all the patients routine anesthetic techniques were used. There were 4 patients who were done using the off-pump technique in the study group. 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. After cardioplegia (intermittent antegrade warm blood cardioplegia), a continuous technique was used to perform the distal anastomoses using a No. 7/0 polypropylene suture. 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.

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 and whether the right coronary system was grafted or not, the total bypass and cross clamp times. 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 hemodynamics, 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 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. Follow-up:

Postoperative echocardiography (after 3-6 months).

After collecting the data, the aim of the study was to evaluate whether CABG alone can correct or reduce moderate IMR and in which set of patients. This set of patients will be compared to the remaining number of patients in the study group to try to elucidate if there are any preoperative or operative variables that can predict the fate of moderate IMR after CABG.

RESULTS

[A] Preoperative Data

The mean age of the study group was 62.0 ± 4.39 years with predominance of males 71.4 % (25 patients). Thirty patients in the study group had previous MI and 12 of those patients had more than one infarction. Diabetes mellitus was present in 21 patients (60%), hypertension in 24 patients (68.6%), dyslipidaemia in 9 patients (25.7%), smoking in 25 patients (71.4%), PVD in 12 patients (34.3%) and COPD in 5 patients (14.3%). Cardiac examination revealed murmur in only 15 patients (42.9 %). Review of the patients' preoperative medications revealed that there were 22 patients on diuretics, 21 patients on B-blockers, and 16 patients on ACE inhibitors. The preoperative ECG revealed that 74.3 % of the patients had either a posterior or an inferior infarction.

The preoperative echocardiographic data showed: The mean jet area was 5.88 ± 0.94 cm2, mean LVESD was 4.02 ± 0.44, mean LVEDD was 5.76 ± 0.58, mean LA dimension was 3.87 ± 0.37 and mean EF was 46.57 % ± 14.30. Coronary angiography revealed that the mean number of vessels with more than 50 % occlusion was 3.89 ± 0.87 per patient.

[B] Operative Data

Patients were submitted to CABG operation with no intervention on the mitral valve. Thirty one patients (88.6 %) were done using cardiopulmonary bypass. The mean total bypass time was 91.42 ± 16.47 minutes and the mean cross clamp time was 57.45 ± 13.76 minutes. During the operation the LIMA was used in all but 2 of the 35 patients. It was discarded because of its low flow. The right coronary artery or its posterior descending branch was grafted in 20 patients (57.1%). The mean number of anastomoses was 3.31 ± 0.63 per patient.

[C] Postoperative Data

The mean period of mechanical ventilation was 7.26 ± 7.33 hours and inotropic support was 20.72 ± 13.05 hours. Two patients needed an IABP to be inserted in the ICU. Patients were discharged from the ICU when haemodynamically stable, on no inotropic support, with no drains and with satisfactory postoperative laboratory results and ECG. There were 5 cases of postoperative morbidity: 2 cases of exploration for bleeding, a case of arrhythmia (supraventricular tachycardia), renal failure and wound infection. The single mortality in the study 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 that 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 performed, and an IABP inserted in the ICU. She passed into a low cardiac output state and died.

Echocardiography was done for all patients prior to discharge. Mean LVESD was 4.02 ± 0.61, mean LVEDD was 5.65 ± 0.54, mean LA dimension was 3.84 ± 0.37 and mean EF was 51.26 ± 17.21%. There were very minute differences in the postoperative LVEDD, LVESD, and LA dimensions as compared to the preoperative echo. There was however an improvement in the ejection fraction.The degree of mitral 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 cm2.

[D]Follow up Data

Follow up was complete in 100% of the 34 hospital survivors. Patients were called after a mean period of 114.09 ± 29.37 days. Twenty six and half percent of the patients were still on diuretics while 17.6 % were on ACE-inhibitors. All the patients had an echocardiogram in the follow up period. Mean LVESD was 3.90 ± 0.46, mean LVEDD was 5.46 ± 0.37, mean LA dimension was 3.82 ± 0.27 and mean EF was 51.26 ± 14.37%. 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).

It was seen that CABG corrected IMR in 20 of the patients in the study group at follow up echocardiography. It, however, failed to do so in the remaining 14 patients (11 remained in 2+ and 3 progressed to 3-4+). As a result of that, the 20 patients who improved (allocated the name IMR 1) were compared with the other 14 patients who did not (IMR 2) to try to find out what variables, if any, can predict which IMR patient will best benefit from isolated CABG.

The following 22 variables in the preoperative and operative data were compared to try to find out if there are any statistically significant differences between the 2 subgroups that can predict the fate of IMR with CABG alone:

Age, sex, the site and number of preoperative infarctions, diabetes mellitus, hypertension, smoking, dyslipidaemia, COPD, PVD, preoperative use of anti-failure medications (diuretics, B-blockers, and ACE-inhibitors), left ventricular size (LVEDD, LVESD) and left atrial dimension on preoperative echocardiography, ejection fraction preoperatively, the number of vessels with more than 50% occlusion on coronary angiography, whether the operation was done On/Off pump, the number of anastomoses, use of the LIMA to graft the LAD, and whether the right coronary system was grafted or not.

There were 5 variables with statistically significant differences between the two groups. These were: the number of preoperative infarctions, LVEDD, LVESD, preoperative EF %, and failure to graft the right coronary system intraoperatively. These are outlined in table (1). All the differences in the other variables between the two groups were statistically insignificant.

	IMR 1 (n= 20)	IMR 2 (n= 14)	P value	Significance
> 1 infarction	1 (5%)	11 (73.3%)	0.001	< 0.001
EF%	55.95 ± 3.20	34.07 ± 13.78	0.001	< 0.001
LVEDD	5.36 ± 0.24	6.31 ± 0.44	0.001	< 0.001
LVESD	3.80 ± 0.29	4.32 ± 0.44	0.001	< 0.001
Failure to graft RCA	3 (15%)	12 (80%)	0.001	< 0.001

Table (1): Statistically significant markers of IMR grade after CABG
Data were expressed as mean ± standard deviation (SD) or number (%).
P< 0.001= Extremely significant

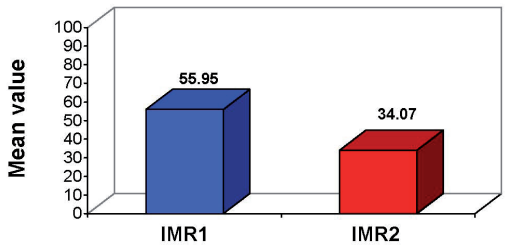

Fig 1 : Preoperative EF% in IMR groups

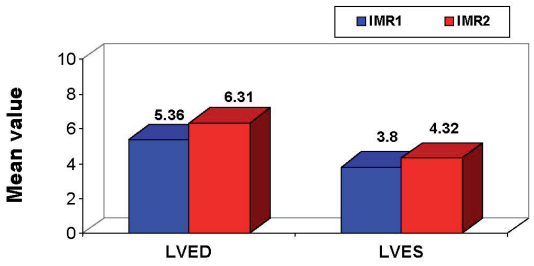

Fig 2: Preoperative LV size in IMR groups

Using Spearman's rank correlation coefficient, a positive correlation was found between LVEDD, LVESD, the number of preoperative infarctions and the grade of IMR after CABG. A negative correlation was found between the preoperative EF%, grafting of the right coronary system and the grade of IMR after CABG. Table (2) and the following figures outline the correlation between these markers and the postoperative grade of IMR.

	R	P	Significance
> 1 infarction	0.604	0.01	< 0.01
Low EF%	-0.607	0.01	< 0.01
LVED	0.740	0.01	< 0.01
LVES	0.529	0.01	< 0.01
Failure to graft RCA	- 0.586	0.01	< 0.01

Table (2): Correlation between IMR grade follow up and different variables
r= Correlation coefficient.
p< 0.01= Highly significant

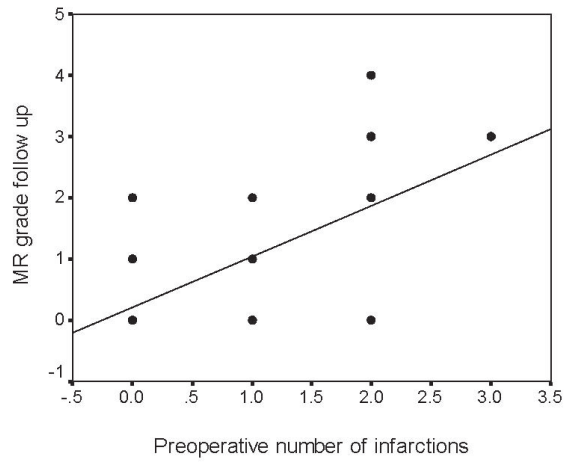

Fig 3: Correlation between IMR grade follow up and preoperative number of infarctions (r= 0.604; p< 0.01)

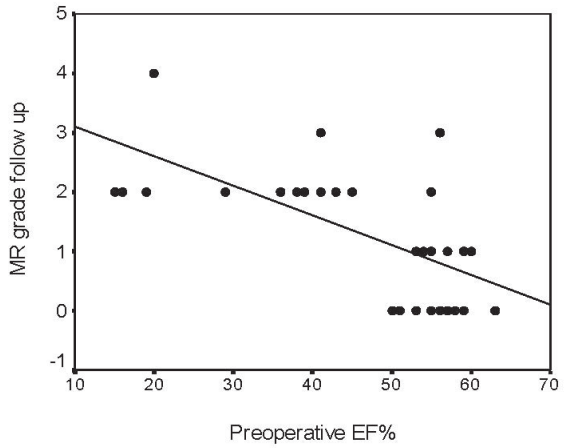

Fig 4: Correlation between IMR grade follow up and preoperative EF% (r= -0.607; p< 0.01).

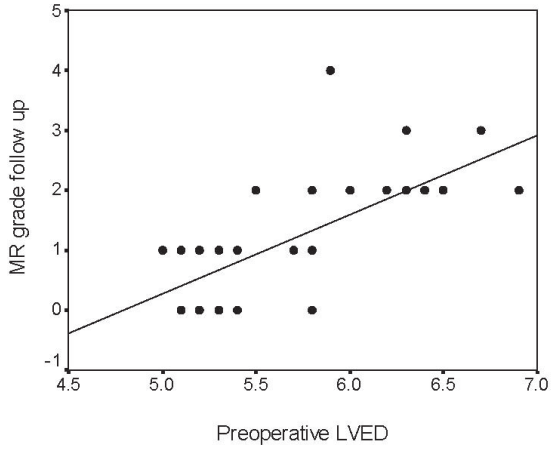

Fig 5: Correlation between IMR grade follow up and preoperative LVEDD (r= 0.740; p< 0.01)

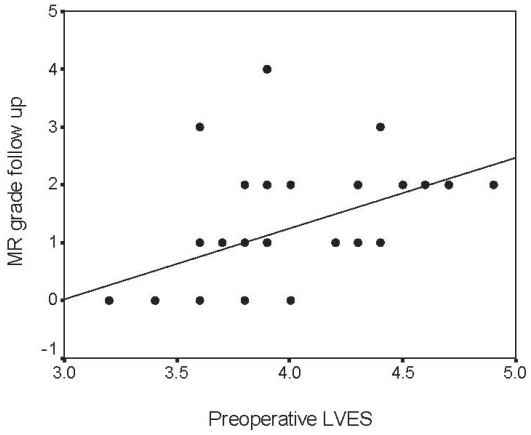

Fig 6: Correlation between MR grade follow up and preoperative LVES (r= 0.529; p< 0.01).

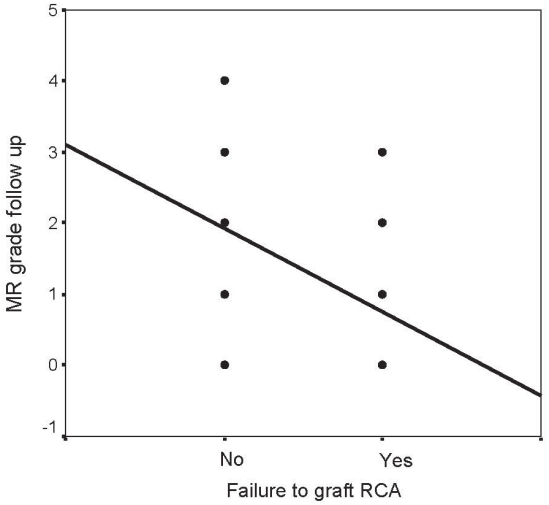

Fig 7: Correlation between IMR grade follow up and failure to graft RCA (r=- 0.586; p< 0.01)

DISCUSSION

There is general agreement that patients with severe (3+ or 4+) IMR should undergo mitral valve surgery at the time of CABG. However, the management of moderate (2+) IMR in such patients is controversial. The results of clinical studies differ as regards the fate of moderate IMR after CABG alone. Therefore, the course of unrepaired moderate IMR after CABG surgery alone was tracked, trying to identify the factors which could predict the fate of moderate IMR after CABG alone. The preoperative profile of patients was similar to patients investigated in other studies (10, 11&12).

In the study by Lam et al., all the patients in their study group had a previous myocardial infarction in order to be accepted as having IMR as opposed to 85.7% in this study. Fifty three percent of their patients had mod-

erate to severe LV dysfunction (EF < 40%) as compared to 31.4% in this series, and finally 6% of their patients had preoperative atrial fibrillation as opposed to none in this series. The series by Campwala and colleagues resembles this series closely. It was found that 74.3% of the patients had a previous posteroinferior infarction (p=0.004). This validates data by other authors that states that, although anterior infarctions are commoner to occur in IHD patients, the occurrence of IMR is more common after a posteroinferior myocardial infarction (13). 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 (14). In-hospital mortality rate in this study (2.9%) compares well with other series; 4.2% of the 168 patient cohort by Kim et al (12) and 2.9% in the study by Aklog et al. (15). There was an improvement in the ejection fraction, 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 patients (20 out of 34). The grade remained moderate in 32.3 %, and increased in only 8.8% of cases. 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 these results. In their patients, the ejection fraction improved from 22.0% to 31.5% ($p < 0.05$) after CABG. The mean grade 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 (16). As regards improvement in the grade of mitral 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 (11). 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 (10,11& 15).

In an attempt to shed the light on factors that might influence the regression of moderate IMR after CABG, 22 preoperative and operative variables were examined that might influence this to occur and compared these between the group of patients in which the grade of IMR decreased (n= 20) to the group in which it remained the same or increased (n= 14). There were 5 variables with statistically significant differences between the two groups. These were: the number of preoperative infarctions, LVEDD, LVESD, preoperative EF%, and failure to graft the right coronary system intraoperatively. Using Spearman's rank correlation coefficient, any correlation that might existed between these variables and the grade of IMR postoperatively was studied. A positive correlation was found between LVEDD, LVESD, the number of preoperative infarctions and the grade of IMR after CABG. A negative correlation was found between the preoperative EF% and failure to graft the right coronary system and the grade of IMR after CABG.

The first four variables (more than one previous infarction, a larger LV dimensions as evidenced by a higher LVEDD and LVESD, and lower preoperative ejection fraction) point to the fact that patients in whom IMR does not regress are those with a sicker ventricle preoperatively. As known, the main mechanism behind the development of IMR is the apical displacement of the papillary muscles with the associated tethering of the leaflets as a result of the underlying LV remodeling. All the above factors lead to worsening of LV remodeling. Failure to graft the right coronary artery or its posterior descending branch might influence the grade of IMR postoperatively by the fact that failure to vascularize hibernating myocardium in this territory, may impair the improvement of left ventricular contractility postoperatively thus preventing regression of mitral regurgitation. Furthermore, the development of new regional wall motion abnormalities in the inferior-posterior LV wall territory due to the development of new ischemia without infarction, may additionally progress IMR post-CABG due to change in regional LV geometry. These results agree with other authors, Campwala and colleagues found failure to graft the PDA territory as an independent predictor of postoperative IMR progression, also the presence of pre-CABG LV dysfunction and larger LV size correlated with progression of IMR. Other factors as poor targets and small vessels are associated with progression (10). Wong and colleagues also identified inferior LV dysfunction as a predictor of worsening IMR grade postoperatively (17). Further studies are requested with bigger number of patients and longer follow up period.

CONCLUSION

• Moderate ischaemic mitral regurgitation progresses to more severe grades in only a minority of patients (8.8 %) in the early follow up period following CABG.

• A higher number of preoperative infarctions, a larger LV size, lower ejection fraction, and failure to graft the right coronary artery territory can all lead to the persistence or progression of moderate IMR following isolated CABG.

