

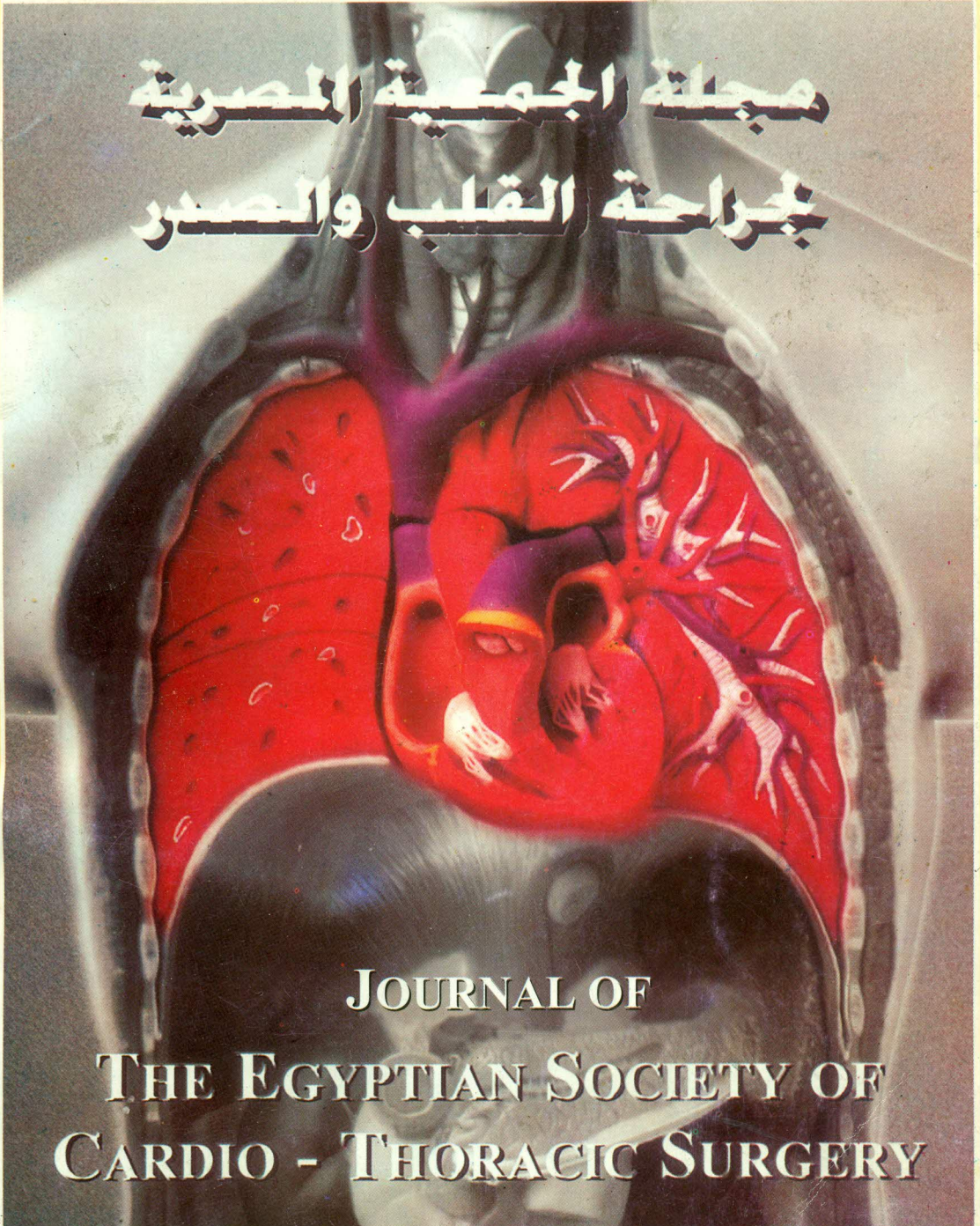
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المجلد الثاني عشر عدد رقم ١، ٢ - ٢٠٠٤

# مجلة الجمعية المصرية بجراحة القلب والصدر



JOURNAL OF  
THE EGYPTIAN SOCIETY OF  
CARDIO - THORACIC SURGERY

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Correspondence to be sent to:

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# Journal of the Egyptian Society of Cardio Thoracic Surgery

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## Contents January, April, 2004

- Egyptian National Data Base Of Cardiac Surgery Project Of National Adult Cardiac Surgical Registry  
Yasser MW Heigazy, COUNCIL OF EGYPTIAN SOCIETY OF CARDIOTHORACIC SURGERY (2000-2003).  
*J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII January No. 1.....* 5-14
- Immediate Surgical Closure Versus Indomethacin In The Management Of Persistent Ductus Arteriosus In Premature Newborns  
Hossameldin Eid, O. Al-Jassim, A. Khan, M. Alaziz, N. Alkhaja  
*J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII January No. 1.....* 15-18
- Influence Of The Inverted, T-Shaped, Posterior Pericardiotomy On Supra-Ventricular Arrhythmias And Pericardial Effusion: Early Results After Coronary Artery Bypass Grafting  
Said Abdel Aziz, MD Yahya Balbaa, MD Diaa Abul Seoud, MD Ahmed H. Gaafar, MD Marawan Mohamed, MD  
*J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII January No. 1.....* 19-25
- Reduction Of The Inflammatory Response To Cardiopulmonary Bypass After Mitral Valve Replacement: Comparative Study Between Aprotinin And Methylprednisolone  
Hossam El-Okda, MD Thanaa Hodhod, MD Adel M.Fahmy, MD and Halla S.El-Sheikh, MD  
*J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII January No. 1.....* 27-38
- Predictors Of Mortality In Elderly Patients Undergoing Coronary Artery Bypass Grafting  
Hosam Fawzy, Ahmed El-Watidy, Atef Farag, Aitizaz Syed, Arto Nemlander  
*J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII January No. 1.....* 39-43
- Radial Artery For Coronary Artery Bypass Grafting  
Hosam F. Fawzy  
*J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII January No. 1.....* 45-54
- Cardiac Surgery In The Elderly Analysis Of Mortality And Morbidity  
Ayman A. Sallam, FRCS, Bakir M.Bakir, MD, Ashraf A.Esmat, MD, Anjum Jalal, FRCS, Mohamed Fouda FRCS, Ahmed Al-Saddique, FRCS.  
*J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII January No. 1.....* 55-62

Surgical Treatment Of Subaortic Stenosis: Results, Risk Factors For Early Mortality, Recurrence And Reoperation Hany A. El Maboud, MD Ahmed Samy, MD Hatem EL Bawab, MD Hassan Moftah, MD Hossam El Okda, MD Mohamed A. El Fatah MD. <i>J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII April No. 2.....</i>	63-76
Role Of Normothermic Papaverine For Managing Intraoperative Mammary Spasm Mohammed Attia, Ahmed Abd EL Aziz, Hesham Abd EL Rahman, Hossam Ezzat, Ahmed sami. <i>J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII April No. 2.....</i>	77-81
Mitral Valve Intervention In Patients With Previous Trial Of Balloon Valvuloplasty Mohamed Attia Hussein, MD <i>J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII April No. 2.....</i>	83-94
Intraoperative Fabrication Of Lateral Chest Wall After Resection Of Primary Tumours Ashraf El-Sebaie Mohammed, MD and Walid Gamal Abou Senna, MD <i>J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII April No. 2.....</i>	95-104
Clinical Evaluation Of Preemptive Use Of Phosphodiesterase III Inhibitors In Patients Undergoing Off Pump Coronary Artery Bypass Grafting Hosam Fawzy, Ahmed El-Watidy, Atef Farag, Aitizaz Syed, Arto Nemlander, Bassel Me Nour El Din, MD Hosam F.Fawzy, MD Alaa Basiouni And El Sayed El Mistekawy, MD <i>J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII April No. 2.....</i>	105-117
Leiomyomas Of The Oesophagus A Clinical Review Aitizaz Uddin Syed FRCS Ed. Amro Serag, MD Hosam Fawzy, MD Arto Nemlander, MD <i>J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII April No. 2.....</i>	119-129
Comparison Of The Oxygen Delivery, Total Body Oxygen Consumption And Oxygen Extraction Fraction In Patients Undergoing Off-Pump And Conventional CABG Elmistekawy E, Fawzy H, Uddin Syed A, Nemlander A and Nooreldin B <i>J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII April No. 2.....</i>	131-140

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## EDITOR

MOHAMED EL FIKY.

79, Ramsis Str.

Cairo - Egypt.

Post Code 11111.

Fax (202) 772535

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## EDITORIAL

# PROJECT OF NATIONAL ADULT CARDIAC REGISTRY EGYPTIAN SOCIETY OF CARDIO THORACIC SURGERY

Yasser MW Hegazy.

J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII January No. 1

### INTRODUCTION

The leap that cardiac surgery took in this country should be recognized throughout both the medical and non medical fields. By adopting our great fathers philosophy; "Civilization if not recorded will never take place in history".

Our Society in that context feels that the need to collect data on patients undergoing Cardiac and Thoracic Surgery will achieve different goals.

- It will record exactly the nature and magnitude of the evolving Cardio Thoracic practice in this country.

- It will enlighten us on areas of weakness and deficiencies to improve and areas of strength to build upon.

- It will help national statistical analysis of our work.

- It will provide a wider base for scientific research and mega studies which will reflect our place and role the international side.

It will eliminate public misconceptions and increase trust in our practice.

It will set a national standard and observe all national centers performance in order to improve any substandard surgical practice

and help various centers to overcome different obstacles.

It will help auditing and retraining programs.

Our society should not re-invent the wheel in establishing such project but we will use already established Western systems with modifications which suit us.

**What are the keys issues to establish such project ?**

**Data-set design**

**Resources**

**Data validation**

**Reporting**

**Collaboration**

**The process**

**Data-set design:**

To put this project in application each unit should collect the society's recommended data set in a format defined by the society. N.B: every center in Egypt will be invited to contribute in setting and altering the data base design until we reach a format agreed upon by the different centers and conform with our national Egyptian practice.



N.B: find enclosed suggested data base with a questionnaire.

### **Resources:**

To collect these data each center should have an electronic export system network, computers, medical & non medical individual responsible for data collection; This has resource implications as It costs MONEY.

### **Data Validation:**

The data validation is a key issue; there is no substitute for good internal review and validation as part of the unit's own audit process, by dedicated individual.

This internal review process must be as well subject to external scrutiny.

### **Reporting:**

This is part of the system and needs allocated personnel to facilitate data reporting in each center making data recording system easy accurate and agreeable to the Surgeons.

### **Collaboration:**

Collaboration is essential between the different Surgeons in the same center, the different centers and even between surgeons and Cardiologists to develop a unified database collecting data on patients from the time of their first cardiological intervention.

### **The process:**

Every center in Egypt is invited to collect data through each hospital intranet computer

connection system to a central merged data base = [interim registries].

These source registries will be copied directly from the hospital system and loaded into an additional discrete data base then sent via the internet web to a central collection point, to produce the; Merged National data registry =[Final target registry] To produce;

-Basic statistical analysis.

-Advanced statistical analysis.

-Risk modelling.

i.e Data from all entries from all hospitals will be used for the basic aggregate data analysis and interhospital comparisons.

NB; No individual patient names, Surgeons names will be hold it will be; Raw Merged Anonymised data.

NB; Parsonnet scores will be in use so that all patients will have a uniform manner of risk scoring.

There is a long way to go, but with the passage of time patient orientated national databases will include pediatric & thoracic surgical databases as well for the time being we will start with the Adult Cardiac one.

Next few windows will demonstrate the frames set by the Egyptian Society of Cardiothoracic Surgeons as an initiation minimum data set for adult cardiac surgical registry through which we can calculate the risk by using the parsonnet scoring system and as well reproduce basic aggregate and advanced statistical analysis after collecting the data from the participating centers.

**Admission Details**

First Name:

Date of Birth:

Gender:  Male  Female

Surname:

Age at Surgery:

Date of Admission:

**Cardiac History**

Angina Status (Canadian)

Dyspnoea Status (New York)

Symptom Status

Congestive Cardiac Failure

Previous "Q wave" MI's

Last "Q wave" MI's

EuroSCORE: Percent MI

**Previous Non-Surgical Intervention**

Previous Cardiological intervention

Thrombolysis within previous 24 hours

Previous PTCA / Stent

Previous Valvuloplasty

Recent Failed intervention

Date of last intervention

**Previous Surgical Intervention**

Previous Surgical Procedure

- None
- CABG
- Ascending aorta or Aortic arch
- Congenital cardiac
- Other cardiac
- Other thoracic
- Valve
- Descending or Abdominal aorta
- Carotid endarterectomy
- Peripheral vascular
- Unknown

Next

Exit

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### Risk Factors For Coronary Disease

Diabetes

Hypercholesterolaemia  $>5.0$  mmol/l or treated

Hypertension (140/90 or treated)

Smoking History

### Catheterisation Data

Was the patient Catheterised

Date of Catheterisation

Catheterised Same Time as Admission

### Additional Medical History\_Risk Factors

GI tract

Renal System

Neurological dysfunction

Peripheral Vascular Disease

Pre-op Arrhythmia

### Coronary Anatomy

Extent or Coronary Vessel Disease

Left Main Stem Disease

**Next**  **Exit**  **Prior**

### Indices and Pressures

PA Systolic  Not measured / unknown

Aortic Valve Gradient  Not measured / unknown

LVEDP  Not measured / unknown

PAWP / LA (mean)  Not measured / unknown

Left Ventricular Ejection Fraction

### Preoperative Support

Pacemaker (temp or permanent)

Cardiogenic Shock

Intravenous Inotropes

IABP

Ventilated

Intravenous Nitrates

### Operation Data

Operation Priority

Operation Sequence

Date of Operation

Surgeon

Consultant

### Patient Bio Data

Height in (cm)

Weight in (kg)

Cumulative Bypass Time

Cumulative XC Time

Body Surface Area

Body Mass Index

Circulatory Arrest Time

Longest Ischaemic Period

### Myocardial Protection and Perfusion Data

Cardiopulmonary Bypass

Predominant Myocardial Preservation

Cardioplegia Method

Non Cardioplegia Myocardial Protection

### Aortic Procedure Data

Concomitant Carotid Endarterectomy

Aortic Procedure

Aortic Site

Aortic Pathology

Aortic Procedure

### Operation Classification by Group

Cardiac Procedures

Other Cardiac Procedures

Other non-Cardiac Procedures

**N**ext

**E**xit

**P**rint

## Valve Procedure Data

Valve Site	Aortic	Mitral	Tricuspid	Pulmonary
Haemodynamic Pathology	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Valve Pathology	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Procedure	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Explant Type	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Explant Prosthesis:	Enter local or Heart Valve Registry Code for valve explant			
	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Implant Type	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Implant Prosthesis:	Enter local or Heart Valve Registry Code for valve implant			
	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Serial Numbers	Valve / Ring Serial Numbers			
	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Implant Valve Size in mm.	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Valve Repair	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

[Next](#)

[Exit](#)

[Print](#)

### Graft Procedure Data

Graft Number	Number 1	Number 2	Number 3	Number 4	Number 5
Graft Sites	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Conduit	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Graft	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Local Proc.	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Next

Exit

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Low Cardiac Output	<input type="text"/>	Arrhythmias	<input type="text"/>
Pc-operation	<input type="text"/>	Blood Used	<input type="text"/>
Sternal Resuturing	<input type="text"/>	Multisystem failure	<input type="text"/>
Days Ventilated (if ventilated >24	<input type="text"/>	Hours Ventilated (if less than 24	<input type="text"/>
Neurological Complications	<input type="text"/>	Infective Complications	<input type="text"/>
Pulmonary Complications	<input type="text"/>	Renal Complications	<input type="text"/>
Stay on ITU	<input type="text"/>	Re-admitted to ITU	<input type="text"/>
Date of Discharge / Death	<input type="text"/>	Gi Complications	<input type="text"/>
Admission to op stay	<input type="text"/>	post-operative stay	<input type="text"/>
Total stay	<input type="text"/>		
Status	<input type="text"/>	Cause of Death	<input type="text"/>
Other cause of death	<input type="text"/>		
Discharge destination	<input type="text"/>		

**Print**

**Exit**

**Save and Calculate**



# IMMEDIATE SURGICAL CLOSURE VERSUS INDOMETHACIN IN THE MANAGEMENT OF PERSISTENT DUCTUS ARTERIOSUS IN PREMATURE NEWBORNS

## ABSTRACT

How often is prostaglandin inhibition by Indomethacin successful in closing the patent ductus arteriosus (PDA)? To answer this question, from October 1999 to October 2003, we have studied 162 patients who were premature newborns with PDA. We divided these patients into two groups: Group (A) (80 patients) surgical closure by double haemoclips was achieved and Group B (82 patients) had prostaglandin inhibition (Indomethacin) therapy.

The mean gestational age for Group A was  $29 \pm 3.2$  weeks and  $30 \pm 2.5$  weeks for Group B. The age of treatment was  $25 \pm 19$  days for Group A and  $26 \pm 2.8$  days for Group B. The birth weight was  $1028 \pm 379$  g for Group A and  $1089 \pm 336$  for Group B patients.

In Group B two patients underwent surgery for PDA closure, one because of failure with two courses of Indomethacin therapy and the other was not given Indomethacin because of delayed diagnosis. Both had no morbidity or mortality.

In Group (A) there was no operative related mortality, but there was 5/82 (4.1%) mortalities in Group B due to gastrointestinal bleeding and renal failure.

Out of this study, it is possible that treatment of PDA with surgical clips closure is safe and simple with less morbidity compared to the use of Indomethacin specially in patients with birth weight less than 1000 grams.

**Key words:** Premature, PDA, Indomethacin, surgical closure.

Hossameldin EID, O. Ai-Jassim, A. Khan\*, M. Alaziz, N. Alkhaja

J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII January No. 1

## INTRODUCTION

Patent Ductus Arteriosus (PDA) with left to right shunt is often associated with respiratory distress in the premature infant, making worse broncho-pulmonary dysplasia lesions (1). Two lines of treatment have been proposed: surgical ligation or medical management using prostaglandin synthetase inhibitor such as Indomethacin (2). Side effects and complications of pharmacological treatment are reported and

must be under consideration with surgical management (3). Failure of ductal closure with Indomethacin is reported between 30% and 40% (4). The failure rate is higher in newborns weighing less than 1000 grams (5). Although surgical closure of PDA in premature infants may be performed with a very low risk by experienced team, however, the anatomy of premature is somewhat different from older child with hazard of misidentification of major vessels (6).

### **Aim of the study**

Through this report we compared our experience in the two lines of management of PDA in premature newborns, to answer the question of which is better ?

### **Patient and methods**

From October 1999 to October 2003, we studied 162 patients of premature newborns with PDA under 34 weeks of gestational age. We divided them into two groups: Group (A) eighty patients who underwent surgical closure by double haemoclips. Group (B) eighty-two patients had medical management. The diagnosis of PDA was established on the typical murmur, wide pulse pressure, cardiomegally and evidence of excess pulmonary blood flow by radiographic examinations. Echocardiography confirmation was obtained in all cases. In Dubai there are two Neonatal units in two different hospitals, one unit prefers medical management for PDA in preterms (B) and the other unit's team prefers the immediate surgical closure (A). The medical management includes: Fluid restriction, anti failure measures, and mechanical ventilation and Indomethacin administration. The dose regimen used was 0.1 mg/kg intravenously for 6 days. During therapy there was routine check of 24-hour urine output, platelet count, serum urea, creatinine and electrolytes on alternate days till the course is over.

Patients with serum creatinine > 1.8 mg%, platelet count < 60,000/mm<sup>3</sup>, stool hematest > 3+, evidence of bleeding diathesis, evidence of increasing intra ventricular hemorrhage or clinical or radiological evidence of narcotizing enter

colitis were excluded from medical treatment.

**Surgical management:** Once diagnosed, the patient is transferred to operating theater in a transport incubator, Under general anesthesia, through poster lateral mini-thoracotomy, the PDA is identified and doubly clipped with medium size Ligaclips, no chest drains were required. All patients in both groups were routinely checked by echocardiography within the first week of treatment, chest x-ray, weaning from mechanical ventilation and the incidence of complications and survival.

Quantitative data were analyzed using the standard error of the difference between percentages (U test). A p value of less than 0.05 was considered significant. Data were expressed as mean ± standard error of the mean.

### **Results**

From October 1999 to October 2003, we studied 162 consecutive premature newborns with PDA, who were classified into two groups (A) surgical and (B) medical. The mean gestational age for Group A was 29 ± 3.2 weeks and 30 ± 2.5 weeks for Group B. The age of treatment was 25 ± 19 days for Group A and 26 ± 2.8 days for Group B. The birth weight was 1028 ± 379 g for Group A and 1089 ± 336 for Group B patients. There was no operative related mortality in-group (A), but there was (4.1%) mortality in-group (B). Two patients (2.4%) from group (B) underwent surgical closure of PDA due to failure of medical management. The follow up echocardiography showed none of the surgically treated patient had residual shunt

**Table (1):**

ITEM of Comparison	Group (A)	Group (B)	P value =
Gestational age	29 ± 3.2	30± 2.5	0.5204
Birth Weight	1028± 379	1089± 336 gm	0.7877
Age at treatment	25± 19 days	26± 2.8 days	0.672
Patency of PDA after treatment	0.0 %	8.5%	P< 0.01
Mortality	0.0%	4.1%	P< 0.06
Bleeding	0.0%	4.8%	P< 0.05
Renal Failure	0.0%	6.0%	P< 0.05
Early weaning from mechanical ventilation	96.25%	94%	P< 0.5
Recurrent Laryngeal Nerve injury	1.25%	0.0%	P< 0.31

**P value < 0.05 is statistically significant.**

at the ductus level, but seven patients in group (B) had patent PDA (5 died of complications + 2 who were referred to surgery). Those who had successful closure of PDA in both groups were early (within 3 days) weaned from mechanical ventilation unless they had associated severe form of respiratory distress syndrome (RDS). Gastrointestinal bleeding (4/82) and renal failure (5/82) were the two main complications of Indomethacin therapy. One patient (1.25%) from group A had recurrent laryngeal nerve injury during operation.

The following table summarizes the comparison between the two groups.

### Conclusion

The closure of shunting PDA benefits premature newborns specially those who have RDS. Although initial trial of prostaglandin inhibitor (Indomethacin) seemed accepted by many neonatologist, we found that in our series the immediate surgical closure is more simple, effective and associated with lower complication rate than Indomethacin treatment specially in

those babies with birth weight less than 1000gms. Medical treatment is suitable for preterms that have no contraindications for Indomethacin and above 1000gms birth weight.

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Said Abdel Aziz, Yahya Balbaa, Diaa Abul Seoud, Ahmed H. Gaafar, Marawan Mohamed

# **INFLUENCE OF THE INVERTED, T-SHAPED, POSTERIOR PERICARDIOTOMY ON SUPRA-VENTRICULAR ARRHYTHMIAS AND PERICARDIAL EFFUSION: EARLY RESULTS AFTER CORONARY ARTERY BYPASS GRAFTING**

## **ABSTRACT**

**Objective:** The aim of this prospective study was to investigate the early postoperative influence of an inverted, T-shaped, posterior pericardial incision in reducing the incidence of pericardial effusions and consequently reducing the related supra-ventricular tachyarrhythmias (SVT), especially atrial fibrillation (AF) after coronary artery bypass grafting (CABG).

**Material and Methods:** This prospective study was carried out between January 2000 and May 2003, in 180 patients undergoing coronary artery bypass grafting (CABG). Patients were divided into two groups; each group included 90 patients. Their ages ranged from 42 to 76 years with a mean of  $57.1 \pm 9.9$  in group A (in which an inverted T-shaped posterior pericardiotomy was performed) and ranged from 38 to 71 years with a mean of  $54.7 \pm 10.3$  in group B (the control group). In group A, an inverted T-shaped incision was made posterior to the left phrenic nerve with its transverse limb parallel to the diaphragm and its longitudinal limb parallel to the phrenic nerve. This posterior pericardiotomy was not performed in the control group B.

**Results:** Early pericardial effusion developed in 11.1% (10 patients) and in 42.2% (38 patients), respectively, in group A and group B ( $P < 0.0001$ ). Atrial fibrillation developed in 9 patients (10%) in group A and in 29 patients (32.2%) in group B ( $P < 0.001$ ). Other supra-ventricular tachyarrhythmias were not statistically significant.

**Conclusion:** The inverted, T-shaped., posterior pericardiotomy incision is a simple, safe and effective technique for reducing the prevalence of early pericardial effusion and related atrial fibrillation.

**Key words:** Postoperative atrial fibrillation, Posterior pericardiotomy, Coronary artery bypass grafting.

Said Abdel Aziz\*MD; Yahya Balbaa\*, MD; Diaa Abul Seoud\*, MD; Ahmed H. Gaafar\*, MD; Marawan Mohamed\*, MD

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## **INTRODUCTION**

Supra-ventricular tachyarrhythmias (SVT) have been recognized as a common postoperative complication of coronary artery bypass grafting (CABG). These

arrhythmias include atrial fibrillation (AF), atrial flutter and paroxysmal atrial tachycardia. Many clinical studies have reported a prevalence of 25% to 40% among patients with CABG, with a peak incidence occurring between the 2<sup>nd</sup> and 4<sup>th</sup>

postoperative days (1,5,6). Postoperative pericardial effusion, which is commonly seen after CABG, adds a wide range of morbidity to the operation as it may impede cardiac filling, reduce cardiac output, and lead to cardiac tamponade. Moreover, It is often incriminated in the development of SVT after CABG operation (2). Several investigators have previously dealt with the clinical features and management of postoperative pericardial effusion and have emphasized the high mortality rates associated with delayed treatment (3,4). Postoperative supra-ventricular arrhythmias, although usually benign, can cause hemodynamic instability, prolong hospital stay and increase cost and, rarely, predispose to cerebrovascular accidents (7). Posterior pericardial drainage has been reported to reduce not only the prevalence of postoperative pericardial effusions and related atrial fibrillation but also delayed posterior pericardial effusion (8,9).

### **Objective:**

The aim of this prospective work was to demonstrate the early postoperative influence of an inverted, T-shaped, posterior pericardial incision in reducing the incidence of pericardial effusions and consequently reducing the related atrial fibrillation after coronary artery bypass grafting.

### **Patients and Methods**

Over a 40-month period (January 2000 to May 2003), 180 patients, who underwent CABG operation, were prospectively studied. Patients were divided into two groups that were well matched for age, sex, and preoperative risk factors. Each group included 90 patients. Their ages ranged from

42 to 76 years with a mean of  $57.1 \pm 9.9$  in group A (in which an inverted T-shaped posterior pericardiotomy was performed) and ranged from 38 to 71 years with a mean of  $54.7 \pm 10.3$  in group B (the control group). Male/Female ratio was 53/37 and 49/41 in group A and B respectively. All patients were subjected to the same preoperative assessment list including cardiac catheterization, echocardiography, chest X-ray electrocardiography (EGG) and routine laboratory investigation. Echocardiography was used to assess the preoperative left ventricular function and also to evaluate the postoperative pericardial effusion. Preoperative left ventricular function was assessed and defined as good (ejection fraction > 50%), moderate (ejection fraction 30-50%), or poor (ejection fraction < 30%). Preoperative data of patients are summarized in Table I.

**Inclusion criteria:** Patients with chronic stable angina, unstable angina and those with different left ventricular functions were included in this study.

**Exclusion criteria:** All patients with the possibility of preoperative arrhythmia, such as patients with hyperthyroidism, chronic obstructive pulmonary disease, renal dysfunction, left ventricular aneurysm, valvular heart disease and preoperative paroxysmal atrial fibrillation were excluded from this study.

**Operative technique:** Anesthetic medications were similar in each group. Median sternotomy, routine aortic and right atrial cannulation and cardiopulmonary bypass using intermittent antegrade warm blood cardioplegia were applied to all patients of both groups. The left internal mammary artery (LIMA) was harvested in

all patients except one in whom the artery was severely diseased as documented by angiography. The left pleural cavity was opened, during harvesting of the (LIMA), down to the phrenic nerve in all patients in order to ensure better drainage of the pericardium into the pleura during the postoperative period. The radial artery was also harvested in 39% and 46% of patients for both groups respectively. A posterior inverted T-shaped pericardiotomy was performed in patients of group A. This window was performed just before coming off bypass. It was done as an inverted T-shaped incision, posterior to the left phrenic nerve with its transverse limb, about 4 cm, parallel to the diaphragm and its longitudinal limb, about 4 cm, extending from the left inferior pulmonary vein downward to the middle of the transverse limb at the diaphragm and parallel to the phrenic nerve. This posterior incision allows free drainage of any collected blood or effusion to the left pleura. This posterior incision was not performed in the control group B patients. Two chest tubes (one in the left pleural cavity and the other in the anterior mediastinum) were routinely inserted and the pericardium was left open anteriorly in both groups. Another third chest tube was inserted in the right pleural cavity when indicated. No drain was placed behind the heart to avoid tube-induced arrhythmias in both groups. Operative data of patients are summarized in Table 2.

**Postoperative Care:** After routine closure of the chest, all patients were transferred to the intensive care unit and continuous negative suction (5 to 10 mmHg) was applied to the drains to ensure tube patency. The amount of fluid drainage in the chest tubes was calculated hourly for each patient. Chest tubes were removed when the drainage was less than 10 ml/hour for 6

consecutive hours. Routinely, all patients of both groups received 2 grams of magnesium sulfate infusion in the first few hours of the postoperative period. Electrocardiograms of patients were monitored continuously for 72 hours for detecting arrhythmias. Standard 12-lead electrocardiogram (ECG) was done routinely to all patients every day and during any event of arrhythmia to detect persistent, clinically relevant AF that would necessitate medication. In the event of SVT the serum potassium level was corrected if less than 4.5 mmol/l and additional 2 grams of magnesium sulfate were given. If the SVT persisted; amiodarone administration was begun. The presence of pericardial effusion was assessed by two-dimensional echocardiography, which was performed in the second postoperative day and before discharge. The presence of pericardial effusion on two-dimensional echocardiography was considered significant if it was greater than 1 cm anteriorly and posteriorly. Clinical data are expressed as the percentage and as the mean  $\pm$  SD in table 3.

## Results

There was no difference between the two treatment groups as regards to age, sex, LV ejection fraction and risk factors. The number of the distal anastomoses, left internal mammary artery (LIMA), radial artery, saphenous vein graft (SVG) usage, duration of aortic cross-clamp time, total bypass time were not statistically significant (Tables 1&2). The duration of intensive care unit (ICU) stay was also comparable in both groups. The mean duration of the chest tube drainage was  $44.8 \pm 8$  hours for group A and  $45.13 \pm 8.1$  hours for group B and it was statistically not significant.

**Morbidity and mortality:** There was one hospital death because of low cardiac

**Table (1): Preoperative data.**

	Group A (n = 90)	Group B (n = 90)	P- value
Age (years)	57.1± 9.9	54.7 ± 10.3	NS
Sex (M/F)	53/37	49/41	NS
Risk factors			
Hypertension	59 (65.5%)	49 (54.4%)	NS
Diabetes mellitus	16 (17.7%)	13 (14.4%)	NS
Smoking	54 (60%)	45 (50%)	NS
Dyslipidaemia	35 (38.8%)	40(44.4%)	NS
Obesity	13 (13.3%)	11 (12.2%)	NS
LV function			
Good (EF ≥ 50)	59 (65.5%)	55 (61.1%)	NS
Moderate (EF 30-50)	22 (24.4%)	24 (26.6%)	NS
Poor (EF ≤ 30)	9 (10%)	11(12.2%)	NS
Previous MI	27 (30%)	31 (34.4%)	NS

EF= ejection fraction. MI = myocardial infarction. NS= not significant.

**Table (2): Operative data.**

	Group A	Group B	P- value
LIMA to LAD	90	89	NS
Radial Artery graft	35 (38.8%)	42 (46.6%)	NS
SVG	77 (85.5%)	75 (83.3%)	NS
No. of RCA or PDA grafts	76 (84.4%)	79 (87.7%)	NS
No. of grafts per patient	3.0 ± 0.5	2.6 ± 0.7	NS
ACC time (minutes)	24-66 (42.3 ± 9.9)	26-69 (41.9 ± 9.3)	NS
Bypass time (minutes)	32-90 (57.8 ± 12)	30-105 (59.6 ± 16.7)	NS

LIMA= left internal mammary artery. LAD= left anterior descending artery. SVG= saphenous vein graft. RCA= right coronary artery. PDA= posterior descending artery. ACC= aortic cross clamp. NS = not significant.

output in group A. Three patients underwent reoperation because of bleeding, One patient in group A (1.1%) due to bleeding from the site of epicardial pacemaker wire on the right ventricle and two patients in group B (2.2%) due to bleeding from a side branch of the LIMA. One patient needed re-wiring of the sternum due to sternal dehiscence in group B.

Early pericardial effusion was detected by trans-thoracic echocardiography. In group A, 10 patients had early pericardial effusion versus 38 patients in group B which was statistically significant ( $P < 0.0001$ ). Before discharge, echocardiography was done to all patients in both groups and no significant pericardial effusion was found. The supraventricular arrhythmias were



**Table (3): Postoperative data.**

	<b>Group A</b>	<b>Group B</b>	<b>P-value</b>
Total arrhythmias	12(13.3%)	34 (37.7%)	<0.001
Atrial fibrillation	9(10%)	29 (32.2%)	0.001
Other SVT	3 (3.3%)	5 (5.5%)	NS
Early pericardial effusion	10(11.1%)	38(42.2%)	<0.0001
Reoperation for bleeding	1 (1.1%)	2 (2.2%)	NS
Re-wiring of sternum	0 (0%)	1 (1.1%)	NS
Mortality	1(1.1%)	0(0%)	NS
Chest tube drainage (hours)	44.8 ± 8	45.13 ± 8.1	NS
ICU stay (hours)	47.9 ± 15.7	48.9 ± 14.1	NS
Hospital stay (days)	10.2 ± 1.9	10.3 ± 2.1	NS

**SVT= supraventricular tachyarrhythmias. ICU = intensive care unit.**

significantly more common in group B (34 patients) than in group A (12 patients) ( $P < 0.001$ ). Arrhythmias were also more commonly associated with the presence of pericardial effusion. Atrial fibrillation was significantly lower in group A than in group B [10% (9 patients) in group A vs. 32.2% (29 patients) in group B]. Other SVTs as paroxysmal atrial tachycardia or atrial flutter were rare and showed no difference between the groups (Table 3). All patients with AF in group A and B were controlled by the administration of amiodarone except for two patients in group B that needed electrical cardioversion. There was no significant difference between the two groups regarding hospital stay ( $10.2 \pm 1.9$ ) for group A and ( $10.3 \pm 2.1$ ) for group B.