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COMBINED ATRIAL FIBRILLATION (AF) ABLATION WITH MITRAL VALVE SURGERY: THE PREDICTORS OF SUCCESS

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Objectives: **To evaluate the efficacy and outcomes of radio frequency AF ablation in patients undergoing Mitral valve (MV) surgery.**
Methods: **Between July 2005 and April 2007, 61 patients, (mean age 65.4 + 10 years, 65% males) underwent exclusive endo-left atrial AF ablation without LA appendage exclusion u sing radio frequency unipolar device (Cardioblate®, Medtronic, USA) in conjunction with 34 MV repairs and 27 MV replacements. AF was paroxysmal in 13 (21%) and chronic in 48 (79%) with a mean duration of 3.6 + 3.5 years. Etiology was mainly degenerative in 35 (57%,) or rheumatic in 17(28%). All patients received amiodarone® postoperatively.**
Results: **Mortality was 0%. There were no thrombo-embolic accidents or device related complications. All patients had intraoperative conversion.41patients (67%) showed postoperative relapse, definitive conversion was achieved in 24 (59%) of them within 3 months. The overall success rate was 74%; it was higher in the repair group (85%) versus MV replacement group (67%, $p<0.05$) with a mean follow up 14 + 8.8 months. The predictors of success included younger age, smaller left atrium and shorter AF duration. Rheumatic etiology and associated CABG were predictors of failure($P<0.05$). The rate of success was similar in chronic and paroxysmal AF.**
Conclusions: **Combined AF ablation with Mitral valve surgery is safe and effective, particularly, when associated with MV repair patients. However, the success rate as defined by definitive conversion to sinus rhythm may vary significantly according to patient characteristics.**

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Atrial Fibrillation (AF) is a well known risk factor for thromboembolism (stroke in 5% per year) [1]. It decreases the cardiac output and in many patients is badly tolerated, being responsible for severe complaints, inspite of medical treatment. Despite extensive, decades-long research, AF remains a major cause of substantial morbidity and mortality [2,3]. Patients with AF can also show intolerance for anti-arrhythmic medication and medically refractory arrhythmia. The incidence of AF increases with aging (6% of above 80y), 2.2 million patients with AF in USA [1]. Several methods for the surgical treatment of AF have been described, the most common approach, in Mitral patients, being the `maze' operation (Cox-Maze III, 1988) [4]. The aim of all these procedures is to build up an electric barrier that would prevent the transfer of the abnormal electrical activity. The original maze procedure that was described for the treatment of patients with atrial fibrillation (besides the surgical difficulties) was followed by an unacceptable incidence of two problems:

(1) The frequent inability to generate an appropriate sinus tachycardia in response to maximal exercise and
(2) Occasional left atrial dysfunction [4].

Evidence has been presented that AF treatment could be achieved by functionally excluding selected areas of the atria, with percutaneous endocavitary radiofrequency ablation; however, aside from being a lengthy procedure with exposure to x-rays, serious thromboembolic complications have been reported in the literature [5].The intra-operative use of this method could, easily, overcome this problem since, even though clots form, they could readily be removed, under direct vision. Radiofrequency AF ablation became a well known procedure despite the different techniques and devices being used [6].

Methods

Between July 2005 and April 2007, 61 patients underwent exclusive endo-left atrial AF ablation without LA appendage exclusion in conjunction with 34 MV repairs and 27 MV replacements. These patients were studied retrospectively trying to analyze the short and mid-term results of this technique. All patients underwent RFA using the Cardioblate surgical ablation pen (Medtronic, Minneapolis, MN). The unipolar RFA device is a saline-irrigated electrode tip that cools the tissue to allow deeper lesions without damaging surrounding tissues. The Cardioblate surgical ablation generator (Medtronic) provided a power output of 20 to 30 W and was used as the power source. Epicardial ablation was not performed in any of the patients.

Variable	Value
Age	65.4 + 10
Sex	27 F, 34 M
DM	29
IHD	7
COPD	6
Hypertension	26
Smoking	31
AVC/TIA history	12
NYHA III/IV	16
Renal impairment/failure	11
reoperation	8
Pathology:	
degenerative	39
rheumatic	22

Table 1: Patients' characteristics

In all cases; the mitral procedure was done prior to the ablation. The radiofrequency catheter was placed inside the left atrium in such a way that a continuous line around the right pulmonary veins was obtained, extending the incision in front of the pulmonary veins around its superior, posterior and inferior limits (cold saline infused inside the atrium). The time of exposure was determined subjectively by the visual changes in the color and texture of the endocardium and atrial tissue (usually 2-5 seconds). No surgical exclusion for the Lt atrial appendage was done. Temporary atrial and ventricular pacing wires were routinely used in all patients.

Postoperative arrhythmias were treated with an intravenous amiodarone bolus (300 mg), followed by a continuous intravenous until patients were tolerating oral intake. Amiodarone was stopped 3 months after the last proved attack of AF.

Follow up was done by the out patient clinic every 2 weeks twice, then every month thrice then every 6 months during the study period.

The ECG at the time of follow up was chosen as the measure of diagnosis/confirmation of rhythm.

Results

There was no mortality. There were no thrombo-embolic accidents or device related complications.

Parameter	MV repair	MV repalcements
Age (mean)	68.1 y	57.8 y
AF since (mean)	1.7 y	3.1 y
LA diam (mean)	48 mm	5.2 mm
Prosthesis used	34 Rings	21 bioprothesis
	6 Gortex chordae	6 mechanical
Relapses	20 (58.8%)	21 (77.8%)
Defenitive SR	29 (85%)	18 (66.7%)27

Table 2: The mitral procedures, predisposers and responses.

All patients had intra-operative rhythm conversion to sinus rhythm. The mean follow up time was 14 + 8.8 months.

Postoperative relapse occurred at least once in 41 patients (67%): 36 (59%) into AF and 5 (8%) into other supra ventricular tachyarrhythmias. Of the relapsing group 24 patients (59%) achieved definitive conversion to sinus rhythm within 3 months.

Permanent conversion of AF to sinus rhythm that

obtained intraoperatively without any relapse (primary definitive conversion) occurred in 20 patients (33%). From the relapsing group 24 patients (39%) regained and maintained sinus rhythm (secondary definitive conversion). AF definitively persisted in 17 patients (28%) after a period of temporary conversion.

Type of conversion	patients
Primary (intraoperatively)	61 (100%)
Primary definitive (intraoperative and maintained)	20 (33%)
Secondary definitive (regained after relapses)	24 (39%)
Failed definitive conversion	17 (28%)

Table 3: types of conversion

Among the studied values there were statistically significant ($P < 0.05$) predictors for successful definitive AF ablation (table 4) and others were significantly associated with failure of achievement of definitive conversion (table 5).

Predictors	P value
Age less than 60 y	0.032
LA diameter less than 45 mm	0.02
Degenerative pathology	0.041
AF duration less than 1 year	0.029

Table 4: Predictors of success

Predictors	P value
Age more than 70 y	0.048
Duration more than 4 y	0.031
MV replacement	0.07
Associated IHD	0.044

Table 5: Predictors of failure

Discussion

Over the past several years, the surgical treatment of AF has evolved rapidly, and a number of devices with various energy sources have been used to create linear lesions in the atria (endocardial, epicardial, or combined). These therapies have been used for both lone AF and AF associated with structural heart disease. [7-12]

The goal of these techniques, however, is to create lines of intra-atrial conduction block that will (1) preclude the development of macroreentrant circuits in the atria, (2) isolate the trigger or triggers for AF in or near the pulmonary vein orifices, or (3) accomplish both goals 1 and 2, while at the same time allowing the atria to resume either a sinus or atrially paced rhythm. Recent clinical evidence has clearly demonstrated that the key mandatory step in the interventional treatment of AF is isolation of the pulmonary vein orifices. [13]

The evaluation of the outcome of the AF ablation in the same patient may vary considerably with the difference in the technique (amount of microwave energy, duration, angle of the probe….etc). It can also vary with the length of follow up and the diagnostic methods used to determine the cardiac rhythm.

The patient age was statistically found to be an important predictor of success if less than 60 years and failure if more than 70. The original pathology and not the type of procedures were proved to be a predictor of success in case of a degenerative pathology or failure in case of rheumatic pathology especially if associated with ischemic myocardium. The duration of AF is a difficult parameter to be objectively evaluated in many patients since a good percentage start to change their rhythm without immediate symptoms and may remain so for a considerable period. In our study we measured the duration of AF proved by objective patient findings on the first referral. Duration of less than 1 year was a predictor of success but more than 4 years of AF was a statistically significant predictor of failure.

The main aim of our study is to identify objectively statistically significant predictors that can help the surgeon to predict the probable result of the AF ablation in concomitance with mitral valve open heart procedures. We tried to evaluate some of the factors thought to be of influence on the outcome of AF ablation. Our results shows that the nature of the associated procedures, patient past history of smoking, hypertension, diabetes, COPD, renal failure, reoperation and degenerative lesions have no statistical significance on the outcome of the ablation.

We noticed that despite the immediate 100% ablation ratio; a considerable percentage of AF relapse occurred in our patients (67%). This information is of particular importance since many patients get depressed with the first AF relapse and it would be better if they would be informed of the different mode possibilities of the out come preoperatively. Permanent ablation from the start (primary definitive conversion) occurred only in 33% of our patients. The total rate of permanent definitive conversion (72% in our study) may vary considerably between the different studies due to many factors; the most important among all is the definition adopted for permanent conversion. We didn't consider the absence of symptoms or signs of AF relapse or follow up visit, online or on phone questionnaires as a proof of outcome.

We only considered a patient was permanently converted into sinus rhythm if he had had sinus rhythm in the ECG traces performed in the last follow up visit.

Our study shows that we are in a need to have a multicentric study on a large volume adopting objective methods in the microwave energy application, the estimation of the effect on the atrial tissue in addition to the objective estimation of the out come to be able to evaluate the vast difference in the results of surgical ablation published by different research groups.

The limitations of this study are: being retrospective, using a visual estimation of the ablation procedure (subjective) and the relatively small volume of patients.

Conclusions

Combined AF ablation with mitral valve surgery is safe and effective, particularly, when associated with MV repair patients.

The predictors of success include patient's age less than 60 years, AF duration less than one year, a degenerative pathology and a left atrial diameter of less than 45mm. The predictors of failure were patient's age older than 70 years, AF duration more than 4 years and ischemic and/or rheumatic pathology.

However, the success rate as defined by definitive conversion to sinus rhythm may vary significantly not only according to the patient characteristics but also the methods of follow up and the definition of conversion.

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EFFECT OF VALVE PROSTHESIS – PATIENT MISMATCH ON SHORT TERM OUTCOME AFTER AORTIC VALVE REPLACMENT

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Background: **Small- size prostheses for aortic valve replacement can be too small in relation to the body size, thus causing valve prosthesis-patient mismatch (PPM) and abnormally high transvalvular pressure gradient. This study was planned to examine the relation between the PPM and the short term outcome after the operation.**

Methods: **Baseline risk factors and short term outcome were analyzed in 23 patients, 19 (82.6%) males and 4(17.4%) females who underwent Aortic valve replacement. The indexed valve effective orifice area (IEOA) was estimated for each type and size of prosthesis implanted. PPM was defined as not clinically significant if patient IEOA is > 0.85 cm2/m2 while clinically significant if patient IEOA is ≤ 0.85 cm2/m2 .**

Results: **Study patients were divided into 2 groups, group "A" (9 patients with IEOA ≤0.85 cm2/m2) and group "B" (14 patients with IEOA > 0.85 cm2/m2). There was no statistical difference between both groups regarding pre-operative patients' demographics. Operative characteristics were similar among patients in both groups with no statistical significance difference. ICU stay was 2.8 + 1.5 days in group A vs. 3.2 + 1.9 days in group B (p =0.08). While total hospital stay was 12.5 + 9.8 days in Group A vs. 13.6 + 9.8 days in group B (p =0.59).The early mortality was encountered in two patients in group A and one patient in group B (p =0.59).**

Conclusion: **Prosthesis-Patient Mismatch has no significant effect on short term outcome in patients undergoing Aortic Valve Replacement.**

Prosthetic valve replacement represents a successful surgical therapy for patients with symptomatic aortic valve disease. Despite an increasing proportion of high-risk patients

presenting for valve surgery, the morbidity and mortality of isolated aortic valve replacement (AVR) remain low1. Small aortic annular size has been reported to be associated with increased operative mortality 1-3. However, considerable controversy

remains regarding the effects of small aortic prostheses on short & long-term survival 4, 5.

In particular, the relation between Prosthesis – Patient Mismatch (PPM) and short -term mortality remains to be determined and it could theoretically be important given that the left ventricle is more vulnerable at that time and that it could be more sensitive to the increased hemodynamic burden imposed by PPM.

The parameter often used in order to define the presence of PPM has been the geometric orifice area (GOA) that is, a measurement deriving from the internal diameter of the prosthesis and measured in vitro by the valve manufacturer. However, the GOA has been shown to overestimate the 'functional area' of valve prosthesis. Following the introduction of echo-Doppler studies, a more reliable parameter has been validated in clinical practice, termed the

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effective orifice area (EOA) 6, 7.

Rahimtoola8 was the first one to define PPM to be present when the effective orifice area (EOA) of the implanted prosthesis is less than that of the normal human valve. Based on this definition, most patients undergoing aortic valve replacement (AVR) thus have at least mild PPM.

Transvalvular gradients observed postoperatively are related not only to the EOA but also to the transvalvular flow. In turn, transvalvular flow is related to cardiac output that at rest is primarily related to the patient's body size. As a consequence, the most reliable parameter to estimate the hemodynamic properties of the valve is the indexed effective orifice area (IEOA) 9, 10.

The IEOA is obtained from the relationship between effective orifice area and body surface area (EOA/BSA), with the EOA being calculated using the continuity equation: EOA= SV/VTI, where SV is the stroke volume and VTI is the velocity time integral of the aortic jet Doppler signal. It is accepted worldwide that moderate aortic valve stenosis is present when the IEOA is <0.9 cm2/m2 and this concept should apply also to valve prostheses. In fact, several studies have demonstrated that when a prosthetic IEOA is <0.9 cm2/m2, a significant transvalvular gradient is present at rest 10, 11.

The aim of this study was to evaluate the impact of valve prosthesis-patient mismatch on the short term outcome after Aortic valve replacement.

Methods

Baseline risk factors and short term outcome were analyzed in 23 patients, 19 (82.6%) males and 4(17.4%) females who underwent AVR with prosthetic valve in the cardiac surgery unit at North West Armed Forces Hospital during the period from May 2002 to May 2004.

Clinical, echocardiography, coronary angiography, operative and post-operative outcome data were retrospectively collected in a computerized database.

Prosthesis

The selection of prosthesis was based on the patient's age, history of previous thromboembolism or bleeding disorder and the preference of the patient and surgeon.

Indexed EOA (IEOA) for each prosthesis was derived from echocardiographic measured value of EOA divided by patient's body surface area (BSA). PPM was defined as not clinically significant if patient IEOA is > 0.85 cm2/m2 while clinically significant if patient IEOA is ≤ 0.85 cm2/m2.

Short term mortality was defined as death from any cause within 30 days after the operation.

Statistical analysis:

Data were expressed as mean ± standard deviation and compared using Chi square test to compare the results obtained in patients with and without mismatch. Values of p less than 0.05 were considered significant

Results

Study patients were divided into 2 groups, group "A" (9 patients with EOA/BSA ≤0.85 cm2/m2) and group "B" (14 patients with EOA/BSA > 0.85 cm2/m2).

Mean age in group A was 53 ± 26 years and was 48 ± 20 years in group B (p =0.91). There was no statistical difference between both groups regarding BSA (1.72 ± 0.16 m2 and 1.65 ± 0.15 m2 in group A & B respectively) (p =0.18). Rheumatic valve disease was found in 10 patients (5 in each group) while degenerative valves were found in 4 patients in group A and 9 patients in group B (p =0.34). Four of the patients were diabetic (2 in each group) (p =1.0). Two patients in group "A" and 3 patients in group "B" had LVEF ≤ 40 % (p =0.68). Euro score was 5 ± 3 for group A and 4.8 ± 2.7 for group B (p =0.80). Pre-operative patients' demographics are presented in table 1.

	Group A EOA/BSA ≤ 0.85 cm^2/m^2 (n= 9)	Group B EOA/BSA > 0.85 cm^2/m^2 (n=14)	*P*
Age (Y):	53 ± 26	48 ± 20	0.91
Male/Female:	7/2	12/2	0.59
BSA:	1.72 ± 0.16	1.65 ± 0.15	0.18
Etiology:			
- Rheumatic:	5	5	0.34
- Degenerative:	4	9	0.34
Diabetes:	2	2	1.0
CVA:	0	0	0
LVEF < 40%:	2	3	0.68
EuroScore: (Standard)	5 ± 3	4.8 ± 2.7	0.80

The following prostheses had been used: CE Standard in 6 patients, SMJ Standard in 13 patients, ON- X valve in 3 patients and SJM Toronto in one patient. Range of valve sizes implanted with in vitro internal diameter in mm, effective orifice area in cm2 and the ratio between the EOA/ BSA in cm2/m2 are shown in Table 2.

Valve	n	ID, mm	EOA, cm2	EOA/BSA
CE Standard:	3	21	1.1	0.688
	3	23	1.3	0.827
SJM Standard:	1	19	1.04	0.556
	4	21	1.38	1.753
	3	23	1.52	0.92
	3	25	2.08	1.194
	2	27	2.65	1.623
SJM Toronto	1	21	1.3	1.149
ON –X	1	19	1.5	0.932
	2	23	2.0	1.105

Operative characteristics were similar among patients in both groups with no statistical significance dif-

ference. Six Patients (2 in group A and 4 in group B) had concomitant coronary artery bypass grafting (CABG). Cardiopulmonary Bypass time was similar in both groups (176 + 120 min vs. 144 + 48 min in group A & B respectively P = 0.69). There was no difference in the Cross clamp duration between both groups (108 + 34 min vs. 103 + 26 min in group A & B respectively P = 0.74). Mechanical valves were implanted in 4 patients (44.4 %) in group A and 12 patients (85.8 %) in group B (p =0.28) , while 5 patients (55.6 %) had Bio-prosthesis in group A and 2 patients (14.2 %) in group B (p =0.28). Patients' operative characteristics are shown in table 3.

	Group A EOA/BSA ≤ 0.85 cm^2/m^2 (n= 9)	Group B EOA/BSA > 0.85 cm^2/m^2 (n=14)	*P*
Concomitant CABG:	2 (22.2%)	4 (28.6%)	NS
CPB Duration (minutes):	176 ± 120	144 ± 48	0.69
Cross Clamp Duration (minutes):	108 ± 34	103 ± 26	0.74
Mechanical Valves:	4 (44.4%)	12 (85.8%)	0.28
Bioprosthetic Valves:	5 (55.6%)	2 (14.2%)	0.28

There was no statistical difference between the two groups in length of ICU stay, total hospital stay and early mortality. ICU stay was 2.8 + 1.5 days in group A vs. 3.2 + 1.9 days in group B (p =0.08). While total hospital stay was 12.5 + 9.8 days in Group A vs. 13.6 + 9.8 days in group B (p =0.59).The early mortality was encountered in two patients in group A one of them died in the ICU from post-op electromechanical dissociation. The second patient had uncontrolled post operative surgical bleeding from the Aortomitral angle. Group B had only one death from post operative chest infection (p =0.59). Post-operative Data is demonstrated in table 4.

	Group A EOA/BSA ≤ 0.85 cm^2/m^2 (n= 9)	Group B EOA/BSA > 0.85 cm^2/m^2 (n=14)	*P*
ICU Stay (Days):	2.8 ± 1.5	3.2 ± 1.9	0.086
Hospital Stay (Days):	12.5 ± 9.8	13.6 ± 9.8	0.59
Early Mortality:	2	1	0.59

Discussion

Patient-prosthesis mismatch is a term often used but vaguely defined, with many variations of the definition used by investigators. It was defined on the basis of small valve size, excessive gradients across the aortic valve, exercise-induced gradients, smaller in vivo prosthetic valve effective orifice area than that of a native human valve, or various combinations of the above. Our definition of PPM has followed the generally accepted method of assessing (IEOA) to allow comparisons with other studies.

Conclusions drawn concerning the impact of PPM on short –term outcome differ greatly among reports. Our results show that there is no significant impact of PPM on the short term out come and mortality following AVR. Other studies have also purported to analyze the influence of PPM on mortality after AVR and they could not identify any major influence 7, 12.

Pibarot and coworkers5 in his series of consecutive AVR patients, the 30-day mortality was 4.6% in the patients without PPM, but was doubled with moderate PPM and increased 11-fold with severe PPM. Although patients with moderate and severe PPM had significantly more risk factors including impaired left ventricular function, older age, female gender, coronary artery disease, and emergent/salvage surgery, the authors nevertheless concluded that PPM was a strong and independent predictor of short-term mortality. Likewise, Rao et al., 6 also noted an increased operative mortality (8 vs.5%) in their series of AVR patients with PPM who similarly had a higher incidence of other risk factors. Finally, Blackstone et al., 11 using multivariable hazard domain analysis with balancing score and risk factor adjustment in AVR patients from nine centers, reported that PPM increased the operative mortality by 1–2%.

A possible explanation for these apparently conflicting results might be an interaction of PPM with pre-existing impairment of left ventricular function. In a multivariate analysis of 52 patients undergoing AVR with a left ventricular ejection fraction below 35%, the only predictor of surgical mortality was smaller prosthesis size 13.

In another observational study in patients undergoing AVR with stentless bioprosthetic valves, baseline left ventricular mass index and PPM were the strongest predictors of the extent of postoperative LV mass regression, implying a more powerful effect of PPM in the impaired ventricle 14.

Limitation of the study

A randomized controlled study with larger number of patients would provide better understanding of PPM and explore different risk factors that might play a role in its occurrence. Intermediate and long-term outcomes need to be addressed.

Conclusion

The effects of PPM are still controversial, and despite the fact that our study showed no significant effect of the PPM on the short term out come after Aortic valve replacement, larger sample size should be studied to demonstrate sufficient statistical effect.

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RELATION OF LEFT VENTRICULAR MASS TO VOLUME AND ITS INFLUENCE ON THE OUTCOME OF AORTIC VALVE REPLACEMENT

Cardiovascular

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Abstract: **Our study included 67 patients With Pure Aortic regurgitation . All of them had undergone open heart surgery for aortic valve replacement in National Heart Institute (NHI) and Qasr Alaini hospitals in the period from November 2004 to September 2006.**
Those patients have been evaluated clinically, radiologically and echocardiographically preoperatively, early post-operative and 6 months late post-operatively. Our results showed that those patients Who had been operated upon with the following criteria .CTR < 0.6 , LVEDD < 7.5 cm, EF >50% and diastolic radius to wall thickness (R/WTh) < 3 have good outcome with better quality of life as regard to LV function , NYHA class and ventricular arrhythmia . Those patients with CTR > 0.6 ,LVEDD > 7.5, EF < 50% , and R/WTh > 3 , showed bad outcome as LV function and NYHA did not improve and they had ventricular arrhythmi

Chronic aortic regurgitation produces LV volume overload that leads to a series of compensatory changes including LV enlargement and compensatory hypertrophy. Wall thickness must increase to compensate for increased ventricular dimensions to minimize or normalize wall stress according to Laplace law. As long as left ventricular wall stress is maintained in the normal average, the LV reserves contractility and EF remains within normal range and patients during this chronic compensated stage remain asymptomatic for long periods. By time LV dilatation increases with change of LV from an elliptical to spherical shape with increase of wall stress, decline in the contractility and EF and the patients start to be symptomatized. LV Function is considered to be one of the most important main factors which affect the early and long term results of AVR for aortic Incompetence. Our study is to detect the parameters upon which we can predict our surgical outcome in patients who have been undergone aortic valve replacement for chronic aortic regurge by correlating pre- and post-operative values of these parameters. .

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Patients and methods

All of our (67) patients were operated upon in NHI and Qasr Alaini hospitals from November 2004 to September 2006. all of our patients had isolated chronic aortic incompetence (52) of them were males and (15) females with age range from (22) years to (47) years and the mean age of 33.6 + 3.2 Years .

All patients were examined clinically, radiologically and echocardiographcally pre-operatively, early post-operatively and then 6 months post-operatively.

Clinically our patients were assessed according to NYHA functional classification. ECG data. study included comment on left ventricular hypertrophy (LVH) and LV strain and presence of arrhythmia. Plain chest X-ray PA view was done to all patients to assess cardiothoracic ratio (CTR).

Echocardiographic study including M.mode, two-dimensional and color Doppler study were done to assess LVEDV., LVESV ., LVEDD and LVESD. EF was calculated from the following formula

$$EF = \frac{\text{Stroke volume (EDV-ESV)}}{EDV}$$

FS Percentage was calculated from the following formula

$$FS = \frac{(EDD - ESD)}{EDD}$$

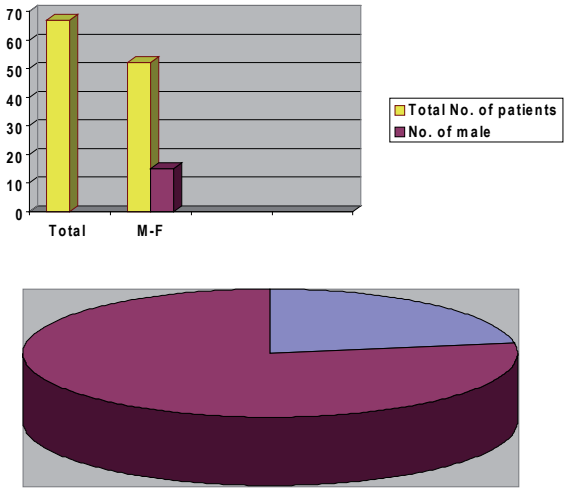
Both EF and FS are used as an indication for LV systolic performance. Compensatory hypertrophy to increased LV volume is assessed for relation of volume to mass ratio. LV volume can be assessed by LVEDD , LV mass can be assessed by posterior wall thickness as expressed by the following formula :-

R (index of LV mass) =2 x posterior wall thickness.

$$R/Th = \frac{EDD}{2 \times \text{posterior wall thickness}}$$

Results

All our 67 patients had undergone isolated aortic valve replacement. The ratio of female to male is 1 : 3.47. The mean age of all 67 patients is 33.6+3.2. The mean age for the males was 35.3 years and for female was 29.7 years.



Male
Female
FIG.1 Male to Female ratio

Our (67) patients were divided into two groups according to the LVEDD and LVESD .

The first group (A) included 45 patients there mean age 25.9 + 4.2.9 of them were in NYHA class I but their LV dimensions were increased to limit which started to affect their LV functions. 30 patients were in NYHA class II ., 6 patients were in NYHA class III . in all patients group (A) CTR was less than O.6 and ECG showed LV hypertrophy by voltage criteria only .The LVEDD < 7.5 cm , LVESD < 5.5 cm EF >50% FS<25% and R/TH ratio was <3 .

The second group (B) included 22 patients with mean age of 35.3+3.9. 10 of them were in NYHA class II ,. 7 were in NYHA class III and 5 were in NYHA class IV . CTR was > 0.6 , ECG showed strain pattern of LVH , LVEDD > 7.5 cm. ,LVESD >5.5 cm. , EF<50% , FS < 25% and R/Th ratio was >3 .

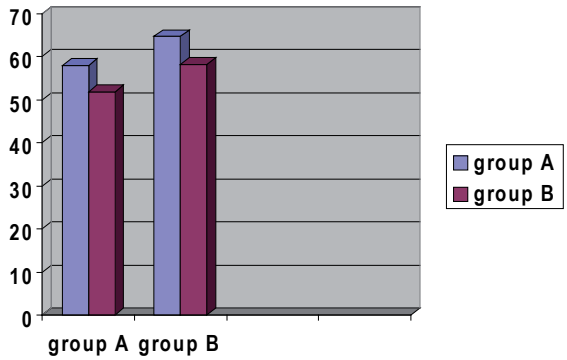
operative data

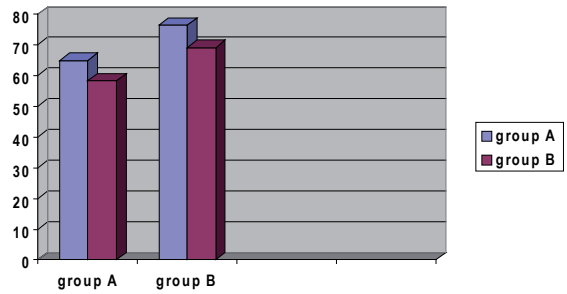
Cold blood antigrade cardioplegia was used in all 67 pts. with systemic and local cooling. Mean cross clamp time was 34.1+ 3.2 min with no big difference between group A and B .the mean bypass time was longer in group B 67.6+5.2 min. while it was 49.8+3.6 min in group A. minimal inotropic support was needed in 11 pts only from group A., while inotropic support was needed in all 22 patients of group B with use of more than one inotropes in 7 patients .

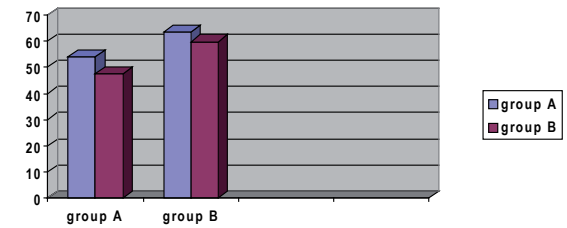
postoperative data

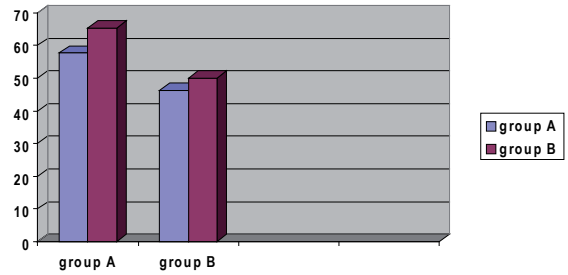
ICU stay and total hospital stay were less in group A .one patients only from group A was re-opened for bleeding and the cause was bleeding from the site of the right upper pulmonary vein vent . No patients re-opened for bleeding in group B. 41 patients from group A were in NYHA class 1 while only 4 patients were in NYHA class 11 one of them was in NYHA class II pre-operatively and the other 3 were in NYHA class III pre-operatively . While in group B there is 12 patients in NYHA class 1 post-operatively, 8 of them were in NYHA class 11 and 3 were in NYHA class 111 and there is 6 patients in NYHA class11 post-operatively , 2 of them were in NYHA class 11 pre-operatively , another 2 of them were in NYHA class 111 pre-operatively and the last 2 were in NYHA class1V ,in NYHA class 111 there is 4 patients post-operatively ,2 of them were in NYHA class 111 pre-operatively and 2 were in NYHA class 1V pre-operatively. Only one patient was in NYHA class 1V post-operatively and this patient was also in NYHA class 1V pre-operatively . Total mortality was 3 pts. (4.48 %) all of them from group B and we lost 5 patients (7.46%)

during follow up 3 of them from group B and the other 2 from group A. correlative study between the pre-operative and post-operative ECG., radiographic and echocardiographic data was made and analyzed in both groups and the results are summarized in the following tables .









	R/ th ratio			
	Group A		Group B	
	Pre	Post	Pre	Post
Rang	2.58.3	2.4.2.8	3.11-3.82	2.91-3.42
Mean	2.76	2.59	3.52	3.21
S.D	1 0.3	+0.26	+0.21	+0.16.9
P	< 0.5			< 0.5

Table 2 Preoperative & Post OP.
End – diastolic radius – to – Wall Thickness ratio (R/Th)

DISCUSSION

With aortic regurge , the left ventricle is exposed to volume over-load and to compensate for this load, the left ventricle increases its stroke volume , end-diastolic volume and myocardial mass with normal or may be reduced ejection fraction . Then at certain limits , these compensatory mechanisms are exhausted and the pump function of the left ventricle start to fail gradually . If this mechanical problem is not corrected by surgical interventional , the left ventricular function will deteriorate more and more with subsequent irreversible left ventricular dysfunction and congestive heart failure as a final result , so , surgical interventional should be done at the appropriate time before the occurrence of irreversible depression of myocardial function .

In our 67 patients, we noticed obvious improvement after aortic valve replacement in some patients; on the other hand, some other patients did not improve or may show marked deterioration. Now, the question, what are the factors which affect our results. .?? . . and to get a clear answer , we correlate our post-operative results with the pre-operative parameters as a regard to clinical and haemodynamic status .