### Discussion

Supraventricular arrhythmias, especially atrial fibrillation, are the most common complication following CABG (1) and occur in up to 30-50% of cases in different studies with the major occurrence 2 days after the operation (5,6). Various causes for postoperative AF have been suggested such

as advanced age, hypertension, right coronary artery involvement, respiratory complications, bleeding and withdrawal of beta blockers (1,10,11,12&13) Previous reports have demonstrated that patients with pericardial effusion had a higher prevalence of supraventricular arrhythmias (2,14). Mulay and associates (9) have demonstrated that a posterior pericardiotomy could drain freely the pericardium into the pleural space, thereby reducing the incidence of pericardial effusion and related supraventricular arrhythmias. Many other authors reported similar results (8,15). In our study, comparable results were obtained, where early pericardial effusion was noted in 11.1% of patients in group A (pericardiotomy) versus 42.2% of patients in group B. Similarly, postoperative AF was lower in group A patients than in group B patients (10% vs. 32%).

On the other hand, Asimakopoulos and coworkers (16) have shown that a posterior pericardiotomy was more effective for pericardial drainage, but they also have shown that atrial fibrillation or SVT

incidence was not significantly reduced (20%) in comparison with the conventional technique (26%). However, there were two potential limitations for their study. First, they did not perform continuous ECG monitoring after 48 hours. Second, they did not perform echocardiography to quantify the incidence or size of any pericardial effusions.

We used echocardiography, as many others (8,9,15), to evaluate the postoperative pericardial effusion.

Unusually, Yorgancioglu et al. (17) experienced the protrusion of a sequential vein graft from the posterior pericardiotomy site, which resulted in squeezing of the vein graft by the edges of the posterior pericardiotomy incision. They recommended that a posterior pericardiotomy should carefully be used with patients in whom posterior wall revascularization was performed, especially by sequential grafting. As regard this, we did not face such a complication in our cases and this could be explained by our inverted T-shaped modification of the incision that allows wide separation between the edges of the pericardiotomy.

In conclusion, the inverted T-shaped posterior pericardiotomy incision is a simple, safe and effective technique for reducing the incidence of early pericardial effusion and related atrial fibrillation.

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Said Abdel Aziz, Yahya Balbaa, Diah Abul Seoud, Ahmed H. Gaafar, Marawan Mohamed  
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## REDUCTION OF THE INFLAMMATORY RESPONSE TO CARDIOPULMONARY BYPASS AFTER MITRAL VALVE REPLACEMENT: COMPARATIVE STUDY BETWEEN APROTININ AND METHYLPREDNISOLONE

### ABSTRACT

**Background:** Exposure of the blood to the foreign surface of the cardiopulmonary bypass machine; including the surfaces of the oxygenator and that of the tubing system, can trigger a series of inflammatory responses which is manifested by increased plasma concentrations of cytokines as IL-6 and 8 as well as various clinical and hemodynamic consequences. The inflammatory responses are the main causes of ischemia-reperfusion injury. Inhibiting these cytokines can improve the outcome in patients undergoing open heart surgeries. The aim of this study is to test the effect of aprotinin and methylprednisolone administration on the levels of IL-6 and 8 as biochemical markers of inflammatory response and to test the hypothesis that they can improve the postoperative clinical course.

**Methods:** Forty-two patients, undergoing elective MVR were divided randomly into three groups: Group A patients who received aprotinin in a dose of 20,000 IU/kg as pre-treatment followed by 7500 IU/kg every 6 hours for 24 hours, Group B patients who received methylprednisolone 30 mg/kg before CPB and another equal dose before declamping of the aorta and Group C patients who received normal saline 20 ml/h during the operative period. Blood samples were drawn: (1) after initiation of CPB, but before applying the aortic cross-clamping; (2) one hour after removal of the aortic cross-clamping; (3) three hours after the end of surgery and (4) twelve hours after the end of surgery. These samples were analyzed to determine the plasma levels of IL-6 and IL-8 with ELISA. Postoperative variables evaluated included body temperature, the occurrence of low COP syndrome and inotropic support needed, alveolar-arterial oxygen gradient and total ventilation time.

**Results:** One hour after removal of the aortic cross-clamp and three and twelve hours postoperatively, the mean IL-6 and 8 levels in groups A and B were significantly ( $p < 0.05$ ) lower than that in group C. Group B patients showed a non-significantly ( $p > 0.05$ ) and a significantly ( $p < 0.05$ ) lower mean values of IL-6 and IL-8 respectively than group A patients; one hour after removal of aortic cross-clamp and also three and twelve hours postoperatively. The mean temperature for the first 24 hours postoperatively was significantly lower in both groups A and B than in the controls. Compared with controls, both aprotinin and methylprednisolone-treated patients had significantly lower alveolar-arterial oxygen gradients during the first 24 hours and required less mechanical ventilation. Both drug-treated groups needed less inotropic support than the control group but with no statistical significance.

**Conclusion:** Administration of either methylprednisolone or aprotinin in open-heart surgeries is associated with a reduction in the postbypass inflammatory response as assessed by cytokine levels and clinical course.

Hossam El-Okda, MD; Thanaa Hodhod, MD; Adel M. Fahmy, MD and Halla S. El-Sheikh, MD. J. of Egypt. Society of Cardiothorac. Surg. 2004, Vol. XII January No.1

### Introduction

The inflammatory response in cardiac surgery is thought to be produced from exposing patients to pro-inflammatory trigger factors. These factors include exposure of blood to the foreign surface of the cardiopulmonary bypass (CPB), ischemia-reperfusion injury, reduction in pulmonary blood flow during aortic cross-clamping, endotoxemia, hypothermia and the surgical technique itself (1). The resulting pro-inflammatory response is manifested by increased plasma concentrations of the pro-inflammatory cytokines: tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and interleukin-1, -6 and -8 (IL-1, -6 and -8)(2,6), complement products, free oxygen radical release, elastase and increase in the adhesion potential of neutrophils (7,8).

It is well known that ischemia-reperfusion injury is mediated primarily by free radicals that are produced by polymorphnuclear leukocytes, complement activation and cytokines upon restoration of oxygen to the tissues (9). Previous reports have shown that ischemia-reperfusion injury was reduced by leukocyte depleted blood (10). Also from previous studies it has been reported that serum levels of cytokines such as IL-6 and IL-8 are elevated after myocardial injury (11,12). The exact mechanism for this elevation is not yet known but it seems likely that those cytokines may be produced possibly via a protease mediated pathway from the myocardium during postischemic reperfusion in patients undergoing CPB (13).

Aprotinin, a natural protease inhibitor derived from bovine lung, inhibits plasmin and kallikrein, thereby directly affecting fibrinolysis. It also inhibits the contact phase

activation of coagulation which initiates coagulation and promotes fibrinolysis. In addition, aprotinin preserves the adhesive glycoproteins in the platelet membrane, rendering them resistant to damage from the increased plasmin levels and mechanical injury that occur during cardiopulmonary bypass. The net effect is to inhibit both fibrinolysis and turnover of coagulation factors and to decrease bleeding (14). Also, from previous studies it has been reported that methylprednisolone (MP), which has been shown to inhibit cytokines in vitro and in vivo (15,17), was given to patients undergoing open heart surgery, and its inhibitory effect on the increased production of IL-6 and IL-8 was recorded (18).

The aim of this trial was to study the effect of aprotinin and methylprednisolone on the postbypass and postoperative course after elective mitral valve replacement using both clinical data as well as biochemical markers of inflammatory response.

### Patients and methods

Forty-two patients, NYHA class II or III, aged between 18 and 46 years, of average body weight, undergoing elective MVR for rheumatic mitral valve disease were included in this study in Ain Shams University Hospitals in the period from January 2002 to May 2003. They were divided randomly into three groups. Group A (Fourteen patients) received aprotinin (Trasylol, Bayer A.G. Leverkusen, Germany) in a dose of 20,000 IU/kg as pre-treatment followed by 7500 IU/kg every 6 hours for 24 hours. Group B (Fourteen patients) received methylprednisolone 30 mg/kg before CPB and another equal dose before declamping of the aorta. Group C (Fourteen patients) received normal saline 20 ml/h during the operative period. The

three groups were comparable with regard to age, sex, weight, height and other demographic variables (table 1). All patients had preoperative ejection fraction (EF) > 0.45. Exclusion criteria were: heart failure, diabetes mellitus, peptic ulcer and blood diseases.

#### **Anesthetic protocol:**

Patients were premedicated with diazepam 0.2 mg/kg IM one hour before induction of anesthesia. On arriving the operative room, ECG and arterial oxygen saturation using a pulse oximeter were monitored. Under local anesthesia and after performing the Allen's test, arterial cannulation was done in the right radial artery to measure the arterial blood pressure invasively and from which blood samples were drawn. A base-line blood gas and electrolyte analysis and activated clotting time (ACT) were measured. All patients then received standard general anesthesia consisting of fentanyl 75-100 µg/kg and vecuronium bromide 0.1-0.2 mg/kg. After endotracheal intubation, mechanical ventilation with isoflurane in nitrous oxide/oxygen mixture was started to maintain the PaCO<sub>2</sub> between 35 and 40 mm Hg using Ohmeda 7000 ventilator. Nasopharyngeal and rectal temperatures were continuously measured using probes. A pulmonary artery catheter was inserted into the internal jugular vein. Heparin was given prior to CPB and activated clotting time was measured and maintained over 400 seconds.

#### **Operative techniques:**

All patients were operated through a standard midline sternotomy. Cardiopulmonary bypass was performed with a roller pump (Sarns 3M, MN, USA) and membrane oxygenator (Dideco SPA). Moderate hypothermia (core temperature

28°C) was used in all patients with a flow rate of 2-2.4 L/min and a mean arterial pressure of 40-50 mmHg. Hematocrit values were maintained at 22-27% throughout the CPB period. The circuit was primed with Ringer' lactate and packed blood cells were only added if the estimated hematocrit was less than 22 %. Myocardial protection was achieved by antegrade cold blood-enriched cardioplegia in a dose of 15 ml/kg together with topical cooling. Weaning from CPB was done using dopamine in a dose of up to 12 µg/kg/min. Epinephrine was used if dopamine was not sufficient.

#### **Biochemical data:**

Blood samples were drawn: (1) after initiation of CPB, but before applying the aortic cross-clamping; (2) one hour after removal of the aortic cross-clamping; (3) three hours after the end of surgery and (4) twelve hours after the end of surgery. All blood samples were taken from the internal jugular vein. These samples were analyzed to determine the plasma levels of IL-6 and IL-8 with a commercially available enzyme-linked immunosorbent assay (ELISA) [IL-6: Toray Fujibionics Inc., Tokyo, Japan[19] and IL-8: RD Systems, Minneapolis, MN, USA[20]]. The release of both cytokines was expressed by the area under the curve (AUC).

#### **Postoperative protocol:**

Intensive care unit (ICU) monitoring was standard for all patients. Each patient was monitored by ECG, invasive blood pressure, central venous pressure recordings, arterial blood gases analysis and urine output. The following findings were recorded for each patient; Mean body temperature, alveolar-arterial oxygen gradients during the first 24 hours, period of total ventilation needed and amount of inotropic support used. For this

**Table (1): Patients Demographic data.**

	Group A (n=14)	Group B (n=14)	Group C (n=14)	(P)
Age (years)	27.1 ± 8.7	26.2 ± 6.5	23.5 ± 7.2	NS
Weight (kg)	48.85 ± 9.6	52.85 ± 9.92	47.1 ± 9.17	NS
BSA (m <sup>2</sup> )	1.57 ± 0.4	1.60 ± 0.3	1.54 ± 0.2	NS
Height (cm)	169.3 ± 4.5	162.1 ± 6.5	163.2 ± 3.5	NS
Sex (male/female)	10/4	9/5	11/3	NS

**Table (2): Preoperative and Intraoperative data.**

	Group A (n=14)	Group B (n=14)	Group C (n=14)	(P)
NYHA (II/III)	11/3	10/4	9/5	NS
Preoperative EF	42 ± 8.2	44 ± 9.7	41 ± 6.8	NS
CPB duration (minutes)	68.1 ± 13.5	72.2 ± 18.2	75.82 ± 13.7	NS
Cross-clamping time (minutes)	39.3 ± 12.5	44.5 ± 18.8	43.1 ± 15.8	NS

**Table (3): Postoperative findings.**

	Group A (n=14)	Group B (n=14)	Group C (n=14)	(P)
Body temperature	37.3 ± 0.4 °C	37.1 ± 0.4 °C	37.9 ± 0.5 °C	P = 0.007
a - A O <sub>2</sub> tension gradient	76.2 ± 41.7	71.6 ± 38.5	112.2 ± 29.9	P = 0.03
Total intubation time (h)	8.3 ± 3.1	7.4 ± 3.8	13.6 ± 5.4	P = 0.04
Inotropic support ug/kg/24 hours	1630 ± 1786	1424 ± 1678	1823 ± 2153	NS
Low COP syndrome	2 (14.3) %	1 (7.15) %	2 (14.3) %	NS

purpose, a total drug dose for each 24 hours was calculated by adding the doses of dopamine (in micrograms per kilogram per minute) and assigning an arbitrary value of 10 µg inotropic drugs per kilogram per minute for each 0.1 µg of epinephrine per kilogram per minute.

#### Statistical analysis:

Data were analyzed with the Statview software. Data were presented as means ± SD or as numbers. Numeric data were analyzed using ANOVA and non-numeric

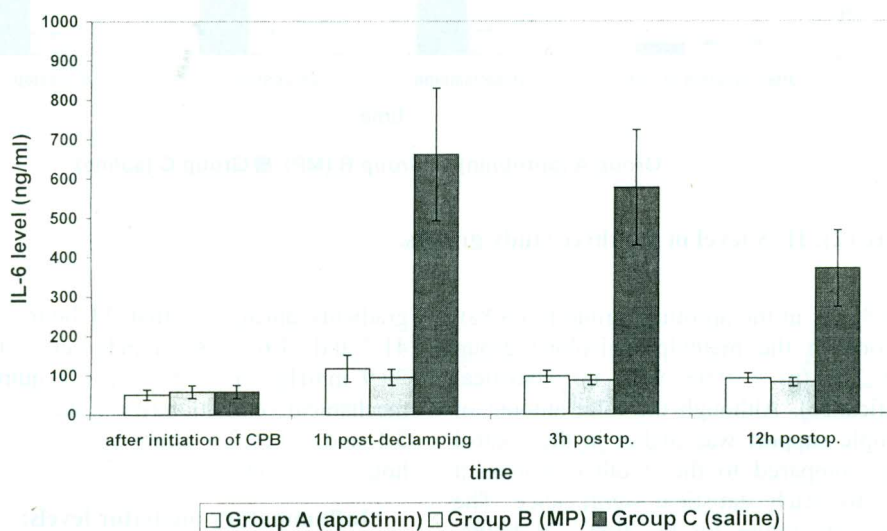
data were analyzed by the Chi-square test. Linear regression was used to identify the different variables that might have influenced the release of IL-6 and IL-8, as expressed by the AUC. Linear regression was also used to study the influence of cytokines release (AUC) on some other variables. P value <0.05 was considered to be statistically significant.

#### Results

Results were expressed as mean (standard deviation) or as numbers. Patients'

**Table (4): Correlation coefficients between AUC of IL-6 and IL-8 and the different preoperative, operative and postoperative variables.**

	AUC IL-6	(P)	AUC IL-8	(P)
Age	+ 0.14	NS	+ 0.09	NS
BSA	+ 0.22	NS	+ 0.17	NS
EF	+ 0.09	NS	+ 0.21	NS
CPB time	+ 0.65	S	+ 0.62	S
Ischemic time	+ 0.57	S	+ 0.49	S
Body temperature	+ 0.66	S	+ 0.71	S
a-A o2 tension gradient	+ 0.52	S	+ 0.28	NS
Total intubation time (h)	+ 0.47	S	+ 0.48	S
Inotropic support ug/kg/24 hours	+ 0.23	NS	+ 0.19	NS



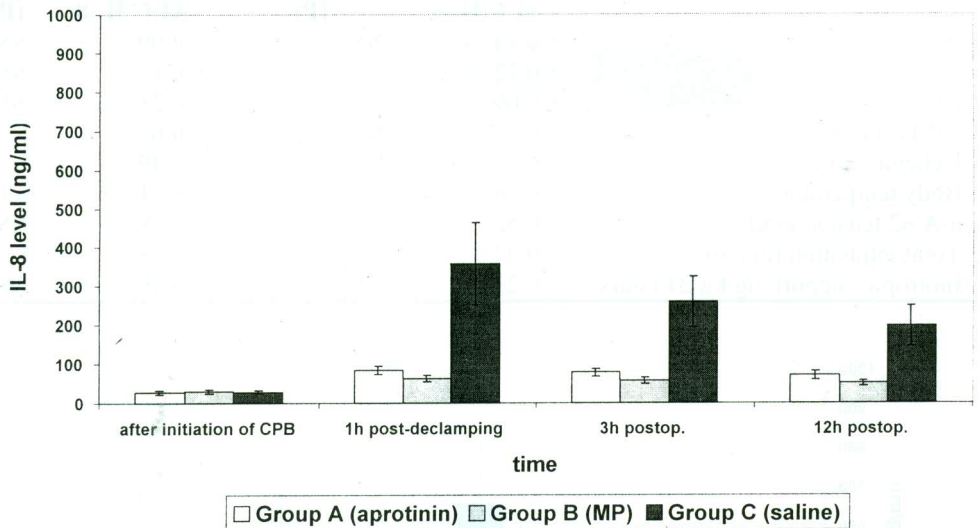
**Figure (1): IL-6 levels in the three study groups.**

characteristics were similar in the three study groups. There were non-significant differences ( $p > 0.05$ ) between the groups as regards age, sex distribution, body weight, height, and body surface area (BSA) (table 1). There were also non-significant differences ( $p > 0.05$ ) between the groups as regards the preoperative clinical data (EF and NYHA class) as well as the operative data (CPB time and aortic cross-clamping time) (table 2).

**Postoperative variables:**

The different postoperative findings are summarized in table 3. There were 2 mortalities in the study group (4.7 %). One patient died from the control group 4 days postoperatively from low COP and multiorgan failure. The second one was from the aprotinin group and died 2 days after operation from low COP. Low COP syndrome was encountered in five patients (11.9 %), 2 patients in the control group





**Figure (2): IL-8 level in the three study groups.**

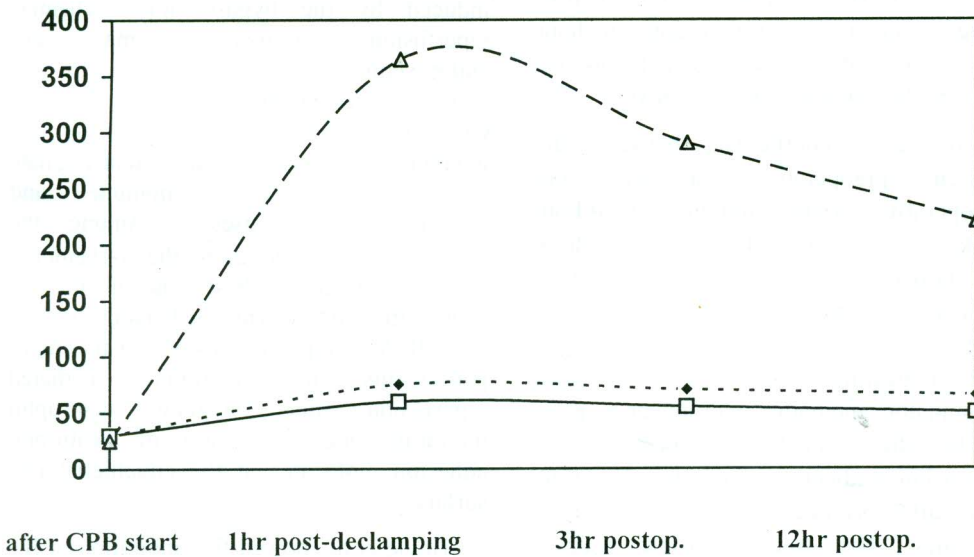
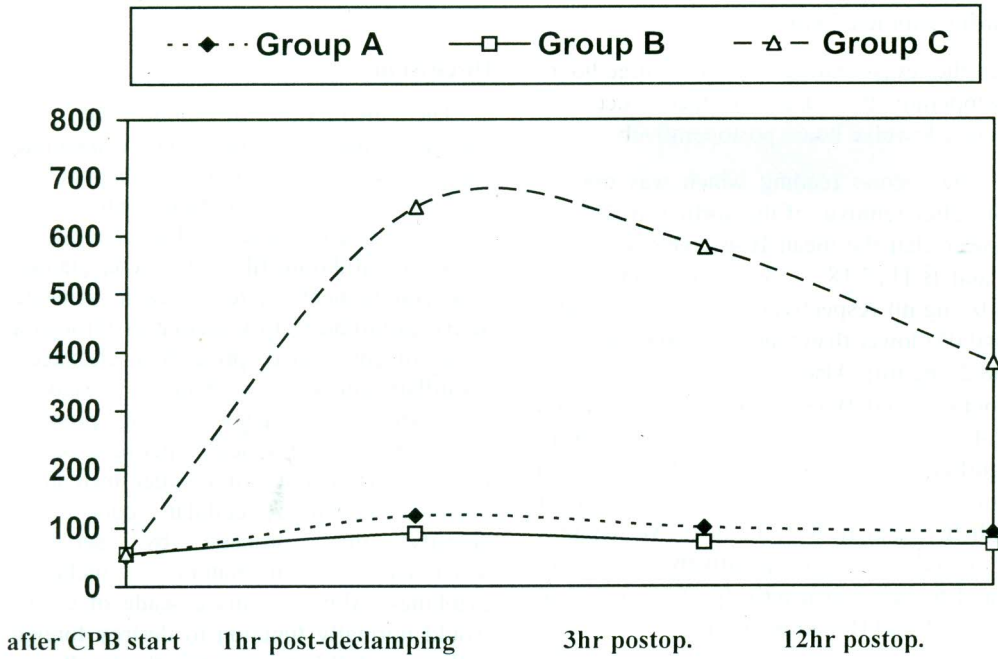
(14.3 %), 2 in the aprotinin group (14.3 %), and one in the methylprednisolone group (7.15 %) ( $p > 0.05$  with no statistical significance). Although the total amount of inotropic support was higher in the control group compared to the 2 other groups, it failed to reach statistical significance. The mean temperature for the first 24 hours postoperatively was significantly lower in both groups A and B than in the controls ( $37.3^\circ \pm 0.4^\circ\text{C}$ ,  $37.1 \pm 0.4$  versus  $37.9^\circ \pm 0.5^\circ\text{C}$ ;  $p = 0.007$ ). Patients in groups A and B had significantly fewer febrile episodes, defined as a mean temperature of  $38.5^\circ\text{C}$  or greater for at least 4 hours. None of the patients in the first 2 groups had a mean temperature of  $38.5^\circ\text{C}$  or greater for the first 8 hours postoperatively, whereas 5 (36%) of the 14 patients in group C did.

Compared with controls, both aprotinin and methylprednisolone-treated patients had significantly lower alveolar-arterial oxygen

gradients during the first 24 hours ( $76.2 \pm 41.7$  and  $71.6 \pm 38.7$  mmHg versus  $112.3 \pm 29.9$  mmHg;  $p = 0.03$ ) and required less mechanical ventilation (mean duration,  $8.2 \pm 3.1$  and  $7.3 \pm 3.5$  hours versus  $13.6 \pm 5.4$  hours;  $p = 0.04$ ).

#### **Inflammatory mediator levels:**

Plasma levels of the two types of cytokines are summarized in figures 1 and 2. The IL 6 and IL 8 levels showed similar dynamics. The total cohort of their dynamics in the 3 groups is shown by figures 3 and 4, which demonstrate the area under the curve (AUC) of both cytokines, representing their total release. The IL-6 and IL-8 levels in blood samples taken after initiation of the cardiopulmonary bypass were non-significantly ( $p > 0.05$ ) different between the three study groups. One hour after removal of the aortic cross-clamp, both IL-6 and IL-8 levels increased in the three study groups,



Figures (3,4): The area under the curve (AUC) for IL-6 and IL-8 respectively (ng/ml).

then the levels started to decline three hours postoperatively and further decrease occurred twelve hours postoperatively.

The second reading which was done 1 hour after removal of the aortic cross-clamp showed that the mean IL-6 levels in groups A and B [ $117.18 \pm 34.2$  ng/ml and  $94.9 \pm 21.07$  ng/ml respectively] were significantly ( $p < 0.05$ ) lower than that in group C [ $660.7 \pm 168.23$  ng/ml]. Also, the mean IL-8 levels in groups A and B [ $83.45 \pm 10.87$  ng/ml and  $62.45 \pm 9.2$  ng/ml respectively] were significantly ( $p < 0.05$ ) lower than that in group C [ $357 \pm 105.5$  ng/ml]. The levels of both IL-6 and IL-8 in the next two readings (3 h and 12 h postoperatively) were also found to be significantly ( $p < 0.05$ ) lower in groups A and B than in group C.

Group B patients (methylprednisolone group) showed a non-significantly ( $p > 0.05$ ) and a significantly ( $p < 0.05$ ) lower mean values of IL-6 and IL-8 respectively than group A patients (aprotinin group) one hour after removal of aortic cross-clamp and also three and twelve hours postoperatively.

Correlation coefficients between the different preoperative, operative and postoperative variables and the AUC of both cytokines are expressed in table 4. These data show that release of IL-6 and IL-8 were not correlated to age, BSA, EF, but was positively correlated to ischemic and CPB time, indicating more release of such inflammatory mediators with longer by pass. On the other hand, body temperature, a-A O<sub>2</sub> tension gradient and total intubation time were all correlated to AUC of both cytokines. The total inotropic support needed was, however, not correlated to their value.

## Discussion

The interaction of blood with the gaseous interface and bioincompatible surfaces of the cardiopulmonary bypass unit indicates activation of three intersecting plasma protease pathways. These pathways, the kinin-kallikrein, fibrinolytic-coagulation, and complement systems, each generate active proinflammatory mediators through a series of consecutive proteolytic cleavages. Proinflammatory mediators activate leukocytes and platelets, and promote vasodilatation and vascular permeability to enhance the activity of cellular mediators. Further, activated cellular components amplify this process by secreting inflammatory mediators, including cytokines. Although this cascade of events would normally function to destroy foreign pathogens, in bypass surgery, the result may be hypotension, fever, coagulopathies, edema, tissue injury, or, in extreme cases, organ failure. In addition to the insult induced by the bypass unit, ischemia-reperfusion, surgical trauma, and endotoxemia can also contribute to this systemic inflammatory response (21,22). Cytokines are a diverse group of intercellular signaling proteins that regulate local and systemic immune and inflammatory responses. Among the cytokines, IL-8 belongs to the  $\alpha$ -chemokine family and it is best known for its chemoattractant activity for leukocytes (23). Thus IL-8 is implicated as one of the major participants in neutrophil mediated reperfusion injury including neutrophil migration and expression of neutrophil adhesion molecules at the endothelial cell surface.

Boyle et al showed that inhibition of IL-8 blocked the myocardial ischemia-reperfusion injury in a rabbit model. They

neutralized the IL-8 with a monoclonal rabbit antibody (ARIL 8.2) and found that ARIL 8.2 inhibited the neutrophil recruitment and thus reduced the degree of myocardial injury (24,25). Sawa et al reported that IL-6 production has been suppressed by a protease inhibitor FUT-175 (11). They also reported that FUT-175 prevents the reperfusion injury of the myocardium (26).

Aprotinin is a low molecular weight, broad spectrum protease inhibitor which has been used in many institutions particularly to prevent blood loss in cardiac operations. It has many diverse properties that inhibits an array of enzymes and activities that participate in coagulation, fibrinolytic and inflammatory processes. It has also been used to treat pancreatitis and hyperplasminemia (27-29). Lord et al showed that aprotinin treatment also reduced the neutrophil activation after major vascular operations (30). Methylprednisolone has been shown to inhibit cytokines in vitro and in vivo (15-17). Yoshikawa and his co-workers showed that methylprednisolone inhibits the release of free oxygen radicals in addition to its anti-shock and membrane stabilizing effect (31).

From all the previous studies, there is a strong possibility that CPB-related inflammatory response as well as reperfusion injury might be controlled if IL-6 and IL-8, which activate neutrophils, are inhibited. Our present study showed that group A patients (who received aprotinin) and group B patients (who received methylprednisolone) showed a significantly lower mean values of both IL-6 and IL-8 in the postoperative period when compared to the control group. Group B patients had a non-significantly and a significantly lower levels of IL-6 and IL-8 respectively when compared to group A patients in all times

following aortic declamping. Correlation coefficients between the area under the curve of IL-6 and IL-8, which represent their total release, and the different variables also gave some valuable data. They were higher with more ischemic and bypass times indicating the strong relation between CPB and inflammatory response. On the other hand, increase in body temperature and depressed respiratory gas exchange could be positively correlated to the increase of circulating cytokines. These findings were supported by the clinical postoperative data which showed that the 2 drugs-treated groups had fewer febrile episodes, improved respiratory gas exchange, required fewer time of ventilation and ICU stay as well as less inotropic support. The reduced incidence of fever may be due, at least in part, to the lower of circulating cytokines, which are known pyrogens. The better respiratory gas exchange, and the less mechanical ventilation required is attributed to the attenuation of the inflammatory cascade as a result of the structural integrity, decreased pulmonary and systemic capillary leak, and decreased interstitial edema formation. On the other hand, the attenuation of the production of inflammatory mediators lessens the development of myocardial ischemia as well as reperfusion injury (32).

In conclusion, this prospective randomized study has demonstrated that the administration of either methylprednisolone or aprotinin in open-heart surgeries resulted in an attenuated inflammatory response as based on biochemical analysis of serum inflammatory mediators and on postoperative clinical courses. Both drugs reduced IL-6 and IL-8 production during and after CPB with subsequent improvements in the clinical outcome. However, aprotinin seems to be less effective than methylprednisolone especially

on IL-8 production. Apart from steroid and aprotinin treatments, other strategies for decreasing inflammatory reactions include depletion of leukocytes, use of colloid-primed and heparin-coated extracorporeal circuits, and ultrafiltration. Minimally invasive coronary artery bypass grafting without CPB can be probably added to this list (33).

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# PREDICTORS OF MORTALITY IN ELDERLY PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING

## ABSTRACT

**Objectives:** Coronary artery bypass surgery has been performed in elderly patients ( $\geq 70$  years) with increasing frequency. The aim of this study was to determine the risk factors for mortality in this age group

**Methods:** Over a 2-year period, 705 patients underwent primary coronary artery bypass grafting at Prince Sultan Cardiac Surgery Center and North West Armed Forces Hospital, Saudi Arabia. One hundred one patients were 70 years of age or older. There were 81 men and 20 women, ranging from 70 to 85 years (median age, 75.5 years). We analysed 7 variables: gender (20 females), unstable angina (34 patients), left main coronary artery stenosis (LMS) (13 patients), emergency bypass (34 patients), left ventricular ejection fraction  $\leq 30\%$  (22 patients), post-operative low cardiac output (C.O.P.) (18 patients) and associated cardiac surgical procedures (8 patients).

**Results:** Overall hospital mortality was 3.96%. Higher mortality rate was found in patients with: female gender (15%), pre-operative unstable angina (12%), LMS (15%), emergency operation (12%), EF  $\leq 30\%$  (14%), post-op low C.O.P. (22%), associated procedures (25%).

**Conclusion:** Predictors of mortality in coronary revascularization in elderly patients are: Pre-operative (female gender, unstable angina, low EF%), Operative (left main stenosis, emergent operation, associated procedures) and Post-operative (low C.O.P.).

Hosam Fawzy, Ahmed El-Watidy, Atef Farag, Aitizaz Syed, Arto Nemlander

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## Introduction

Over the last 30 years, advances in operative technique, myocardial protection, and technology have resulted in improved results in cardiac surgery. The late 70s justified expansion of the potential patient population. Elderly patients who had previously been considered high-risk candidates for cardiac operations are now being considered reasonable candidates for surgical intervention (1). By the mid 80s, results in octogenarians suggested that select groups of octogenarians would benefit from cardiac operations. Initially, only the healthiest octogenarians were considered for

operation. However, as experience was gained, patients with mild-to-moderate ventricular dysfunction as well as patients with pre-existing illnesses such as diabetes or peripheral vascular disease were considered reasonable candidates. (2)

Presently, in some centers, approximately half of the patients undergoing coronary artery bypass grafting are in the elderly category. (3)

It has been an impression that these elderly patients frequently have more aggressive anginal syndrome prompting their referral for coronary artery bypass



grafting, despite their advanced age and associated medical problems. Others have reported an increase in operative mortality in the elderly undergoing coronary artery bypass grafting. (4)

The results of open-heart surgical procedures in elderly patients are being scrutinized because past studies have documented increased mortality, complications, and length of hospitalization in elderly patients. (5)

However, the greatest risk of mortality is in those patients who present urgently with unstable anginal syndromes leaving few options for management other than surgical intervention. (6)

Recent reports reveal that cardiac operations for selected elderly individuals who have otherwise good physical and mental health can improve mortality, morbidity, and even quality of life. (7)

With recent advances in myocardial preservation and intensive care, the risks of coronary artery bypass surgery in the elderly may in fact be less than those in the past. (8)

Coronary artery bypass grafting has become an increasingly common procedure in the elderly population. Numerous clinical series have documented the increasing proportion of elderly patients undergoing CABG, as well as the increased morbidity and mortality in this population. (9)

Most reviewers have discussed their experience with elderly patients undergoing CABG as an isolated group without direct comparison with a concurrent group of younger patients. (10)

If cardiac surgical operative mortality and morbidity rates continue to improve, the goals of shorter postoperative hospital stays, a favorable long-term survivals with good quality of life will be accomplished. (11)

### **Aim Of the Work**

The purpose of this study was to identify determinants of operative mortality in elderly patients undergoing coronary artery bypass grafting. Elderly was arbitrarily defined as 70 years of age or older.

### **Material and Methods**

#### **Patients:**

Over a 2-year period, 705 patients underwent primary coronary artery bypass grafting at Prince Sultan Cardiac Center and North West Armed Forces Hospital, Saudi Arabia. One hundred one patients were 70 years of age or older. There were 81 men and 20 women, ranging from 70 to 85 years (median age, 75.5 years). Fifty-two patients (51%) were diabetics whereas forty-five (45%) had hypertension. Sixty-seven (66%) were identified as having stable anginal syndrome with varying degree. They were ranging from Canadian Class III to IV angina status. Thirty-four patients (34%) had unstable angina that dictated emergency surgical interference, with the majority residing in the coronary care unit. These patients all required pharmacological or mechanical resuscitation, or both, before their operative procedures. Sixty-seven (66%) of the patients underwent elective coronary artery bypass grafting, whereas 34 patients (34%) had emergency procedures. Fifty-nine patients (60%) had triple vessel disease and thirteen patients (13%) had left main stenosis. Twenty-two patients (22%) had poor Left ventricular functions (with  $EF \leq 30\%$ ).

**Table (1): Univariate Analysis of Predictors of Mortality in Elderly people.**

Variable	Risk Factor Present (Deaths/patients,%)	Risk factor Absent (Deaths/patients,%)	P-Value
Female Gender	3/20 (15%)	1/81 (1.2%)	0.009
Unstable Angina	4/34 (12%)	0/67 (0%)	0.006
Left Main Stenosis	2/13 (15%)	2/88 (2.3%)	0.037
Emergency Operation	4/34 (12%)	0/67 (0%)	0.006
EF ≤ 30%	3/22 (14%)	1/79 (1.3%)	0.014
Post-op low C.O.P.	4/18 (22%)	0/83 (0%)	<0.001
Associated Procedures	2/8 (25%)	2/93 (2.2%)	0.005

**Table (2): Selected Published Reports of Operative Mortality in Patients 70 Years and Older Undergoing Primary coronary Bypass Grafting.**

Authors	Study Years	Patients Age Range	No. Of patients	Deaths	Mortality (%)
Horneffer, et al (3)	1980-1984	70-85	228	21	9.2%
Acinapura, et al (12)	1981-1986	70-85	685	54	7.9%
Horvath, et al (6)	1977-1986	75-88	222	24	10.8%
Curtis, et al (1)	1978-1991	70-90	668	35	5.2%

### Operative Technique:

All patients received moderate systemic hypothermia (30-32oC) with cardiac arrest achieved by antegrade crystalloid (37%)/ blood (63%) Cardioplegia. Complete surgical revascularization was the goal of operation in all patients. Left internal mammary artery was used in fifty-nine patients (58%). Overall average grafts per patients were 3.2 grafts. Endarterectomy was done in nine patients (9%). Associated procedures were done in eight patients (8%): AVR in four patients, MVR in two patients, Left Ventricular Repair in one patient and VSD closure in one patient.

### Statistical Methods:

Seven clinical or hemodynamic variables were hypothesized. As potential predictors of mortality were scrutinized, univariate

analyses were conducted, examining the variables individually.

### Results

Overall operative mortality (hospital and 30-day death) was 3.96%.

Operative mortality was significantly greater in women, patients undergoing coronary revascularization for unstable angina, those with associated procedures and those requiring preoperative pharmacological or mechanical resuscitation. In 20 women who underwent coronary revascularization, three (15%) did not survive (p = 0.009). In 67 consecutive patients with stable angina there was no operative mortality. Operative mortality in 34 consecutive patients with unstable angina was (12%) (p = 0.006). Out of the thirteen patients with left main stenosis, two patients (15%) died (p = 0.037). Emergency

procedures were carried out in 34 patients; four of them (12%) did not survive ( $p = 0.006$ ). In patients with preoperative low EF% ( $\leq 30\%$ ), three patients of 22 (14%) did not survive ( $p = 0.014$ ). Post-operative low C.O.P was manifested in eighteen patients, four of them (22%) died ( $p < 0.001$ ). With associated procedures, the mortality rate increased. Two of eight patients (25%) who had associated procedures died ( $p = 0.005$ ). Analysis of potential predictors of hospital mortality is shown in table No. (1).

### Discussion

Increasingly, elderly patients are being referred for coronary artery bypass grafting. Acinapura and colleagues (12) reported that the number of patients more than 70 years of age referred for coronary bypass increased from 8% in 1981 to 33% in 1987. We noticed the same observation. As this trend is likely to continue, it seems important to evaluate determinants of operative mortality in the elderly to select the best treatment modality for this group of patients with ischemic heart disease. It seems that the operative mortality for coronary artery bypass grafting in the elderly is greater than that for younger patients. Important comparative information was generated by the Collaborative Study in Coronary Artery Surgery (CASS) (4), wherein 6, 630 patients operated on at 15 institutions showed conclusively that operative mortality increased with age. Operative mortality was 0% in the group 20-29 years of age and increased to 7.9% in the group 70 years of age and older. In addition to advanced age, this large, well-controlled study identified female sex, symptoms of heart failure, left main coronary artery stenosis, impaired left ventricular function, and nonelective operation as other factors associated with

higher operative mortality. The overall operative mortality in this series of only patients 70 years of age and older is similar to that reported by others. Selected Published Reports of operative mortality in elderly patients undergoing coronary artery bypass grafting are shown in table No. (2). We found that female sex is a risk factor for operative mortality, an observation that has been debated by others. Jeffery and colleagues (13) reported no difference in operative mortality between men and women over the age of 70 years undergoing coronary artery bypass operation. It has been suggested by Fisher et al. (14), that the increased operative mortality observed in women is related to body size, the acuity of anginal syndromes and other factors rather than sex alone. Horvath and colleagues (6) reported that anginal syndrome and urgency of operation are predictive of increased operative mortality in elderly patients undergoing myocardial surgical revascularization. Horneffer et al. (3) reported that operative risk increased significantly from 2% in patients undergoing elective operations to 14% in emergency operation.

### Conclusion

Operative mortality after coronary artery bypass grafting increases with advancing age. Despite increased operative mortality in elderly patients undergoing coronary bypass grafting, actuarial survival and functional status of survivors supports the continued use of surgical revascularization in that group of patients.

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# RADIAL ARTERY FOR CORONARY ARTERY BYPASS GRAFTING

## ABSTRACT

**Background:** Use of the radial artery for coronary artery bypass grafting is still controversial. This study was designed to define the feasibility of the radial artery as a conduit for coronary revascularization.

**Methods:** Between January 2001 and December 2003, the radial artery graft was used in 67 patients undergoing coronary artery bypass grafting. To prevent spasm, the radial artery was not skelatonized and papaverine was administrated routinely.

**Results:** No patients sustained a perioperative myocardial infarction in an area revascularized with a radial artery. The overall mortality was zero and there were no cases of radial artery graft failure requiring reoperation. No ischemia of the hand was observed after harvesting of the radial artery. One patient developed post-operative wrist drop due to radial nerve injury.

**Conclusion:** Radial artery is an excellent alternative conduit for myocardial revascularization and may be used safely especially in patients with poor-quality or unavailable saphenous veins.

Hosam F. Fawzy

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## Introduction

The internal mammary artery (IMA) is the best conduit currently available for coronary artery bypass grafting, with a patency rate of 85%-95% after 10 years (1). Use of the left IMA is associated with an improved 10-year survival and fewer late events, such as recurrent angina, myocardial infarction and reoperations (2&3). This encourage many surgeons to use other arterial conduits like right gastroepiploic artery and redial artery in an attempt for total arterial revascularization especially with the high incidence of early saphenous vein graft occlusion. Coronary artery bypass grafting (CABG) using radial artery was first introduced by Carpentier in 1973 (4). However, two years later, he abandoned its

use because of the unexpected high incidence (35%) of graft narrowing and occlusion (5). He explained that graft failure by the spasm of the denervated radial artery. Curtis in 1975 (6) and Fisk in 1976 (7) also reported early radial artery graft failure, caused by intimal hyperplasia.

Twenty years later, Acar and associates (8) revived the use of the radial artery because of unexpected good long -term patency rate of radial artery grafts on angiography in several patients who were initially considered to have occlusion.

These observations, together with the new available antispastic drugs, encouraged us to reinvestigate the use of the radial artery for coronary revascularization.

## Patients and Methods

### Patients:

Between January 2001 and December 2003, the radial artery graft was used in 67 patients undergoing coronary artery bypass grafting. Their mean age was 53.8 years (range, 37 to 77 years). There were 60 (89.5%) male and 7 (10.5%) female patients. The proportion of the operations using the radial artery increased steadily during the study period (Figure 1). Patient characteristics are shown in table 1. Seventeen patients (25.4%) received exclusively total arterial grafts. In 50 patients (74.6%) saphenous vein was used. Eleven patients (16.4%) presented with unstable angina and were operated on an emergency basis. Two patients (3%) presented with redo coronary surgery. Six patients (9%) had severely impaired left ventricular function (ejection fraction < 30%). Fifty-two patients (77.6%) underwent CABG using conventional technique while 15 patients (22.4%) had off pump technique. Conversion from OPCAB to conventional CABG was done in 2 patients (3%). Left anterior descending coronary artery (LAD) endarterectomy and roofing using a small saphenous vein patch (2.5-5 cm) was performed in two patients (3%). Associated mitral valve repair with St. Jude Taylor ring was done in one patient only (1.5%).

### Preoperative preparation:

Allen's test was routinely performed before surgery. The radial artery was chosen from the nondominant forearm. The left forearm was chosen in right-handed patients (n = 63, 94%), the right forearm in left-handed patients (n = 3, 4.5%) and both forearms in one patient only (1.5%). All

peripheral intravenous and arterial lines were placed in the dominant arm.

### Anesthetic technique:

The patients were premedicated using nitrozapam 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. Maintenance was done using Sevoflurane 1-3% with N2O/O2 50/50% in all OPCAB patients. While in conventional CABG, anesthesia was maintained by Sevoflurane 0.5-1%, Pancronium 0.06 mg/kg, Fentanyl 1-2ug/kg during cardiopulmonary bypass time.

### Harvesting Technique:

The entire arm was prepared circumferentially and positioned over an arm-board. An incision was made from the wrist (over the radial pulse) to the mid-antecubital fossa (over the brachial artery pulse). The course of the radial artery was found to very constant and predictable. After the antebrachialis fascia was incised, the brachioradialis muscle was retracted laterally in its entire length before dissection of the radial artery. This maneuver allowed excellent exposure of the entire length of the radial artery. After exposure of the radial artery in one patient, we found entire calcification of the artery which was discarded. Since that time, we shifted to another technique of harvesting that we used a short incision (5cm) over the distal forearm exposing the distal end of the radial artery. Palpation for calcification was followed by digging under the muscles up to the elbow exposing the entire length of the radial artery bit by bit. To avoid spasm, the radial artery was not skeletonized and

papaverine was used routinely. Therefore, the two satellite veins and the surrounding adipose tissue were left attached to the radial artery to preserve its blood supply as much as possible. Initially, the branches of the radial artery were divided with a scissors between haemostatic clips. Recently, we used (Ultracision Harmonic Scalpel) (Johnson & Johnson) to cut the branches of the radial artery. We avoid use of the electrocautery to prevent thermal injury of the artery. This is very important because patency of arterial grafts may be jeopardized by using the electrocautery (9). The entire length of the radial artery was then covered with a sponge soaked with a solution containing papaverine hydrochloride. The radial artery pedicle was then ligated and divided at both ends. The distal 2 or 3 cm frequently were discarded, because the distal end is usually tortuous and is more prone to spasm. To avoid intimal trauma, no metallic probes or dilators were used. The radial artery graft was irrigated very gently with heparinized saline solution and stored in a solution containing papaverine until used. Hemostasis was verified carefully before the arm incision was closed. The antebrachialis fascia was approximated with few interrupted sutures to avoid a compartment syndrome. Skin was closed using skin clips. After the arm incision was closed and dressings and elastic bandages were applied, the arm was repositioned parallel to the patient's body using an elbow pad. The arm and hand again were examined carefully before leaving the operating room. The time required to harvest the radial artery graft ranged from 45 to 60 minutes. However, total operating time was not prolonged because the assistant harvested the radial artery while the attending surgeon opened the sternum and prepared the internal mammary artery while the saphenous vein graft was harvested by another assistant.

### **Radial Artery Characteristics:**

The length of the radial artery graft ranged from 14 to 25 cm (mean, 18 cm) and the internal diameter ranged from 1.5 to 3.0mm (mean, 2.0 mm). The free blood flow measured after dividing the distal end, ranged from 60 to 120 ml/min (mean, 85 ml/min).

### **OPCAB procedures:**

Off - pump surgery was performed with mechanical stabilization using "Medtronic Octopus 3 stabilizers". Intra coronary shunts were used in all the patients. For grafting the distal obtuse marginal vessels the apex of the heart was displaced anteriorly and to the right by carefully pulling on a gauze swab placed behind the heart and held in position by a deep silk suture in the posterior pericardium. Occasionally a "Medtronic Star Fish" suction device on the apex of LV was used to aid the exposure.

### **Cardiopulmonary Bypass (CPB) Management:**

Anticoagulation was achieved with 300 IU/kg Heparin sodium, with an additional dose of 10, 000 IU added to the prime of the cardiopulmonary circuit to ensure an activated clotting time (ACT) of over 480 seconds throughout CPB. The institution of CPB was accomplished using an ascending aortic cannulation and single two-stage venous cannulation (Callmed Laboratories, CA, USA) via the right atrium. Method of acid-base management employed was Alpha - stat.

Standard CPB circuit (Beldico SA/NV, Mache, Belgium) was used, which included a 40- $\mu$ m arterial filter (Gish Biomedical, Inc., CA, USA), a COBE Century roller pump (Cobe Cardiovascular, Inc., CO, USA) and a Terumo Capiiox SX18 hollow-fiber oxygenator (Terumo Corporation, Tokyo, Japan). The extracorporeal circuit

was primed with 1000 ml of Plasmalyte-A solution, 500 ml Gelofusine, 40 mg lasix, 8 mg Dexamethasone and 1.5 g Zinacef. Laminar flow was used with a flow rate of 60-80 cc/kg/min, maintaining cardiac index of 2.4 L / min / m<sup>2</sup> , throughout bypass. Mean arterial pressure (MAP) was maintained at 50 to 80 mmHg during CPB using Phenylephrine. Sevoflurane was used to maintain anesthesia. The patient was cooled down to 32 degrees Celsius during cross-clamping. Mechanical ventilation was discontinued during CPB, but the tracheal tube was not disconnected from the ventilator. No positive air way pressure was maintained during bypass, however a valsalva maneuver was routinely performed at the end of bypass to inflate the lungs prior to starting mechanical ventilation.

#### **Distal Anastomoses:**

All distal anastomoses were performed using continuous 7/0 or 8/0 polypropylene suture. We tried to use the radial artery (RA) together with LIMA and RIMA to achieve total arterial revascularization. However, saphenous vein graft had to be added in many cases when many distal anastomoses were required. A total of 232 distal anastomoses were performed (mean 3.5 grafts per patient), included 71 LIMA, 11 RIMA and 71 saphenous vein grafts. The remaining 79 distal anastomoses were performed with radial artery grafts (mean, 1.2 graft per patient). The radial artery was used as a single graft in 49 patients (including one patient in whom both radial arteries were used), as a sequential graft in 14 patients, and as a Y grafts in 2 patients. A piece of the radial artery was used to extend LIMA in 2 patients and RIMA in one patient. The most frequent targets were the obtuse marginal branches of the circumflex artery (Table 2).

#### **Proximal anastomoses:**

Using a partial aortic occlusion clamp on the ascending aorta, the proximal anastomoses were performed using continuous 6/0 polypropylene suture. In some cases of conventional CABG, it was done while the aortic cross clamp still in situ to avoid application of the aortic side occlusion clamp to aorta. In 2 patients, the proximal end of the radial artery was anastomosed to the internal mammary artery. These patients had a heavily calcific aorta, which precluded the safe application of the aortic side occlusion clamp.

#### **Statistical analysis:**

Univariate analysis and comparison of risk factors was conducted using Chi-square test to compare results obtained with a similar group of patients who underwent CABG without the use of the radial artery at our institution during the same period of the study. P-values less than 0.05 were considered statistically significant.

#### **Results**

There were no ischemic or functional complications in the arm or the hand after removal of the radial artery. One patient developed dropped left wrist after harvesting the radial artery of the left forearm most likely due to compression of the radial nerve in the spiral groove of the humerus. Five patients developed transient dysesthesia of the thumb with no functional abnormalities was observed. All patients were followed up for a period ranging from 2 to 12 months (mean, 6 months). All were alive and free of symptoms. No functional disturbances related to radial artery harvesting were reported. Three patients (4.5%) had a superficial infection of the arm, which was managed successfully with simple draining



**Table (1): Patient Characteristics.**

Characteristics	Number	Percent
Age > 65 years	12	18%
Age < 65 years	55	82%
Female Patients	7	10.4%
Male Patients	60	89.5%
Diabetes Mellitus	31	46.3%
Congestive Heart Failure	3	4.5%
LVEF < 30%	6	9%
Recent MI (< 90 days)	19	28.4%
Left Main Stenosis	6	9%
Previous CABG	2	3%
Elective operations	56	83.6%
Unstable Angina	11	16.4%
Pre-op IABP	4	6%

**Table (2): Distal Anastomoses Using The Radial Artery Graft.**

Vessel grafted	Single (n =49)	Sequential (n =28)	Y-graft (n =2)	Total (n =79)
LAD	4	2	0	6
Diagonals	2	3	1	6
RI	6	5	0	11
Obtuse marginals	33	16	1	50
RCA	2	0	0	2
PDA	2	2	0	4

LAD = Left Anterior Descending Coronary Artery.

RI = Ramius Intermedius Coronary Artery.

RCA = Right Coronary artery.

PDA = Posterior Descending Coronary Artery.

**Table (3): Univariate Analysis of Preoperative Risk factors: Comparison of CABG Patients With and Without The Use of Radial Artery Graft.**

Risk Factor	CABG with RA (n = 67)	CABG without RA (n = 88)	P-value
Age > 65 years	12 (18%)	35 (40%)	0.004
Female Patients	7 (10.5%)	22 (25%)	0.02
Diabetes Mellitus	31(46.3%)	48 (54.5%)	NS
LVEF < 30%	6 (9%)	23 (26%)	0.007
Recent MI (< 90 days)	19(28.4%)	21 (23.9%)	NS
Left Main Stenosis	6 (9%)	8 (11. 9%)	NS
Previous CABG	2 (3%)	0 (0%)	NS
Unstable Angina	11 (16.4%)	18 (20.1%)	NS
Pre-op IABP	4 (6%)	10 (11.4%)	NS

**Table (4): Univariate Analysis of Post-operative Complications and Mortality: Comparison of CABG Patients With and Without The Use of Radial Artery Graft.**

Complications	CABG with RA (n = 67)	CABG without RA (n = 88)	P-value
Perioperative MI	1 (1.5%)	3 (3.4%)	NS
Post-op CHF	2 (3%)	3 (3.4%)	NS
Graft failure	0 (0%)	1 (1.1%)	NS
Renal Failure	1 (1.5%)	3 (3.4%)	NS
Pneumonia	4 (6%)	4 (4.5%)	NS
Sternal Infection	4 (6%)	4 (4.5%)	NS
Neurological	2 (3%)	1 (1.1%)	NS
Need for IABP	5 (7.5%)	10 (11.4%)	NS
Mortality	0 (0%)	5 (5.7%)	0.047

and antibiotics. No re-exploration for bleeding from the radial artery-harvesting site was found in our series.

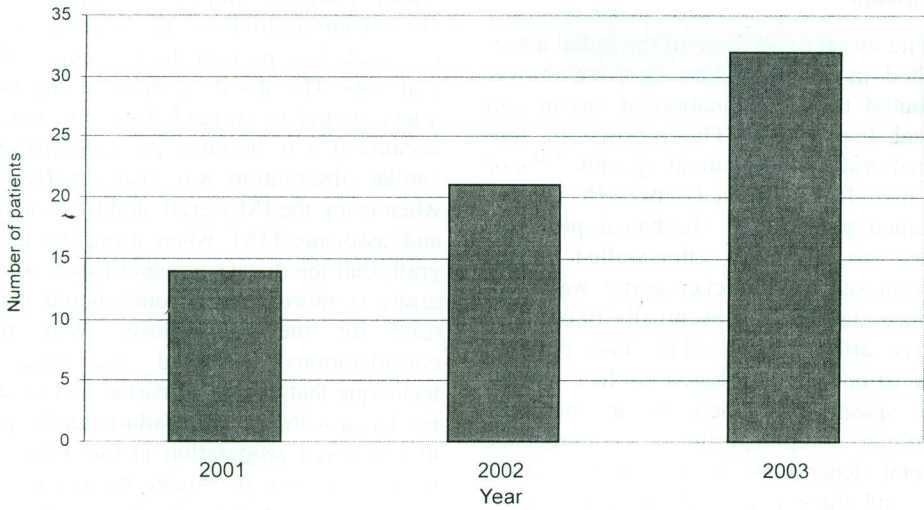
There was no statistically significant difference in the prevalence of the risk factors, when our present series was compared with a group of patients who underwent coronary artery revascularization without the use of radial artery at our institution (Table 3). One patient (1.5%) sustained a perioperative myocardial infarction. That was not in the area supplied by the radial artery graft. There was an accidental cut of the LIMA graft to LAD during hemostasis. LIMA was ligated followed by reanastmosis of LAD using a piece of the saphenous vein graft. Afterward, the patient suffered anterior wall myocardial infarction. Post-operative congestive heart failure occurred in 2 patients (3%), both improved with medical treatment. In our present series, there were no cases of radial artery graft failure requiring reoperation. Post-operative low cardiac output was encountered in 5 (7.5%) patients; all of them required IABP

insertion. Post-operative renal failure developed in one patient (1.5%) who improved with hemodialysis for short period. Post-operative pneumonia developed in 4 patients (6%), they responded well to antibiotics and chest physiotherapy. One of them required reintubation for proper pulmonary toilet. Four patients (6%) developed sternal wound infection; one of them required removal of two sternal wires that caused wound sinus. The other three had superficial wound infections that responded well to proper antibiotics.

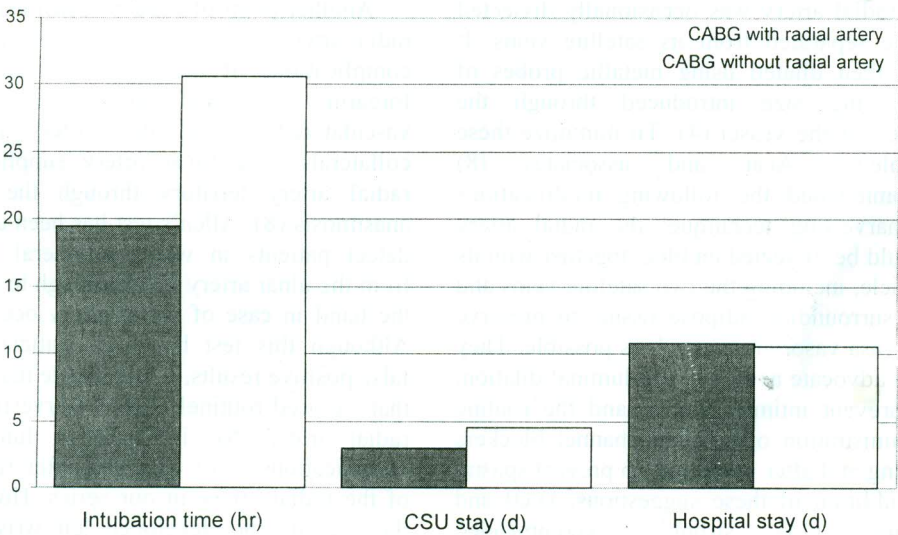
Univariate analysis of post-operative complications comparing radial group results with the results of non-radial artery group, showed no statistically significant difference between both groups. The 30-day hospital mortality was zero and that was significantly less than in non-radial group (see table 4).

Ventilation time recorded a lower mean in radial artery group than non-radial group. While intensive care unit and hospital length of stay were comparable in both groups (see Figure 2).

**FIG. 1 Number of CABG patients with RA**



**FIG. 2 Comparison of CABG patients with and without RA**



## Discussion

The initial experience of the radial artery resulted in a high failure rate, which was attributed to a combination of spasm and intimal hyperplasia. The patency of free arterial grafts is suboptimal, as only 77% of the free IMAs studied after 18 months remained patent (10). Technical problems related to a small, thin-walled vessel anastomosed to a thicker aortic wall may produce stenosis and eventually thrombosis of free arterial grafts (11). Two possible explanations are attributed to free arterial graft spasm: that there is an increased reaction to norepinephrine, as a consequence of total denervation of free arterial grafts (12), and there is a total disruption of the vasa vasorum at both ends (13). Early failure of the radial artery graft also has been attributed to generalized intimal hyperplasia (6). The harvesting technique itself as well as the preparation of the graft used 20 years ago could have been responsible for spasm: the radial artery was occasionally dissected alone separated from its satellite veins. It was then dilated using metallic probes of increasing size introduced through the lumen of the vessel (4). To minimize these problems, Acar and associates (8) recommended the following modifications in harvesting technique: the radial artery should be dissected en bloc, together with its pedicle, including the two satellite veins and the surrounding adipose tissue, to preserve the vasa vasorum as much as possible. They also advocate avoiding intraluminal dilation, to prevent intimal trauma, and the routine administration of calcium channel blockers during and after operation, to prevent spasm. In addition of these suggestions, Dietl and Benoit (14) strongly recommended retracting the belly of the brachioradialis muscle before dissecting the radial artery pedicle, to minimize the risk of injury or

spasm. They also emphasized that the use of electrocautery to divide the branches should be avoided, to prevent thermal injury of the graft (9). The distal segment of the radial artery should be discarded in some patients because it may be more prone to spasm. A similar observation was made by He (15), when using the IMA graft, and by Grandjean and associate (16), when using the RGEA graft, that the distal segment of these arterial grafts is more reactive and should not be used for the anastomosis. With these considerations in mind, we used our technique that described earlier and we were not faced with any graft failure due to spasm that required reoperation in our series. We used papaverine to irrigate the radial artery graft instead of calcium channel blockers. Curtis and associates (6) reported a graft failure rate of 65% in their series of 29 patients while Fisk and co-workers (7) reported 50% graft failure rate in their series.

Another point of concern when using the radial artery is the potential risk of ischemic complications of the hand. However, the forearm and the hand are mainly vascularized by the ulnar artery and its collaterals. The ulnar artery supplies the radial artery territory through the distal anastomosis (8). Allen's test has been used to detect patients in whom collateral flow from the ulnar artery is not enough to supply the hand in case of radial artery occlusion. Although this test has been criticized for false positive results, it is a simple maneuver that we used routinely before harvesting the radial artery. No ischemia or functional complications were observed after removal of the radial artery in our series. However, the patient who developed left wrist drop post-operatively, neurological explanation was found to be most likely due to compression of the radial nerve in the spiral

groove of the humerus during outstretching of the arm against the arm board during the all time of surgery. Thereafter, once the arm incision was closed and dressings and elastic bandages were applied, the arm was repositioned parallel to the patient's body using an elbow pad. The patient showed slight improvement by physiotherapy. Transient dysesthesia of the thumb with no functional disturbances was observed in 5 patients, probably due to surgical trauma of the superficial branch of the radial nerve. Acar et al, (8) reported 8 patients in his series who developed transient dysesthesia of the thumb. Three patients (4.5%) developed superficial radial artery harvesting site infection. They were managed successfully with simple draining, antibiotics and control of hyperglycemia.

Trick et al, (17) reported 12.3% of harvest site infection (HSI) of his 309 patients who underwent radial artery harvesting during CABG procedure. They explained this high rate of infection by that the radial artery harvest site; if on the right, is close to the surgeon's back, which is not sterile, and if on the left, is close to the surgical assistant's back. This close proximity may make it difficult to perform radial artery graft harvesting without contaminating the incision site.

In summary, use of the radial artery does not increase morbidity or mortality in our study. Perioperative myocardial infarction, congestive heart failure, and need for intra aortic balloon pump (IABP) were not related to failure of the radial artery graft.

### Conclusion

Radial artery graft is an excellent alternative conduit for myocardial revascularization and it can be used safely, especially in patients with unsuitable or unavailable saphenous veins. Stress should be made on using proper harvesting

technique, to prevent intimal damage, and minimizing the risk of spasm and intimal hyperplasia, to improve long-term patency. However, a randomized study including large number of patients with control angiogram and long-term follow up is necessary before reaching any definite conclusion.

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## CARDIAC SURGERY IN THE ELDERLY ANALYSIS OF MORTALITY AND MORBIDITY

### ABSTRACT

**Objective:** Analysis of mortality and morbidity in the elderly undergoing cardiac surgery. Identification of risk factors using logistic regression analysis.

**Patients & Methods:** Patients seventy years or older were included in this analysis. The data of 100 consecutive patients operated from 01.01.2000 to 31.01.2003 were revised from the database of our department and the hospital medical records section. There were 73 male and 27 female patients. Their age was  $74.76 \pm 4.3$  (mean  $\pm$  S.D.) years. The median Euro score was seven, which corresponded to the 7.5% predicted mortality. The pre-operative ejection fraction and pulmonary artery pressure were  $41.76 \pm 4.3\%$  and  $30.49 \pm 11.54$  mmHg respectively. Seventy-four patients were diabetic, 67 were hypertensive, seven had left ventricular failure, nine had recent myocardial infarction, nine were on intra-aortic balloon pump, nine had COPD and seven had carotid artery disease. Over 35 pre and post-operative variables were identified and the data was analyzed by electronic spreadsheet Microsoft® Excel. Analysis was carried out on post-operative ventilation time, Intensive care and hospital stay, morbidity and mortality.

**Results:** The mean post-operative ventilation time was  $37.51 \pm 10$  hours and the total hospital-stay was  $14 \pm 9$  days. The 30-day mortality in the group was eight percent that is surprisingly better than the predicated mortality set by Euro score. There was one superficial wound infection and one patient developed mediastinitis both however have survived. The short-term follow-up was 100% successful and the mean follow-up time is 18.5 months. Nevertheless, there is statistically significant difference of post-operative ventilation and mortality between the groups. The patients requiring coronary bypass grafting with valve replacement and on pump beating coronary artery bypass had the highest mortality followed by those who underwent conventional coronary bypass surgery. The off pump coronary bypass graft group had no mortality ( $P = 0.016$ ).

**Conclusions:** Patients should not be denied heart surgery because of their age. Although there is some increased intensive care as well as hospital stay most of these patients usually do benefit from surgery and live a meaningful life. The off pump coronary artery bypass technique proved to be the least harmful to these patients and should therefore be utilized whenever technically is possible.

**Keywords:** Old age, cardiac surgery, risk predictive, coronary artery bypass grafting. Cardiac surgery in the Elderly analysis of mortality and Morbidity.

Ayman A. Sallam, FRCS, Bakir M. Bakir, MD, Ashraf A.Esmat, MD, Anjum Jalal, FRCS, Mohamed Fouda FRCS, Ahmed Al-Saddique, FRCS.

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## INTRODUCTION

With the unprecedented improvement in health care people are generally living much longer than they ever used to and the number of the senior population is on the rise. A considerable number of them would inevitably need cardiac surgery at some point of their life. In fact in some places they constitute a sizable number of the patients' population, for instance, in Germany 37% of patients undergoing heart surgery in the year 2000 were 70 years of age and older (1). The progress in anesthesia, surgical techniques and post-operative care has made heart surgery possible for this age group. Despite the decrease in overall perioperative mortality over the last two decades in cardiac surgery patients; age is still considered an independent risk factor for both morbidity and mortality. This is obviously due to no small part to the increased incidence of co-morbid conditions and diminished physiologic reserve (2). The risk of neurologic events is higher among individuals above seventy years of age (3). Age has always been recognized as an important factor in patients' selection for cardiac procedures (4,5). But despite of all apparent negativity favorable outcomes can still be expected in elderly patients undergoing cardiac surgery. The aim of this work is to analyze the pattern of morbidity and mortality in the elderly patients subjected to cardiac surgery.

## Patients and Methods

Patients seventy-years or older were included in this study. One hundred patients that were operated from January 2000 to January 2003 and were available for analysis. The data was obtained from the department's database and from the medical records of these patients. Details of pre-

operative, operative and postoperative course have been thoroughly examined. The thirty days mortality was included even if it occurred outside the hospital.

There were 73 males and 27 females with a mean age of 74.76 ( $\pm$  4.3) years. 51 patients were subjected to conventional coronary artery bypass grafting (CABG); 24 patients Off-pump beating CABG (OPCAB); 11 patients On-pump beating CABG; six patients subjected to CABG with Single valve replacement, four patients to CABG with mitral and aortic valve replacement, three required valve replacement and one patient had Bentall's procedure. Over 35 pre-operative and post-operative variables were identified and entered into Microsoft® Excel. These parameters were examined post-operative ventilation time, Intensive care unit (ICU) stay, hospital stay, morbidity and mortality. This was done on the group as a whole and then separately for the various procedures carried out. Conventional CABG, OPCAB, and on-pump beating CABG. The differences of mortality were compared using Chi-square test for the categorical variable and either t-test or ANOVA for continuous variable using © SPSS for Windows © SPSS Inc., In addition these patients are being followed-up for any cardiac event and for their quality of life after surgery.