As regard to NYHA classification, correlation between pre-operative and post-operative data revealed that our result is nearly the same as Mousa et al ; as those patients who improved to class 1 had mean CTR < 0.6 with moderate dilatation of left ventricle (LVEDD < 7.5 cm & LVESD < 5.5 cm) and the left ventricular function was preserved as the LV dilatation compensated by enough hypertrophy to preserve LV function (mean R / TH < 3) ,also less bypass time , less need to inotropic support and less morbidity and mortality was noticed in those group of patients .We noticed also both of our results and Mousa et al , results correlate with many studies as Cunha et al ; and Henry et al; . In our Series were classified according to preoperative heart size , left ventricular dimensions and function into 2 group to correlate these parameters with postoperative quality of life .We found that 75% of group A became in class 1.12.5 in class II : but in group B we found that 17.6 % only in class I and 31.4 in class II and 33.4 in class III and IV

. It observed that patients with subnormal preoperative ejection fraction and fibre shortening have significantly worse late postoperative prognosis than that of patients with normal left ventricular function .

It is assumed that long standing volume load leads to irreversible left ventricular dysfunction before or coincident with the onset of preoperative symptoms . In the earlier phase of chronic volume sufficient left ventricular hypertrophy develops to normalize the left ventricular wall stress . Ejection fraction becomes depressed when hypertrophy is inadequate to compensate for progressive volume load 2.8,10,12,23 .

Mousa et al 7 , found that patients with EF of 60% or more and % ΔD of 30 had better prognosis than those with lower values Bonow et al 8 reported that the preop. EF less than 50% affected the 3 years postoperative survival . H Al-Faleh et al 23 reported that impaired left ventricular function correlates with the extent of ultrastructural degenerative changes rather than with the extent of fibrosis .

Therefore correct timing of operative intervention is one of the most difficult problems because , as mentioned before, volume overload is well tolerated yet significant degenerative changes may occur in association with physiologic adaptation to chronic volume overload . As result , when corrective valve surgery is performed there may be irreversible left ventricular dysfunction which may preclude an optimal surgical result 9,13,17 . In conclusion good result were observed with properative CTR <60%, EDD <68mm , ESD<57mm , EF > 55%, fibre shortening more than 25% and R/th ratio of 3 or less particularly if the patient was in functional class 1 or II .

The observed finding have led us to propose operation generally at the onset of first symptoms and even before the onset of symptom in cases of voluminous chronic aortic incompetence accompanied by patent signs of left ventricular impairment.

Finally operation is indicated in

1 . All symptomatic patients with moderate & sever regurge .
2 . Asymptomatic patients with :
   a . LV dysfunction (EF < 55% &ΔD < 25%)
   b . progressive enlargement of LV (CTR > 60 & EDD > 68)
   c . Ineffective compensatory hypertrophy (R/Th <3)
   d . ESD of 57 mm or more , if less , for follow-up .

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RETROGRADE VERSUS ANTEGRADE BLOOD CARDIOPLEGIA FOR CABG PATIENTS: DOES IT AFFECT MYOCARDIAL PRESERVATION?

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Ghada Ali,
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Background: **The method of delivery of cardioplegic solution in coronary artery grafting is still controversial regarding optimal myocardial protection.**

Aim: The current work aimed to evaluate the adequacy of myocardial protection with either ways of delivery of cardioplegic solution (antegrade versus retrograde)

Methods: **40 patients scheduled for elective coronary artery bypass grafting were randomly assigned to 1 of 2 groups according to route of cardioplegic administration either antegrade or retrograde. ECG, cardiac troponin (cTnI) and CK-MB were done preoperatively and at 2, 12, 24, 48 and 72 hrs postoperatively. Echocardiograhpy was done preoperatively and before discharge.**

Results: **There were no differences in both groups regarding operative parameters. The antegrade group showed significantly higher CK-MB levels at 2 hrs postoperatively as well as the sensitive and highly specific marker; cTnI concentrations till 24 hrs.**

Conclusions: **Retrograde application of cardioplegia provides better myocardial protection as indicated by lower levels of cTnI concentrations.**

Despite the popularisation of off-pump coronary artery bypass surgery (CABG), a large percentage of myocardial revascularization procedures are still performed on cardiopulmonary bypass (CPB) (1). The cardioprotective strategies available for intraoperative management during the CPB phase are numerous. In the field of cardioplegia, the multiplicity of solutions available, their method of delivery, patient selection and the methods used to determine and quantify myocardial preservation versus injury have made it difficult to accurately decide which form of cardioplegia is best (2).

However, there is some clinical evidence that in certain subsets of patients, blood cardioplegia provides better myocardial protection (3).

The method of delivery of cardioplegic solution in coronary artery during grafting is still controversial regarding optimal myocardial protection (4). Applying antegrade cardioplegia, homogenous perfusion of all segments of the heart may be limited in cases of badly collaterized coronary artery stenosis. Retrograde administration through the coronary sinus seems to offer a solution for this problem. However non homogenous cardiac protection will result if there is rare shunt or short coronary sinus (5-7).

Recently cardiac troponin I (cTnI) has been shown to be a sensitive and highly specific marker of myocardial injury during open-heart operations (8). It has already been used to compare different methods of myocardial protection (9-11).

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The aim of this study was to compare two routes of intermittent warm blood cardioplegia delivery in patients undergoing elective CABG using clinical, echocardiographic and biochemical results for evaluating the adequacy of myocardial protection.

METHODS

After approval of institutional ethics review board and informed patient consent, 40 ASA II-III patients admitted for elective CABG surgeries were assigned randomly to 1 of 2 groups of cardioplegia administration, antegrade (group-A, n=20) and retrograde (group-R, n=20).

Exclusion criteria included Left ventricular ejection fraction (EF) <40%, previous cardiac surgery, myocardial infarction within 4 weeks preoperatively, associated valvular disease, chronic obstructive pulmonary disease, severe hepatic impairment (defined as serum protein <3 g% and serum bilirubin >3 mg%) or renal dysfunction (defined as predicted creatinine clearance (CLcr) <50 ml/min) and history of neurological disorder.

Anesthetic Technique

Premedication was achieved by 0.1 mg/kg morphine intramuscularly one hour preoperatively. Induction with 0.03 mg/kg midazolam, 10-15 µg/kg fentanyl, sleep dose of propofol and atracurium 0.5-0.7 mg/kg. Anesthesia was maintained by 40 µg/kg/hr atracurium and fentanyl boluses administration at 1-3 µg/kg every 20 minutes together with isoflurane up to 1.5 MAC as needed.

Standard monitoring was used in all patients including 5-lead ECG, pulse oximetry, capnography, esophageal temperature, continuous arterial blood pressure and central venous pressure monitoring.

Operative Technique

All operations were performed by one surgeon. In all patients, median sternotomy was done, followed by dissection of left internal mammary artery while simultaneously harvesting the radial artery and saphenous vein. Cannulation for the CPB was carried out in the usual fashion with a 2 stage venous cannulation technique. After full heparinization (300 IU/kg) with activated clotting time (ACT) of 480 seconds or greater, CPB was initiated.

The standard cardiopulmonary bypass circuit was used with a membrane oxygenator and a non-pulsatile roller pump flow rate of 2.4 L/m2/min.

A cardioplegia delivery cannula with separate vent line was inserted into the ascending aorta of all patients. In patients of the retrograde group (group R) an additional coronary sinus catheter with autoinflating silicone cuff was positioned by a closed trans-arterial technique.

After aortic cross clamping, 1000 ml of blood cardioplegia was delivered to all patients according to the group of selection either antegrade (group A) or retrograde (group R). After the first dose, additional doses of 300-500ml were reinfused after 30 min of cross clamp time. No combinations of antegrade and retrograde cardioplegia were given. Aortic cross clamp was removed after the distal anastomoses were done. Proximal anastomoses were done with aortic partial clamping.

Electrocardiogram

A 12-lead ECG was recorded before the operation, 2 hrs after admission to intensive care unit (ICU), then daily after the operation for the next 3days. ECG monitoring was continuous for 48 hrs post operatively in the ICU. New Q-waves >0.04 ms and/or a reduction in R-waves >25% in at least 2 leads were diagnostic for perioperative infarction, while transient ischemic events were diagnosed with ST-segment elevation >1mm. The ECG interpretation and analysis was done by a cardiologist blinded to experimental protocol.

Measurements

Blood samples from the central vein for measurement of cardiac cTnI and CK-MB concentrations were taken preoperatively and 2, 12, 24, 48 and 72 hrs postoperatively. They were stored at -20°C until analysis. CK-MB activity was assayed by immunologic ultraviolet technique with a sensitivity of 5U/L and assay coefficients of variance <2% (normal value ≤ 24U/L). As for cTnI, electrochemiluminescence sandwich immunoassay technique was utilized with a sensitivity of >0.1ηg/ml and coefficients of variance <5% (normal value, < 0.6ηg/ml).

Echocardiography

All studies were performed by the same operator preoperatively and just before hospital discharge. EF was recorded as well as wall motion score index (WMSI).

Statistical analysis

Numerical data are presented as mean ± SD, otherwise total number or % of total as apropriate. Demographic data were analyzed using Student's t-test for numerical variables. Categorical data were analyzed using the x2 analysis or Fisher's exact test as appropriate. cTnI and CK-MB were analyzed using repeated measure ANOVA, where group (A) and group (R) are the independent variables, if significance is reached a tukey post.

hoc test is used to identify level of significance. $P < 0.05$ was considered as statistically significant. Statistical analysis was performed using Instant Graphed, version 2 statistical package for windows.

RESULTS

There were no significant differences between the two groups regarding age, sex, ejection fraction and risk factors as shown in (Table 1).

	Group A (n=20)	Group R retrograde (n=20)
Mean age (yrs)	63.7±7.9	65.0±8.4
Sex (M/F)	13/7	12/8
Ejection Fraction (EF %)	46±13	46±11
Two vessels with > 70% stenosis	18	17
No. of diseased vessels	2.6±0.5	2.6±0.5
Hypertension	8	9
Diabetes	8	7
Smoking	7	8
History of CHF	1	1
Family History of CAD	3	4
Dyslipidemia	7	6
Old Myocardial Infarction	12	13

Table 1: Demographic Data and Patients Characteristics. Continuous data are presented as mean±SD. Categorical variables are presented as number and/or proportion. There were no statistical differences between the 2 groups. Group A = antegrade, Group R = retrograde.

Operative and Postoperative Data

Operative and postoperative characteristics are shown in Table 2. Patients of group-R had shorter operative, bypass and cross clamp times but with no statistical significance. The left internal mammary artery was used in all patients. Volume of cardioplegia used was not significantly different between the 2 groups.

At time of weaning from CPB, 6 patients in group-A required inotropic support in the form of epinephrine infusion, 2 in low dose (up to 50 ηg/kg/min) and 4 in moderate dose (up to 100 ηg/kg/min) as compared to 3 patients in group-R, 1 in low dose and 2 in moderate dose.

Intraoperative defibrillation of the heart was necessary in 8 patients in group-A and in 7 patients in group-R. None of our patients required intra aortic balloon pump or re-thoracotomy.

Postoperative ventilation was shorter in group-R (6.6±6.2 hrs) as opposed to group-A (8.1±6.9 hrs) but still not significant (table-1).

Also ICU time and hospital time in days were shorter in group-R than in group A however not reached a statistical significant.

Three patients developed perioperative myocardial infarction, 2 patients in group-A and 1 patient in group-R.

	Group-A (n=20)	Group-R (n=20)
Operation Time (min)	186 ± 31	175 ± 29
CPB time (min)	86 ± 22	78 ± 18
Minimal Core Temperature During CPB (°C)	32.1 ± 1.6	32.1 ±1.4
Aortic Cross Clamp Time	49 ± 12	41 ± 11
Number of Grafts	3.7 ± 0.7	3.6 ±1.1
LIMA Used (no)	20	20
Volume of Cardioplegia (ml)	1306 ± 273	1390 ± 331
Intraoperative Inotropes	6	3
Intraoperative Defibrillation	8	7
Postoperative Ventilation (hr)	8.1 ± 6.9	6.6 ± 6.2
ICU Time (days)	1.8 ± 1.2	1.4 ± 0.9
Hospital Time (days)	9.2 ± 2.4	8.8 ± 1.7
Perioperative Infarction	2	1

Table 2: Operative and Postoperative Data. Data are presented as absolute number or mean±SD as appropriate. Group A = antegrade, Group R = retrograde. CPB = cardiopulmonary bypass, LIMA = left internal mammary artery. There were no statistical differences between the 2 groups.

Biochemical Results

The concentrations of cTnI of both groups are shown in figure 1.

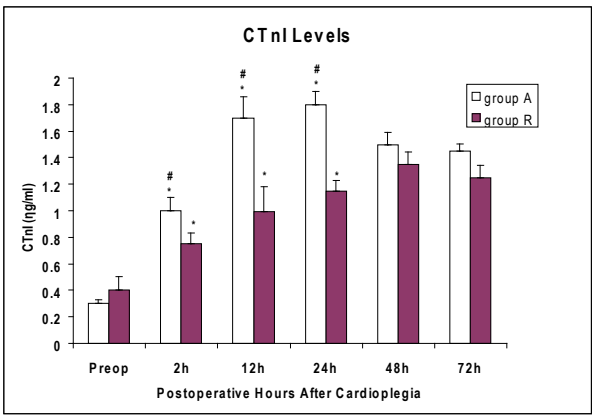

Figure 1: Serum cardiac troponin-I [CTnI] levels (ηg/ml) measured at various time points after infusion of blood cardioplegic solution whether antegrade [Group A] or retrograde [Group R]. *Significant against preoperative values; #significant against Group R; (P<0.05).

Both groups showed an increase in cTnI levels that was statistically significant until 24 hrs postoperatively, as compared to the preoperative values. The rise in cTnI levels in the antegrade group was more than the rise in the retrograde group, this was statistically significant until 24 hrs only, and after that the difference was not statistically significant.

The changes in CK-MB levels are shown in figure 2. They showed a pattern similar to that of cTnI levels but the statistically significant rise in CK-MB level was at 2 hrs postoperatively. However, the increase in both;

cTnI and CK-MB never fulfilled the criteria of myocardial infarction except in 3 patients, 2 in group-A and 1 in group-R.

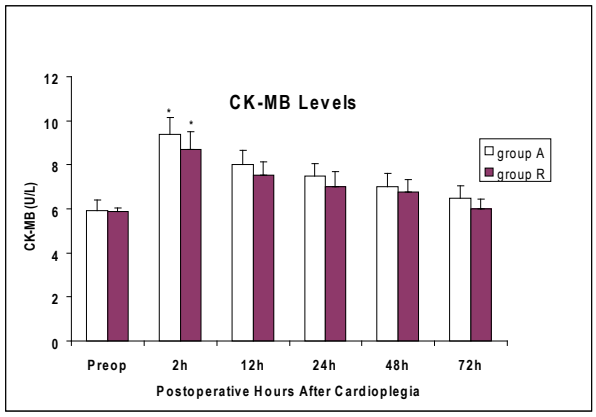

Figure 2: Serum creatine kinase–MB [CK-MB] activity (U/L) measured at various time points after infusion of blood cardioplegic solution whether antegrade [Group A] or retrograde [Group R]. *Significant against preoperative values; (P<0.05).

Echocardiography

Postoperatively, both groups showed mild improvement in left ventricular EF, in group-A from 46±1.3% to 49±2.5% and in group-R from 46±1.1% to 50±1.7%.

Left ventricular WMSI also showed a mild improvement in both groups postoperatively. In group-A from 1.42±0.37 to 1.13±0.16 and in group-R from 1.61±0.28 to 1.12±0.13.

DISCUSSION

The optimum route of delivery of cardioplegia for myocardial protection in patients with coronary artery disease is still under debate. This controversy arises from the large amount of studies done during the last 2 decades with vexing and perplexing conclusions. Although many cardiac surgeons suggest routinely the retrograde route of administration (12.13), others prefer the antegrade route (14,15).

In our study we examined both; the antegrade and retrograde methods of administration of warm intermittent blood cardioplegia. The administration of cardioplegic solution through the aortic root produces very quick diastolic arrest and preservation of myocardial function. Although applying cardioplegia by this method produces homogenous perfusion of all segments of the heart, this may be limited in cases of badly catheterized coronary artery stenosis. This can lead to myocardial injury and depressed postoperative left ventricular function.

Infusion of retrograde cardioplegia results in better distribution, myocardial protection and recovery of the function in the area distal to the occlusion (16,17). However, veno-venous shunts and the thebesian channels draining into the ventricular cavity may limit retrograde distribution of cardioplegia.