## Results

Where different types of cardiac surgery have been performed on 73 males and 27 females, 74% of patients were diabetics and 67% hypertensives. 57% of patients had a Euro score varied between 6-10. 30% had a Euro score less than 5 and 13% more than 10, with overall predicted mortality around 15%. Carotid artery stenosis was present in



**Table (1): Pre-operative categorical variables are shown.**

Parameter	Frequency
Gender (Male)	73
Diabetics	74
Hypertensive	67
Congestive Heart Failure	6
Pre-operative IABP	9
Recent myocardial infarction	8
Carotid artery stenosis	8
COPD	9
Renal failure	18
Cerebro-vascular events	1
EURO-SCORE	
0-5	30
6-10	57
>10	13

**IABP = Intra-aortic balloon pump.**

**COPD = Chronic obstructive pulmonary disease.**

eight patients as diagnosed by carotid duplex imaging.

Renal failure was thought to be present when serum creatinine exceeded 200 mmol/l. eighteen patients had renal failure. Congestive heart failure was present in 6 patients, 9 had COPD. Recent Myocardial infarction in 8, and 9 were taken to surgery with intra-aortic balloon inserted preoperatively.

The mean ejection fraction was 41.65% (range between 20%-60%) and the mean

pulmonary artery pressure was 32.42 mmHg (range between 30-65 mmHg).

Post-operative variables (table 3, 4) revealed that the mean ICU stay in hours was 93.61 hours and the mean ventilation time in hours was 43.84 hours with a considerable standard deviation explained by the variations between the patients as some needed short ICU stay of 48 hours or less and other for months and same observation was found in ventilation time. The mean hospital stay was 14.46 days.

Out of the 18 patients with renal failure, two needed dialysis (11.1%) with the use of hemofiltration in ICU. Four patients had superficial wound infection, and one had sternal dehiscence due to mediastinitis. Two patients of the nine with COPD required re-intubation and mechanical ventilation. Six patients developed atrial fibrillation treated with anti-arrhythmic drugs. Four developed low cardiac output syndrome due to peri-operative myocardial infarction. The overall mortality rate was 8 % mainly due to peri-operative myocardial infarction, multiple organ failure, bleeding and cerebrovascular accident.

86 patients were underwent isolated CABG. This group of patients are divided them into 3 subgroups; group A; conventional CABG (51patients), group B: OPCAB (24 patients) and group C; On-pump beating CABG (11 patient). Comparison of pre operative categorical variables is shown in table V.

**Table (2): Operative categorical variables are outlined.**

Variables	Frequency
Valve replacements	03
CABG	86
CABG+ single valve replacement	06
CABG+ Double valve replacement	04
Bental procedure	01

**Table (III): Showing different variables:**

Variable	Mean	Standard error mean	Standard deviation
Pre-operative:			
Age (years)	74.79	0.43	4.29
Ejection Fraction (%)	41.65	4.29	12.89
Pulmonary Artery Pressure (mm Hg)	32.42	1.34	13.40
Post-operative:			
ICU-stay (hours)	93.61	11.49	114.16
Ventilation (hours)	43.84	12.92	129.22
Hospital stay (days)	14.46	01.03	10.30

ICU= Intensive Care Unit.

**Table (IV): Presenting post-operative complications.**

Complications	Frequency
Renal impairment	18
Pulmonary problems	09
Superficial wound infection	04
Sternal dehiscence	01
Atrial fibrillation	06
GI-bleeding	03
Low COP syndrome	04
Mortality	08

GI = gastro-intestinal. COP = cardiac output.

**Table (V):**

Variable	Group A	Group B	Group C	Chi-square	P-value
Male: female	39:12	20:04	09:02	0.22	0.77
Diabetes					
Yes: No	41:10	24:06	10:01	1.21	0.55
Hypertension					
Yes: No	34:17	21:03	10:01	0.77	0.69
CCF					
Yes: No	03:48	01:23	0:11	0.72	0.69
Recent MI					
Yes: No	04:47	02:22	01:10	0.02	0.99
Renal Failure					
Yes: No	09:42	03:21	02:09	0.35	0.84

CCF= congestive heart failure. MI= myocardial infarction.

**Table (VI): Comparisons of post-operative complications in the different groups of CABG are outlined.**

Complication	Group A	Group B	Group C	Chi-square	P-value
Renal failure					
Yes: No	10:41	05:19	01:10	5.0	0.28
Wound infection	01:50	02:22	01:10	9.25	0.05
Yes: No					
Lung problems	08:43	0:24	01:10	8.0	0.09
Yes: No					
AF					
Yes: No	02:49	01:23	02:09	4.18	0.38

AF = atrial fibrillation.

**Table VII compares the mortality in the different three groups of CABG.**

Mortality	Group A	Group B	Group C	Total	Chi-square	P-value
Alive	49	24	08	81		
Dead	02	Nil	03	05	11.07	0.004
Total	51	24	11	86		

The highest mortality was in-group C of patients 37.5% but this is statistically difficult to accept since the number of patients was small 11patients. In addition this group of patients was a relatively at higher risk than those falling in group A and B as seen from their higher pulmonary artery pressure and lower ejection fraction which reflects disturbed left ventricular function.

Group B patients had less ventilation time because they sailed through without any complications. There were no significant differences among these groups of patients in terms of ICU and Hospital stay.

In the 92 patients who survived, the initial post-operative stress has been followed up for a period of 18.5 months. During this time five patients had recurrent

symptoms of angina (5.4%); coronary angiography was not done, as they felt comfortable on medical treatment. One patient (1.07%) died seven months post-operatively; the cause of his death was unclear. Out of the survivors 85 patients (93.3%) enjoy a healthy life.

### Discussion

The number of the elderly patients going for cardiac surgery is definitely on the rise. This study shows cardiac surgery can be performed safely with reasonable risk albeit higher than in younger patients. Early on some have reported operative mortality to be three times higher (6,7) it is our estimation that the on-going trend of doing CABG off-pump technique will further decrease the risks. As it is less stressful and would be better tolerated by those individuals with

limited physiologic reserve and co-morbid conditions that might coexist (8).

The overall mortality in this group of patients was around 8 %. It is interesting to note that most of these patients had a Euro-score of 10 or more that usually corresponds to a mortality rate around 15%. This we believe is largely due to improved surgical techniques and also due to the great improvement in the post-operative care. It is worth mentioning that our policy in ICU calls for the liberal use of Prisma dialysis, mechanical ventilation, and or intra-aortic balloon pump. The main cause of death was low cardiac output syndrome associated with renal failure seen in six patients, one patient because of bleeding diathesis that was not controllable and one patient died because of status epilepticus that led to coma and eventually death. These results are in line with what is currently reported in the literature. Gatti et al published a series of 73 patients with mortality rate of 8.2% and the main cause was myocardial infarction and low cardiac output (9). Other reports have contributed their in-hospital mortality mainly to atrial fibrillation and diabetes (1). Analysis of data revealed that there was no mortality in the group who underwent CABG alone using off-pump technique (OPCAB). We believe that this is largely due to the fact that these patients do not experience the systemic inflammatory response syndrome that cardiopulmonary bypass entails and those frail patients with limited reserve have difficulty coping with. Stamou and colleagues reported a less than 2% in-hospital mortality rate for octogenarians subjected to CABG by off-pump technique (10). This notion has been supported by other published reports (2,11).

Patients who underwent CABG on-pump beating heart technique had the highest mortality rate in this group. It is worth mentioning that these were the sickest of the group. Their parameters of high pulmonary artery pressure and lower ejection fraction are guarantors of a dismal outcome and they would have not survived conventional CABG. Most of these patients were planned for OPCAB but we had to convert to on-pump beating CABG as their hearts could not tolerate the slightest manipulation.

Other complications were superficial wound infection (4%), sternal dehiscence (1%), atrial fibrillation (6%), gastrointestinal bleeding (3%) & Low cardiac output syndrome due to peri-operative myocardial infarction (4%). All these complications are familiar problems to cardiac surgery and their rate of occurrence is similar with what is mentioned in the literature relative to this age group (12,13). Stamou et al (10) showed that all in-hospital adverse events increased with advancing age as he compared elderly patients to those younger than 50 years of age and found that they are 3 times more likely to develop respiratory failure, 3.9 times more likely to develop renal failure.

Ennabli & Pelletier showed a higher rate of preoperative myocardial infarctions in elderly patients than in younger (14). Fruitman and colleagues reported 42.5% rate of atrial fibrillation in octogenarians (15). Interestingly this was not the case in our group of patients. There was no significant difference in the hospital stay between the subgroups.

All recorded preoperative, operative and post-operative data were analyzed for relative risk for post-operative mortality.

Preoperative IABP, renal failure, COPD, combined CABG and single or double valve replacement, sternal dehiscence, and the need for dialysis for renal failure, were significant risk factors for early death. Prolonged ventilation and postoperative cerebrovascular stroke were significant risks for late death. Therefore, attention should be paid to asepsis, renal function, ventilation and nutritional status for elderly patients.

It is interesting to note that in this study we didn't find that urgent or emergent operation did not add to the risk for post-operative mortality. Most of these patients had in addition other co-morbid conditions.

As overall we were able to conclude that the use of OPCAB surgery reduces the postoperative morbidity and mortality. Similar results have been shown by others like Boyd et (16) who showed significant decrease in morbidity and mortality furthermore he reported a saving of 14% per patient when OPCAB is performed in 70 years and older in comparison with conventional revascularization with cardiopulmonary bypass. Hirose et al (17) concluded in their study that OPCAB successfully facilitates early recovery and reduces the incidence of post-operative complications among elderly patients.

We conclude that cardiac surgery can be performed at a reasonable risk in elderly patients. Adopting the OPCAB technique will significantly lower the risk of mortality and post-operative morbidity. Furthermore, one should always be optimistic for these individuals because even after a prolonged stay in intensive care services many manage to improve and live long enough to enjoy a quality of life as good as their healthy colleagues.

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## **SURGICAL TREATMENT OF SUBAORTIC STENOSIS: RESULTS, RISK FACTORS FOR EARLY MORTALITY, RECURRENCE AND REOPERATION**

### **ABSTRACT**

**Objectives:** The aim of the study was to analyze the long-term results of subaortic stenosis relief and the risk factors associated with recurrence and re-operation.

**Methods:** During the last two decades, 250 patients with subaortic stenosis were operated upon. The mean age of our patients at the time of surgery was 8 years (range 1-30 years). Sixty percent of our patients were asymptomatic, 30% presented because of shortness of breath on severe exertion (NYHA I -II) & 10 % were in NYHA III -IV. Aortic regurgitation (AR) of mild to moderate degree was diagnosed in 75 patients (30%) while severe aortic regurge was present in only 8 patients (3.2%). Preoperatively, the mean gradient across the left ventricular outflow tract (LVOT) was  $79 \pm 25$  mmHg (range 30- 150). Twenty three patients (9%) had previous operations, PDA ligation (5 patients), coarctation repair (8 patients), & VSD closure in (10 patients). Discrete subaortic stenosis was present in 225 patients (90%) while tunnel obstruction was present in only 25 patients (10%). For patients with discrete stenosis membranectomy was done in 95 patients (36%), myotomy in addition to membranectomy in 55 patients (22%) & myectomy was added in 75 patients (30%). For patients with tunnel obstruction, myomectomy was performed in 13 patients, modified Konno in 7 patients (2.8%) & Konno-Rastan in 5 patients (2.2%).

**Results:** For all patients, early mortality was 2.8% (7 patients), 5 patients (2.2%) from the discrete subaortic group while two patients were from the tunnel group. Four patients (1.6%) developed complete heart block and required insertion of permanent pacemaker and 5 patients (2.5%) were re-explored because of excessive postoperative bleeding. Within  $5.5 \pm 2.8$  years a recurrent gradient more than 30 mmHg was found in 40 patients (16%), 22 of those who had reoperation. According to multivariable Cox regression analysis, preoperative NYHA functional class III- IV influenced survival ( $p = 0.01$ ), while recurrence and reoperation were influenced by immediate postoperative left ventricular outflow tract gradient & surgical technique performed at initial operation. Relief of subaortic stenosis improved the degree of AR in 73 patients & stabilizes it in 7 cases. Actuarial survival at 1, 5, 10, and 15 years was 97.4%, 96%, 95%, and 94% respectively.

**Conclusion:** Surgical treatment of subaortic stenosis provides excellent results. Myectomy in conjunction with membranectomy provides superior results in patients with discrete subaortic stenosis as regards recurrence of subaortic stenosis and reoperation, while for patients with tunnel obstruction, performing myectomy alone was associated with high incidence of recurrence of LVOT obstruction and reoperation when compared to modified Konno and Konno-Rastan aorto-ventriculoplasty.

Hany A. El Maboud MD; Ahmed Samy MD; Hatem EL Bawab MD; Hassan Mofteh MD  
Hossam El Okda MD; Mohamed A. El Fatah MD.

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## INTRODUCTION

Left ventricular outflow tract (LVOT) obstruction caused by subaortic obstruction covers a wide range of anatomic lesions that can be subdivided into 2 main categories, discrete and diffuse subaortic stenoses. Subaortic stenosis can be isolated or associated with other heart defects, particularly with multilevel LVOT obstruction. Discrete subaortic stenosis was first reported by Chevers (1) in 1842 and 2 distinct anatomic types, membranous and fibromuscular, have since been identified (2).

Although subaortic stenosis is generally considered a progressive lesion, the rate of progression is variable. Apart from the risk of progression of the subaortic stenosis, affected patients face an increased risk of bacterial endocarditis and of aortic insufficiency when fibrous strands extend into the base of aortic leaflets (3). Myocardial hypertrophy as a result of the hemodynamic stress may be more or less important and is generally more pronounced at the septal insertion of the membrane. More severe forms of subaortic stenosis are those caused by either short- or long-segment fibromuscular tunnel (4). The aortic annulus may be small with a normal aortic valve, but valvular aortic stenosis may coexist. In those cases concentric left ventricular hypertrophy is usual.

Subaortic stenosis may also be the consequence of abnormal mitral valve insertion (5) or accessory tissue (6), abnormal insertion of mitral papillary muscle (7), abnormal muscular bands within the LVOT (8), or posterior displacement of the infundibular septum without ventricular septal defect (9) associated or not with a subaortic membrane. Finally, subaortic

stenosis can be part of a more complex syndrome of multilevel left ventricular obstruction (Shone complex) (10) for which the optimal strategy remains to be defined.

Membranectomy, with or without septal myotomy or myectomy, has been the accepted method for treatment of fixed subaortic stenosis, and many centers have reported early and intermediate-term follow-up (11). There remain, however, controversies regarding operative methods and uncertainties about recurrence of subaortic obstruction after repair and development of late aortic valve insufficiency.

To study the early and long-term effects of operation for subaortic stenosis on relief of the LVOT gradient and on development of aortic valve insufficiency, we analyzed the data of all patients who have had surgical treatment of fixed subaortic stenosis at Ain Shams University hospitals.

## Patients and Methods

During the last two decades, 250 patients underwent surgical correction of subaortic stenosis at Ain Shams University hospitals. Patients having operation for hypertrophic obstructive cardiomyopathy or Shone's syndrome were excluded from our study.

The lesions were classified as discrete stenosis or tunnel stenosis. Discrete subaortic stenosis is characterized by a complete or incomplete encirclement of the LVOT by a membrane or short-segment stenosis consisting of fibrous tissue or fibromuscular tissue. In patients with tunnel stenosis, there is hypertrophy of the ventricular septum with endocardial thickening of variable length.

Age of our patients ranged from 1 to 30 years with a mean of 8 years. Sixty percent



of our patients were asymptomatic and discovered during routine clinical examination while 30% had shortness of breath on moderate and severe exertion (NYHA I-II). The rest of our patients (10%) were in NYHA class III to IV.

In all patients the diagnosis was established by transthoracic echocardiography and confirmed by direct observation during surgery. Cardiac catheterization was done for only 20% of our patients. The peak systolic pressure gradient (PSPG) measured across the LVOT was used to quantify the degree of obstruction. It ranged from 30–150 mmHg with a mean of  $79 \pm 25$  mmHg. Discrete subaortic stenosis was diagnosed in 225 patients (90%), while tunnel obstruction was diagnosed in 25 patients (10%). Aortic valve regurgitation (AR) was detected in 83 patients (32%). Mild AR was found in 50 patients (20%), moderate in 25 patients (10%), and severe in only 8 patients (2.8%). Valvular aortic stenosis was present in 15 patients (6%) and in 9 patients (3.6%) there were hypoplastic aortic annulus. Associated anomalies are summarized in table (1).

In symptoms free patients the decision for surgical repair was taken when the PSPG was 50 mmHg or more. Unless more than mild AR was diagnosed before surgery, at that time, we accept lower gradient across the LVOT (30 mmHg or more). Previous operations were performed in 20 cases (table 2). PDA ligation in 5 patients, aortic coarctation repair in 8 patients, and VSD closure in 10 patients. Aortic valve replacement was done in all 11 cases presented with severe aortic regurgitation. Other associated cardiac anomalies were treated simultaneously.

### Operative procedures:

Were always conducted with hypothermic cardiopulmonary bypass. Myocardial protection was ensured by crystalloid or blood cardioplegic administration. The mean cardiopulmonary bypass time was  $75 \pm 23$  minutes and the mean cross clamp time was  $38 \pm 18$  minutes. Obstructive lesion was approached through an oblique aortotomy in all cases. After careful inspection of the aortic cusps, they were retracted and the membrane was carefully excised with combined sharp and blunt dissection. Septal myotomy or wedge myectomy were additionally performed below the commissure between the right and left coronary cusps. The goal was to obtain a free patent subaortic area that would admit without friction a Hegar dilator matched with body surface area.

The myotomy consisted of a deep incision made at the nadir of the right aortic cusp into the septal muscle that protruded into the LVOT. When left ventricular septal myectomy was performed, a second incision was made caudal to the commissure between the right and left aortic cusps. These incisions were joined by another incision at their superior ends, and a deep wedge of septal muscle was resected. The width of the resected wedge ranged between 5 and 20 mm. Additional tissue was resected back to the mitral valve and apically to the level of the papillary muscles to provide maximal relief of the obstruction.

In patients with discrete subaortic stenosis, isolated membranectomy was done in 95 patients (38%), membranectomy together with myotomy in 55 patients (22%), and septal myectomy in 75 patients (30%) (Figure 1). On the other hand, for the group of patients with tunnel obstruction, myectomy was performed in 13 patients

**Table (1): Cardiac anomalies associated with SAS.**

Associated anomaly	No. Of Patients
Atrial septal defect	
Ostium secundum	10
Ostium primum	2
Aortic valve stenosis	
Valvular stenosis	15
Annular stenosis	9
Aortic valve regurgitation	83
Ventricular septal defect	15
Pulmonary stenosis	8
Supravalvular aortic stenosis	2
Patent ductus arteriosus	10
<b>Total</b>	<b>154</b>

(5%), modified Konno procedure in 7 patients (2.8%), and Konno-Rastan aorto-ventriculoplasty procedure in 5 patients (2.2%) (Figure 2).

In situations of severe tunnel subaortic stenosis in which the aortic valve annulus was near normal in size and there was no significant disease of the aortic valve, a modification of the Konno-Rastan operation has been performed. For this procedure, an oblique aortotomy was made toward or across the commissure between the left and right aortic cusps, a transverse incision was made in the right ventricular outflow tract, and a curved clamp was passed through the aortotomy and palpated thorough the septum. The interventricular septum was incised longitudinally from the base towards the apex to the left of the nadir of the aortic cusps, and the edges of the incision were retracted, so the septal obstruction on the left ventricular side could be visualized fully and resected. The ventricular septal incision and the right ventriculotomy were then closed either with a patch or by suture (12).

Fifteen patients with valvular aortic stenosis had additional aortic commissurotomy while 8 patients had aortic valve replacement, in 5 patients this was part of Konno-Rastan procedure. Other associated anomalies were treated simultaneously.

#### Statistical analysis:

Data are expressed as mean  $\pm$  SD, continuous variables were compared by unpaired or paired student's test and ANOVA, and discrete variables were compared by the  $X^2$  test. Risk factors associated with early and overall mortality rates were assessed by univariate analysis, as well as for recurrent subaortic stenosis and reoperation. Multi variable logistic regression was used to assess independent factors affecting early mortality rate. Cox regression models were used to assess independent factors affecting long-term survival and recurrence of subaortic stenosis and reoperation.

#### Follow up:

All surviving patients were regularly followed up achieving a median follow up of 12.3 years (range 1-18 y). Follow up was done clinically and by echocardiography and directed mainly towards recurrence of subaortic stenosis and to the function of aortic valve.

#### Results

##### Preoperative clinical features:

##### Early mortality and morbidity:

Seven patients died during hospitalization or within 30 days of operations, for an early mortality of (2.8%). Five patients died from the group with discrete subaortic stenosis (2.2%) and two

**Table (2): Showing previous cardiac surgical procedures.**

Type of procedure	No. Of Patients
VSD repair	10
PDA ligation	5
Aortic coarctation repair	8
Total	23

**Table (3): Preoperative clinical features.**

■ Total number of patients	250 patients	
* Age:		
Mean	8 yrs.	
Range	1-30 yrs.	
* Sex:		
Male	135 pts	54%
Female	115 pts	46%
* Pathology:		
Discrete subaortic stenosis	225 pts	90%
Tunnel subaortic stenosis	25 pts	10%
* Aortic valve regurgitation (AR)		
Mild AR	50 pts	20%
Moderate AR	25 pts	10%
Severe AR	8 pts	3.2%
* NYHA functional class		
NYHA I-II	75 pts	30%
NYHA III-IV	25 pts	10%

patients from the group with tunnel subaortic stenosis (8%). Four patients died from low cardiac out put (LCOP), they had poor LV function before surgery and presented in NYHA class III-IV, two patients died from iatrogenic severe AR and multi-system organ failure respectively while the last patient died from unsuccessful Konno-Rastan aorto-ventriculoplasty. Univariate analysis showed that only preoperative NYHA functional class III-IV significantly increased the risk of early death

( $P= 0.0002$ ), at the same time multivariable analysis showed that NYHA class was found to be an independent risk factor for early death ( $P= 0.007$ ).

Within the group of patient with discrete subaortic stenosis there was no difference in early death when pts were grouped according to operation (membranectomy alone 2%, membranectomy and Myotomy 1.8%, membranectomy and myectomy 2.6%.

**Table (4): Showing previous cardiac surgical procedures. ME = Membranectomy, AVR = Aortic valve replacement, SAMR = subaortic membrane resection.**

Patients	Initial lesion	First operation	Recurrent LVOT gradient	Interval	Secondary lesion	Second operation
1	Discrete	ME.	45	3	Discrete and Severe AR	Myectomy and AVR
2	Discrete	ME.	70	4	Discrete and Severe AR	Myectomy and AVR
3	Discrete	ME.	40	7	Discrete and Severe AR	Myectomy and AVR
4	Discrete	ME.	60	10	Discrete and moderate AR	Myectomy and AVR
5	Discrete	ME.	100	5	Tunnel	Myectomy
6	Discrete	ME.	75	2	Tunnel	Myectomy
7	Discrete	ME.	80	2	Tunnel	Myectomy
8	Discrete	ME.	55	6	Discrete	Myectomy
9	Discrete	ME.	60	10	Discrete	Myectomy
10	Discrete	ME.	95	8	Tunnel	Myectomy
11	Discrete	SAMR and Myotomy	45	4	Discrete	Myectomy and SAMR
12	Discrete	SAMR and Myotomy	55	3	Discrete	Myectomy and SAMR
13	Discrete	SAMR and Myotomy	75	10	Tunnel	Modified Konno
14	Discrete	SAMR and Myotomy	85	11	Tunnel	Konno
15	Discrete	Myotomy	65	2	Tunnel	Konno
16	Discrete	Myectomy	70	4	Tunnel	Konno
17	Discrete	Myectomy	75	1	Tunnel	Konno
18	Tunnel	Myectomy	85	5	Tunnel	Konno
19	Tunnel	Myectomy	65	6	Tunnel	Konno
20	Tunnel	Myectomy	70	4	Tunnel	Konno
21	Tunnel	Myectomy	75	8	Tunnel	Modified Konno
22	Tunnel	Myectomy	100	7	Tunnel	Modified Konno

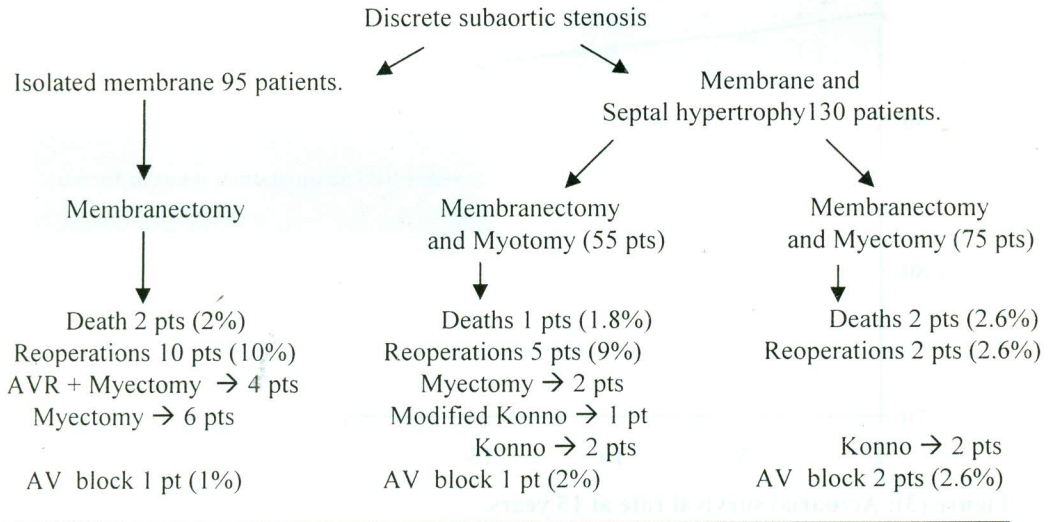


Figure (1): Surgical procedures for discrete SAS and their results.

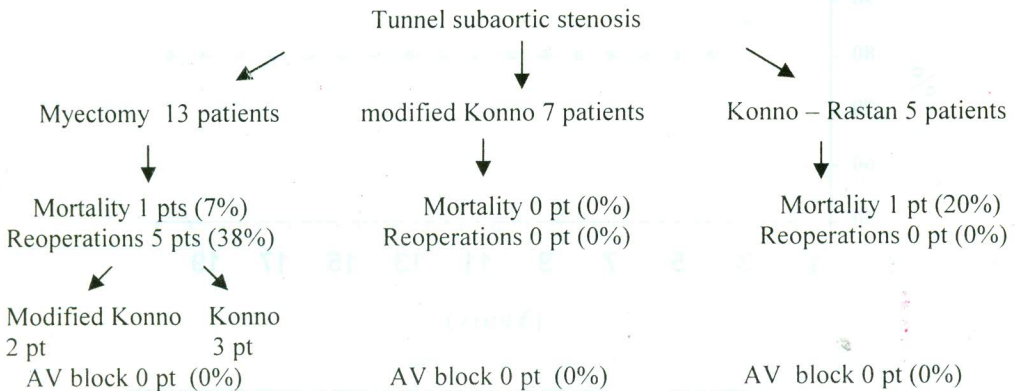


Figure (2): Surgical procedures for Tunnel SAS and their results.

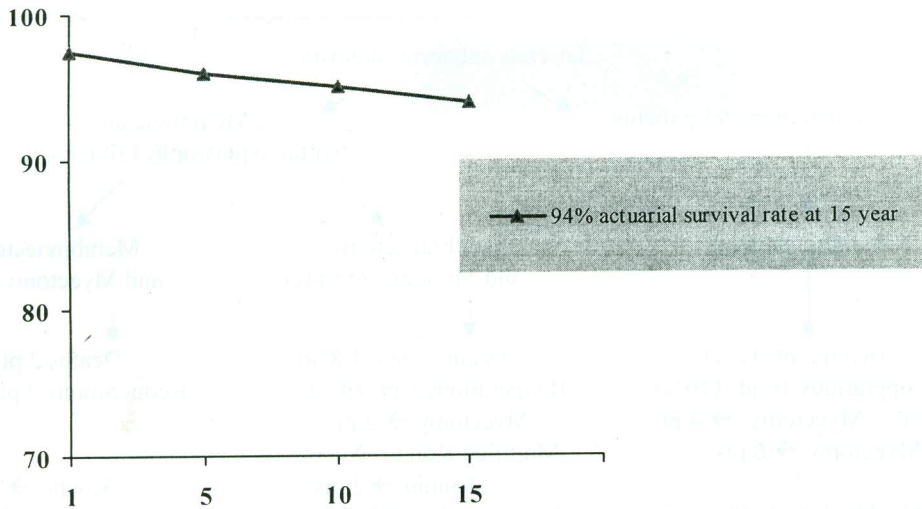


Figure (3): Actuarial survival rate at 15 years.

### Actuarial recurrence-free rate

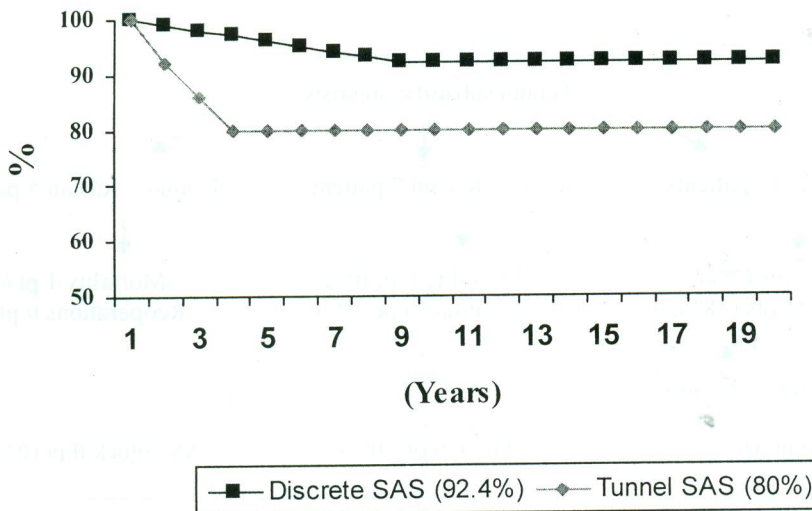


Figure (4): Actuarial recurrence free rate. Comparison between both the discrete SAS group and the tunnel SAS group.

Four patients developed complete heart block and required insertion of permanent pacemaker and five patients were re-explored because of excessive bleeding.

Eight patients had aortic valve replacement, 5 patients from the group with tunnel subaortic stenosis as a part of Konno-Rastan aorto-ventriculoplasty and 3 patients from the discrete subaortic stenosis whom presented with severe AR.

#### **Overall Morality and Long Term Follow Up:**

There were 8 late deaths (3.2%), three pts after a second reoperation while the other 5 pts died from non-cardiac causes.

Actuarial survival at 1, 5, 10, and 15 years was 97.4%, 96%, 95%, and 94% respectively (Figure 3).

As regard late mortality, six patients were related to the group of discrete subaortic stenosis resulting in 11 patients total mortality from this group (5%), while two patients were belonging to the group with tunnel stenosis resulting in total mortality of 16% from this group. Overall mortality rate was influenced by anatomic factors mainly tunnel subaortic obstruction. ( $P= 0.001$ ) and small aortic annulus ( $P= 0.001$ ). Also multivariable analysis showed that tunnel obstruction was a predictor for over all mortality rate.

During follow up which extended up to 20 years, the majority of surviving patients were in NYHA class I and II respectively while 4 patients whom developed severe AR were in NYHA III-IV. As regard the gradient across LVOT it was reduced from  $79 \pm 25$  mmHg preoperatively to  $18 \pm 13$  mmHg Post operatively.

#### **Aortic Valve Function:**

Ninety Eight patients (36%) were known before surgery to have variable degrees of aortic valve disease. 15 patients had isolated AS, 50 patients had mild AR, 25 pts had moderate AR while 8 patients had severe AR. The degree of regurgitation at initial examination correlated with age ( $P = 0.02$ ) but not with LVOT gradient  $P = 0.38$ , relief of subaortic stenosis improved the degree of AR in 73 pts and stabilized it in 7 cases.

At the same time it appeared in 15 pts without preoperative AR following aortic commissurotomy for valvular AS, in most of these cases, it was of mild degree.

#### **Recurrence of subaortic stenosis and re-operation:**

The gradient across the LVOT was reduced from  $79 \pm 25$  mmHg preoperatively to  $18 \pm 13$  mmHg after surgery no significant differences ( $P > 0.05$  for all variables) in reduction of LVOT were observed when the degree of reduction in LVOT was examined in relation to preoperative anatomy. LVOT gradient, status of aortic valve, surgical technique and age during follow up 40 patients (16%) developed a gradient more than 30 mmHg, in 3 of them associated severe AR was evident with deterioration of LV systolic function.

The interval between primary operation and recurrence of gradient was ( $5.5 \pm 2.8$  years), by using univariate analysis anatomic and surgical factors were strong predictors for recurrence. The anatomic factor was tunnel subaortic obstruction. Membranectomy and myotomy were associated with higher rates of recurrence in discrete subaortic stenosis ( $P= 0.02$ ,  $P= 0.03$ ) respectively while myectomy was associated with higher rate of recurrence in

the tunnel subaortic stenosis group ( $P=0.001$ ).

In multivariate analysis tunnel subaortic stenosis and immediate postoperative gradient across LVOT were independent risk factors for recurrence ( $P=0.001$  and  $0.005$  respectively).

Twenty two patients had re-operation 17 from the group with discrete stenosis and 5 patients from the group with tunnel obstruction (Figure 4).

Four patients had AVR and Myectomy, 8 patients had extensive myectomy and resection of recurrent SAM, 3 patients had modified Konno operation and 7 patients had Konno-Rastan operation. Three patients died after re-operation, one following Konno and two patients whom had poor left ventricular function (table 4).

## Discussion

Subaortic stenosis occurs constitutes 8% to 30% of all forms of left ventricular outflow tract obstruction (13). The anatomic spectrum, natural history, and progressive nature of this lesion have been well documented (11). There remains, however, considerable uncertainty about the rapidity of progression and the timing of surgical repair (14,15). Although significant left ventricular hypertrophy and aortic insufficiency are clear indications for surgery, controversy persists whether to remove the membrane in symptom-free patients with an isolated membrane (16). In addition to the timing of surgical repair, the surgical technique remains an area of discussion.

Although the etiology of subvalvular aortic stenosis is still incompletely understood, there is strong clinical and experimental evidence that it is an acquired

malformation (17). Subaortic stenosis is rarely identified in neonates and young children and has not been reported in the developing heart (11). Possible developmental mechanisms include genetic predisposition and hemodynamic abnormalities associated with other cardiac lesions such as conoventricular malalignment in association with interrupted aortic arch or coarctation, accessory endocardial cushion tissue in atrioventricular canal defect, perimembranous ventricular septal defect, anterolateral deviation and thickening of the anterior part of the septum, anterior displacement of the mitral valve, or malattachment of chordae and papillary muscles (17).

It may also occur after surgical repair of other cardiac defects such as partial or complete AV septal defect or VSD (18). In this series 10 patients 4% developed subaortic obstruction following VSD repair.

The hypothesis that discrete subaortic stenosis is a dynamic, progressive disorder of the LVOT is supported by our study as well as serial hemodynamic and angiographic investigation (17). In our series, 9 patients 53% of 17 patients who had discrete membranous subaortic stenosis at initial operation and required re-operation were found to have tunnel obstruction at re-operation. These data support the concept that in patients who develop subaortic stenosis, there may be a preexisting nidus that is stimulated by hemodynamic forces. An additional mechanism may be present in those patients who develop tunnel subaortic stenosis months to years after operation for discrete subaortic stenosis in whom extensive fibrous tissue is found surrounding the LVOT. These findings suggest that an abnormal healing response (perhaps an internal keloid) may contribute to the



recurrent obstruction in some individuals. If discrete, membranous subaortic stenosis is untreated or inadequately relieved, LVOT obstruction may ultimately lead to concentric left ventricular hypertrophy, damage of the aortic valve, and bacterial endocarditis. Our data also confirm previous reports that the routine addition of a generous myectomy to membranectomy for relief of fixed LVOT obstruction may reduce the incidence of recurrent obstruction (19).

In this series, the risk of operative mortality was 3%, for patients with discrete obstruction the risk was 2.2% while it reached up to 8% for patients with tunnel obstruction. The variables that were associated with increase mortality were the tunnel obstruction and NYHA functional class III-IV.

Our results coincide with the results of other groups (20,21).

The first group (20) had an operative mortality 4.7% with no difference in mortality was found between the discrete and the tunnel group while in the other group (21), mortality was 3.1% and they concluded that only preoperative NYHA functional class III and IV and the older age at operation significantly increased the risk of early death.

As regard late mortality in this series, it was 3.2%, we have eight late deaths six of them were related to the group of discrete obstruction (5%) while two patients were related to the tunnel group (16%).

Other groups demonstrated late mortality up to 10% (20). In our series the risk of operative mortality was not related to the surgical technique in the group with discrete stenosis while Konno Rastan was associated

with operative mortality 20% for the tunnel obstruction group.

Several previous studies have emphasized the progressive nature of aortic valve insufficiency in patients with subaortic stenosis; incidence and severity of aortic valve insufficiency is greater in adults than in children (13,22). The mechanism responsible for the aortic valve insufficiency is believed to be repetitive trauma caused by the jet of blood through the subvalvular stenosis impinging on the aortic valve cusp at the beginning of systole (23). Moreover, there is both clinical and experimental evidence that the aortic valve in subaortic stenosis closes early, which may lead to enhanced damage to the valve leaflets (24). Histological studies indicate that fibroelastic tissue may extend from the subaortic lesion into the aortic cusps. In this study, 83 patients (33%) were diagnosed to have variable degrees of aortic insufficiency preoperatively, relief of subaortic stenosis improved the degree of AR in 73 of them and stabilized it in 7 cases at the same time 3 pts had AVR with resection of subaortic stenosis. This result coincides with the result of other group (21), in addition they showed also that addition of myectomy to membranectomy resulted in much lower incidence of AR than membranectomy alone or membranectomy plus myotomy.

During follow up of our patients which extended up to 20 years a recurrent gradient more than 30 mmHg was demonstrated in 40 patients (16%), 22 of them were re-operated upon. In our experience and that of Ashraf and associates (25) addition of myotomy to membranectomy didn't significantly alter the risk of recurrent obstruction. Therefore we favor generous myectomy as a routine adjunct to membranectomy both in discrete and tunnel subaortic stenosis. Although, this operation

is generally effective as the initial surgical treatment in discrete membranous subaortic stenosis, it was associated with a recurrence rate up to 38% in patients with tunnel subaortic stenosis. Therefore, in selected patients with severe primary tunnel lesion we consider performing modified Konno; with preservation of the native aortic valve as the initial operation if the cusps look normal with no evidence of AR or Konno-Rastan if there is associated significant aortic valve disease.

In patients who require re-operation for recurrent LVOT obstruction, a generous myectomy may be done for discrete lesion if the initial operation was limited to a membranectomy other wise if myectomy is not effective in relieving subaortic obstruction, we favor a modified Konno-Rastan operation for patients with healthy aortic valve or Konno-Rastan for patients with diseased aortic valve.

Because a big number of patients with subaortic stenosis in this series (60 %) are asymptomatic and because there is little correlation between symptom and magnitude of LVOT gradient, timing of the operation is a crucial issue. It is difficult to establish rigid criteria for operation on subaortic stenosis based on LVOT gradient. In general we follow the same guidelines for valvular aortic stenosis that we operate on LVOT obstruction if gradients more than 50 mmHg unless there is more than mild AR or evidence of progressive AR at that time we operate on lesser gradient.

In view of the potential for development of late aortic insufficiency and or recurrence of subaortic stenosis long term follow up evaluation by two dimensional Echocardiography is needed in patients who have and have not been operated upon.

### In conclusion

- Surgical treatment of subaortic stenosis produces excellent result as regard mortality and recurrence.
- For discrete obstruction addition of generous myectomy to membranectomy provides excellent results regard postoperative LVOT gradient and recurrence of obstruction than membranectomy alone or membranectomy and myotomy.
- For patients with tunnel obstruction a generous myectomy is the primary treatment. In case of recurrence, modified Konno is advised for patients with healthy native aortic valve and Konno-Rastan aorto-ventriculoplasty for patients with diseased aortic valve.
- Timing of surgery is advised in patients with gradient above 50 mmHg unless there is evidence of more than mild AR or progressive Aortic insufficiency, we accept lower gradient up to 30 mmHg for surgery.
- Patients who had VSD and subaortic membrane should have resection of SAM during VSD closure even if there is no gradient across LVOT.

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## ROLE OF NORMOTHERMIC PAPAVERINE FOR MANAGING INTRAOPERATIVE MAMMARY SPASM

### ABSTRACT

**Background:** After mobilization, vasospasm often reduces flow through the internal thoracic (mammary) artery. An established method of relaxing the artery and increasing flow is to use papaverine at ambient temperature (20 to 22°C) as a topical vasodilator. However, the pharmacologic actions of papaverine generally have been assessed at 37°C.

**Methods:** In 90 patients in whom the left internal mammary (thoracic) artery was used for myocardial revascularization, at Cardiothoracic Surgery Unit, Ain Shams University, between Jan. 1999 and Dec. 2000, we investigated the effects of normal saline solution at 20°C (Group I), papaverine at 20°C (Group II), and papaverine at 37°C (Group III). Under controlled haemodynamic conditions, free flow was measured before any pharmacologic intervention and a median of 18 minutes after pedicle had been sprayed with one of the agents.

**Results:** Normal saline solution at 20°C produced a small increase in flow from  $37.5 \pm 8.1$  ml/min to  $50 \pm 10.2$  ml/min. A significant increase occurred with papaverine at 20°C from  $38.05 \pm 6.5$  ml/min to  $78.75 \pm 21.2$  ml/min ( $P < 0.0001$ ). Papaverine at 37°C, however, produced an increase in flow from  $36.9 \pm 12.6$  ml/min to  $102.5 \pm 42.8$  ml/min ( $P < 0.0001$ ) and proved to be more effective than papaverine at room temperature ( $P = 0.0174$ ).

**Conclusions:** We recommend topical use of papaverine at 37°C to relieve intraoperative spasm of the internal mammary artery.

**Key words:** (Mammary artery, papaverine, spasm, temperature 37°).

Mohammed Attia, Ahmed Abd EL Aziz, Hesham Abd EL Rahman, Hossam Ezzat, Ahmed sami.

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### INTRODUCTION

The internal thoracic (mammary) artery (ITA) is the conduit of choice for coronary artery operations because it has a better long-term patency rate than saphenous vein grafts (Okies et al., 1984 and Tector, 1986). Numerous references have suggested that survival is superior when the left ITA rather than a saphenous vein is used to graft the anterior descending coronary artery (Okies et al., 1984; Tector, 1986 and Ivert et al., 1988). Operative preparation of the ITA

often results in vasospasm with reduction in early graft flow, which could cause perioperative morbidity and even death in high-risk patients (Sarabu et al, 1987). An established method of dealing with this problem is to spray papaverine solution on the ITA graft and to wrap the artery in a papaverine-soaked swab before grafting.

Papaverine is frequently used during surgical procedures at an ambient temperature (20° to 22°C), whereas the pharmacologic actions of papaverine

generally have been assessed at 37°C (Demesy-Waeldele and Stocklet, 1975, and Wells et al., 1975). In this study, therefore, we compared the effects on ITA free flow of normal saline solution at room temperature, papaverine at room temperature, and papaverine at 37°C to identify the best method for the treatment of ITA spasm.

### Patients and Methods

We studied 90 patients whose left ITA was mobilized and who were undergoing elective coronary artery bypass operation at Cardiothoracic Surgery Unit, Ain Shams University, between Jan. 1999 and Dec. 2000 (Table 1). All patients received calcium antagonists, blockers, and nitrates until the date of operation. Each patient was randomly allocated to one of three equal-sized groups. The ITA was dissected on a pedicle, from the subclavian artery to just beyond the bifurcation into the superior epigastric and musculophrenic arteries, with the aid of diathermy and metal ligature clips. Five minutes after systemic heparin treatment, the artery was divided distally and the first flow was determined by measuring the volume of blood expelled from the end of the bleeding artery in a 30-second period. Time of measurement, heart rate, and mean arterial and central venous pressures were also recorded. The tip of the artery was occluded with bulldog clamp, and the artery, with the nonfascial surface anterior, was laid on a moist swab beneath the left sternal edge.

Normal saline solution at 20°C (in group I), papaverine at 20°C (in group II), or papaverine at 37°C (in group III) was then sprayed from a syringe and needle along the artery. After cannulation, blood was transfused from or returned to the pump to restore the mean arterial and central venous

pressures as nearly as possible to the previous values. Systemic vasopressors or vasodilating agents were not used. Time, heart rate, and mean arterial and central venous pressures were recorded, and second flow was measured after removing the bulldog clamp.

The topical solutions consisted of the following: (1) normal saline solution at room temperature (20°C), 4mL of 0.9% sodium chloride solution; (2) papaverine at room temperature (20°C), 6 mg in 4 mL of 0.9% sodium chloride solution; and (3) papaverine at 37°C, 6 mgm in 4mL of 0.9% sodium chloride solution.

All values are expressed as mean  $\pm$  standard deviation. Differences between the groups in the flow measurements were determined by Student's t test and analysis of variance. A P value  $< 0.05$  was considered statistically significant.

### Results

Sex, ratios and ages of the three groups are shown in Table (1). The differences among groups in body surface area and time between flow measurements were not significant ( $P > 0.05$ ). Heart rates mean arterial pressures and central venous pressures at the time of the first and second flow measurements were not significantly different ( $P > 0.05$ ), either within or between groups.

Medians of the first and second flow measurements for each method are shown in Table (2). There was no significant difference among the first flow rates of the three groups. As regards the second flow normal saline solution at 20°C produced a small increase in flow from a median of  $37.5 \pm 8.1$  mL/min to  $50 + 10.2$  ml/min. ( $P < 0.05$ ).

**Table (I): Clinical Characteristics of the Patients and Haemodynamic Data<sup>a</sup>**

Characteristic	Group I (n =30)	Group II (n =30)	Group III (n =30)
Male/female	22/8	25/5	24/6
Age (y)	54.6 ±8.2	55.5 ± 7.9	54.3 ± 9.4
Range	39-69	39-67	40-69
Body surface area(m <sup>2</sup> )	1.85±0.13	1.82 ±0.14	1.85 ±0.14
Range	1.56-2.05	1.62-2.08	1.61-2.12
Heart rate 1 (beats/min)	74.3 ±10.9	73.5 ±9.6	73.5 ±10
Heart rate 2 (beats/min)	77.9 ±14	74.9 ± 9	78 ±12.9
MAP 1 (mm Hg)	68.9 ±5.6	70.2 ± 6.5	69.6 ±6.2
MAP 2 (mm Hg)	69.9 ±5.6	69.2 ± 5.2	71.2 ±5.2
CVP 1 (mm Hg)	2.5±1.8	3.2 ±2.1	2.8 ±1.5
Range	0-6	0-7	0-6
CVP 2 (mm Hg)	1.9±1.1	2.55 ±1.7	2.35 ±1.5
Range	0-4	0-7	0-5
Time (min)	16.95±4.9	16.75±3.9	17.10±4.2

<sup>a</sup> Data are presented as mean ± standard deviation, except as noted. CVP = central venous pressure; MAP= mean arterial pressure.

**Table (2): Flow rates before and after application of topical agents<sup>a</sup>**

Measurement	Group I (n=30)	Group II (n=30)	Group III (n=30)
First flow (mL/min)	37.5 ±8.1	38.05 ±6.5	36.9 ±12.6
Second flow (mL/min)	50.0 ± 10.2	78.8±21.1 <sup>b</sup>	102.5±42.8 <sup>b,c</sup>

<sup>a</sup> Data are presented as mean ± standard deviation.

<sup>b</sup> P< 0.05 versus first flow.

<sup>c</sup> P< 0.05 versus second flow in group II.

A significant increase occurred with papaverine at 20°C from 38.05 ± 6.5 ml/min. to 78.75 ± 21. ml/min. (P< 0.0001). Papaverine at 37°C, however, produced an increase in flow from 36.9 ± 12.6 mL/min to 102.5 ± 42.8 mL/min (P < 0.0001) and proved to be more effective than papaverine at room temperature (P = 0.0174).

## Discussion

The ITA is frequently in spasm with reduced flow immediately after mobilization. Spontaneous relaxation does not occur in the time between the end of

mobilization and the start of cardiopulmonary bypass. To solve this problem, papaverine is frequently used at an ambient temperature (20° to 22°C) (Bilgen et al., 1996). Papaverine causes relaxation by blocking the intracellular enzyme phosphodiesterase in vascular smooth muscle cells. This prevents the breakdown of cyclic 3'5' adenosine monophosphate, which promotes vascular smooth muscle relaxation. Because enzyme activity is progressively reduced at lower temperatures, blocking of phosphodiesterase by papaverine may result in less relaxation at

an ambient temperature than at 37°C. Studies have shown papaverine to be an effective dilator of isolated animal blood vessels at 37°C (Levy, 1973; Berti et al., 1974; Toda, 1974; Demesy-Waeldele & Stocklet, 1975 and Wells et al., 1975;). Rusch and colleagues (1992) have shown that papaverine is a slower and less potent dilator of canine saphenous veins at 25°C than at 37°C. That study did not examine the effect of papaverine at 37°C to relieve intraoperative spasm of the ITA.

The concentration of papaverine used in this study was that proposed by Mills and Bringaze (1989). A volume of 4 mL was adequate to cover the ITA pedicle. He and co-workers (1989), in an *in vitro* study, found that glyceryl trinitrate was more potent than papaverine in relaxing precontracted segments of human ITA. Nifedipine also produced maximal relaxation, but took longer time than glyceryl trinitrate to achieve this. Cooper and co-workers (1992) compared the effects on ITA free flow of normal saline, papaverine, nifedipine, glyceryl trinitrate, and sodium nitroprusside. They found that the most effective vasodilator was sodium nitroprusside. In this study, all topical vasodilators were used at room temperature (18° to 20°C).

In another study, the ability of various vasodilators to inhibit ITA contraction was investigated using discarded segments of human ITA that were not used in coronary artery bypass grafting (Jett et al., 1992). This study concluded that papaverine should be used for the treatment of vasospasm seen during isolation of the ITA intraoperatively, whereas nifedipine may be a better drug for the treatment or prevention of perioperative ITA spasm.

Several other means to improve flow through the ITA have been suggested. Among these are gentle massages of the pedicle or the use of an appropriate-sized probe or a balloon catheter to dilate the entire length of the artery. More recently, intraluminal dilation with papaverine has been shown to produce a dramatic increase in ITA free flow to a mean value of 229 mL/min (Mills and Bringaze, 1989). However, Van Son and co-workers (1992) have shown that hydrostatic dilation of the internal mammary, musculophrenic, and superior epigastric arteries may have detrimental effects on the histologic characteristics of the intima and the internal elastic lamina. They advocated wrapping the ITA with a papaverine-soaked sponge as an appropriate technique to increase ITA flow.

In conclusion, papaverine is frequently used as a topical vasodilator for treatment of ITA spasm intraoperatively at an ambient temperature (20° to 22°C). The mechanism of papaverine-induced relaxation involves inhibition of enzyme activity, which is a temperature-dependent process. Our findings showed that papaverine at 37°C was a more effective topical vasodilator for ITA (internal thoracic artery) free flow than was papaverine at 20°C because cooling produces vasospasm.

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Mohammed Attia, Ahmed Abd EL Aziz, Hesham Abd EL Rahman, Hossam Ezzat, Ahmed sami.

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# MITRAL VALVE INTERVENTION IN PATIENTS WITH PREVIOUS TRIAL OF BALLOON VALVULOPLASTY

## ABSTRACT

The use of balloon Valvuloplasty for the management of mitral stenosis has much increased in the last decade In spite of the improvement in manual practice and the development in the manufacture of the balloon used including valvulotome, complications still occur in a considerable percentage of patients so, in this work we have studied a number of patients who required mitral valve intervention after variable periods of balloon mitral valvotomy trying to find the criteria which optimize the selection of patients for either surgery or balloon valvotomy. The studied patients (96 patients) were classified into group A (22 patients) who required emergency mitral valve intervention because of tamponade with either penetration of the apex in 6 patients (6.25%) or injury of the left atrium in 5 patients (5.2%), acute pulmonary oedema in 4 patients (4.17%) and acute mitral regurge in 7 patients (7.29%). They were of different ages and sex, having sinus rhythm and their echo scoring of the mitral valve at balloon valvotomy ranged between 6 and 12. The surgical procedure done in this group was closed mitral valvotomy in 10 patients, open mitral valvotomy in one patient and mitral valve replacement in 11 patients in addition to surgical procedure done for associated lesions or tears.

group B (74 patients) who required elective mitral valve intervention because of mitral restenosis in 32 patients (33.3%) (6-12 months after valvuloplasty) and mitral restenosis with significant mitral regurge in 42 patients (43.75%) (6-18 months after valvuloplasty). They were of different ages and sexes, having sinus rhythm, their echo scoring of the mitral valve at balloon valvuloplasty ranged between 8 and 12, the mitral valve area after valvuloplasty ranged between 1.5 and 2.0 while it ranged between 0.9 and 1.2 at the time of surgical intervention. The surgical procedure done in this group was mitral valve replacement in all patients in addition to the surgical procedures done for the associated lesions of other valves.

Mohamed Attia Hussein, MD.

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## Introduction

Rheumatic heart disease remains a major cardiac problem in developing countries, (1) With mitral stenosis being the most common presentation. (2) The concept of mitral commissurotomy was first proposed by Brunton in 1902, (3) and successful surgical mitral commissurotomy was performed in the 1920s. (3-5). By the late 1940s, transatrial and transventricular

closed surgical commissurotomy had become accepted procedures. (6-9) Early and long term clinical follow-up of these patients demonstrated that closed and open surgical mitral commissurotomy dramatically improved their functional status and longevity. (10-13) since the introduction of percutaneous balloon mitral valvuloplasty by Inoue et al, (14) in 1984, it has become the treatment of choice for mitral stenosis in selected cases. Percutaneous balloon mitral

commissurotomy is appealing because the mechanism of valve dilation closely parallels the mechanism of surgical mitral commissurotomy. (15) The technique of balloon mitral commissurotomy has evolved rapidly, with improvement in balloons, guide wires, the application of double-balloon techniques (16,17) and the use of the newly developed percutaneous metallic valvulotome by Cribier et al 1997 (18) several investigators have reported improved hemodynamics and low procedure-related morbidity in patients with isolated mitral stenosis (17,19-21) however, it has been concerned that these excellent results might, not be achieved when put into broad practice or when applied routinely to certain subgroups such as elderly patients who often have heavily calcified valves or other associated valvular or ischemic heart disease. (22,23) So, in this work we tried to find the different causes which worsened the prognosis of balloon valvuloplasty, in order to judge the patients from the start to the appropriate procedure suitable for their management whether surgical or non-invasive, which can provide the optimal results.

### Patient and methods

This study included 96 patients who were diagnosed as cases of rheumatic mitral stenosis and who came to the department of cardiothoracic surgery at Ain Shams University Hospital between April 2000 and March 2003 for mitral valve intervention after a previous trial of balloon mitral valvuloplasty. 22 patients (group A) presented for mitral valve intervention on an emergency basis while 74 patients (group B) required elective mitral valve intervention.

In group A (Table 1) the causes of emergency mitral valve intervention were

1. Cardiac tamponade in 11 patients (11.45%) whose ages ranged between 18 and 36 years, 5 were males and 6 were females, all of them had sinus rhythm, 3 patients had tricuspid regurg grade I, III and the Echo scoring of the mitral valve at balloon valvuloplasty ranged between 6 and 9 (mean  $7.0 \pm 0.2$ ).

2. Acute pulmonary oedema with failure of valve dilatation in 4 patients (4.17%), 1 was male and 3 were females, their ages ranged between 28 and 45 years, all of them had sinus rhythm and their Echo scoring of the mitral valve at balloon valvuloplasty ranged between 9 and 12 (mean  $10.0 \pm 0.5$ ).

3. Acute mitral regurg in 7 patients (7.29%), 2 were males and 5 were females, their ages ranged between 30 and 48 years, all of them had sinus rhythm, 2 patients had tricuspid regurg grade II and 2 patients had aortic regurg grade II and the Echo scoring of the mitral valve at balloon valvuloplasty ranged between 9 and 12 (mean  $10.0 \pm 0.7$ ). In group B (table 2) 32 patients (33.3%) required elective mitral valve intervention because of mitral restenosis (6-12 months after balloon valvuloplasty), 13 patients were males and 19 patients were females, their ages ranged between 36 and 48 years, all of them had sinus rhythm, tricuspid regurg grade III, IV was present in 12 patients.

The echo-scoring of the mitral valve at valvuloplasty and intervention ranged between 9 and 12 (mean  $10.0 \pm 0.8$ ), the mitral valve area after valvuloplasty ranged between 1.5 and 2.0 cm (mean  $1.7 \pm 0.2$ ) while at the time of intervention it ranged between 0.9 and 1.1 cm (mean  $1.0 \pm 0.05$ ). 42 patients (43.75%) required elective mitral valve intervention because of mitral restenosis with the development of

significant mitral regurge grade III, IV (6-18 months after balloon valvuloplasty), 12 patients were males and 30 patients were females, their ages ranged between 38 and 48 years all of them had sinus rhythm, tricuspid regurge grade III, IV was present in 12 patients, the Echo scoring of the mitral valve at valvuloplasty and intervention ranged between 10 and 12 (mean  $10.0 \pm 0.9$ ), grade I mitral regurge was present in 16 patients at valvuloplasty, the valve area after valvuloplasty ranged between 1.6 and 2.0 cm (mean  $1.8 \pm 0.1$ ), while at intervention it ranged between 1.0 and 1.2 cm (mean  $1.0 \pm 0.2$ ),

### **Surgical procedures:**

Group A (Table 3) for patients presented by cardiac tamponade, the heart was explored through the left antrolateral thoracotomy, a longitudinal pericardial incision parallel to the phrenic nerve was done and the pericardial cavity was evacuated, repair of the tear in the left atrium (5 patients 5.2%) or in the apex (5 patients 5.2%) was done using mattress stitches supported with Teflon pledgets followed by closed mitral valvotomy using the Tubb's dilator. The stitches used for repair of apical tear were not tightened till completion of the valvotomy.

In only one patient (1.05%) the apical tear was so extensive causing maceration of the myocardium, so its repair required multiple mattress stitches over two strips of Teflon. Two weeks after control of bleeding, mitral valve replacement was done using median sternotomy.

For patients with acute pulmonary oedema, the mitral valve was explored through median sternotomy where open mitral valvotomy was done in 1 patient and mitral valve replacement was done in 3 patients. For patients with acute mitral

regurge, the mitral valve was explored through median sternotomy where mitral valve was replaced in the 7 patients (7.29%) and repair of the tricuspid valve was done in 2 patients and replacement of the aortic valve was done in 2 patients.

Group B (Table 4) the patients of this group presented electively for mitral valve intervention where the mitral valve was explored through median sternotomy. In patients with mitral restenosis (32 patients 33.3%) the mitral valve was replaced in all of them and repair of tricuspid valve was done in 12 patients.

In patients with mitral restenosis and associated significant mitral regurge (42 patients 43.75%) the mitral valve was replaced in all of them, repair of the tricuspid valve was done in 6 patients and aortic valve replacement was done in 12 patients.

### **Results**

The patients presented with tamponade had simple tear in the apex of the heart or in the left atrium and had Echo score between 6 and 9 so, repair of the tear was easy followed by closed mitral valvotomy with good outcome only one patient had extensive tear in the apex which required multiple stitches over strips of Teflon and two weeks later when the valve was explored through median sternotomy, there was a tear in the posterior cusp of the valve (which means multiple trials during balloon valvuloplasty) so, the valve was replaced.

In only one patient with acute pulmonary oedema (Echo score 9) open mitral valvotomy was done, while in other patients with the same presentation and in those with acute mitral regurge and mitral restenosis with or without mitral regurge (Echo score 9-12) the mitral valve was replaced.

Table (1): Data of the patients presented for emergency mitral valve intervention Group A.

Cause of Emergency Mitral Valve Intervention	Number of Patients	Sex		Age	Rhythm	Associated lesions	Echo Scoring of the Mitral Valve at balloon valvuloplasty
		Male	Female				
1. Tamponade with							
A. Penetration of the apex.	6 (6.25%)	4	2	18-32 y	Sinus	Tricuspid regurge grade I-II in 3 Patients	6-8 (mean 7.0 ± 0.1)
B. Injury of the left atrium.	5 (5.2%)	1	4	18-36 y	Sinus		7-9 (mean 7.0 ± 0.6)
2. Acute Pulmonary oedema							
With Failure of Valve Dilatation	4 (4.17%)	1	3	28-45 y	Sinus		9-12 (mean 10.0 ± 0.5)
3. Acute Mitral Regurge							
	7 (7.29%)	2	5	30-48y	Sinus	Tricuspid regurge grade III in 2 patients Aortic regurge garde II in 2 patients	9-12 (mean 10.0 ± 0.7)

Table (2): Data of the patients presented for elective mitral valve intervention Group B.

Cause of elective mitral valve intervention	Number of patients	Age	Sex		Rhythm	Echo score of the mitral valve at valvuloplasty and intervention	Valve area after valvuloplasty	Valve area at mitral valve intervention	Associated Lesions
			Male	Female					
1. Mitral restenosis (6-12 months after valvuloplasty)	32 (33.3%)	36-48y	13	19	Sinus	9-12 (Mean 1.0 ± 0.8)	1.5-2.0 (Mean 1.7 ± 0.2)	0.9-1.1 (Mean 1.0 ± 0.05)	Tricuspid regurge in 12 patients
2. Mitral restenosis with the development of significant mitral regurge grade III-IV (6-18 months after valvuloplasty)	42 (43.75%)	38-48y	12	30	Sinus	10-12 (Mean 10.0 ± 0.9)	1.6-2.0 (Mean 1.8 ± 0.1)	1.0-1.2 (Mean 1.0 ± 0.2)	Tricuspid regurge grade III-IV in 6 patients Aortic regurge grade II in 12 patients

Table (3): Surgical procedures done for patients presented for emergency mitral valve intervention.

Number of patients	Cause of emergency mitral valve intervention	Surgical procedure
11 (11.45%)	1. Cardiac tamponade	-Repair of the tear in the apex or left atrium. - Closed mitral valvotomy in 10 patients.
4 (4.17%)	2. Acute pulmonary oedema with failure of valve dilatation	-Mitral valve replacement was done 2 weeks after control of bleeding in one patient. -Open mitral valvotomy in 1 patient.
7 (7.29%)	3. Acute mitral regurg	-Mitral valve replacement in 3 patients. -Mitral valve replacement in 7 patients. -Repair of the tricuspid valve in 2 patients. -Aortic valve replacement in 2 patients.

Table (4): Surgical procedures done for patients presented for elective mitral valve intervention.

Number of patients	Cause of elective mitral valve intervention	Procedure done for mitral valve	Procedures done for associated lesions
32 (33.3%)	Mitral restenosis	Mitral valve replacement in 32 patients	Repair of the tricuspid valve in 12 patients
42 (43.75%)	Mitral restenosis with development of significant mitral regurg	Mitral valve replacement in 42 patients	Repair of the tricuspid valve in 6 patients Aortic valve replacement in 12 patients



Fig. (1): Showing one of the replaced valves with marked thickening, fibrosis and calcification.



Fig. (2): Showing the ventricular aspect of a replaced valve with shortened and amalgamated chordae and with adherence of the cusps to the tips of the tips of the papillary muscle.



Table (5): Postoperative echocardiographic data.

The surgical procedure	Number of patients	Mitral valve area	Mitral regurge	Gradient across the mitral valve
Closed mitral valvotomy	10	2.2 – 2.6 (Mean 2.3 ± 0.3)	No	3.2 – 4.2 (Mean 3.4 ± 0.7)
Open mitral valvotomy	1	2.5	No	2.8
Mitral valve replacement	85	Opening orifice of the prosthesis 1.7 – 2.3 (Mean 1.9 ± 0.6)	No valvular or para valvular mitral regurge	4.5 – 6.8 (Mean 5.1 ± 0.5)

In the patients who subjected to mitral valve replacement, the native valve was found to be markedly thickened, fibrosed with variable degrees of calcification. (Fig1) Also, the chordae were extensively shortened and amalgamated with adherence of the cusps to the tips of the papillary muscles (Fig. 2).

The post operative Doppler's echocardiography (Table5) revealed adequate valve area with no mitral regurge in patients with closed and open valvotomy and good functioning prosthetic valve with adequate opening area in patients with mitral valve replacement.

Apart from superficial wound infection in 2 patients there was no morbidity. There was only one mortality, who presented with acute pulmonary oedema and subjected to mitral valve replacement, the patient remained hypoxic for 2 days with loss of consciousness complicated by severe low cardiac output which terminated in cardiac arrest.

### Discussion

Although the prevalence of rheumatic mitral valve disease is declining in most industrialized nations, the disease continues to be endemic in much of Asia, latin America, Africa, and the middle East (1,2). Treatment of rheumatic mitral stenosis by surgical closed miral commissurotomy was first attempted in 1923 (4) and was reported successful beginning in the 1940s (6). Percutaneous balloon mitral commissurotomy was first described in 1984 (14) as an alternative to the surgical approach. Descriptive studies have reported successful short – term (23) results without significant recurrence in early follow-up. (19-22) However, early and late complications of this new technique have

been reported in many studies (24-28). The selection of the patient is an important factor affecting the end results of any procedure. So, we believe that echocardiographic evaluation of the mitral valve plays a pivotal role in the selection of the patients with mitral stenosis for percutaneous mitral valvuloplasty. Echo cardiographic evaluation of the valvular and subvalvular structures of the mitral valve is the most powerful predictor of the outcome of percutaneous mitral valvuloplasty. Patients with high echo cardiographic scores (9-16) do not do as well as patients with lower echo cardiographic scores (0-8) in early or late outcome (24-26).

This explains the high echo score (9-12) of the mitral valve of the majority of the patients of this work either presented early (emergency) or late (elective) after balloon valvuloplasty.

Cardiac tamponade is one of the recorded complications of balloon mitral valvuloplasty. It may occur due to improper positioning of the balloon too close to the left ventricular apex causing ventricular tear or occur at the time of transseptal catheterization causing left atrial perforation (26) it may also occur due to improper operator experience or repeated unsuccessful attempts of valvuloplasty (25). In this work 22 patients presented with cardiac tamponade at the time of balloon valvuloplasty. These patients were relatively of young age (18-36 years), had sinus rhythm and no associated lesions except functional tricuspid regurgitation I-II in 3 patients. Repair of the tear in the ventricle or atrium and successful mitral commissurotomy was done. Only one patient who had very wide tear in the apex due, to repeated trials, repair of the tear was done over two strips of Teflon and two weeks later open heart surgery was done

where the valve was replaced because there was a tear in the posterior leaflet of the valve.

The newly developed percutaneous metallic valvulotome by Cribier et al 1997 (18), offered promising results. The device based on the old Tubb's dilator used for surgical mitral commissurotomy, can be sterilised for multiple uses without loss of performance. It dilates stenotic mitral valve by a different mechanism compared to the balloon, with the former depending on forces applied to the plane of the mitral commissures while the latter on forces applied radially to the mitral valve. This device encouraged the operators to try dilatation of mitral valve with relatively high echo score (between 9 and 12). This may be responsible for the presentation of 7 patients with acute mitral regurgitation who required emergency mitral valve replacement. Although Abascal et al (20) in their relatively small study concluded that valvular anatomy is not a predictor of an increase in mitral regurgitation after valvuloplasty, other investigators (24-28) have stressed the importance of valvular and subvalvular anatomy in this complication.

The patients of this work who required mitral valve replacement early or late after balloon valvuloplasty because of the development of the mitral regurgitation or mitral stenosis were found to have severely thickened, fibrosed valves with variable degrees of calcification.

Also, the chordae tendinae were extensively shortened and fused together with adherence of the cusps to the tips of the papillary muscles. This means that the anatomy of the mitral valve is a predictor of unfavorable results of balloon valvuloplasty in the form of mitral stenosis or

development of new or increase of already present mitral regurge.

In addition to the mentioned complications, there are certain factors which may restrict the routine use of balloon valvuloplasty. Among them is the presence of atrial fibrillation with left atrial thrombus or the presence of associated lesions of other valves. In the contrary, through surgery we could dilate or replace the diseased mitral valve and at the same time we could repair the associated tricuspid regurge or replace the stenotic or regurgitant aortic valve.