Cardiac troponin-I (cTnI) is a relatively new marker with high specificity for cardiac damage compared to CK-MB and troponin-T measurement (18,19). It is not influenced by peripheral muscular disease and is unchanged after non cardiac operations. The result of the current work shows a significantly high level of cTnI in all patients in the antegrade than the retrograde group started 2 hrs postoperatively and remained elevated until 48 hrs postoperatively, then started to decline, while CK-MB shows non significant differences between the 2 groups. Therefore it is widely accepted that cTnI should be able to detect even minor differences of myocardial ischemia (19).

These results indicate better myocardial protection by retrograde delivery of cardioplegia and this agrees with the results of Carrier et al 1997 and Jasinsta et al 1997.

The advantages of retrograde blood cardioplegia perfusion are the establishment of aerobic arrest; protection in areas distal to acute MI, ungraftable vessels, and acute occlusion; and elevation of the heart rate and dissection of coronary arteries while administering cardioplegia (20,21).

In conclusion, both methods of delivery allow myocardium protection, however; retrograde delivery of blood enriched cardioplegic solution offers a better myocardial preservation as indicated by cTnI; the most sensitive myocardial injury detector to date.

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IMPACT OF HIGH THORACIC EPIDURAL ANALGESIA ON INCIDENCE OF PERIOPERATIVE STRESS RESPONSE IN OFF PUMP CABG

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Background: **Most randomized control studies in this area have focused on hemodynamic effects and the stress response to surgery. Studies assessing the important issue of potential cardioprotective effects of TEA have yielded conflicting results. The aim of this prospective randomized study was to investigate effects of TEA as an adjunct to GA in patients undergoing Off-Pump CABG as regards hemodynamics, postoperative release of biochemical markers of myocardial damage and myocardial morbidity.**

Methods: **64 patients were randomly allocated into two groups (G I n=33) patients underwent Off-Pump CABG under GA without TEA and (GII n=31) patients underwent Off-Pump CABG under GA with adjunct TEA.**

Results: **mean heart rate was increased significantly in G I during chest closure and after arrival to ICU and mean arterial pressure was lower in G II. The incidence of perioperative AF, ventricular extrasystole and peak plasma levels of ANP, BNP and catecholamines were significantly lower with TEA. The serum concentration of cTnT and CK-MB is significantly higher without TEA.**

Conclusion: **TEA is advantageous as adjunctive analgesia to patients in Off-Pump CABG. It effectively suppressed the sympathetic activity, reducing incidence of post operative arrhythmia. Combination of TEA with GA during CABG exerted a beneficial effect on the perioperative stress response as indicated by reduction of Catecholamines, ANP and BNP. The use of epidural techniques as adjuncts to GA gives better results as regard level of biochemical markers cTnT and CK-MB which detect minor myocardial injury.**

Post operative morbidity occurs because of factors related to surgical procedure, concomitant medical disease, or the severity of the neuroendocrine response to the surgery (1) especially Sympathoadrenal reflexes (2). Coronary artery bypass grafting (CABG) is associated with exaggerated hormonal and inflammatory responses (3,4). Activation of myocardial sympathetic nerves is associated with the genesis of silent myocardial ischemia in patients with coronary artery disease (5). Perioperative arrhythmias such as atrial fibrillation (AF) are the most common complications in patients undergoing CABG (6). General anesthesia (GA) is the most commonly used anesthetic technique and is considered the (gold standard) for CABG performed either On-pump or Off-pump (7). Within the past few years, however, thoracic epidural analgesia (TEA) as an adjunct to GA has become more prevalent and has been shown to be potentially beneficial in patients with coronary artery disease (8).

Potential advantages of TEA include thoracic sympathicolysis with subsequent improvement of coronary perfusion, decrease heart rate, decrease endogenous stress response, and a reduced risk of perioperative myocardial ischemia

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(9). Most randomized controled studies in this area have focused on hemodynamic effects and the stress response to surgery. Studies assessing the important issue of potential cardioprotective effects of TEA have yielded conflicting results (10). The release of cardiac troponin T (cTnT) has been shown to be a sensitive and specific marker of myocardial cell necrosis with significant prognostic importance after cardiac surgery (11). Natriuretic peptides are produced by the heart and regulate arterial blood pressure, electrolyte balance, and fluid volume (12).

The aim of this prospective randomized study was to investigate effects of TEA as an adjunct to GA in patients undergoing Off-Pump CABG as regards hemodynamics, postoperative release of biochemical markers of myocardial damage and myocardial morbidity.

METHODS

After obtaining informed written consent, patients were given a full explanation of the anesthetic techniques. Exclusion criteria were severe alteration of left ventricular function (Ejection fraction < 30%), symptomatic mitral or aortic valvular disease, liver dysfunction (alanine aminotransferase, aspartate aminotransferase >40U/L), renal insufficiency requiring hemodialysis, contraindication to dural puncture (chronic back pain or previous spinal surgery in the area of puncture, localized infection, therapy with anti platelet drugs <3 days before surgery), abnormal blood coagulation tests and patients undergoing emergency operation.

67 patients were operated upon for CABG during the period from January 2006 to December 2007 by one surgeon, 3 patients were excluded, 1 patient because TEA did not function postoperatively and due to the need of postoperative pacing in 2 patients. The remaining 64 patients were randomly allocated into two groups (G I n=33) patients underwent Off-Pump CABG under GA without TEA and (GII n=31) patients underwent Off-Pump CABG under GA with adjunct TEA. There were no statistically significant differences in demographic and preoperative clinical variables (Table 1).

Demographic Data	G I	G II
Age	64±9	63±9
Sex (male/female)	33/2	31/3
Body mass index (Kg/m2)	27.6 ± 3.8	27.1 ± 2.7
Previous M.I.	5	4
Hypertension	4	3
D.M.	2	2
Previous stroke	0	0
COPD	0	1
Ejection fraction	57 ± 10	58 ± 9

Table (1): Demographic data

Preoperative cardiac medications were continued until the day of surgery. Premedication consisted of medazolam 7.5 mg orally in the evening before surgery and 2 h before induction of anesthesia. On arrival in the holding area intravenous access and direct blood pressure monitoring by catheterization of the radial artery were established. An 8.0 F pulmonary artery catheter was inserted into pulmonary artery via the right jugular vein. In patients of G II a16G epidural catheter was inserted through a tuohy needle at the T1-T2, T2-T3 using median approach and loss of resistance technique. Proper position was tested by injection of 2 ml of bubivacaine 0.5% epidural analgesia was induced 8-14 ml of bubivacaine 0.5%. Somatosensory blockade was evaluated by touching the skin with ice and performing pinprick test bilaterally at mid clavicular line after 30-40 minutes. An extension from at least T1-T10 was accepted.

The block was maintained with bubivacaine 0.5%, with infusion rate of 4-8 ml /h, until the patient arrived at the intensive care unit (ICU). Then analgesia was achieved by a continuous infusion of bubivacaine (2 mg/ml) and fentanyl (2µg/ml) epidurally (3-7ml/h) until the end of study on the 3rd post operative day. TEA was performed successfully in all patients without any observed complications.

Electrocardiogram (ECG) monitoring was initiated. GA in all patients was induced with medazolam (0.05-0.1mg / kg), fentanyl (7-15µg/kg), Propofol (20mg increments as required), and rocuronium (0-6 mg /kg). GA was maintained with propofol 3-6mg .kg -1.h-1. Further doses of Rocuronium 10 mg were given only for overt patient movement. Positive pressure ventilation with O2 50% in air was used. Tidal volume (8-10ml/kg -1) and respiratory rate (10-12 min -1) were adjusted according to end tidal pressure of carbon dioxide to achieve normal ventilation (end-tidal pressure of carbon dioxide 35-45 mmhg).

In all patients mammary artery were harvested in skeletonized fashion using low voltage electrocautery and dilated with local injection of a mixture of Papaverine, Heparin and Isopten. Saphenous venous grafts were harvested and used when needed; the redial artery was not used.

Intravenous heparin was given in a standard dose of 150 IU/kg after thoracic artery dissection. After creating pericardial cradle, pericardial sutures were taken and snared to rotate the heart in the direction needed. The target vessels were exposed and Octopus stabilizer was used for stabilization of the target vessels. Anastomoses were performed in standard beating heart bypass technique using proximal temporary occlusion of the target coronary artery with a vessel loop and suction to clear

the anastomotic site.

Heparin was reversed with protamine 3 mg /kg. Further protamine (0.5-1mg/kg) was given to return the activated clotting time to baseline or as initial management of bleeding.

Heart rate (HR), Mean arterial pressure (MAP), Right atrial pressure (RAP), Mean pulmonary artery pressure (MPAP), Pulmonary capillary wedge pressure (PCWP), systemic vascular resistance (SVR) were recorded at the following interval: Prior to induction, 5 min after intubation, 1-2 min post sternotomy, during chest closure, and after arrival in ICU. Patients were carefully monitored with intraoperative continuous ECG monitoring system with automatic arrhythmias and ST segment analysis. Thereafter, twice daily 12-lead ECG was performed until hospital discharge. Arrhythmias were classified as supraventricular, ventricular, or conduction defects. Supraventricular arrhythmias were further divided into atrial flutter or fibrillation. Ventricular arrhythmias were subdivided into tachycardia, fibrillation, or multiple ventricular ectopics (>6 min). Conduction defects were classified as 1º, 2ºor 3º (complete) heart block.

Postoperative myocardial infarction was diagnosed with ECG analysis (new Q waves, ST segment increase >3 mm) and confirmed by samples of blood for cTnT were collected in correlation with ECG Changes. Transmural infarction was defined as new Q waves, ST segment increase > 3 mm and cardiac troponin I cTnT > 15µg/l.

Postoperatively, respiratory weaning was started by intermittent mandatory ventilation, follwed by continuous positive airway pressure breathing. Patients were extubated as soon as they fulfilled extubation criteria.

Venous blood samples were obtained preoperatively (T0), on arrival in ICU (T1), and in the morning of the first (T1) and second (T2) postoperative day, they were stored at -30 º C until analysis. The following variables were determined using commercially available laboratory kits: ANP for which normal values are 10-70 pg /ml in healthy men < 65 yr (13), BNP for which values >80pg /ml are indicative of neurohormonal activation (12, 14) and Catecholamines (epinephrine/or epinephrine) which was performed by using a reverse phase high performance liquid chromatography assay on anisocrotic liquid chromatography interfaced with an electrochemical detector.

Cardiac-specific contractile protein troponin T serum level was measured on an autoanalyzer using an enzyme immuno-method. The lower limit of detection of this test is 0.02 ng/ml. (concentration measured 30 times in the zero standard ± 3 sd). The measuring range was up to 15 ng /ml. The interassay coefficient of variation was from 2.0% (mean concentration of troponin T 14.9 ng /ml) to 9.5% (mean concentration of troponin T 0.07ng/ml). The reference range derived from healthy subjects was 0.0-0.1 ng /ml values of > or equal 0.1ng/l were therefore considered to be positive. The monoclonal antibodies used in this test are highly specific for cardiac troponin T and therefore, for myocardial damage. No significant antibody cross-reaction with skeletal muscle troponin T has been observed (< or equal 0.004%). Creatinine kinase MB (CK-MB) measured by micriparticle enzyme immuonoassay technique, Abbot AX SYM system, Abbot laboratories, Chicago, IL. Samples collected and Data recording at preceding the induction of GA, on arrival to ICU and 24 h after ICU admission.

Statistical analysis

Continuous normally distributed data were compared using paired and unpaired student's t-test or analysis of variance for repeated measures. When multiple comparisons were made, the Bonferroni correction was applied. Data were expressed as mean ± SD.P values of <0.05 were considered statistically significant. The baseline characteristics and for both groups were compared by x 2 contingency or the fisher exact test for categorical data and the Man-Whitney U test for continuous variables. Descriptive statistical analysis was done with the state view statistical software package 5.0.1 (SAS institute,Inc,Cary,NC).

RESULTS

There was no hospital mortality in either group. There were no statistically significant difference between the two groups as regards the mean number of grafts per patient and the total operating room time excluding the time needed for TEA. The surgical results are shown in table (2).

	G I	G II
Number of grafts (mean ± std dev.)	2.7 ± 0.5	2.9 ±0.3
Operative time	158 ± 20	162 ±18

Table (2):Surgical results

The mean upper sensory blockade level extended to C5-6(+/- 1.5 segments), and the lower blockade extended to t10-11 (+/-3.5 segments) in both groups.

There is no significant difference in HR prior to induction of GA, 5 min after induction, and 1-2 min post sternotomy, however, mean heart rate was increased significantly in G I during chest closure and after arrival to ICU. (Figure 1). Mean arterial pressure was lower in G II (P=0.0006) but the other hemodynamic variables were

not different (Table 3).

No patient developed perioperative myocardial infarction detected by ECG (new Q waves, ST segment increase > 3 mm and cTnT > 15).

One patient developed ventricular fibrillation in each group. The incidence of perioperative AF was significantly lower (P<0.01) in G Π (0.4%) than in G I (3%). Time of onset of AF did not differ between the two groups, 1.9 days (44.47 +/- 20.5 hours), 1.8days (44.41+/- 19.9 hours) in GI and GΠ respectively. Five patients in G I and one patients in G Π developed non sustained ventricular extrasystole and which was significant (P<0.01). No patient developed any other type of arrhythmias.

Preoperative epinephrine and norepinephrine were similar in both groups. The surgical procedure resulted in a significant increase in both plasma catecholamines but peak plasma level of epinephrine and norepinephrine was significantly smaller in GΠ (p<0.05) (Figure 2)

Preoperative ANP and BNP concentrations were similar in both groups (G I: 3.4 +/-1.8 and 2.7 +/- 12.3 pgm /ml, G Π: 3.1 +/- 2.0 and 25.9 +/- 13.0 pgm /ml respectively). Both variables remained increased for the duration of the study period with peak plasma ANP and BNP concentrations were (13.4 +/- 4.1 pgm /ml, 161.2 +/- 44.7 pgm/ml in GI and 8.3+/-3.2 pgm/ml, 92.1+/-31.9 pgm/ml in GΠ respectively) at T1 (on arrival to ICU) which significantly lower P <0.05. (Figure 3)

Variable	Timing	G I	G II	P value
	Prior to induction	96	90	
	5 min after intubation	90	82	
MAP (mm hg)	1-2 min after sternotomy	92	81	0.006*
	During chest closure	97	76	
	After ICU arrival	85	87	
	Prior to induction	6	9	
	5 min after intubation	7	9	
RAP (mm hg)	1-2 min after sternotomy	7	8	0.017
	During chest closure	10	10	
	After ICU arrival	8	10	
	Prior to induction	19	22	
	5 min after intubation	19	21	
MPAP (mm hg)	1-2 min after sternotomy	18	19	0.146
	During chest closure	20	22	
	After ICU arrival	18	21	
	Prior to induction	13	14	
	5 min after intubation	9	10	
PCWP(mm hg)	1-2 min after sternotomy	10	10	0.291
	During chest closure	11	12	
	After ICU arrival	11	13	
	Prior to induction	2.7	2.9	
	5 min after intubation	2.7	2.8	
CI(mm hg)	1-2 min after sternotomy	2.5	2.4	0.329
	During chest closure	2.6	2.6	
	After ICU arrival	3.2	2.9	

Table (3) Perioperative hemodynamic variables
G I: CABG (No TEA), G II CABG (TEA), *: significantly different P value.

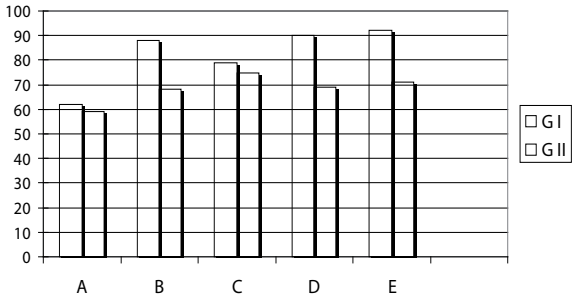

Figure (1) : Perioperative heart rate monitoring. A: prior to induction, B: 5 mins. after intubation, C: 1-2 mins. poststernotomy, D: during chest closure, E: after arrival to ICU. G I: CABG (No TEA), GII: CABG (TEA).

The serum concentration of cTnT and CK-MB increased in both groups but more pronounced in G I with significantly higher values compared with GΠ. (Table 4)

		Preinduction of GA	On Arrival to ICU	At 24 Hr
Troponin T (ng/ml)	Group I	0.02 ± 0.05	0.60±0.70 +*	1.30 ± 1.98 +*
	Group II	0.02 ± 0.04	0.03 ± 0.10	0.40 ± 0.50 *
CK-MB(ng/ml)	Group I	1.4±0.5.	6.3±3.4 +*	8.1±3.4 +*
	Group II	1.2±0.4	1.4±0.5	4.2±1.5 *

Table (4) Cardiac enzymes in the two groups recorded at different intervals
Data are mean ±SD, *P<0.005 significantly different from at preceding induction of GA in same group, +P<0.5 significantly different from GΠ.

DISCUSSION

Despite continuous development in minimizing surgical, anethesiologic, or cardiopulmonary bypass trauma in CABG procedures, perioperative morbidity and clinical complications are still significant (15). Common philosophies in convential minimally invasive CABG surgery focus on avoiding cardiopulmonary bypass (16,17) , limiting surgical access (18) and attenuation of the adrenergic response to surgical stress without jeopardizing hemodynamic stability (19). The use of thoracic epidural analgesia as supplement to general anesthesia and controlled ventilation may provide both intraoperative and post operative benefits. Intraoperative palliative effects largely occurred from sympatholysis associated with neuroaxial blockade (20,21). Postoperative benefits occurred as a result of the profound analgesia afforded by TEA (22,23). Instrumentation of the epidural space

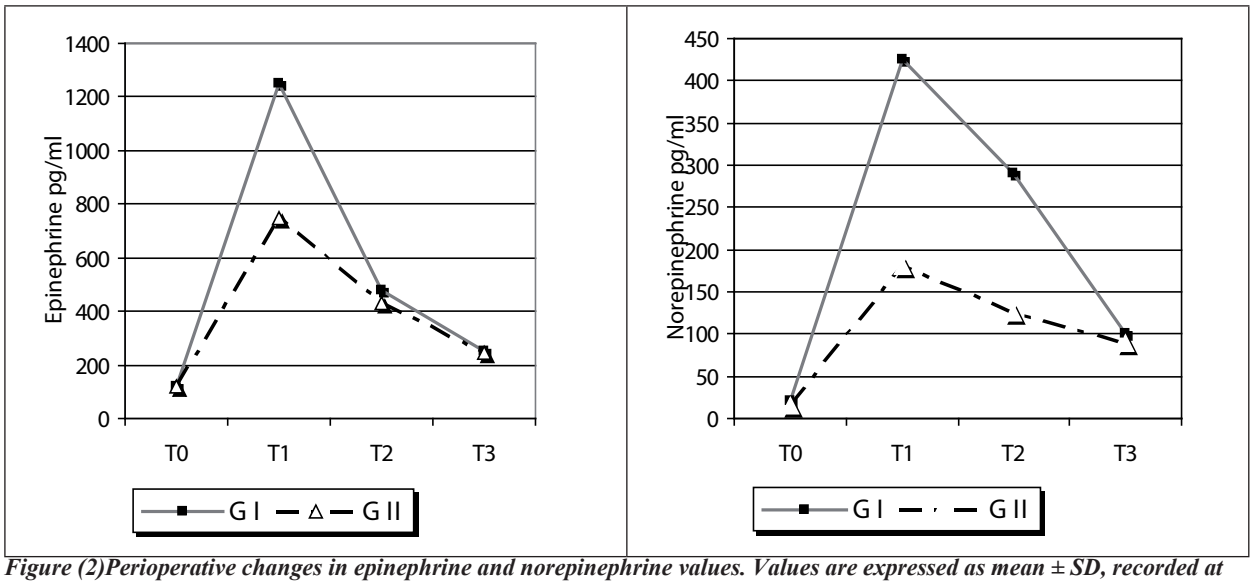

Figure (2)Perioperative changes in epinephrine and norepinephrine values. Values are expressed as mean ± SD, recorded at preoperatively (T0), on arrival to I.C.U. (T1), first day post operative (T2) and on second day postoperative(T3).

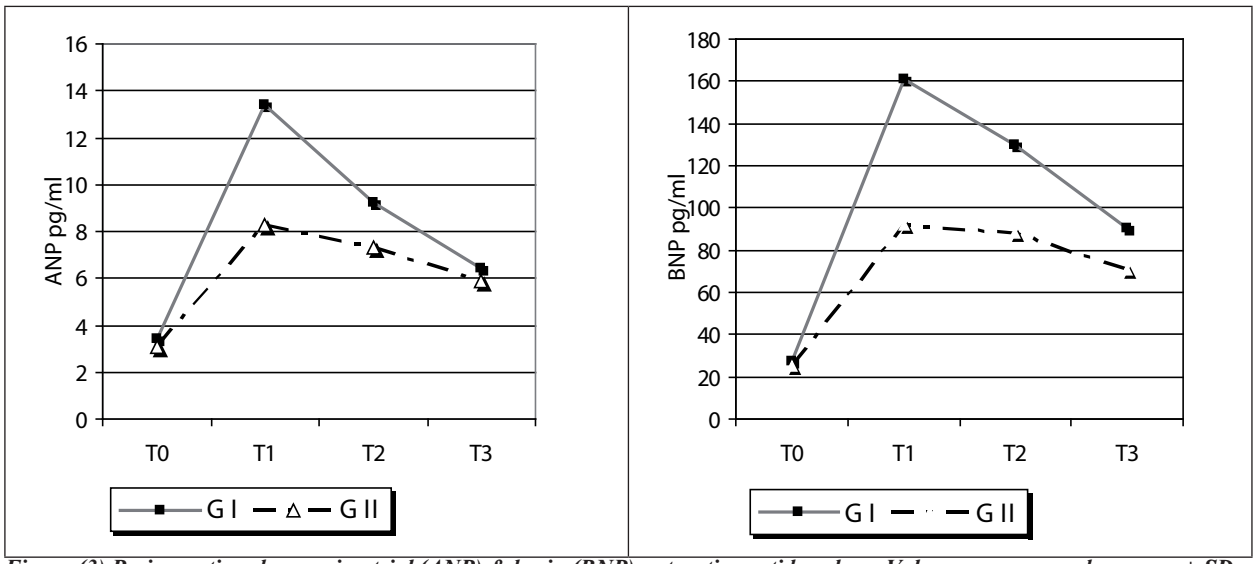

Figure (3) Perioperative changes in atrial (ANP) & brain (BNP) naturetic peptide values. Values are expressed as mean ± SD, recorded at preoperatively (T0), on arrival to I.C.U. (T1), first day post operative (T2) and on 2 day postoperative(T3).

may lead to unrecognized bleeding, hematoma formation, nerve root compression, ischemia, and paralysis. Unfortunately, the true prevalence of an epidural hematoma among patients requiring anticoagulation for heart surgery is unknown. A recent meta-analysis calculated the risk for epidural hematoma formation in cardiac surgical patients with a 95% confidence to be less than 1 of 150,000 for epidural anesthetics (24) compared with an incidence of 1/143.000 in the overall population receiving epidural anesthesia (25). Scott and coworkers (22) reported that non of their 202 patients suffered any adverse neurologic events associated to the use of TEA which is similar to result of current study. The entire spectrum of ischemic heart disease, including stable and unstable angina without myocyte necrosis is characterized by activation of the natriuretic peptide system (12, 14).

Natriuretic peptides are produced by the heart and regulate arterial blood pressure, electrolyte balance and fluid volume (12). Atrial natriuretic peptide ANP is synthesized and secreted by the atrial myocardium in response to atrial stretch (13). Brain natriuretic peptide (BNP) is released almost exclusively by the ventricular myocardium in response to increased left ventricular

wall tension and volume (12,14). Both cardiac natriuretic peptides act as counter regulatory hormones to the increased sympathoadrenal and neurohormonal activation in response to ischemic myocardial injury (26).

Continuous Perioperative TEA modulate the release of both ANP and BNP, which are reported to be the biochemical markers of choice for evaluating the acute risk of nonsurgical patients with cardiovascular condition ranging from myocardial ischemia without ST segment elevation to acute transmural myocardial infarction. The results of this study were that peak plasma level concentration of both cardiac natriuretic peptides was significantly smaller in GII in which TEA was used than GI. The effect of TEA on the autonomic nervous system and the question whether it inhibits the sympathetic outflow induced by surgery have been evaluated in previous studies. Accordingly, TEA was shown to inhibit the increase of catecholamine levels after CABG in several studies (27-29). Further more, if combined with general anesthesia during and after CABG, TEA exerted a beneficial effect on the perioperative stress response and postoperative myocardial ischemia, as indicated by a reduction in heart rate, catecholamines and cTnT (7,21,30,31). Findings are consistent with results of this study showing that peak plasma epinephrine and norepinephrine were significantly smaller in GII.

Geenson and colleagues (32), showed that after CABG 48% of patients had CK-MB isoenzyme elevation of more than 5 times the upper limit of normal and 21% of patients had peak troponin values more than 80 times the upper limit of normal. Although cTnT has been superior to conventional measurement of CK-MB for detection of minor myocardial injury both are included in this study and data demonstrates that serum concentration of troponin T and CK-MB increased in both groups but more pronouncly in GI, with significantly higher values compared with GII. These findings suggest that there is less myocardial damage if TEA supplements general anesthesia for Off-Pump CABG and correspond with previous studies that demonstrated a beneficial effect of TEA on myocardial outcome (21, 27, 33). No patient developed myocardial infarction with ECG analysis (new Q waves, ST segment increase > 3 mm and CTnT > 15).

Four decades of clinical research have failed to find a general anesthetic techniques that attenuate the stress response and resultant adverse sequelae associated with surgery and cardiopulmonary bypass. In contrast, spinal cord anesthesia that is, the selective blocking of spinal nerve roots prevents the surge in stress hormones that accompanies cardiac procedures (20, 21, 28,30).

The sympathetic fibers from T1 to T5 innervate the myocardium and coronary vasculature and play a critical role in determining coronary blood flow and distribution. After anesthesia induction there were no significant hemodynamic differences between groups except that increased mean heart rate in GI significantly during chest closure and after arrival to ICU, mean arterial pressure was lower in G II. There were a higher incidence of perioperative AF in GI with no statistical difference between groups as regard time of onset and the incidence of nonsustained ventricular extrasystole was significantly lower in GII.

Scott etal (22) found in a large study a significantly reduced incidence of AF with the use of TEA which is consistent with this study and in contrast with two studies performed by Priestly MC et al and Jideus et al (34,35). However in the study of Scott, etal. the epidural infusion included clonidine, which may have contributed to the less frequent incidence of AF. Blockade of the cardiac accelerator fibers may be responsible for the decreased prevalence of Perioperative cardiac arrhythmia observed in patients managed with a TEA thus the application of regional techniques as a supplement to GA may be considered therapeutic as well as facilitative.

There is a limitation of this study because it only evaluates immediate intra- and postoperative effects of continuous TEA as an adjunct to GA. Therefore we can only speculate a potential beneficial long term effects of this combination. It is believed that this would be a worthwhile area of future investigation, perhaps with multicenter approach.

IN SUMMARY

Results of current study showed that TEA is advantageous as adjunctive analgesia to patients after Off-Pump CABG. It effectively suppressed the sympathetic activity, reducing incidence of post operative AF and ventricular extrasytole and decreasing heart rate. Combination of TEA with GA during CABG exerted a beneficial effect on the Perioperative stress response as indicated by reduction of Catecholamines (epinephrine and norepinephrine), ANP and BNP. The use of epidural techniques as adjuncts to GA gives better results as regard level of biochemical markers cTnT and CK-MB which detect minor myocardial injury. These findings merit further multicenter prospective clinical trials that should focus on underlying mechanisms and long term follow-up and out come.

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ACQUIRED NON- OESOPHAGEAL EXTRATHORACIC BRONCHIAL FISTULAS

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Background: **Extra- thoracic bronchial fistulas (ETBF) are rare conditions that arise due to an abnormal communication between the entero-pancreatico-biliary system and the tracheo-bronchial tree though there have been very rare reports of other unusual distal locations of ETBF such as the spleen and the kidney-ureter complex. We herein review our experience in managing this entity.**

Methods: **This was a retrospective study of patients with non-oesophageal extra-thoracic bronchial fistulas managed at the Alexandria University Hospital, Egypt between 1990 and 2007 (18years).**

Results: **There were 23 patient with a significant male preponderance (male: female ratio of 6.7: 1) and a mean age of 41.5+/-5.3 years.**

Bronchobiliary fistula occurred in twenty patients (87%) due mainly to ruptured amoebic liver abscess. Gastrobronchial fistulas occurred in 2 patients (8.7%) and were due to a neglected subphrenic abscess in one case while the other occurred as a complication of a gastric decompressive surgery for portal hypertension. One patient (4.3%) developed colobronchial fistula as a sequela of a pneumonectomy and involved the splenic flexure. 13 patients had lower lobectomy while nine patients were had pneumonectomy. One patient was treated by fistulectomy, primary repair of the colonic end and closure of the bronchial stump using an intercostal muscle pedicled flap. There was one mortality and ten morbidities.

Conclusion: **Acquired extrathoracic bronchial fistulas still remains an unfortunate complication with attendant high morbidity. Adequate preoperative preparation and appropriate anaesthetic and surgical techniques are emphasized to improve patient outcomes.**

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Fistulas are abnormal communications between two endothelial-lined surfaces (1). Extra- thoracic bronchial fistulas (ETBF) are rare conditions that arise due to an abnormal communication between the entero-pancreatico-biliary system and the tracheo-bronchial tree (2, 3). There have been reports of other unusual ETBF (4-10). Infections such as hydatid disease (11, 12) and amoebiasis (13) represent the principal causes in the tropics and subtropics but other aetiologic factors such as iatrogenic; traumatic; malignancy; inflammatory bowel disease and pancreatico-biliary pathologies must be considered.

The diagnosis may difficult necessitating the utilization of a variety of diagnostic tools such as plain and contrast radiographs, computed tomography, endoscopy and others depending on the suspected site of the fistula.

Management can be challenging and may be complicated by secondary

pulmonary changes due to the exposure of the lung parenchyma and airways to the noxious enteric contents as well as the general poor condition of the patient due to the underlying systemic pathology.

A variety of minimal interventional procedures can be used but surgery still plays a pivotal role in the cure of the patient. Surgical resection and direct closure is the treatment of choice.

This study was conducted to review our experience with the management of this condition as well as highlighting the main aetiologic conditions in our practice.

Patients and Methods

This was a retrospective study of patients with non-oesophageal extra-thoracic bronchial fistulas managed at the Alexandria University Hospital, Egypt between 1990 and 2007 (18years). The case notes were retrieved and analyzed for age, sex, presentations, diagnosis, treatment and outcome.

The preoperative evaluation of the patients was done taking into cognizance the diagnosis, any systemic disease as well as the nutritional state of the patient.

All patients had rigid bronchoscopy with simultaneous enteral methylene blue feeding to diagnose the bronchial component of the fistula while other investigations such as dilute barium studies, ultrasonography and computed tomography was done to identify the enteric component.

Nutritional deficiencies were corrected usually by feeding jejunostomy for enteric lesions above the jejunum and total parenteral nutrition for those patients with lesions distal to the jejunum and those with severe malnutrition on presentation. Acid base deficits, electrolyte imbalances and anaemia were corrected.

Tube thoracostomy was instituted in patients with empyema while percutaneous drainage was done in patients with subphrenic abscess. Nasogastric decompression and bronchial lavage were commenced in all patients

Preoperative broad spectrum antibiotics consisting quinolones and metronidazole were given in all patients. This was later modified based on results of culture and sensitivity from bronchial aspirates and blood cultures. Albendazole was given to the patients with hydatid liver disease.

Chest physiotherapy was begun preoperatively in all patients and was continued postoperatively to improve respiratory function.

All patients had open surgery under general anaesthesia and single lung ventilation.

Statistical Analysis

All data were collected and stored in a personal IBM- compatible computer. Continuous variables are presented as mean +/- standard deviation and categorical variables were expressed as percentages. The data were subjected to independent and paired student t-test and chi- square to determine statistical significance. Differences were considered statistically significant if the p value is less than 0.05.

Results

Variety of extrathoracic bronchial fistula	Aetiologic factors	Frequency	%
BRONCHOBILIARY FISTULA	Amoebic Liver Abscess	11	48
	Hydatid disease of the liver	5	21.8
	Subphrenic abscess	2	8.7
	Gall stone disease	1	4.3
	Choledochal cyst (post operative)	1	4.3
GASTROBRONCHIAL	Subphrenic abscess	1	4.3
	Post operative gastric surgery	1	4.3
COLOBRONCHIAL	Post Left Pneumonectomy	1	4.3
Total		23	100

Table 1: Variety and aetiologic factors of non- oesophageal extra-thoracic fistulas in Alexandria, Egypt.