### Conclusion

Our findings suggest that balloon valvuloplasty may achieve results at least as favorable as surgical closed commissurotomy, with significantly less discomfort and a markedly shorter hospitalization, it likely will complement and not replace the currently available surgical alternatives.

Closed commissurotomy is the most common surgical procedure in most countries where rheumatic mitral stenosis is endemic where there are limited facilities and resources, closed commissurotomy is by far the less costly procedure. In industrialized countries, open mitral commissurotomy or mitral valve replacement remain the first choice for many patients despite much higher cost, because of less favorable anatomy and because of the availability and superiority of an approach using cardiopulmonary bypass where surgery can be performed under direct vision.

Both of which may be more appropriate choices for those with severe subvalvular disease, left atrial thrombus, severe leaflet

calcification or the presence of associated lesions of the aortic or tricuspid valves.

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## INTRAOPERATIVE FABRICATION OF LATERAL CHEST WALL AFTER RESECTION OF PRIMARY TUMOURS

### ABSTRACT

**Background:** Chest wall tumors comprise those of bone and soft tissues. They include both benign and malignant primary neoplasms.

**Material and Methods:** We reviewed our surgical results in 10 cases in whom resection of soft tissue or bone tumors of the chest wall was done in the department of Cardiothoracic Surgery Faculty of Medicine Cairo university, between March 2001 and March 2003. Their ages ranged from 16 to 65 years (with a mean age of 32 years) at the time of diagnosis. pathological types were 4 patients had chondrosarcoma (40%), one patient had rhabdomyosarcoma (10%), one had angiosarcoma (10%), one had liposarcoma (10%), one had chondroma (10%), two had fibrous dysplasia (20%) There were 6 males and 4 females in our study. In all our cases wide excision of the tumor with an adequate safety margin was done followed by chest wall reconstruction. The techniques used for chest wall reconstruction included combined use of bone cement sandwiched between two layers of non-absorbable mesh and muscle flaps to cover the synthetic material. This full-thickness reconstruction is planned to match anatomically the normal chest wall i.e. our new idea was to fabricate separate ribs from the bone cement having the exact size of the resected ribs while leaving spaces inbetween the ribs simulating intercostals spaces.

Ashraf El-Sebaie Mohammed , M.D.\*\* and Walid Gamal Abou Senna, M.D\*.

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### INTRODUCTION

Primary chest wall tumours are uncommon. They include both bone and soft tissue neoplasms. Among bony tumours, neoplasms of the ribs are far more common than those of the sternum (1). The primary rib tumours are benign as frequently as malignant, while benign tumours of the sternum are uncommon (2).

In the past the principle difficulty in the management of chest wall tumours was concerned with limitations imposed by the size of the defect that could be closed safely and tolerated physiologically. With current reconstructive techniques using myocutaneous flaps or muscle flaps in

addition to fasciocutaneous closure after using prosthetic material, masses can be resected aggressively, knowing that stabilization of the chest wall is possible (3).

The majority of them present as painful and enlarging swelling. Some of them may present as tumors that recur or persist after previous resection and or irradiation (3).

Surgical excision, sometimes, is considered the only line left for management (4). Advancement in the surgical techniques used in chest wall reconstruction occurred primarily through the newly-recruited refinements in muscle transposition and the better understanding of the functional anatomy of blood supply of the trunk

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*From department of surgery\*\* and department of Cardio thoracic surgery\* Cairo university.*

muscles (5), (6), (7). The combined influence of all these factors resulted in a boost to the trend towards aggressive resection of these kinds of tumors (8), (9).

Since such lesions are rare. Relatively small-numbered series have been reported in the literature addressing the Subject dealing with such chest wall neoplasms (4), (10).

Resection of the entire sternum or large anterolateral chest wall without subsequent reconstruction, is usually hazardous as it jeopardizes the safety of the different mediastinal structures (6), causes paradoxical movement of the thorax (9), and consequently leads to impaired ventilation (10). Skin, soft tissue, muscles and or prosthetic materials) can be successfully used according to preference to bridge the residual gap and fill the defect whatever, may be its size (7). (11).

### **Aim of the work**

In this work we described a new simple method of reconstruction of the chest wall defects with isolated intraoperative fabrication of polymethylmethacrylate ribs then muscle or myocutaneous coverage of the prosthetic fabricated ribs to complete ideal full thickness reconstruction.

### **Patients and Methods**

#### **Population, age and gender:**

Ten patients had primary chest wall tumours were managed at the cardio-thoracic surgery department, Cairo university hospitals during the period between March 2001-till March 2003. Six patients were males while four were females. Their ages ranged from 16 to 65 years (with a mean age of 32 years) at the time of diagnosis.

Pathological types. 4 patients had chondrosarcoma (40%), one patient had rhabdomyosarcoma (10%), one had angiosarcoma (10%), one had liposarcoma (10%), one had chondroma (10%), two had fibrous dysplasia (20%) Table 1 shows the demographics, patient characteristics, clinical and operative details).

#### **Presenting complaint:**

Presenting complaint: all the patients in our study presented complaining of a chest wall palpable mass. The palpable masses were painful in 6 cases (60%) and painless in 4 cases (40%).

Patient evaluation Clinical evaluation of the patients included careful history, physical examination followed by plain chest x-ray, computed tomography to delineate soft tissue, pleural, mediastinal and pulmonary involvement.

#### **Preoperative Investigations:**

Non-invasive and or invasive investigations were preoperatively done. Non-invasive ones included plain chest radiographs in the erect postero-anterior & the lateral views CT scanning of the chest, and pulmonary function tests. Invasive ones included bone scanning and fine needle aspiration and or biopsy. Fine needle aspiration and or biopsy positively diagnosed all cases and determined their histopathologic types before surgery. In all our cases, Plain radiography and or CT scans succeeded to reveal the mass itself (and clarify its extent), with any "lytic properties" when present. Bone scan was undertaken to show the extent of bony involvement of the mass, and to detect the presence of bone metastases to another distant site, as well as to determine the extent of affection of the sternal bone.

### **Preoperative biopsy:**

When the diagnosis was still in question a needle biopsy (fine or cutting needles) is performed or open incisional biopsy was fashioned to include the biopsy site and tract within the excised block during the definitive surgery. The reason for biopsy was to obtain the histopathologic identity of the tumour mass to plan for preoperative radiotherapy or chemotherapy if possible.

Adjuvant oncotherapy no single patient of our patients needed to have oncotherapy in the perioperative period.

### **Surgical technique:**

Skin incision is made according to the site of the mass. If the mass is located in the anterior chest wall, the skin incision is made vertically over the midportion of the sternum and extended inferiorly beneath the breast. A flap of skin and subcutaneous tissue is elevated over the anterior chest wall. The tumour mass is apparent beneath the pectoralis major muscle. If the tumour mass is situated posteriorly, a standard posterolateral thoracotomy incision is performed, then the posterior chest wall muscles and scapula are retracted superiorly. In some cases the incision is planned in a different way according to the planned muscle flap and the previous biopsy incision.

The tumour mass is removed en block, guidelines to be followed during tumour resection include a 2-3 cm clear margin of soft tissue and 5 cm above and below the tumour of the rib. If the tumour is near the sternum a portion of the sternum medially is removed to ensure safety margin. Violation of the tumour should be avoided, then full-thickness chest wall resection is carried out including the parietal pleura and contiguous structures invaded by the tumour if possible included with the specimen. However, overlying skin should always be taken if it is

adherent to the tumour or if it is the site of previous biopsy.

### **\* Technique of intraoperative fabrication of isolated ribs:**

Our new idea was to refashion intraoperatively the resected segment as follows. First the defect is measured (deficient ribs and intercostal spaces) then a polypropylene doubled layered mesh is used to match the defect and 2-3 cm. are left beyond the confines of the defect. Then the methylmethacrylate (bone cement) is prepared, and is put between the 2 layers of mesh, in such a fashion to reconstruct solid flattened rods with the same tilt, curvature and inclinations of the resected parts of the ribs. The process is repeated to construct the total number of the resected ribs and leaving in-between areas matching the intercostal spaces as well (formed only of 2 layers of mesh) (fig. 1) Then fixation is done using thick absorbable sutures to fix the mesh borders to the remains of the pleura and intercostal muscles all around where the designed rib segments are fixed to both rib ends left after excision using stainless steel wires to allow for solid fixation. (fig.2)

Then closure of such full-thickness chest wall defect is done over an intercostal tube drain with under water seal. The final step is to cover the whole area of prosthetic material with lattissimus muscle flap which can reach any site on the lateral chest wall (fig.3)

### **Results:**

All our patients had an immediate postoperative P.A and lateral views X-rays (3<sup>rd</sup> post op day) repeated daily till removal of the intercostals tube drainage and complete re-expansion of the lung. (Fig 4) There was not any pleural collection or lung inflation problems. As regard the physiologic tolerability of the reconstructed





Figure 1.

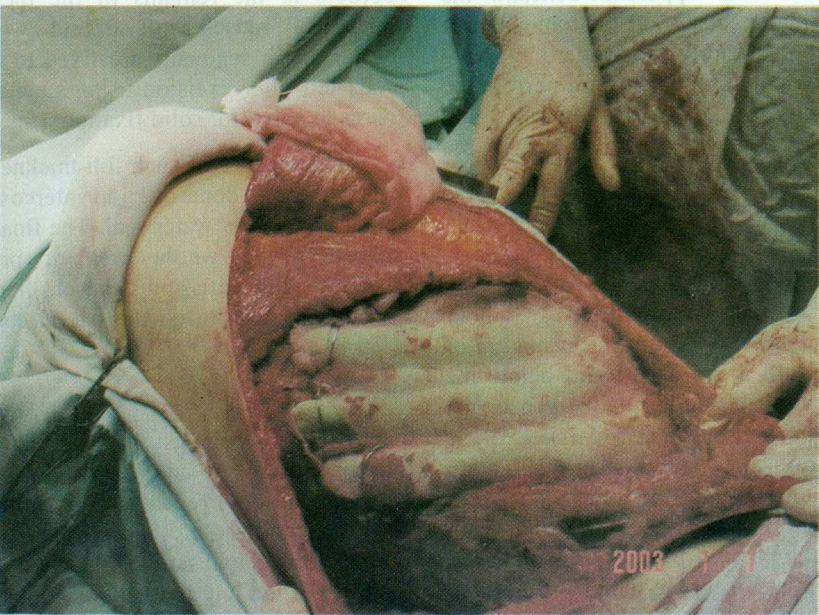


Figure 2

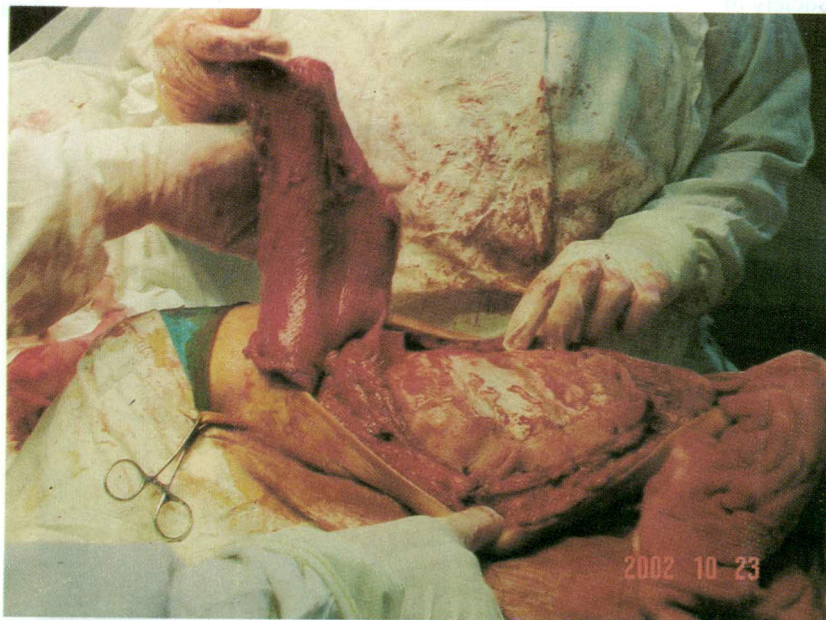


Figure 3

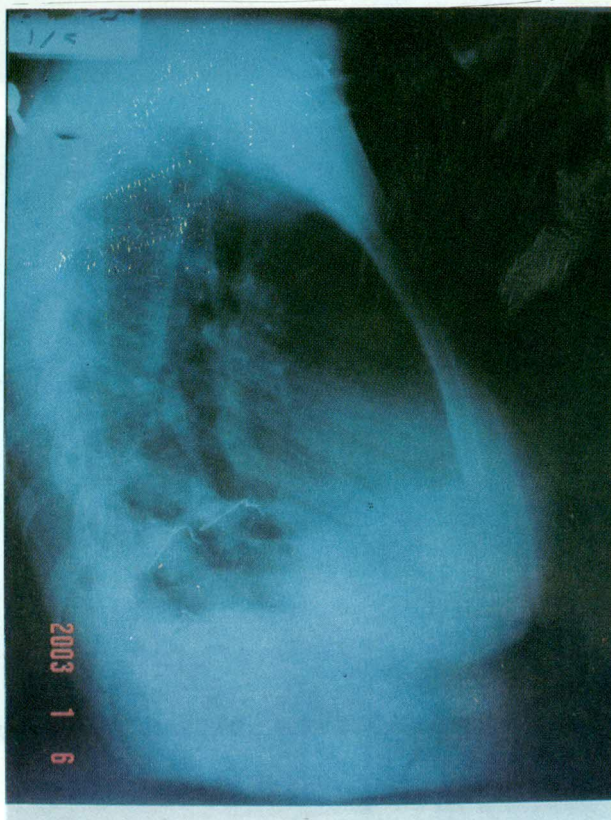


Figure 4

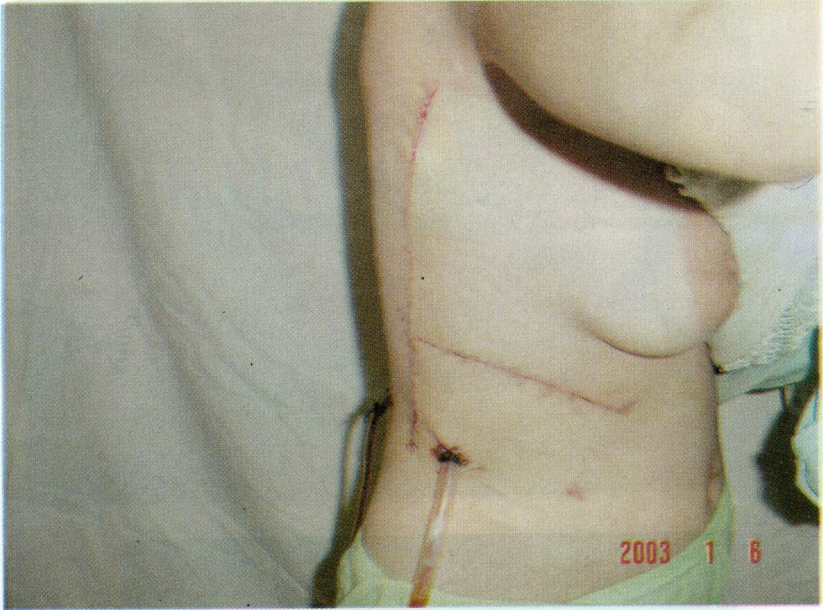


Figure 5

**Table (1): Demographic data, patient characteristics, clinical and operative details.)**

Patient no	sex	age	diagnosis	site	Extent of defect
1	F	16	Rhabdomyosarcoma	Lt. lateral	2-6 ribs
2	M	28	chondrosarcoma	Rt.lateral	8-11 ribs
3	M	34	chondrosarcoma	Rt.lateral	3-5 ribs
4	F	65	liposarcoma	Rt.lateral	4-8 ribs
5	F	35	chondrosarcoma	Lt.lateral	3-9 ribs
6	F	39	chondrosarcoma	Rt.lateral	4-8 ribs
7	M	22	Fibrous dysplasia	Rt.lateral	6-9ribs
8	M	31	angiosarcoma	Rt.lateral	5-9 ribs
9	M	34	Fibrous dysplasia	Rt.lateral	6-8 ribs
10	M	21	chondroma	Lt.lateral	3-5 ribs

chest walls, all patients weaned off the ventilator 30-120 minutes after operation with excellent blood gases analysis. Patients were left on an oxygen mask for 24 hours maximum. The oxygen tension ranged from 140-200 and carbon dioxide tension from 32-43.

In some cases (3 cases) there was an expiratory bulge in the intercostals spaces between the fabricated ribs (paradoxical movements) which disappeared 3-5 days after surgery.

There was no incidence of wound infection in our study due to the muscle flap coverage and overlying safe skin closure, the subcutaneous suction drain was left at the latissimus donor site and overlying the muscle flap for 5-8 days. About ipsilateral tilt, after the pain disappears from surgical trauma, patients were able to do ipsilateral tilt successfully, and without limitation on the reconstructed side, and without pain. (1 week after surgery). (Fig.5). The hospital stay ranged from 6-15 days to ensure good physiologic function and wound healing

## Discussion

Primary chest wall tumours are uncommon (1), (12). Resection of these tumours is often indicated for palliation from pain or ulceration. However, under

various conditions, it may lead to lasting tumour control and substantial freedom of the disease might be achieved (13), (14).

It is the belief of many surgeons that chest wall tumors suspected of being primary neoplasms should be diagnosed by excision rather than incision or needle biopsy (11),(15). Patients with tumors diagnosed as malignant should then undergo wide excision. However, the extent of resection should not be compromised to allow the ability to close the residual chest wall defect (8),(5),(10).

In our study, all our patients were biopsied and histologically diagnosed before surgical extirpation was done. In 9 cases, a sure histopathological result was readily-available preoperatively. This was not the case in one patient, where the biopsy report was either angiosarcoma or rhabdomyosarcoma which was proven postoperatively as angiosarcoma.

In our technique, it was so important to decide the nature of the tumour before surgery, to plan the margin of resection and it does not matter the size of the residual defect as it is going to be ideally reconstructed. Opinions in this context, differ as to what constitutes wide resection?? (2),(8),(9),(10). In all our

patients who had malignant tumors, we planned our margin of resection at least 5 cm around the tumor. The extent of the resected margin, in our opinion, showed no influence on survival. Our observation was also reported by other workers like King and colleagues (16) and Zuslu et al (17), who reported that the extent of the margin resected did not influence patient-survival but may have affected the rate of tumor recurrence. They could not demonstrate a significant difference in survival because all of their patients had a margin of resection of at least 2 cm. Many surgeons agree with the opinion that a margin grossly free, by several centimeters from macroscopic tumor growth would be considered an 'adequate resection'. Although this may be sufficient for benign and low-grade malignant primary tumors such as chondrosarcoma, higher-grade tumors such as rhabdomyosarcoma, and osteosarcoma have the potential to spread within the marrow cavity, along the periosteum or along the parietal pleura. Consequently, excision of these higher grade tumors with a 2-cm margin would not be an "adequate resection" (4), (15).

Reconstruction was planned and performed routinely with plastic surgeons. The fact that lattissimus muscle have an axial blood supply permits elevation and rotation with or without their overlying skin (5), (9). Lattissimus dorsi muscle flap was used in all our patients to cover antero-lateral chest wall "rib-defect" after tumor resection. We noticed that previous radiation therapy did not compromise the viability of these flaps (1). In one case there was an incision crossing the anterior border of lattissimus dorsi muscle which was only a skin incision to reach the tumour mass and to take open biopsy before case referral to us. During surgery the Lattissimus muscle pedicle was identified first to ensure it was

not injured during the biopsy procedure and it was found intact.

Large chest wall defects frequently result from treatment of primary tumors. Chest wall reconstruction should include stabilization of the bony thorax and coverage of any soft tissue defect (1). Defects with a maximum diameter less than 5 cm anywhere on the thorax are usually not constructed. Posterior defects of less than 10 cm do not require reconstruction because the overlying scapula provides support (6),(7).

Since the introduction of muscle, myocutaneous, fasciocutaneous, the reconstruction of full thickness chest wall defect is still a challenge. (1)

However, reconstruction of sufficient stability is needed for large defects of the antero-lateral chest wall and sternum (18), to prevent flail chest and paradoxical insufficient breathing and hence the necessity for postoperative mechanical ventilation. (19). It should also provide a cosmetically near normal contour of the chest wall.

The difficulty in reconstruction of skeletal defects of the chest wall can be judged by the availability of large number of procedures. Although autogenous rib grafts in various forms are ideal, there are problems of its availability and harvesting with prolonged time of surgery and its complications.

The reconstruction using one or more prosthetic materials is a more common and popular method. The most common is the use of synthetic mesh (polypropylene) with or without sandwich. Polymethylmethacrylate is not a new material for chest wall reconstruction. It is presently used in combination with various

materials as a sandwich or plate. This innovative technique of reconstruction of the bony chest wall defects with fabricated heat-cure polymethylmethacrylate ribs provide many advantages, it does not require much experience, less time consuming and also provides stability and rigidity to the chest wall. Also it is inexpensive material compared with various implants in use. This advantage is a very important consideration for the developing countries like ours. The technique also results in a near normal contour and configuration of the chest wall, with good ipsilateral tilt. Also the danger of tissue damage caused by exothermic reaction and monomer emission is nonexistent. However, the risk of postoperative infection and extrusion is the same as with the other available implants.

In the study of Agrawal and his co-workers, the complication that was encountered, was the sinus formation at the a stainless steel wires after 1 year in one patient, necessitating the removal of the prosthesis through the previous incision, by time the fibrous capsule around the prosthesis was quite tough and it stabilized the chest wall. (20)

Multidisciplinary planning between the departments of thoracic surgery plastic & reconstructive surgery, pathology radiology, medical oncology, and radiation therapy, was routinely used in our planned case management.

### Conclusion

Accurate diagnosis is the first step in successful management of any chest wall tumor. Wide as well as adequate chest wall resection, depending on the prior knowledge of the tumors histopathological type, is the key to their successful management. Our new technique generally, allows the surgeon to widen the surgical margin of resection as safely required and regardless the defect size

is, and to ideally reconstruct the rib defects in such a way to fabricate ribs and intercostal spaces to allow for painless lateral tilt of the patients to the same side, in the same time give excellent chest wall support like normal (best physiologically tolerated), and excellent cosmetic appearance with short hospital stay and early weaning from ventilators.

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# CLINICAL EVALUATION OF PREEMPTIVE USE OF PHOSPHODIESTERASE III INHIBITORS IN PATIENTS UNDERGOING OFF PUMP CORONARY ARTERY BYPASS GRAFTING

## ABSTRACT

**Background:** Deterioration in ventricular function is not uncommon after off pump coronary artery bypass grafting (OPCAP). We hypothesized that Phosphodiesterase III inhibitors like milrinone or amrinone may reduce their occurrence and may decrease catecholamine requirements and cellular enzyme levels in patients undergoing (OPCAP).

**Methods:** In 30 patients, we randomly administered milrinone 50  $\mu\text{g}/\text{kg}$  plus 0.5- $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  infusion for 10 h, amrinone 1.5 mg/kg plus 10  $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  infusion for 10 h, or Placebo before systemic heparinization. Hemodynamic variables, dopamine requirement, and laboratory values were recorded.

**Results:** At the postoperative period, stroke volume index was higher in the Milrinone and Amrinone groups (mean (SD), 28.2 (6.0) and 27.6 (5.2) vs. 22.4 (5.6 mL  $\cdot \text{min}^{-1} \cdot \text{m}^{-2}$  per beat,  $P < 0.0001$ ). The postoperative dopamine requirement was less 6.9 (2.7) and 7.3 (2.6) vs. 12.4 (2.0) mg/kg,  $P < 0.008$ ), and postoperative serum lactate, alanine and aspartate aminotransferase, lactate dehydrogenase, creatinine kinase and glucose levels were less ( $P < 0.01$ ). The mean postoperative heart rate was faster in the Milrinone group than in the Amrinone and Placebo groups (101.8 (10.3) vs. 85.9 (9.5) and 84.8 (10.8) bpm,  $P < 0.01$ ).

**Conclusion:** We concluded that preoperative milrinone or amrinone administration in OPCAP patients not only ameliorates postoperative deterioration in cardiac function, but also reduces dopamine requirement and limits the increases in serum lactate, glucose, and cellular enzymes, although milrinone may increase heart rate.

**Key words:** Amrinone - Coronary artery bypass grafting (CABG) - Milrinone - Off pump coronary artery bypass grafting (OPCAP) - Phosphodiesterase inhibitors.

Hosam Fawzy, Ahmed El-Watidy, Atef Farag, Aitizaz Syed, Arto Nemlander, Bassel ME Nour El Din, MD\*, Hosam F.Fawzy, MD\*\*, Alaa Basiouni\*\* and El Sayed El Mistekawy, MD\*\*\*

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## INTRODUCTION

Many patients undergoing cardiac surgery require inotropic support immediately after cardiopulmonary bypass

(CPB) (1). Some practitioners use positive inotropes routinely in nearly every cardiac surgical patient, whereas others use them based on clinical assessment, considering

\*Assistant professor - Ain Shams University, Cairo, Egypt and Consultant Cardiac Anesthesiologist, NWAFFH, Tabuk, KSA

\*\* Senior Registrar Cardiothoracic Surgery, NWAFFH, Tabuk, KSA

\*\*\* Registrar Cardiothoracic Surgery, NWAFFH, Tabuk, KSA



target values for cardiac output or other variables (2-5). There is no consensus regarding the best inotropic drugs for use in either patients undergoing routine CABG or those undergoing OPCAP surgery (6,9).

Phosphodiesterase III inhibitors provide an alternative means of inotropic support via non- $\beta_1$ -adrenergic pathways (10); they induce vasodilatation (11) and are effective for improving cardiac function immediately after CPB in patients undergoing cardiac surgery (12). Several pharmacokinetic and pharmacodynamic evaluations have established the most effective dose regimens for amrinone and milrinone (13-15); however, the clinical effectiveness of these two drugs has never been studied in OPCAP surgery. Furthermore, there are accumulating evidences that the timing of the pharmacological intervention with the Phosphodiesterase III inhibitors is crucial as well. However, no study has explored this hypothesis or clarified the different characteristics of preemptive use of milrinone and amrinone in OPCAP surgery.

In this study we examined inpatients undergoing OPCAP surgery whether preemptive use of milrinone or amrinone reduces deterioration in ventricular function, reduces dopamine and nitroglycerine requirements, as well as limits increases in lactate, glucose, and cellular enzymes.

### Patients and Methods

At the Departments of Anesthesia and Cardiac service at the North West Armed Force Hospital (NWAFFH) - Tabuk-KSA, We studied 30 adult patients (mean age, 68 ( $\pm$  9 yr) who underwent isolated OPCAP surgery either because of unstable ( $n = 10$ ) or stable, progressive angina pectoris ( $n = 20$ ). All patients had 90% or greater stenosis of two or more coronary arteries. Criteria for

exclusion included a planned concomitant valve procedure, emergency surgery, and history of persistent ventricular tachycardia or obstructive cardiomyopathy, myocardial infarction within 4 weeks before surgery, preoperative inotropic support, or use of an intraaortic balloon pump at the time of surgery.

After Institutional Review Board approval and informed written consent, 30 patients were enrolled in this trial. A standardized protocol for general anesthesia was applied. All patients were premedicated with midazolam 15 mg orally 90 minutes before scheduled operative time. After insertion of right radial artery cannula with local lidocaine 1% infiltration, Induction of anesthesia was performed with midazolam 0.04-0.07 mg/kg, propofol (bolus of 0.5-1.5 mg/kg and total operative dose lower than 15  $\mu$ g/kg). Muscle relaxation was obtained with pancuronium bromide (bolus of 0.1 mg/kg and further administrations of 0.03 mg/kg as needed). Nitrous oxide/O<sub>2</sub> 50/50% and sevoflurane 2-3% were added to maintain appropriate anesthetic depth as indicated by hemodynamics monitoring. A central venous catheter and pulmonary artery thermodilution catheter (Baxter Healthcare Corp, Irvine, CA) were inserted after endotracheal intubation. The same team of surgeons, with standardized surgical procedures, did all the interventions. All patients were operated on through full median sternotomy. The left internal mammary artery was then taken down concurrent with saphenous vein and/or left radial artery harvest. Before anastomosis, porcine heparin, 100-150 U/kg, was administered, and supplemental doses were added, as needed, to maintain a celite-activated clotting time (ACT) between 200-250 s. The proximal anastomoses were then

performed using a partial occlusion clamp followed by distal anastomoses of left anterior descending coronary artery, right coronary artery and circumflex marginal branches when indicated. Each artery was stabilized in turn using the Medtronic Octopus II Tissue Stabilization System (Medtronic, Inc, Minneapolis, MN). Intracoronary shunts were used when feasible to maintain distal coronary perfusion during the distal anastomosis of the grafts. After termination of the anastomoses, the total dose of heparin was reversed with protamine (1:1 ratio). Further doses of 50 mg of protamine were administered if ACT was greater than the baseline

We randomly assigned 30 patients to either Amrinone, Milrinone, or Placebo (Control) group immediately before anesthetic induction. Before systemic heparinization, we randomly administered a bolus of milrinone  $50 \mu\text{g}/\text{kg}$  plus  $0.5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  (Milrinone group), a bolus of amrinone  $1.5 \text{ mg}/\text{kg}$  plus  $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  infusion (Amrinone group), or same volume of normal saline bolus and infusion (Placebo group). The initial loading dose was administered over 10–15 min, and infusion was continued for 10 h. The loading dose syringe was covered with aluminum foil to assure blinding because the study protocol required all clinicians to be blinded to drug identity.

Dopamine  $5\text{--}10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  and nitroglycerine  $0.5\text{--}1 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  infusions were used to maintain a cardiac index  $>2.0 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ , a systolic blood pressure between 90 and 130 mm Hg, a heart rate at  $<110 \text{ bpm}$ , and a pulmonary-capillary wedge pressure  $<18 \text{ mm Hg}$  throughout all the interventions and during the postoperative period. For each patient, the total individual doses of dopamine and nitroglycerin administered (in  $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ )

min<sup>-1</sup>) were recorded, and the mean total dose was calculated for all patients. Patients were weaned from mechanical ventilation when they were hemodynamically stable and alert and were usually discharged from the ICU after extubation and discontinuation of all vasoactive drug infusions.

Hemodynamic measurements (heart rate, mean arterial blood pressure, cardiac index stroke volume index, mean pulmonary artery occlusion pressure and systemic vascular resistance index) were obtained after anesthetic induction (Time 1), before heparinization (Time 2), at 15 and 30 min after conclusion of anastomosis, and every hour for the first 24 h postoperative

Cardiac index was determined in duplicate by the thermodilution technique using 10-mL boluses of saline injected through a pulmonary artery catheter during the expiratory pause phase of the ventilator cycle. Cardiac index was calculated automatically with each output measurement. In the ICU, cardiac output was measured by means of continuous thermodilution cardiac output measurements (16); the duplicate thermodilution technique described previously was also repeated every 6 h. Hemodynamic indices were calculated from pressure and cardiac output by use of standard formulas (17).

An electrocardiographic ischemic episode was evaluated off-line retrospectively, and it was defined as reversible ST depression of 0.1 mV or more from baseline at J + 60 ms or as ST increase of  $>0.2 \text{ mV}$  at the J point lasting for at least 1 min. Possible episodes of ischemia were reviewed and verified by two investigators who were blinded to treatment group assignment. Three or more consecutive ventricular premature beats were recorded as an episode of ventricular tachycardia.

Arterial oxygen contents, hemoglobin, and lactate levels were measured before and after anesthetic induction, before heparinization and at 30 min and 2, 3, 5, 10, 15, 20, and 24 h postoperative.

Blood samples for laboratory examination were obtained in all patients preoperatively and on postoperative days 1, 2, and 3. Laboratory values included those for lactate, creatine kinase, lactate dehydrogenase, aspartate or alanine aminotransferase, creatinine, C-reactive protein, glucose, and platelet count. These laboratory examinations were conducted as routine tests for cardiac surgical patients.

Comparisons of demographic data were made by one-way analysis of variance, followed by the Bonferroni multiple comparison test. Comparisons of hemodynamic and laboratory values among the treatment groups were made by analysis of variance with repeated measures in which the within-subject variables were treatment groups and time. After tests on the main effects, multiple comparisons between treatment groups at a specific time were performed by using the Bonferroni procedure adjusted for repeated measures, maintaining an experiment-wise  $\alpha$  level of 0.01. The number of patients with a postoperative electrocardiographic ischemic episode or ventricular tachycardia and who received allogeneic blood transfusion were analyzed by the  $\chi^2$  test, supplemented by Fisher's exact test for pairwise comparisons. All statistical tests were two-sided. Statistical analysis was performed with statistical software (SAS; SAS Institute, Cary, NC). The calculated P values that indicated significance are given in the tables. All data are expressed as mean (SD).

## Results

There were no significant differences among the three groups with respect to any of the patient characteristics, as summarized in (Table 1) There were no significant differences in any hemodynamic or laboratory values among the three groups before cardiac surgery (Table 1).

The data for hemodynamic variables are shown in (Figure 1-6. The effects of amrinone and milrinone on cardiac index ( $P = 0.005$  and  $P = 0.009$  respectively) (Figure 3), and on stroke volume index ( $P = 0.0002$  and  $P = 0.01$ , respectively) (Figure 4) on comparison with placebo were significantly greater than those of placebo. The effect of milrinone on heart rate was significantly greater than that of placebo ( $P = 0.011$ ) or amrinone ( $P = 0.011$ ) (Figure 1). Cardiac index at the postoperative nadir in the Amrinone and Milrinone groups was higher ( $2.5 (0.25) \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ ,  $P < 0.0001$ ; and  $2.5 (0.4) \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ ,  $P < 0.0001$ , respectively, versus  $1.95 (0.5) \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$  in the Placebo group (Figure 3), and stroke volume index at the nadir was higher  $26.7 (4.0) \text{ mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ ,  $P < 0.0001$ ; and  $28.3 (3.3) \text{ mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ ,  $P < 0.0001$ , respectively, versus  $21.5 (5.1) \text{ mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$  per beat in the Placebo group (Figure 4).