There were 23 patients managed during this period; there was significant male preponderance with twenty males and three females (p=0.001) giving a male: female ratio of 6.7:1. The age range was 18- 65 years with a mean age of 41.5+/-5.3 years.

The most common variety was bronchobiliary fistula which occurred in twenty patients (87%) due to ruptured amoebic liver abscess occurring in 11 patients, 5 patients with hydatid disease of the liver, 2 patients with neglected post-laparotomy subphrenic abscess and one patient each with complicated gall stone disease and after surgical correction of a choledochal cyst. Gastrobronchial fistulas occurred in 2 patients (8.7%) and were due to a neglected subphrenic abscess in one case while the other occurred as a complication of a gastric decompressive surgery for portal hypertension. Only one patient (4.3%) developed colobronchial fistula which occurred as a sequela of a left-sided pneumonectomy and involved the

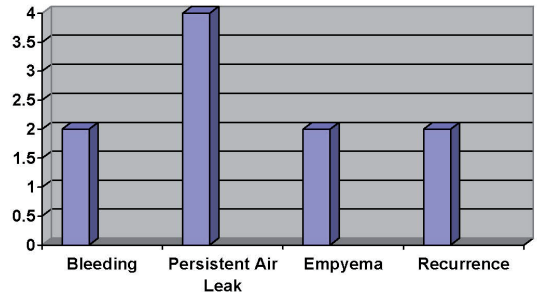
splenic flexure of the transverse colon (Table 1).

All patients after adequate preoperative stabilization had standard posterolateral thoracotomy under general anaesthesia and single lung ventilation. The fistulous tract was dissected, resected and sent for histopathologic and bacteriologic examination.

Additional procedures were done in twenty-two of the patients (95.6%) and included lower lobectomy in 13 patients (10 were right- sided and 3 left- sided) while nine patients were treated by pneumonectomy (seven were right-sided while 2 were left- sided). The patient who had a colobronchial fistula complicating a left pneumonectomy was managed by fistulectomy, primary repair of the colonic end and closure of the bronchial stump using an intercostal muscle pedicled flap.

All patients had repair of the diaphragm either by direct two-layer non-absorbable suture closure or using synthetic mesh prosthesis in large defects.

There was one post-operative mortality (4.3%), a male patient who had a right pneumonectomy due to extensive destruction of the right lung from a ruptured hydatid disease of the liver. His surgery was complicated by post- pneumonectomy empyema and bronchopleural fistula. He was managed conservatively but died two weeks later due to septicaemia and respiratory failure.



Ten patients (43.3%) developed significant post-operative morbidity (figure 1); two patients had to be re-explored within 6 hours after surgery for significant bleeding (more than 200ml/ hour through the intercostal tube). The source of the bleeding was due to a lacerated posterior intercostals artery at the site of the intercostal tube in one patient while the other had diffuse oozing following a difficult right lower lobectomy for a bronchobiliary fistula. Persistent air leak occurred in 4 patients (17.2%); two of them were successfully managed conservatively with repeated autologous blood patch and a Heimlich valve, one had a fibreoptic bronchoscopic sealing after failed conservative treatment while another patient had re-thoracotomy due to a major air leak due to a bronchial stump disruption. This was then successfully closed with a pericardial patch.

Two cases developed empyema which was successfully managed with tube thoracostomy, antibiotic irrigation though one of the patients needed prolonged open drainage for 6 months.

Two patients developed recurrence of their bronchobiliary fistula. They had amoebic liver disease which was managed conservatively using metronidazole and tube thoracostomy drainage.

Discussion

Acquired extrathoracic bronchial fistulas still remains an unfortunate complication of some gastrointestinal and hepatobiliary pathologic conditions with its attendant high morbidity and mortality due to the contamination of the bronchial tree with toxic and or bacteria- laden entero- biliary contents.

This condition in our series arises mainly as a complication of transdiaphragmatic ruptured amoebic liver abscess leading to an abnormal communication between the bronchial and biliary trees. Amoebic liver abscess unfortunately maintains a high incidence in relatively less wealthy societies despite the availability of highly effective antibiotics (14, 15). The infective organism, *Entamoeba Histolytica* induces an inflammatory condition of the liver and colon. The resulting liver abscess arising from liquefactive necrosis of the hepatocytes usually communicates with numerous bile lakes. If left untreated, the natural history may result in resolution or rupture into the various adjourning cavities such as the peritoneum, pleura, bronchial tree and even through the skin. Neglected amoebic abscess rupturing into the pleural cavity eventually exits by communicating with the bronchial tree. This may result in the cure of the condition by the expectoration of the abscess. However as we have shown, a persistent bronchobiliary fistula may remain with its attendant dire consequences if left untreated.

The diagnosis of extra-thoracic bronchial fistulas is suspected by the peculiar history of coughing out bilious, anchovy sauce-like, faecal or recently ingested food material depending on the abdominal location of the fistula. The predominantly right sided bronchial and lung location is expected because most of the aetiologic factors identified in our study are right sided. Clinical suspicion is confirmed by various investigations such as contrast gastrointestinal series, chest and abdominal computed tomography, endoscopic retrograde cholangiopancreatography, HIDA scan and bronchoscopy. Bronchoscopic evaluation usually reveals the bronchial end of the fistula however in equivocal cases, methylene blue ingested orally a few minutes before bronchoscopic examination should help reveal this site (16). Also, the

pH of the bronchial aspirate can hint at the possible distal end of the fistula; a strongly acidic aspirate suggesting a gastrobronchial fistula (17) and a strongly alkaline aspirate suggesting a duodenal or pancreatobiliary site.

The patients usually present in poor general condition with fluid and electrolyte derangement, anaemia, malnutrition, poor lung function, pneumonia and septicaemia.

Attention should be paid to stabilization of any preoperative deficits otherwise a prohibitively high mortality and morbidity rate may ensue. This stabilization consists of correction of the fluid, electrolyte and nutritional deficits as well as preoperative broad spectrum antibiotics. Chest physiotherapy consisting of deep breathing exercises as well as postural drainage is essential to the overall survival of the patient. We elected to commence chest physiotherapy on our patients preoperatively and continued it into the post-operative period as soon as the patient recovered from the effects of general anaesthesia until discharge from the hospital.

Associated empyema thoracis was managed by tube thoracostomy. This also helped improve the overall respiratory reserve of the patients making them better surgical candidates.

It is helpful to relieve any distal obstructing lesion on the gastro-intestinal system which may be perpetuating the fistula such as the use of endoscopic stenting and sphincterotomy of the biliary tract in cases of bronchobiliary fistulae associated with bile duct obstruction.

The use of bronchial stents is also important in preventing continued soilage of the airways especially in moribund patients with very poor respiratory reserve whose surgery may be delayed for adequate preoperative care. Biliary stenting has recently been advocated and applied in some patients with bronchobiliary fistulas (18, 19).

Surgery is the best treatment for these patients since conservative measures usually eventually fail or leave the patients with significant morbidity as well as an unacceptably high mortality. Operative measures usually entail fistulectomy, separation and repair of the bronchial and enteric ends of the fistula. Any diaphragmatic defect present is usually repaired at the time of the primary surgery. While repair of the bronchial end by vascularized pedicled tissues is the ideal, this is usually not possible in most cases due to the extensive destruction of adjourning lung parenchymal tissues necessitating lobectomy in most cases or even pneumonectomy. In our series, thirteen of our patients (56.6%) had a lobectomy, nine (39.1%) had a pneumonectomy while only one patient (4.3%) was managed by fistulectomy with separate vascularized repair of the bronchial stump as well as closure of the enteric component.

Surgery is greatly facilitated by the use of double lumen endotracheal tubes. This allows for single lung ventilation and enhanced access to the involved non-ventilated lung.

We routinely utilize an epidural catheter for intra and especially post-operative pain management. This helps improve respiratory function by eliminating or greatly decreasing pain sensation after thoracotomy.

The high morbidity (43.3%) emphasizes the fact that these patients usually present in a grave condition. Aggressive perioperative management is essential to limit morbidity and mortality. This condition exerts a great burden on the health facilities due to the resources, drugs, personnel and equipment required to manage a single patient. Such a demanding care requires the understanding and patience of the health care providers particularly thoracic surgeons, nurses and physiotherapists to obtain good results in the long term.

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BILATERAL BULLECTOMY THROUGH MEDIAN STERNOTOMY

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Background: Emphysematous bullae represent a form of emphysematous lung destruction. Surgical resection has traditionally been indicated when there is hyperexpansion of the chest, compromised pulmonary function, and evidence of underlying, relatively normal compressed lung. Different approaches to LVRS have been proposed; these include median sternotomy, thoracosternotomy and video-assisted thoracoscopic surgery (VATS) technique.

Methods: Nine patients underwent resection of emphysematous bullae at Kasr Elaini hospital between February 2006 and July 2007. All had limiting dyspnea and radiological evidence of hyperinflated bullae compressing adjacent lung parenchyma. All the patients had bilateral lesions. We did median sternotomy, with one-lung ventilation under a standard general anesthetic technique to avoid rupture of bulla, in all patients to do resections bilaterally in the same sitting.

Results: Postoperative complications included persistent air-leak, failure of early extubation, readmission to ICU and chest infection. We had two mortalities one due to ARDS and the other due to chest infection.

Conclusion: we recommend the use of sternotomy approach in highly selected patients with good target areas, as it is only subject the patient for one procedure instead of two and we can avoid the possibility of spontaneous pnemothorax on the opposite side, while doing bulletomy in lateral position through thoracotomy. In our experience there were no difficulties in dissection of lung adhesions or attack any target areas through this approach.

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Emphysema, a form of chronic obstructive pulmonary disease, is a condition characterized by abnormal and permanent enlargement of the air spaces distal to the terminal bronchioles and accompanied by destruction of their walls without obvious fibrosis(1).

Lung volume reduction surgery (LVRS) is a palliative operation to be considered in selected patients suffering severe dyspnea from the end stage of diffuse nonbullous emphysema, who are not responding to maximal medical management. Bullectomy has been an established technique for patients with

bullous emphysema, since the work of Brantigan and Mueller 40 years ago (1).

A bulla is defined as an air-filled space 1 cm or greater in diameter within the lung parenchyma that forms as a result of destruction of the alveolar walls. Rarely one or more bullae enlarge to such a degree that they occupy more than one third of the hemithorax. The term giant bulla is then applied. These easily distensible reservoirs are preferentially filled during inspiration, causing the collapse of adjacent, more normal, lung parenchyma. Because of the alveolar destruction, bullae lack any meaningful alveolar-capillary interface and the thoracic volume they occupy is wasted. The resulting hyperinflation of the chest interferes with normal respiratory mechanics, increasing the work of breathing with associated exercise limitation and dyspnea (2).

The concept of LVRS was developed by Cooper and colleagues inspired by Brantigan's earlier work. He modified the approach of Brantigan and Mueller by using a median sternotomy, thus allowing access to both lungs and used a buttressed staple excision technique. The hyperinflated and relatively functionless parts of both lungs were removed and it was proposed that this would result in improvement in the function of the remaining lung, palliate the dypsnea, improve exercise ability, and provide a positive change in quality of life (3).

The fundamental concept of LVRS is to improve elastic recoil, reduce airflow limitation and improve the mechanics of respiration by excision of some of the most destroyed portions of the lung for patients with severe emphysema (4).

Patients suitable for LVRS are those with heterogenous disease having target areas for resection, which is most commonly associated with centrilobular emphysema. Giant bullae, with relatively normal but collapsed adjacent lung, may represent the most heterogenous end of a spectrum of disease. Traditionally, bullectomy has been performed to alleviate the collapse of under-lying normal lung tissue. On the other hand, the primary benefit of LVRS has been attributed to the reduction of thoracic hyperinflation and improvement in respiratory mechanics. It is probable that both mechanisms are at work after bullectomy (5).

A variety of different approaches to LVRS have been proposed; these include median sternotomy, thoracosternotomy and video-assisted thoracoscopic surgery (VATS) technique. There are both unilateral and bilateral approaches (1).

The areas or surgical removal are identified before surgery by computed tomography and radionuclide ventilation-perfusion scanning. Methods for sealing the site of resected lung include the use of staples or a laser; however, prolonged air leak is a common postoperative complication (6).

Lung volume reduction surgery is a procedure that requires appropriate selection of patients who have been suitably informed of the risks of this procedure. The number of patients who qualify for LVRS are a small percentage of those originally assessed (7).

The majority of patients 5 years post LVRS experience enhanced exercise capacity, a reflection of reduced hyperinflation and gas trapping (8).

The optimal surgical approach for LVRS for advanced bilateral emphysema is unknown. Case series and early randomized trials have demonstrated the superiority of stapled over laser resection and of bilateral over unilateral operations. Case series support the use of either median sternotomy (MS) or video-assisted thoracoscopic (VATS) approaches (9).

Compared with medical management, LVRS produced a significant improvement in function for patients with upper lobe emphysema and improved survival for the subset of patients with upper lobe emphysema and a low baseline exercise capacity (10).

Surgical therapy has been used for bullous emphysema since the mid-20th century. The best surgical candidates are often those with giant pulmonary bullae rather than those with diffuse disease (11).

In this study we tried to show our experience in Kasr Elaini hospital in bilateral LVRS and bullectomy through median sternotomy, the exposure, accessibility, results and outcome.

Patients and Methods:

From February 2006 to July 2007, 9 patients scheduled for elective bilateral bullectomy through median sternotomy in Kasr Elaini hospital were enrolled in the study.

Inclusion criteria:

Patient selection criteria and the clinical evaluation consist of: (1) marked hyperinflation evident by inspiratory and expiratory chest radiographs; (2) radiographic evidence of heterogenous emphysema with clear target zones for resection; (3) severe functional impairment (forced expiratory volume in 1 s (FEV1) < 1.2 or predicted FEV1 20-35%, total lung capacity (TLC) >120%); (4) poor quality of life; (5) dyspnea despite optimized medical therapy; (6) abstinence from smoking, acceptable nutritional status; and (7) rehabilitation potential.

I Exclusion criteria:

Contraindication to surgery included age older than 75 years, current cigarette smoking, symptomatic car-

diac disease, and pulmonary hypertension (pulmonary artery pressure >35 mmHg).

II. Preoperative Assessment:

All patients of the study were assessed in the preoperative period by medical history taking and detailed clinical examination with a special emphasis on any respiratory problems, full laboratory investigations with special emphasis on complete blood picture, coagulation profile, arterial blood gases and pulmonary functions.

Radiological investigations in the form of plain chest x-ray and high resolution computed tomography.

Chest physiotherapy, started preoperatively, to help in clearance of respiratory tree from secretions.

Preoperative echocardiography was done routinely to assess the preoperative cardiac conditions.

III. Operative Management:

Anesthetic technique:

All patients were not premedicated except for inhaled bronchodilators administered prior to induction of anesthesia. Anesthesia was planned to be a combination of thoracic epidural and general anesthesia.

Routine monitors were used including 5 leads ECG, continuous invasive arterial blood pressure monitor and frequent blood gases analysis via a radial 20G cannula, pulse oximeter, capnography, right internal jugular catheter for central venous pressure monitoring and urinary catheter.

Thoracic epidural catheter was placed under local anesthesia in the awake patient, in the sitting position between T5 and T8 via a paramedian approach using loss of resistance to saline. After confirmation of proper epidural placement using test dose 4 mL. of bupivacaine 0.5% and epinephrine 1/200,000, the catheter was firmly fixed in place and 6 mL of bupivacaine 0.5 % as well as 100 microgram fentanyl were injected as a bolus followed by a continuous infusion of 4-6 mL / h of bupivacaine 0.5%, throughout the operation to be reduced to 0.125% bupivacaine in the first 48 hours postoperatively.

General anesthesia was induced intravenously using propofol 1.5 mg/ kg, fentanyl 200 microgram, and succinylcholine 80 mg to facilitate intubation. A left double lumen tube was placed and anesthesia was maintained by sevoflurane 2-3% in oxygen/air mixture with a FiO2 0.5 with supplemental infusion of propofol 3-6 mg/kg/ hour.

Spontaneous ventilation was resumed and continued till the time of sternotomy; when a bolus of fentanyl 100 microgram and pancuronium 6- 8 mg was given, and after complete relaxation the sternum was divided while the lungs were deflated then mechanical ventilation was started.