There were no significant differences among the three groups in the number of patients with postoperative electrocardiographic ischemic episodes or ventricular tachycardia in the first three postoperative days. Ventricular tachycardia was observed in three patients in the Milrinone group ( $P = 0.51$ ) and two patients in the Amrinone group ( $P = 0.47$ ), as compared with four patients in the Placebo group. An ischemic episode was observed in one patient in the Milrinone group ( $P = 0.10$ )

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**Table (1): Demographic Data and Preoperative Clinical Data.**

Variable	Control (n = 10)	Milrinone (n = 10)	Amrinone (n = 10)
Age (yr)	66 (9)	70 (8)	68 (8)
Sex (M/F)	6/4	5/5	7/3
Height (cm)	163 (5)	164 (6)	166 (7)
Weight (kg)	77 (4)	78 (8)	80 (7)
Body surface area (m <sup>2</sup> )	1.6 (0.1)	1.6 (0.2)	1.6 (0.4)
Diabetes mellitus (n)	4	2	4
Preoperative medications (n)			
β-adrenergic antagonist	4	5	5
Calcium-channel blocker	3	3	4
Diuretic drug	2	3	3
Digoxin	2	2	2
Angiotensin-converting enzyme inhibitor	2	2	3
Operation time (min)	260 (46)	261 (51)	250 (53)
Anesthetic time (min)	371 (40)	368 (45)	363 (51)
Grafts (n)	4.1 (1.0)	4.0 (1.0)	4.2 (0.9)
Preoperative ejection fraction (%)	62.4 (12.8)	61.7 (11.9)	60.8 (11.7)
NYHA (class)	3.1 (0.4)	3.0 (0.4)	2.9 (0.4)
Extubation time (h)	6.0 (4.6)	5.4 (4.6)	5.3 (4.5)
Intraoperative bleeding (ml) (a)	284 (183)	313 (133)	252 (143)
Postoperative chest-tube drainage in the first 24 h (ml) (b)	350 (156)	348 (140)	291 (184)
a + b (ml)	633 (239)	660 (221)	543 (244)

Values are means (SD) unless otherwise noted.

and two patients in the Amrinone group ( $P = 0.46$ ), as compared with four patients in the Placebo group (Table 3).

Three patients in the Placebo group (900, 450, and 850 mL), one patient in the Amrinone group (150 mL), and two patients in the Milrinone group (700 and 1000 mL) received allogeneic blood transfusion during surgery, but no patient received blood transfusion postoperatively. There was no significant difference in the number of the patients who received allogeneic blood transfusion among all groups (Table 3).

The mean total dose of dopamine administered in the Amrinone and Milrinone groups was smaller than in the Placebo

group during the first 24 h after surgery 6.8 (2.6) mg/kg,  $P = 0.004$ ; and 6.2 (2.2) mg/kg,  $P = 0.008$ , respectively, versus 10.5 (2.0) mg/kg in the Placebo group (Table 3). At the postoperative nadir of cardiac function, the dopamine infusion rate in the Milrinone and Amrinone groups was slower than in the Placebo group 4.0 (2.2)  $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ,  $P = 0.004$ ; and 4.5 (2.3)  $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ,  $P = 0.005$ , respectively, versus 6.9 (1.9)  $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  infusion in the Placebo group. The mean total dose of nitroglycerin administered in the Milrinone and Amrinone groups was smaller than in the Placebo group during the first 24 h after surgery 3.5 (0.5) mg/kg,  $P = 0.007$ ; and 3.6 (0.5) mg/kg,

**Table (2): Perioperative Enzymatic Values in the Milrinone, Amrinone, and Placebo Groups.**

Enzyme	Before surgery	Postoperative Day 1	Postoperative Day 2	Postoperative Day 3
<b>Creatinine kinase (U/L)</b>				
Control	83.4 (29.5)	2158.2 (1055.1)*	1032.0(273.3)*	439.6 (139.4)*
Milrinone	89.3 (64.5)	893.0 (332.4)*†	608.1(216.3)*†	334.0 (173.1)*
Amrinone	119.5(82.3)	1105.7(535.4)*†	555.0(263.0)*†	290 (177.1)*
<b>Aspartate aminotransferase (U/L)</b>				
Control	21.3 (4.5)	139.1 (59.1)*	78.3 (56.1)*	39.5 (22.6)*
Milrinone	22.3 (7.3)	61.9 (33.1)*†	44.2 (26.2)*†	28.3 (11.1)*
Amrinone	27.9 (9.0)	81.9 (39.4)*	38.1 (24.6)*	27.7 (10.1)*
<b>Alanine aminotransferase (U/L)</b>				
Control	18.3 (7.5)	42.7 (22.7)*	26.5 (13.4)	20.5 (10.5)
Milrinone	20.3 (8.8)	23.1 (7.0)†	18.8 (8.2)	22.9 (9.1)
Amrinone	23.4 (15.7)	33.1 (18.3)	24.9 (11.6)	27.5 (13.7)
<b>Lactate dehydrogenase (U/L)</b>				
Control	179.1(20.7)	655.1 (261.2)*	532.0 (196.7)*	449.4 (167.4)*
Milrinone	178.7(29.0)	489.9 (164.8)*†	413.9 (139.1)*†	378.6 (108.5)*
Amrinone	211.7(39.3)	464.3 (176.1)*†	368.5 (89.3)*†	343.9 (73.5)*†
<b>Lactate (mmol/L)</b>				
Control	0.8 (0.2)	3.8 (1.1)*	2.2 (1.1)*	2.7 (1.0)*
Milrinone	0.8 (0.2)	2.2 (1.1)*†	1.8 (0.8)*	1.3 (0.4)*
Amrinone	0.8 (0.2)	2.7 (1.0)*†	1.9 (0.7)	1.5 (0.7)*
<b>C-reactive protein (mg/dL)</b>				
Control	0.2 (0.2)	9.3 (2.6)*	10.1 (4.0)*	6.0 (2.6)*
Milrinone	0.2 (0.2)	7.1 (1.3)*†	6.7 (2.4)*†	5.0 (2.9)*†
Amrinone	0.2 (0.2)	6.0 (2.9)*†	5.5 (3.5)*†	4.8 (3.4)*†
<b>Creatinine (mg/dL)</b>				
Control	0.79 (0.32)	0.89 (0.25)	0.89 (0.36)	0.77 (0.39)
Milrinone	0.95 (0.17)	1.10 (0.38)	0.99 (0.34)	0.89 (0.38)
Amrinone	0.85 ( 0.22)	0.84 (0.27)	0.71 (0.29)	0.71 (0.24)
<b>Platelet (per mm<sup>3</sup>)</b>				
Control	22.7 (5.9)	9.9 (2.1)*	11.5 (2.1)*	15.0 (3.5)*
Amrinone	25.7 (5.2)	10.3 (2.9)*	11.8 (2.5)*	14.1 (3.2)*
Milrinone	21.8 (5.8)	10.4 (2.7)*	10.0 (2.8)*	12.2 (3.1)*
<b>Serum glucose (mg/dL)</b>				
Control	119 (33)	223 (63)*	234 (66)*	231 (63)*
Amrinone	121 (26)	202 (59)*	188 (24)*†	178 (45)*†
Milrinone	110 (26)	211 (47)*	186 (18)*†	169 (35)*†

Values are means (SD).

\* P < 0.01 versus before surgery.

†P < 0.01 versus Control.

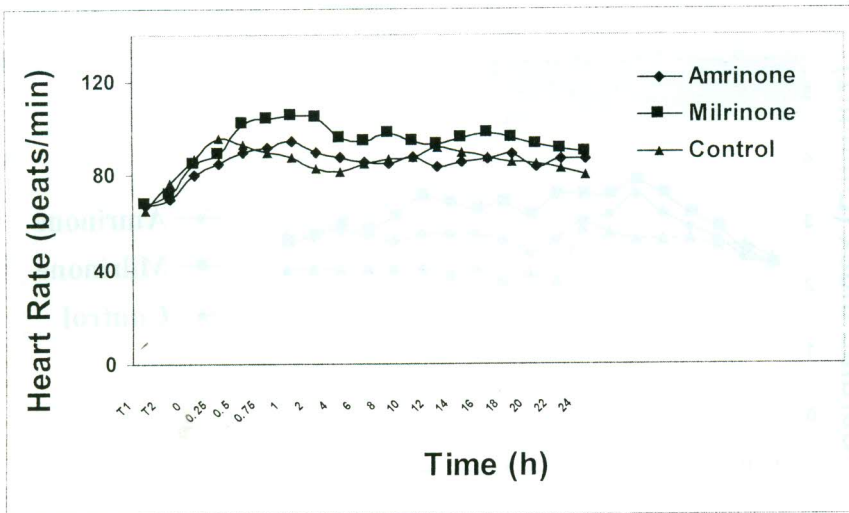


Figure 1. Mean (SD) changes in heart rate in the Amrinone, Milrinone and Control groups at baseline and at the specified intervals.

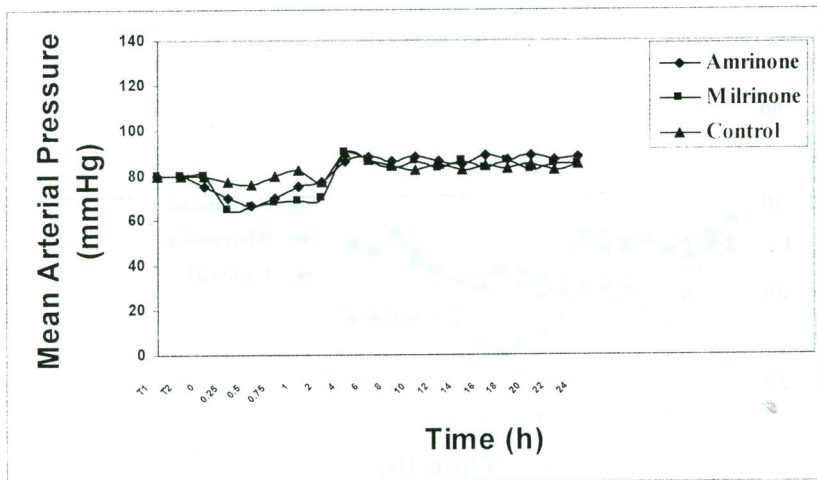


Figure 2. Mean (SD) changes in mean arterial pressure in the Amrinone, Milrinone and Control groups at baseline and at the specified intervals

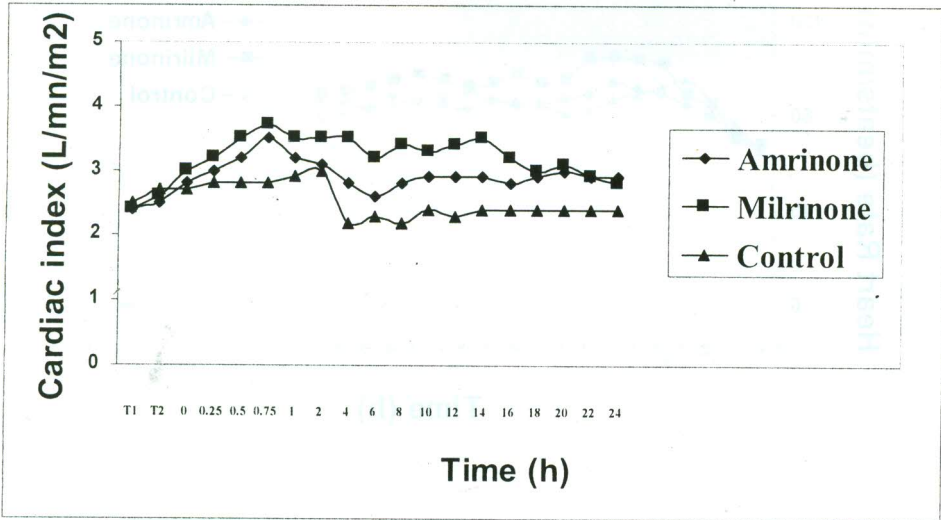


Figure 3. Mean (SD) changes in cardiac index in the Amrinone, Milrinone and Control groups at baseline and at the specified intervals.

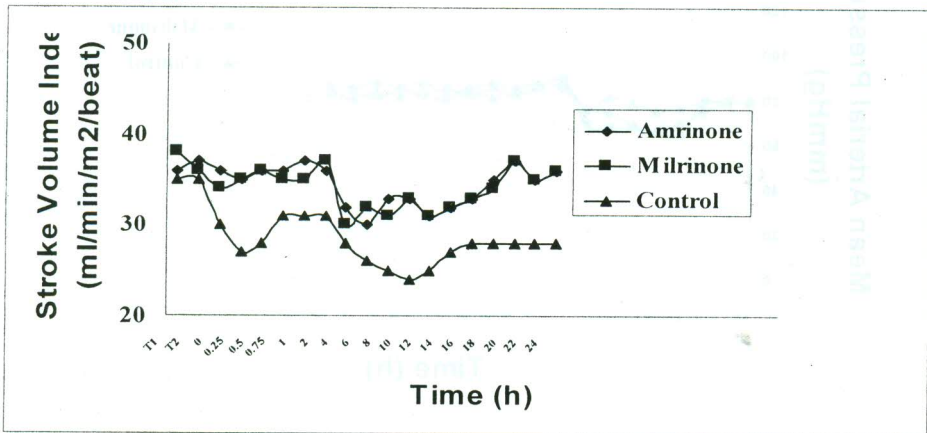


Figure 4. Mean ((SD) changes in stroke volume index in the Amrinone, Milrinone and Control groups at baseline and at the specified intervals.



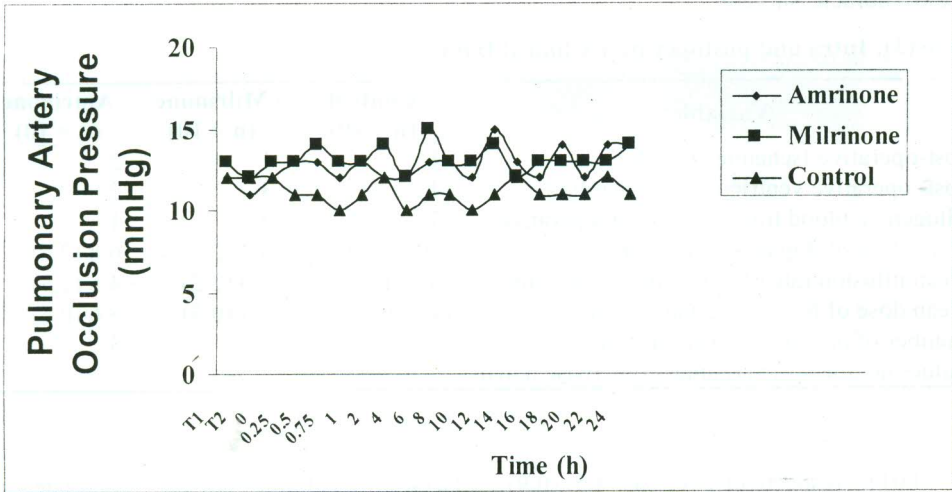


Figure 5. Mean (SD) changes in pulmonary artery occlusion pressure in the Amrinone, Milrinone and Control groups at baseline and at the specified intervals.

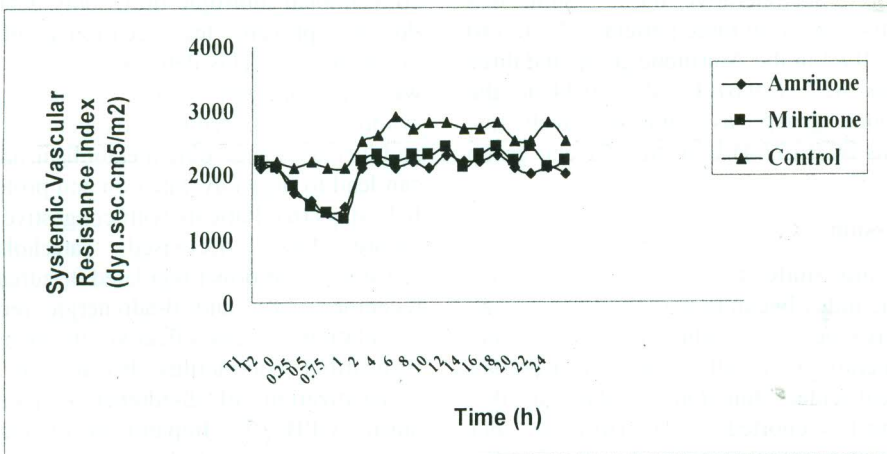


Figure 6. Mean (SD) changes in systemic vascular resistance index in the Amrinone, Milrinone and Control groups at baseline and at the specified intervals.

**Table (3): Intra and postoperative Clinical Data.**

Variable	Control (n = 10)	Milrinone (n = 10)	Amrinone (n = 10)
Post-operative Ischemic episodes	4	1	2
Post-operative ventricular tachycardia	4	3	2
Allogeneic blood transfusion (Intraoperative)	3	2	1
Mean dose of dopamine (mg/kg)	10.5 (2.0)	6.2 (2.2)	6.8 (2.6)
Mean infusion rate of dopamine (ug/kg/min)	6.9 (1.9)	4.0 (2.2)	4.5 (2.3)
Mean dose of Nitroglycerine (mg/kg)	4.5 (0.9)	3.5 (0.5)	3.6 (0.5)
Number of patient received Insulin	5	3	3
Values are means (SD) unless otherwise noted.			

P = 0.011, respectively, versus 4.5 (0.9) mg/kg in the Placebo group (Table 3).

We observed larger increases in lactate, creatinine kinase, lactate dehydrogenase, aspartate or alanine aminotransferase, C-reactive protein, and glucose in the Placebo group than in the Milrinone and Amrinone groups (P < 0.01), as shown in (Table 2) In the three postoperative days, insulin was administered IV in three patients 67.7 (33.6) U, P = 0.82 in the Amrinone group and three patients 62.7 (39.6) U, P = 0.44 in the Milrinone group, as compared with five patients 60.0 (37.4) U in the Placebo group (Table 3).

### Discussion

In this study, cardiac index and stroke volume index began to worsen at three hours and reached a nadir at 7–10 hours postoperatively in all groups, deterioration in ventricular function similar to that previously reported (2,4). However, our results show that, compared with placebo, milrinone and amrinone not only attenuated the postoperative nadir of cardiac function but also reduced the requirements for dopamine and nitroglycerin, as well as the blunted the postoperative increase of serum

lactate, creatinine kinase, aspartate or alanine aminotransferase, lactate dehydrogenase, glucose, and C-reactive protein levels.

Previous studies have shown that postoperative ventricular dysfunction continues to be common problem in patients undergoing CPB surgery and that conventional inotropic drugs only delay but do not prevent the occurrence of this problem (2,4). This deterioration, associated with postoperative low cardiac output syndrome (18), reduces oxygen transport and increases anaerobic metabolism, and this can lead to organ dysfunction and prolonged ICU stays (6). Patients with congestive heart failure have decreased catecholamine sensitivity and down regulated  $\beta_1$ -adrenergic receptors (7,8), and  $\beta$ -adrenergic receptor stimulation is less effective in increasing myocardial contractility because of acute desensitization of  $\beta$ -adrenergic receptors during CPB (9). Impairment of receptor sensitivity to catecholamines may explain why conventional inotropic support with catecholamines fails to prevent ventricular dysfunction. Phosphodiesterase III inhibitors increase ventricular function in patients who receive catecholamine and nitroglycerin

therapy immediately after separation from bypass and have a potential to prevent acute ventricular dysfunction in the early postoperative period (13,14). In this study, milrinone and amrinone reduced the deterioration in ventricular function and total necessary doses of dopamine and nitroglycerin. This indicates that milrinone and amrinone are useful in reducing the risk of low cardiac output syndrome after cardiac surgery.

There are some important differences between the methods and results of this study and those of previous reports (12,15). First, two previous reports examined the hemodynamic effects of milrinone or amrinone during the initial 10 minutes after separation from CPB and concluded that both milrinone and amrinone can effectively improve hemodynamic status and cardiac function in patients who had already undergone conventional therapy with catecholamines and nitroglycerin (12,15). Other previous studies focused mainly on the postoperative hemodynamic effects of milrinone (13,14). In this study, we investigated the advantages of preemptive use of phosphodiesterase III inhibitors in cardiac surgical patients and found that both milrinone and amrinone can contribute to overcoming the limits of conventional treatment with catecholamines and vasodilators for postoperative ventricular dysfunction.

This study showed another advantage of phosphodiesterase III inhibitors: they attenuate postoperative increases in lactate, cellular enzymes, and glucose levels. Second, in this study we chose the time of the systemic heparinization as the start point of phosphodiesterase III inhibitor administration and gave a loading dose of the drug for 10–15 minutes, whereas the phosphodiesterase III inhibitors in the previous reports were administered after

separation from CPB (12–15). The time of systemic heparinization and before any manipulations of the heart is the earliest point at which milrinone or amrinone can be delivered to the myocardium to assist in recovery from any expected surgical ischemia-induced reperfusion injury. In addition, because phosphodiesterase III inhibitors decrease arterial pressure because of a potent vasodilatory effect, rapid administration of a loading dose of milrinone or amrinone tends to increase the requirement for additional volume transfusion that's why early infusion at the time of heparinization gives more time—usually around 15-20 minutes to stabilize the hemodynamics before any serious cardiac manipulation.

Certain differences in the effects of milrinone and amrinone on cardiac performance deserve attention. In our study, although amrinone did not increase heart rate in the postoperative period compared with placebo, milrinone treatment was associated with significantly faster heart rates than with amrinone or the placebo at 10–20 hours postoperatively (Fig. 1). This observation is consistent with findings in previous hemodynamic studies (13, 14). The mechanism of milrinone-induced tachycardia may be caused by an increase in conduction through the atrioventricular node causing sinus tachycardia (19,20) or to increased peripheral vasodilation, although we found no difference between the Milrinone and Amrinone groups in postoperative systemic vascular resistance index (Fig.6).

In this study, C-reactive protein was significantly low in the Milrinone and Amrinone groups (Table 2), and this finding may be attributable to the potential of phosphodiesterase III inhibitors for immunomodulation by inhibiting intracellular cyclic nucleotide

phosphodiesterase, which increases the intracellular concentration of cyclic adenosine monophosphate.

Postoperative hyperglycemia was attenuated in the Milrinone and Amrinone groups in this study, probably because of reduction of dopamine requirement and subsequent decrease in stimulation of glycogenolysis and gluconeogenesis. Inhibition of phosphodiesterase III increases insulin secretion in islets of Langerhans in the human pancreas (22), and an increase in insulin secretion induced by milrinone or amrinone might contribute to attenuation of postoperative hyperglycemia.

Preemptive use of milrinone or amrinone in OPCAP patients not only attenuates postoperative deterioration of ventricular function, but also reduces the necessary doses of dopamine and nitroglycerin and the postoperative increase of lactate, glucose, and certain cellular enzyme levels. These results support a rationale for the use of milrinone or amrinone as a supplement to conventional catecholamine and vasodilatory therapy for maintenance of cardiac function. Because we conducted this study in patients with relatively good ventricular function, our findings should not be extrapolated to patients with impaired ventricular function, and further study of the impact on ICU stays, long-term outcome, and cost issues is required.

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## LEIOMYOMAS OF THE OESOPHAGUS A CLINICAL REVIEW

### ABSTRACT

**SUMMARY:** Benign tumours of the oesophagus are relatively rare. Leiomyoma is probably the most frequently encountered benign oesophageal tumour. It is an interesting diagnostic challenge, though once confirmed, the treatment is usually straight forward.

Leiomyomas of the oesophagus may present as vague symptoms of oesophageal or pulmonary disease to a range of health care personnel like General Physicians, Surgeons, Radiologists, Gastroenterologists, Respiratory Physicians and Thoracic Surgeons. As probably no one has seen a many of these lesions during a life time of his or her career, clinical diagnosis is virtually never made. This article presents an overall review of the subject, which may be of interest to medical professionals of a variety of disciplines and an attempt has been made to outline the latest modalities of investigations and treatment.

● Aitizaz Uddin Syed FRCS Ed. \*Amro Serag MD., ●Hosam Fawzy MD., ●Arto Nemlander MD, Ph D.

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### History:

The earliest record of benign oesophageal tumours dates back to 1559. The early literature has some spectacular reports of regurgitant benign oesophageal tumours presenting in the mouth of the patients (1). As a matter of fact some of these tumours have been reported to be successfully excised through the mouth after ligating the pedicle. Munro in 1797 (2) gave the first precise description of a localised intramural growth of the oesophagus. The histological features of the oesophageal leiomyoma were elaborated by Virchow in 1863 (3).

In 1932, Sauerbauch excised an oesophageal leiomyoma by oesophageal resection (3). In the following year Ohsawa successfully enucleated an oesophageal leiomyoma (4).

### Incidence:

It is very difficult to determine the exact incidence of oesophageal leiomyomas (5). Nearly all the available figures are from the ones published in the English literature. Moreover, a large number of single cases go unreported. A thorough review of the subject was published in 1976 by Seremetis et al., who collected a total of 838 cases of oesophageal leiomyomas reported worldwide up to that time (2). The paper concluded that oesophageal leiomyomas account for only 5 % of all the leiomyomas of the gastrointestinal tract (2). It has been claimed that leiomyomas represent 0.8% of all oesophageal tumours (6). Table 1 outlines the reported incidence of oesophageal leiomyoma.

### **Relation To Oesophageal Malignant Tumours:**

Geographical distribution of the leiomyoma is the same as that of oesophageal carcinoma. Statistically the ratio of oesophageal leiomyoma to oesophageal carcinoma has been variably reported from 1:10 to 1:1000 (7). Table 2 depicts the incidence ratio of oesophageal leiomyoma in relation to oesophageal carcinoma in different studies.

Only very few cases of malignant transformation in oesophageal leiomyoma have been documented. The best known case is that of Biasini 1949 who reported an oesophageal leiomyoma of 4.5X6 cm. with a small zone of leiomyosarcoma in it (8).

Callahan suggested that oesophageal leiomyoma may promote the development of carcinoma by causing stasis (9).

### **Age And Sex Incidence:**

Over 90% of oesophageal leiomyomas are seen in the age group of 20 to 60 years. Male to female ratio is 2:1. In general oesophageal leiomyomas occurs at an earlier age than oesophageal carcinomas. Oesophageal leiomyomas have been reported in children as young as 12 years of age (2).

Contrary to the predominantly solitary leiomyoma in the adults, over 91% of the cases in children are diffuse lesions. Bourque et al reviewed the literature in paediatric population in 1988 and concluded that the nature of the disease is different from the adult population, though the tumour is extremely rare in children. Enucleation is possible in less than 11 % of the cases, while surgical resection is required in 78 % of children with a 21% post operative mortality (10).

### **Genesis Of Oesophageal Leiomyomas:**

Piacentini (11) speculated three possible sites of origin of leiomyoma in Oesophagus namely; muscularis mucosa, Vessel wall muscle and embryonal rest.

Kramer et al (12) reported that oesophageal leiomyomas arise in muscularis mucosa in 20% of cases, the inner circular layer of muscularis propria in 75% of the patients and the longitudinal muscle layer in 5% of cases.

Washsmuth cited 4 cases of leiomyoma of oesophagus in one family (13). He proposed a genetic basis for the tumour, but there is no other report of familial involvement.

### **Growth Characteristics Of Oesophageal Leiomyomas:**

Leiomyomas growing in to the lumen of the oesophagus may present with signs and symptoms indistinguishable from other mucosal lesions. Extra mural leiomyomas occur in only in 3% of cases (5). The expanding intramural tumour may become horseshoe or annular in shape. Growth inside the lumen of oesophagus may assume elongated polypoid shape with long pedicle. The majority of the leiomyomas are solitary, and eccentrically growing. Multiple lesions are found in less than 3% of cases (5).

### **Histology Of Oesophageal Leiomyomas:**

Microscopically, these lesions are made up of spindle-shaped smooth muscle cells, arranged in interlacing bundles. The nuclei may show palisading; resembling a neurilemmoma. Neurilemmomas, however, have a true capsule. The main issue histologically; is to differentiate leiomyomas

**Table (1): Incidence of oesophageal leiomyomas.**

Series	Incidence %
Plachta A 1962 (46)	0.5%
Dillow et al 1970 (22)	0.015%
Postlewait & Musser 1974 (Autopsy series) (47)	5%
Seremetis 1976 (?)	0.9%
Tokubu et al 1981 (48)	7.9%
Domergue et al 1986 (6)	0.5%

from leiomyosarcomas. The number of mitotic figures and the absence or poor development of intracellular organelles is considered a reliable indicator of malignancy (14).

### Symptoms Of Oesophageal Leiomyomas:

Many oesophageal leiomyomas are asymptomatic, incidental discovery as a mediastinal mass on chest X-ray is quite common (15). Unsuspected leiomyomas have been found in association with epiphrenic diverticulæ and at oesophageal hiatal hernia repairs (16, 17).

Commonly documented symptoms are dysphagia, dyspepsia, retrosternal pain, nausea, vomiting, regurgitation, epigastric discomfort, weight loss and occasionally haematemesis. Even large oesophageal leiomyomas seem to cause no difficulty in swallowing. Normal distensibility of the opposite wall of the oesophagus and non involvement of the mucosa can explain this discrepancy (17). The symptoms occur over a long period and are usually mild. Sixty seven percent of the symptomatic patients have dyspepsia, while dysphagia is observed in 50% of the cases. Concomitant pathologies possibly contribute to some of the symptoms of oesophageal leiomyomas.

Though nearly 50% of the gastric leiomyomas present with bleeding (18), haematemesis and melaena are extremely

rare in oesophageal leiomyomas. Johnston and associates proposed that bleeding results from regurgitation of acid gastric contents or from ischemia and necrosis of the mucosa overlying the tumour (19).

Large tumours may produce pulmonary symptoms due to their compressing effects on the neighbouring trachea and bronchi. Cough, respiratory infections (20), collapse of a lobe and pleural effusion have been frequently documented in patients with oesophageal leiomyomas (1).

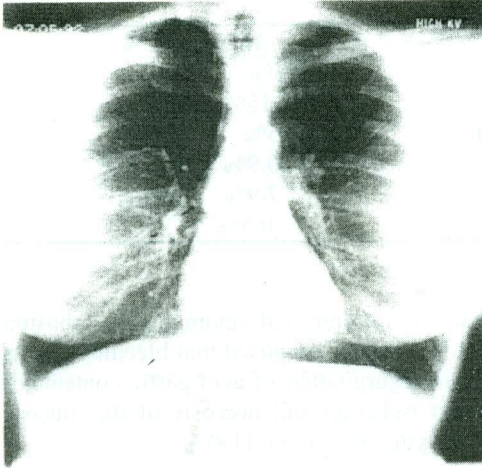
Cardiac compression due to oesophageal leiomyoma is extremely unusual. Mc Manus and Mathews described a case of 62 year old lady who presented with atrial fibrillation which reverted to sinus rhythm following excision of an oesophageal leiomyoma (21).

### Associated Conditions

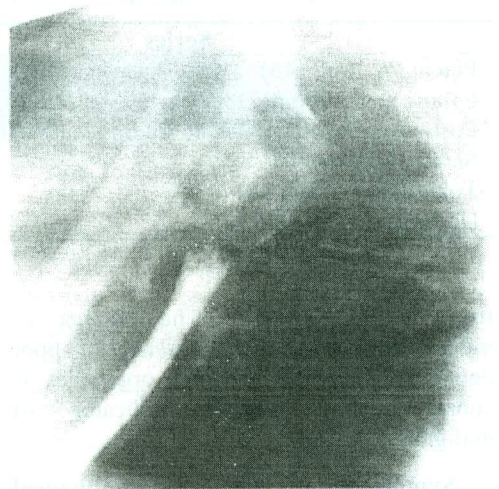
Most common co-existing pathology is hiatal hernia of the oesophagus. This association is probably coincidental as the age range and the site, i.e. lower third of the oesophagus, are shared by both lesions (17). Hodge estimates that the ratio of occurrence of leiomyoma to hiatal hernia is 1: 24 (16).

Twelve cases of oesophageal leiomyomas in epiphrenic diverticulæ have been reported, however the issue of cause and effect relationship is debatable (16). This is an important finding because the diverticulum often obscures the presence of





**Figure (1):** Chest X-ray of a patient which shows a distinct soft tissue shadow in the area of the right pulmonary hilum (arrows).



**Figure (2):** Barium swallow showing submucosal compressing lesion with normal oesophageal mucosa.

tumour and makes the diagnosis of leiomyoma difficult.

Other associated conditions are oesophageal carcinoma, gastric ulcers, Barret's oesophagus and bronchial carcinomas (22).

Multiple oesophageal leiomyomatosis is a recognized entity (23), such patients are known to present with multiple or recurrent tumours (24). And there are also reports of an autosomally dominant inherited syndrome of oesophageal muscular hypertrophy, Alport like nephropathy and bilateral cataracts (25).

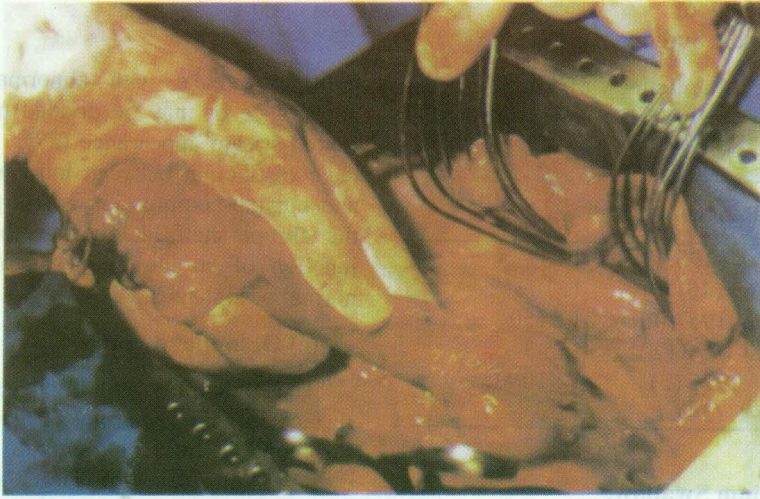
### **Investigations:**

#### **(a) Plain Chest X-ray:**

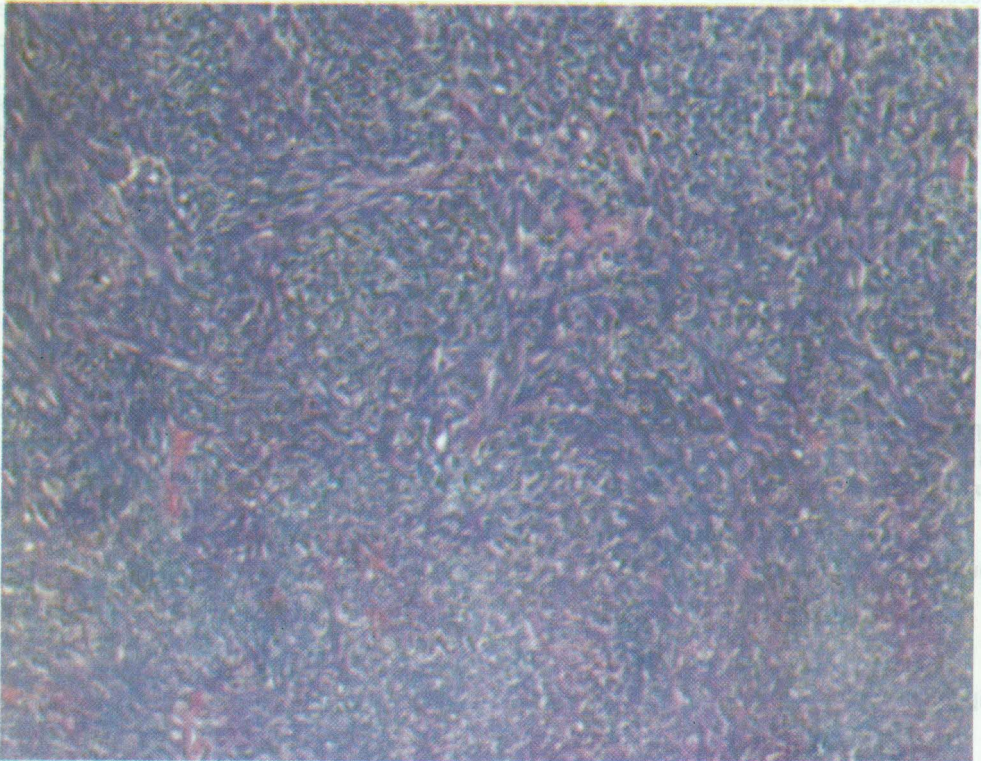
A soft tissue mediastinal mass on plain X-ray may finally turn out to be a leiomyoma. Overlying heart shadow can

obscure some of these lesions in a postero-anterior chest film. Lateral radiographs of the chest are usually more informative under such conditions (26). On fluoroscopy these mediastinal masses are seen to move on swallowing (1). Some calcification may be present in about 1.8% of all oesophageal leiomyomas (2). However plain chest films are almost always unable to resolve the issue of a mediastinal mass completely. Some of the leiomyomas of oesophagus have transmitted pulsation from the neighboring aorta, such lesions justify an aortogram to exclude aortic aneurysms (27).

Though, Plain chest X-rays do not provide the definitive diagnosis, they may be helpful in delineating the tumours of middle third of the oesophagus which project distinctly in the mediastinal border over the pulmonary hilar shadow (Figure No. 1).



**Figure (3): Operative photograph of multiple large oesophageal leiomyomas requiring subtotal oesophagectomy**



**Figure (4): Typical histological appearance of oesophageal leiomyoma with palisading smooth muscle cells.**

**Table (2): Incidence of oesophageal leiomyomas in relation to oesophageal carcinomas.**

SERIES.	INCIDENCE %.
Johnston et al 1953(19)	1 : 15
Plachta 1962 (46)	1 : 10
Watson et al 1967 (49)	1 : 150
Dillow et al 1970 (22)	1 : 43
Seremetis 1976 (2)	1 : 1000
Huang 1991 (34)	1:30

**(b) Barium Swallow:**

Barium swallow is very useful in the diagnosis of oesophageal leiomyomas. According to Schatzki and Howes (28) the characteristics of a benign intramural oesophageal tumour on barium swallow are;

(a) Mucosal folds are normal and clearly visible.

(b) Upper and / or Lower margins of the lesion appear to make a sharp angle with the normal segment of the oesophagus.

(c) The swelling can be demonstrated to move with the oesophagus on swallowing.

(d) The lumen of the oesophagus may appear constricted in one plane, however on films taken at different angles it is stretched and widened in another diameter.

(e) The mass is clearly defined in outline.

(f) The oesophagus is not rigid.

Some of these features can be easily appreciated in Figure No. 2.

Large oesophageal leiomyomas can produce bizarre pictures on barium swallow. Column of the contrast may be broken in to

multiple streaks with abnormal mucosal appearance or may be divided producing a forked-stream appearance (27). However a clear distinction between intramural lesions and outside compression is still possible by the abrupt shelf like borders between the junction of an intramural tumour and the normal oesophagus.

**(c) Oesophagoscopy:**

These tumours usually have a smooth surface with normal mucosa and surprisingly little intramural obstruction even in the case of large leiomyomas. Oesophagoscopy appearance may be normal in majority of the cases.

Though oesophagoscopy is mandatory in all patients undergoing thoracotomy, the role of endoscopic biopsies in a suspected case of oesophageal leiomyoma is controversial. It is argued that an endoscopic biopsy damages the intact mucosa and makes it adherent to an otherwise freely mobile tumour, thus making it difficult to enucleate at a future operation (22). Endoscopic biopsy is definitely indicated in cases with mucosal damage and in pedunculated tumours.

**(d) Endoscopic Ultrasonography:**

This is a reliable and convenient method of investigation. Endosonography is claimed to be superior to barium studies and CT scans in detection, staging and follow up of oesophageal wall tumours (29).

It is possible to differentiate between submucosal and extra luminal masses, and to detect very small ie; less than 5 mm tumours by endoscopic ultrasonography. On endosonography the leiomyomas are seen as hypoechoic masses with clearly demonstrable boundaries and normal overlying mucosa and submucosa. However

in tumours larger than 4 cm in diameter, a central ulcer or large blood vessel may lead to nonhomogenous echo pattern making it difficult to differentiate between leiomyomas and leiomyosarcomas of the oesophagus (30).

#### (e) C.T. Scans:

Computed tomography is extremely useful in deciding the exact site and nature of mediastinal masses. Leiomyomas are generally homogenous with a rather regular shape, in contrast to leiomyosarcomas of the G.I. tract, which are variably non homogenous and irregular in shape (31). Moreover CT scan of chest may show distant metastases in a tumour of malignant nature.

C T scans are claimed to be superior to oesophageal manometry and barium contrast studies in differentiating diffuse oesophageal leiomyomatosis from achalasia (32).

#### (f) Other Investigations:

Aortograms and other radiological and biochemical investigations may be advisable in investigating unusual mediastinal masses, some of which later turn out to be leiomyomas of oesophagus. Bronchoscopy in conjunction with oesophagoscopy is indicated in tumours producing respiratory symptoms (33).

#### Treatment:

Surgical enucleation of the oesophageal leiomyomas was the traditional practice in the past. However with the advent of video assisted thoracoscopic surgery and ingenious endoscopic removal techniques surgical excision is rarely warranted.

Sauerbruch is credited with the first successful resection of oesophageal leiomyoma (3), Ohsawa in 1933 (4) demonstrated the possibility of enucleation

of this tumour, thus preserving the oesophageal wall integrity.

The surgical approach depends upon the location of the tumour and the need to perform an associated procedure e.g. anti-reflux procedure. The surgical access may be via cervical, right thoracotomy, left thoracotomy or thoraco-abdominal incision.

Enucleation is the procedure of choice, and can be accomplished easily in 90% of oesophageal leiomyomas (34). Leiomyomas are well defined and can be easily shelled out through a longitudinal incision in the muscular wall of the oesophagus. The defect in the muscular wall of oesophagus is repaired by approximating the splayed muscle with interrupted stitches. Appreciable motility or swallowing disorders have not been reported in patients; with even large gaps in the oesophageal musculature after enucleation of the leiomyomas. There is only one report of a sacular diverticulum at the previous site of enucleation of a leiomyoma (35).

Plastic reinforcement of the oesophageal wall following enucleation of leiomyoma has been practiced by Russian Surgeons (36). Fujita et al (37) have reported using a latissimus dorsi muscle flap after enucleation of a giant leiomyoma measuring 11.5 cm. Other authors have reported use of diaphragmatic pedicle, Lung flap or Ivalon graft to reinforce the oesophagus after enucleation of a large leiomyoma (34).

An associated antireflux repair must be performed following enucleation of tumours of gastro-oesophageal junction since the extent of dissection required, disrupts the normal antireflux mechanisms (5).

#### Indications Of Oesophageal Resection:

Oesophageal resection is required in about 10% of oesophageal leiomyomas. The indications are, large tumours (over 8cm),

annular leiomyoma. high degree of adhesions of mucosa and tumour (2), ulcer formation (39), a combination with cancer and diverticulum (40), suspicion of malignancy and injury to the mucous membrane during dissection (41) or accidental extensive damage to oesophageal wall which appears to present danger of post-operative leakage. Figure No. (3) shows an operative picture of a case with multiple large leiomyomas necessitating an oesophagectomy.

Many series have reported no operative mortality but in general it is less than 2% with enucleation and less than 10% with resection (44).

#### **Video Assisted Thoracoscopic Surgery (Vats) For Enucleation Of Esophageal Leiomyoma:**

With the advent of videoassisted thoracoscopic surgery in the recent past; it has been possible to successfully enucleate oesophageal leiomyomas by Video thoracoscopy (42). Though no large series have been published so far but experience with limited number of cases suggests that Videoassisted thoracoscopic resection is possibly a better option in cases where a definite diagnosis of leiomyoma of the oesophagus is made before the operation (43).

The simplicity and safety of the thoracoscopic approach, combined with reduced surgical trauma, post-operative pain and functional and cosmetic advantages, make this technique the approach of choice for the removal of esophageal leiomyoma (44).

A new VATS technique for enucleation of esophageal leiomyoma, is to assist the dissection with balloon dilators. The use of

the balloon dilator facilitates separation of the tumor from both the mucosal and muscular layers of the esophagus, and may help prevent perforation (45). Possible complications of VATS approach are, esophageal perforation, fistulas, and oesophageal pseudodiverticulum (46).

#### **Endoscopic Removal Techniques:**

Another interesting surgical option is endoscopic removal in selected cases (38). In 1985, Taka Hara et al., (39) performed an endoscopic polypectomy for a less than 2 cm diameter pedunculated leiomyoma of oesophagus. The combination of endoscopic procedure with or without VATS represents a minimally invasive approach with correspondingly minor surgical trauma. Using simultaneous esophagoscopy and transillumination (diaphanoscopy) of the esophageal wall, the safety and accuracy of the dissection is increased, and the risk of mucosal perforation minimized (47). The presence of the endoscope also provides transillumination that improves visualisation of the operative field and stabilizes the esophagus.

Endoscopic laser ablation has been carried out with safety in stenosing leiomyoma of the esophagus (48).

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# COMPARISON OF THE OXYGEN DELIVERY, TOTAL BODY OXYGEN CONSUMPTION AND OXYGEN EXTRACTION FRACTION IN PATIENTS UNDERGOING OFF-PUMP AND CONVENTIONAL CABG

## ABSTRACT

**Objectives:** The relationship between oxygen delivery and consumption undergoes a marked change during cardiopulmonary bypass. Off-pump coronary artery bypass grafting (OPCAB) obviates the need for cardiopulmonary bypass (the pump). It was perceived that the oxygen metabolism is markedly different between the two techniques.

**Methods:** We prospectively studied 30 consecutive CABG patients the patients were divided into two groups: Group 1: conventional CABG using cardiopulmonary bypass (n =15). Group 2: Off-pump coronary artery bypass grafting (n =15). All the patients received the same type of anesthetic management and postoperative care. Oxygen metabolism indices were calculated from the start of the operation up to 24 hours postoperatively.

**Results:** Oxygen consumption ( $VO_2$ ) and Oxygen extraction fraction ( $ExO_2$ ) increased in the immediate postoperative period. The oxygen delivery ( $DO_2$ ) decreased significantly compared with the baseline. The pattern of change in oxygen delivery, consumption and oxygen extraction fraction was similar in both groups up to 24 hours.

**Conclusion:** Cardiopulmonary bypass is known to induce a profound inflammatory response. However the same pattern of oxygen metabolism changes occurs in OPCAB surgery. This suggests that the surgical trauma itself causes a significant inflammatory response in OPCAB patients.

**Key words:** Coronary artery bypass grafting, Cardiopulmonary bypass, Oxygen metabolism.

Elmistekawy E., Fawzy H., Uddin Syed A., Nemlander A. and Nooreldin B.\*

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## Introduction

Initial attempts of coronary artery bypass grafting were made on beating heart, until the advent of cardiopulmonary bypass (CPB) and cardioplegia in late 1960,s (1). Recognition of the deleterious effects of cardiopulmonary bypass (CPB) led to renewal of interest in off pump coronary artery bypass grafting (OPCAB) in the

recent few years (2). Each of these two techniques has its advantages and disadvantages however they share in many attributes such as the surgical trauma, anesthetic challenges, heparin use and the use of suction devices (3)(4)(5)(6) .

The postoperative course of patients undergoing coronary artery bypass grafting using CPB is one of the hypermetabolic response, characterized by changes in the

whole body oxygen consumption and other oxygen metabolism indices, that attributed to the cardiopulmonary bypass (7)(8)(9)(10)(11)(12)(13). Somewhat similar changes are reported after major non-cardiac surgical conditions and critical illnesses (14) (15) (16).

Increasing use of off -pump CABG raises a question: whether there any difference in the oxygen metabolism in patients getting off-pump coronary artery revascularization as compared with conventional CABG patients.

We conducted this study to compare oxygen metabolism behavior in both conventional and off- pump CABG patients.

## Methods

### Patient's population:

Thirty consecutive patients were prospectively enrolled in this study.

Patients who needed emergency CABG and those who developed low cardiac output after surgery were excluded from the study.

### The patients were divided into two groups:

**Group I:** included patients who underwent conventional CABG utilizing CPB (No.15).

**Group II:** included patients who underwent off pump CABG (No.15).

Our Hospital Medical Research Ethical Committee approved the study.

### Anesthetic technique:

The patients were premeditated using Nitrazepam 0.1 mg/kg PO 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 1-2 mg/kg, and Pancuronium 0.1 mg/kg. Maintenance was done using Sevoflurane 1-3% with N<sub>2</sub>O/O<sub>2</sub> 50/50%. During cardiopulmonary bypass time, anesthesia was maintained by Sevoflurane 0.5-1%, Pancuronium 0.06 mg/kg, and Fentanyl 1-2 ug/ kg.

Before induction of anesthesia arterial line was inserted usually in the Rt. radial artery or femoral artery. Swan Ganz thermodilution pulmonary catheter (Baxter Health Care Corp.) was inserted in all patients.

### Conventional CABG:

All operations are done via median sternotomy. Conduits used for bypass depended on patients characteristics and included left internal mammary and right internal mammary arteries (IMAs), left radial, and saphenous vein grafts. At the final steps of IMA dissection, Heparin was given in a dose of 300 U. /kg. Cannulation of the ascending aorta, 2 stage venous cannulation, and aortic root cardioplegic and vent lines were inserted. Roller, non-pulsatile CPB (Cobe-Century-USA), and membrane oxygenator (Capiiox Sx-Turumo-Corp.Tokyo-Japan) were used. Cold antegrade multidose blood cardioplegia (Modified St. Thomas Cardiologic solution) was used for cardiac standstill. The patient core temperature during CPB was around 30-32 °C and cardiopulmonary bypass flow was maintained at 2.4 L./min./m<sup>2</sup> with hematocrite above 20% at all times.

### Off- pump CABG:

All patients were operated through median sternotomy. After harvesting conduits and making pericardial sling, Heparin at 150 U/kg. was administered, and supplemental doses were added, as needed,

to maintain Activated Clotting Time (ACT) between 200- 250 seconds. The proximal anastomosis were then performed using a partial aortic occlusion clamp followed by distal anastomosis to left anterior descending coronary artery, right coronary artery and circumflex marginal branches as indicated. Each artery was stabilized in turn using the Medtronic Octopus III Tissue Stabilization System (Medtronic, Inc, Minneapolis, MN). Starfish (Medtronic, Inc, Minneapolis, MN) was used alone or with deep pericardial stitch for positioning and exposure of the heart. Intracoronary shunts were used when feasible to maintain distal coronary perfusion during the distal anastomosis of the grafts. After completing of the anastomoses, the total dose of Heparin was reversed with Protamine (1:1 ratio). Cell saver (Bret2, Cobe Cardiovascular. Inc. Division of Sorin Biomedica USA) was usually used from the start of the operation in 2/3 of the patients.

**Postoperative care:**

All patients were returned to cardiac surgical intensive care unit, exactly postoperative management were done in both groups this included homodynamic parameters (Heart rate, Invasive blood pressure, Central venous pressure and pulmonary artery pressure), temperature, and fluid balance were recorded every hour. Mean arterial blood pressure was kept between 65 -90 mmHg and heart rate between 60 -100 beat / minute. Weaning from mechanical ventilation was done as soon as hemodynamic and ventilatory stability was achieved and the patient was awake and able to maintain patent airway.

**Study design:**

Blood samples were drawn from the arterial line and from the distal port of Swan Ganz catheter at the following time points:

Before skin incision (base line), after skin closure, at 1 hour, 6 hours, 12 hours and 24 hours postoperatively. At all those time points measurements of arterial, mixed venous oxygen partial pressure and saturation and hemoglobin concentration were done. Cardiac output and Cardiac index were calculated using thermodilution technique (using Datascope monitoring system) at each time points.

The following formula were used to calculate oxygen metabolism indices (11) (13):

$$CaO_2 = Hb \times SaO_2 \times 1.33 + PO_2 \times 0.0031$$

$$CvO_2 = Hb \times SvO_2 \times 1.33 + PvO_2 \times 0.0031$$

$$Do_2 = CI \times CaO_2 \times 10$$

$$Vo_2 = CI \times 10 \times \{CaO_2 - CvO_2\}$$

$$Exo_2 = Vo_2 / Do_2 \times 100$$

**Where:**  $CaO_2$  = Arterial oxygen content (mlO<sub>2</sub>/100 ml bl.),  $CvO_2$  = Venous oxygen content (mlO<sub>2</sub>/100 ml bl.), **Hb** =Hemoglobin content of the blood (gm/dl),  $SaO_2$  = Arterial oxygen saturation (%),  $SvO_2$ = Mixed venous oxygen saturation (%),  $PO_2$  = Arterial blood oxygen partial pressure (mmHg),  $PvO_2$ = Venous blood oxygen partial pressure (mmHg), **CI**= Cardiac index (L./min./M<sup>2</sup>),  $Do_2$  =Oxygen delivery (ml/min./M<sup>2</sup>),  $Vo_2$  = Oxygen consumption (ml/min./M<sup>2</sup>),  $Exo_2$  = Oxygen extraction ratio (%), 1.33 = binding coefficient and 0.0031 = oxygen solubility coefficient.

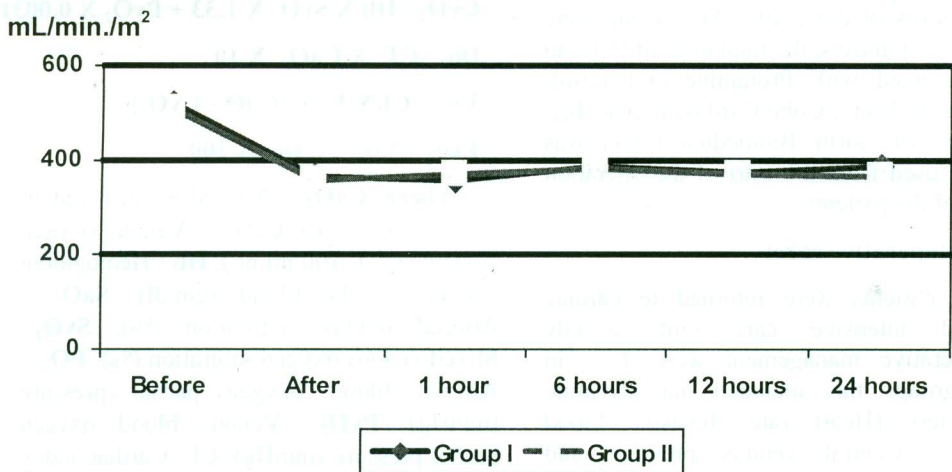
**Statistical Analysis:**

Statistical analysis was performed using SPSS program version 10 for Windows. The data were presented as the mean ± standard deviation. A 95% confidence interval was applied with p < 0.05 to be considered significant. Independent samples t-test have

**Table (1): Demographic data of the two groups.**

	Group I	Group II	Significance
Age (Years)	55.80±9.80	55.86±10.49	NS
Sex			
Female	2	1	
Male	13 (86.66%)	14 (93.33%)	NS
BSA (m <sup>2</sup> )	1.78±18	1.73±0.13	NS
BMI	27.50±2.44.	26.28±3.32	NS
EURO SCORE	2.71±1.84	2.93±4.9	NS
Number of Diabetic patients	5/15	6/15	
Number of Hypertensive patients	8/15	7/15	
Number of smokers	5/15	6/15	

Data presented as Mean ± Standard deviation. P value < 0.05. NS = Non Significant.



**Figure (1): Oxygen delivery changes in the two groups.**

compared means of different variable for two groups, for parametric tests while two-independent samples test have compared two groups of cases on one variable, for the nonparametric tests.

## Results

### 1-The demographic and clinical variables:

The demographic characteristics and clinical variables of the two groups are

reported in table No.1 and table No.2. There is no statistical significant difference between the two groups regarding age, sex, body surface area (BSA), body mass index (BMI), ejection fraction (EF%) and Euro score.

There was no significant difference in the number of distal anastomosis, total drainage, intubation time, intensive care duration and length of hospital stay. One patient in group I developed postoperative

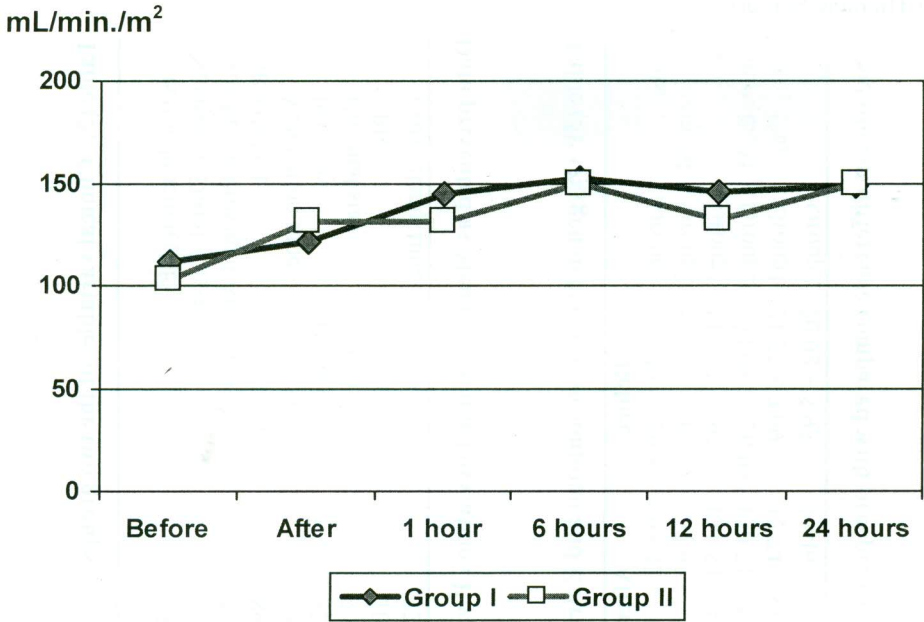


Figure (2): Oxygen consumption changes in the two groups.

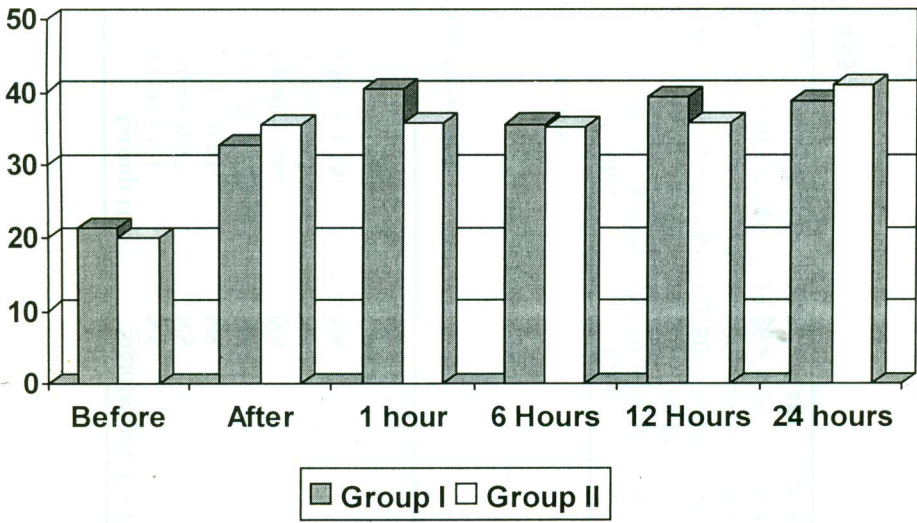


Figure (3): Oxygen extraction ratio changes in the two groups.

Table (2): Clinical variables of the two groups.

	Group I		Group II		Significance P value <0.05
Ejection Fraction (EF) %	49.66 ± 9.95	49.00 ± 9.1	NS		
Number of Distal Anastomosis	3.26 ± 0.96	2.66 ± 0.97	NS		
Number of Proximal Anastomosis	1.37 ± 1.03	1.13 ± 0.91	NS		
DRAINAGE: (ml/24 hours)	891.20 ± 382.92	694.20 ± 248.47	NS		
Ventilation time (Hours)	13.40 ± 11.51	10.00 ± 5.83	NS		
ICU stay (Hours)	32.53 ± 8.92	32.00 ± 9.7	NS		
Hospital stay (days)	7.93 ± 2.6	6.86 ± 1.18	NS		
CPB (minutes)	107.46 ± 36.00	-	-		
Cross clamp time (minutes)	72.4 ± 28.49	-	-		

Data presented as Mean ± Standard deviation . P value < 0.05. NS = Non Significant.

Table (3): Oxygen delivery, Consumption and Extraction ratio in the two groups.

	Before		After		1hr.	6hr.	12hr	24hr
Do <sub>2</sub> (ml/min./M <sup>2</sup> )	Group1	518.80 ± 56.10	363.32 ± 74.59*	357.92 ± 52.04*	385.71 ± 85.92*	374.39 ± 58.16*	384.97 ± 65.52*	
	Group2	509.17 ± 62.21	357.92 ± 37.19*	371.19 ± 55.23*	383.65 ± 84.74*	369.11 ± 60.85*	366.23 ± 49.41*	
Vo <sub>2</sub> (ml/min./M <sup>2</sup> )	Group1	111.93 ± 93	121.54 ± 42.85*	145.12 ± 37.99*	135.96 ± 35.56*	145.80 ± 31.99*	148.60 ± 37.85*	
	Group2	103.05 ± 36.95	130.71 ± 51.81*	131.38 ± 31.07*	133.53 ± 25.61*	132.26 ± 40.33*	149.42 ± 34.12*	
Exo <sub>2</sub> (%)	Group1	21.57 ± 7.09	32.74 ± 8.60*	40.36 ± 8.30*	35.30 ± 7.78*	39.26 ± 8.29*	38.82 ± 8.10*	
	Group2	20.02 ± 5.95	35.46 ± 11.16*	35.74 ± 8.0*	35.30 ± 5.45*	35.76 ± 9.48*	40.86 ± 8.0*	

\* Significant difference compared with preoperative value. P. value < 0.05.

pneumonia and pleural effusion while one patient in group II had renal impairment.

2-Oxygen metabolism variables: (Table N.3)

#### **Oxygen delivery (Do<sub>2</sub>):**

Compared with the baseline, oxygen delivery decreased significantly after skin closure at 1 hr. and 6 hr. postoperatively. This difference was less marked at 12 and 24 hours postoperatively in both groups but still significant. There was no statistical significance difference (p value < 0.05) between the 2 groups at any time point. (Figure No. 1)

#### **Oxygen consumption (Vo<sub>2</sub>):**

Compared with the baseline, oxygen consumption increased significantly after skin closure, at 1hr., 6 hr., 12 hr., and 24 hr. postoperatively in both groups. There was no statistical significance difference between the 2 groups at any time point. (P value <0.05) (Figure No. 2).

#### **Oxygen extraction (Exo<sub>2</sub> %):**

Compared with the baseline, oxygen extraction was increased significantly in the postoperatively in both groups. There was no statistical significance difference between the 2 groups at any time point. (P value < 0.05) (Figure No. 3). From our data we found that the behavior of Do<sub>2</sub>, Vo<sub>2</sub> and Exo<sub>2</sub> were similar in the 2 groups.

#### **Discussion**

Optimization of tissue oxygenation (delivery and consumption) in the perioperative period is essential for reduction of both morbidity and mortality after cardiac surgery (13) (17) (18) (19). Tissue oxygen balance relies on three factors: pulmonary gas exchange, Oxygen delivery and systemic gas exchange. Studying the relationship between Do<sub>2</sub>, Vo<sub>2</sub>

and Exo<sub>2</sub> assists in identification of those patients at risk of developing defective tissue oxygenation (20) (21). Because of the defective tissue oxygenation, the cells resort to anaerobic metabolism resulting in elevated lactate level and other anaerobic metabolites with its drawbacks. (18)

The use of cardiopulmonary bypass is often linked to impairment of tissue oxygenation and oxygen debt accumulation that may extend into the postoperative period (8) (9) (22). This effect was explained by diminished ability of the tissues to extract oxygen, increased tissues oxygen demand or both (23). Also the cardiopulmonary bypass is known to induce lung injury as well as release of a plethora of inflammatory mediators and cytokines that may affect oxygen metabolism. (7) (23) (24) (25). Hass et al., (20) attributed these changes to clamping of the aorta, they presumed that repayment of the debt was delayed and extent to ICU due to thermoregulatory vasoconstriction .

In contrast to these findings systemic oxygenation was not impaired by using cardiopulmonary bypass for cardiac surgery as reported by Ganuschak et al., (13) in their study that included 15 patients who underwent CABG using hypothermic CPB, they found that oxygen extraction begin to rise and reach maximum at 12-18 hours postoperatively, they attributed this changes to body temperature and stress of weaning.

Interestingly it was demonstrated that oxygen metabolism alteration occurs also in all major surgical procedures as well as stress conditions (26) .

In our study we found that oxygen consumption and extraction ratio was increased immediately after closure and in the postoperative period (1hr.-24 hr.). At the same time oxygen delivery was decreased during the same periods. Comparing those

changes with perioperative values statistically significant difference was present up to 24 hours postoperatively (P value < 0.05). Comparing those changes in between the 2 groups, no statistically significant difference was found between the two groups i.e. oxygen metabolism indices were behaving more or less the same manner in both off pump and on pump CABG.

Similar finding was reported by Parolari et al (27) who studied two groups of patients who underwent CABG the first group (n. 14) underwent on pump CABG and the other underwent off pump CABG (n.11) they compared oxygen metabolism indices (oxygen delivery, consumption and extraction ratios during 18 hours follow up postoperatively, they did not find statistical significant difference between the two groups regarding these parameters. They said that a hypermetabolic status ensues often after both on pump and off pump CABG as reflected by increased oxygen consumption with respect to base line and oxygen extraction ratio with respect to the base line values. The time and extent of response of those variables was similar in the both groups.

The increased metabolic rate after both on pump and off pump CABG observed in our study (and other studies of patients undergoing cardiac or non cardiac operations) may be caused by perioperative inflammation induced by surgical trauma and stress (11) (14) (15) (16) (20).

It is known that the temperature (which reduces metabolic rate) has an important role in the metabolic process including oxygen, but in our study the role of temperature was not studied as we did our measurements while the patients are

normothermic in both groups (temp.36-37 Oc).

### **Conclusion**

We concluded that similar changes of oxygen transport indices (delivery, consumption and extraction ratio) occur in the perioperative period after CABG these changes occur irrespective of the use of CPB.

We presumed that these changes may be due to surgical trauma and stress response on oxygen metabolism.

### **Limitation of our study:**

Small number of the patients is one of the limitations of this study also correlation of oxygen metabolism indices was not correlated with body temperature and hemodynamics.

### **Acknowledgement:**

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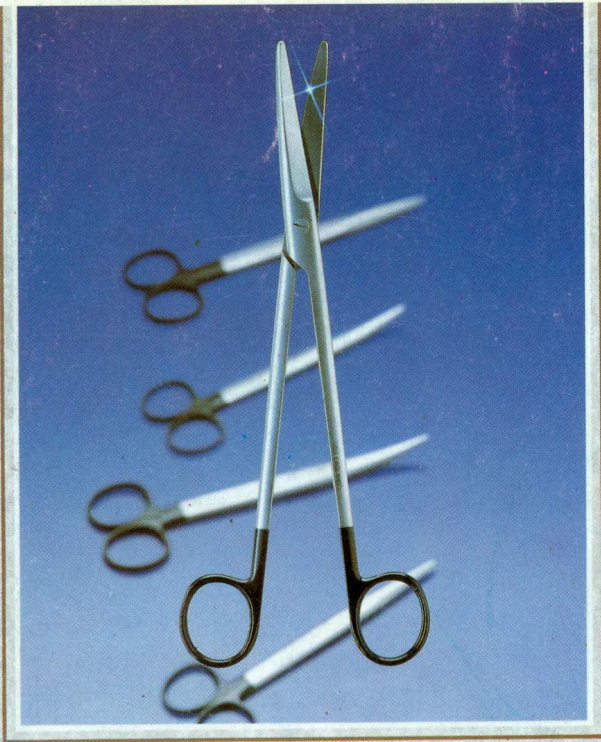
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