After strenotomy; anesthesia was maintained by 2% sevofluraine and bolus doses of pancuronium 1 mg / h. One lung ventilation was used and FiO2 was increased to 1.0.Tidal volume was set between 6-8 mL, and respiratory rate between 12-14/ min with a PEEP of zero. Ventilator settings were adjusted to maintain peak airway pressure ≤ 25 cm H2O, and arterial tension of CO2 around 40 mmHg or within 20% of the awake baseline readings. When oxygen saturation dropped below 90 percent brief periods of two-lung ventilation were necessary.

At the end of surgery spontaneous breathing was resumed and muscle relaxant was reversed. The patients were extubated in the theater and transferred to the intensive care with an epidural infusion and supplemental oxygen.

Surgical technique:

Patients underwent median sternotomy. Bilateral procedures were performed as a rule. The side with better-preserved perfusion was operated on first. Dissection of all adhesions between the lung and chest wall, should be done firstly, to let the lung totally free.

The target zones for resections were assessed preoperatively by high resolution computed tomography.

In many cases when there is giant bulla, a division of the anterior bulla wall done firstly, then control of the feeding bronchus was done by interrupted proline 3/0 sutures. In smaller bullae the bases are controlled either by silk suture or by continuous proline 3/0 sutures, and then bullae were excised.

Before closure of the chest, mediastinal and pleural tubes were positioned in the mediastinum, one retrosternal two tubes in each pleural space; each of the plural tubes was placed laterally at the level of anterior axillary line.

IV. Postoperative assessment:

Postoperative pain relief was achieved with a thoracic epidural placed prior to induction of anesthesia at the level of the fourth thoracic vertebral body.

Early and vigorous chest physiotherapy and ambulation were performed.

Outcomes included mortality, complications, hospital stay duration, ICU stay, need for mechanical ventilation, and status at initial hospital discharge.

Results:

A total of 9 patients underwent bullectomy through

median sternotomy during the analysis interval.

All the nine patients were men with an average age of 65.2 ±8.1 years.

Baseline pulmonary functions and arterial blood gases are shown in table (1).

FEV1 (% of predicted)	32.9±5.6
TLC (% of predicted)	127.4±15
Pa O2 (mm Hg)	66.4±10.3
Pa CO2 (mm Hg)	52.8±6

Table (1) preoperative pulmonary functions and arterial blood gases.

The mean operating time was 115 minutes.

Intraoperative complications are shown in table (2). The major complication that occurred in all patients was uncontrolled air-leak which varies from mild to moderate, depending on the extent of affection of the lung parenchyma.

Patients with mild air-leak at closure of the sternum were 6 (66.6%), 2 (22.2%) patients were with moderate air-leak and 1 (11.1%) patient had major air-leak.

Regarding the duration of air leak postoperative, 3 patients stopped air-leak in the first postoperative week, 2 patients in the second postoperative week; the other two patients stopped air-leak after two weeks of surgery. No patients were reopened for air-leak.

N.B. The two mortalities were omitted from this parameter.

Arrhythmia	2(22.2%)
Hypoxia	3(33.3%)
Cardiac arrest	none
Uncontrolled air leak	9(100%)

Table (2) ***Intraoperative complications.***

Intraoperative arrhythmia were in the form of some atrial ectopics may be related to some hypoxia.

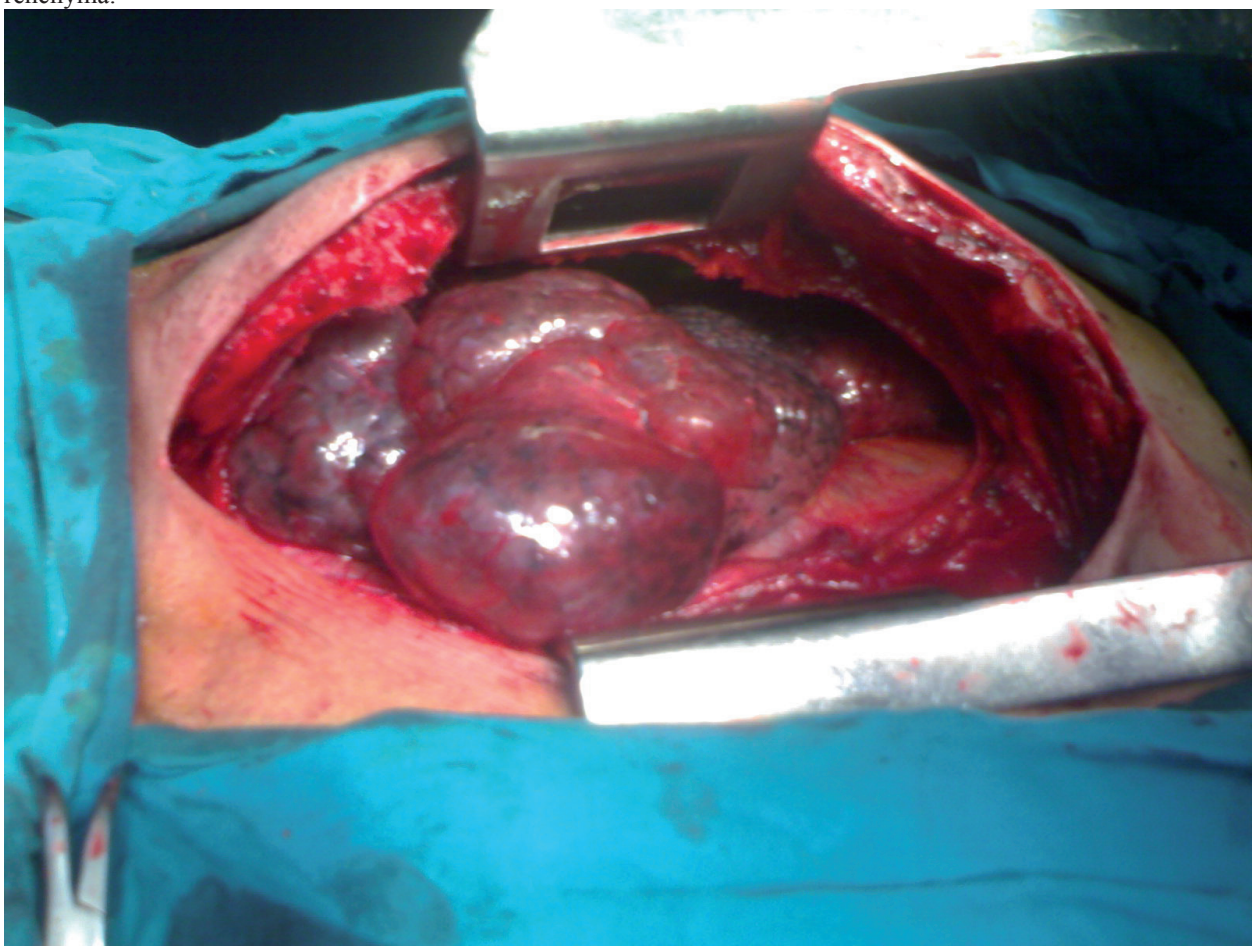

Fig. (1) ***Multiple apical bullae in right upper lobe through median sternotomy***

Postoperative complications were listed in table (3).

Arrhythmia	3(33.3%)
Failure of early extubation	3(33.3%)
Failure to wean	1(11.1%)
Readmission to ICU	4(44.4%)
Chest infection	7(77.7%)

Table (3) postoperative complications.

Regarding postoperative ICU stay, 4 patients stayed only one day in the ICU, 2 patients for two days and 3 patients for more than two days, including the 2 mortalities. The 3 patients failed to be extubated on table, one of them weaned from mechanical ventilation on the same day, one in the second day, and the third failed to be weaned till his death in the sixth day postoperative.

Hospital length of stay was 17±10 days.

There were no intraoperative mortalities. The hospital mortality was 2(22.2%). (12).

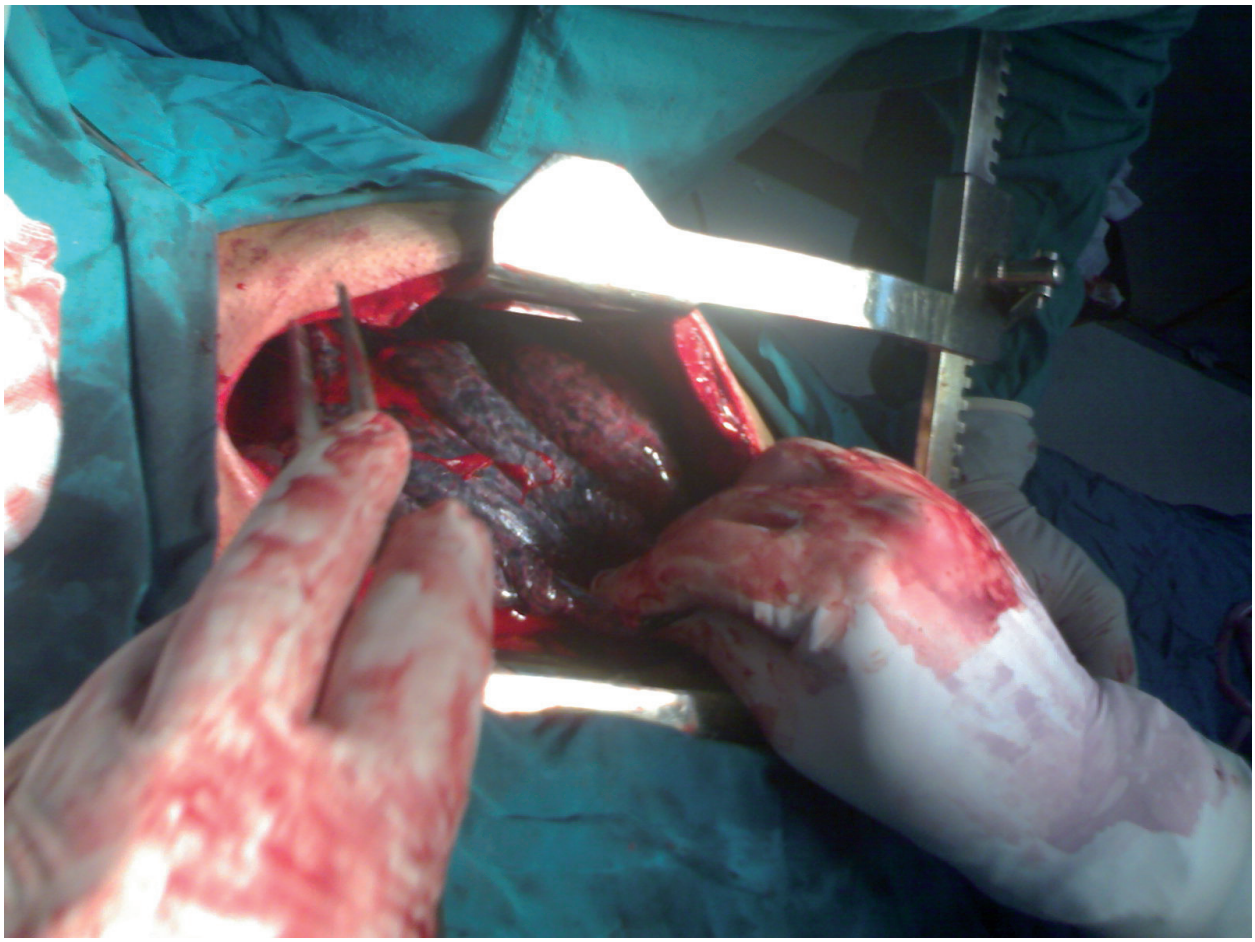

Fig. (2) Right lung after bullectomy

In our study all our patients had FEV1 less than 50% and their CT scan showed mostly normal surrounding lung parenchyma, which was very important criteria in selection of patients as it is very crucial factor in the end result of surgery. In our study we were stick to the definition of a bulla as an air-filled space 1 cm or greater in diameter within the lung parenchyma.

Air-leak lasting 7 or more days is the most commonly reported complication after LVRS and occurs in approximately half of patients (9).

The NETT (National Emphysema Treatment Trial) data for air-leak are similar to published data. The VATS (video assisted thoracoscopic surgery) patients had a higher incidence of air-leak at closure than the median sternotomy patients; this is presumably because intraoperative identification and elimination of air-leaks is more difficult for a VATS approach than for a median sternotomy approach (13).

Schipper and his colleagues reported that their most frequent complication was air-leak, occurring in half the patients. They approach air-leaks initially with prevention and they put no suction on the chest tubes. If the

air-leak persists, a Heimlich valve is placed to decrease further the resistance to expelling a pnemothorax and the barotrauma on the remaining lung. They were very reluctant to return to the operating room for an air-leak, believing that reoperations create more leaks than are repaired (5).

In our study patients with persistent air-leak more than a week were 4 patients (57% of living patients), which is similar to the published data. It was the second most common complication after chest infection. In our study we had more incidence of air-leak at time of closure due to the difference in the technique of resection of bullae, in different studies they used buttressed staple lines (with bovine pericardium), in our case we used continuous proline 3/0 sutures. This was only affecting the rate of air-leak at time of closure but did not affect the rate of persistant air-leak for more than 7 days. We managed persistent air-leak by chest physiotherapy, no suction was applied to the chest tubes, and control of chest infection. We also did not reopened any of our patients for persistent air-leak as we also believe in more damage produced by reopening than repair.

Because LVRS is a palliative, elective procedure, one of the greatest concerns was the mortality rate for the procedure. Reported operative mortality rates were generally 3.5% to 10%, but some were as high as 19.1%. Moreover, on the basis of data for Medicare patients who underwent LVRS between October 1995 and January 1996, a mortality rate of 14.4% was found at 3 months. However, in the prospective multicenter study, the NETT observed 90-day mortality for LVRS of 5.9% for median sternotomy and 4.6% for VATS (13).

Schipper and his colleagues reported that their hospital mortality of 2.3% is low and consistent with the mortalities ranging from 0% to 9% reported by other authors(5).

Fujimoto and his colleagues reported that there should be a balance between the extent of resection that offers the maximal functional improvement and the extent that causes the minimal perioperative morbidity and mortality. On the one hand, the larger the volume of non-functional lung parenchyma is resected, the greater the functional improvement can be achieved. On the other hand, the pulmonary vascular bed, which can be represented by diffusing capacity (DLCO), may limit the possible extent of resection, (which is not routinely done) and this may lead to rapid development of adult respiratory distress syndrome (ARDS), which will lead to death (14).

Regarding our mortality we had two mortalities, one due to ARDS died on the sixth day postoperative, this was may be due to the small amount of lung tissue left after resection (increased amount of resection with left unhealthy tissue). The other mortality was due to severe chest infection after discharge from ICU with increased bronchial tree secretions, which necessitate readmission to ICU, but patient died out of respiratory failure on fifth day postoperative. Sputum culture which appeared after his death showed infection with MRSA bacteria.

Our mortality rate is to an extent higher than most of the literature but this could be attributed to the small number of patients in our study, which make a single mortality represents more than 10%. Selection of cases may be another cause as we have no specific facilities as measuring diffusing capacity of the lung, and we depend only on pulmonary functions and CT appearance of the lung parenchyma, with the gross pathology seen by the surgeon intraoperatively.

Since the inception of the LVRS program at Barnes Jewish hospital, more than 800 patients have been evaluated on site for potential emphysema surgery. Forty-three of these patients were found to have bullae fitting previously published criteria for bullectomy (5).

As regards the number of patients in this study, it is related to many factors as, selection criteria of the patients to be indicated which were very obvious that it is a limiting factor by itself. Many of the emphysematous patients have diffuse pathology with no target areas, or affection of the lung parenchyma left small residual apparently healthy lung that could not permit suitable oxygenation of the body.

Second factor is general health of the patients as they may be unfit for a major surgery like this due to their general medical condition.

Lastly, many patients refused to do surgery especially when they knew the nature of this surgery being palliative one and the symptoms will recur again after few years.

Stirling and his colleagues reported 2001 that LVRS using the stapling-excision technique and the median sternotomy approach, in highly selected cases, has proved to be a safe and reasonably efficacious procedure. These results have been shown to be reproducible by other workers (1).

The data from the NETT showed there is no difference between median sternotomy and VATS patients with respect to the functional results at 12 and 24 months after randomization. They concluded that the choice of approach is a matter of the surgeon's preference and experience (13).

In conclusion we recommend the use of this approach in highly selected patients with good target areas and sufficient amount of residual lung parenchyma, as it is only subject the patient for one procedure instead of two

and we can avoid the possibility of spontaneous pnemothorax on the opposite side, while doing bulletomy in lateral position through thoracotomy. In our experience there were no difficulties in dissection of lung adhesions or attack any target areas through this approach, except for some difficulties in lower lobe lesions (which is not common).

We recommend doing study on long duration or multicenter studies to help in getting more number of patients for better results analysis.

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