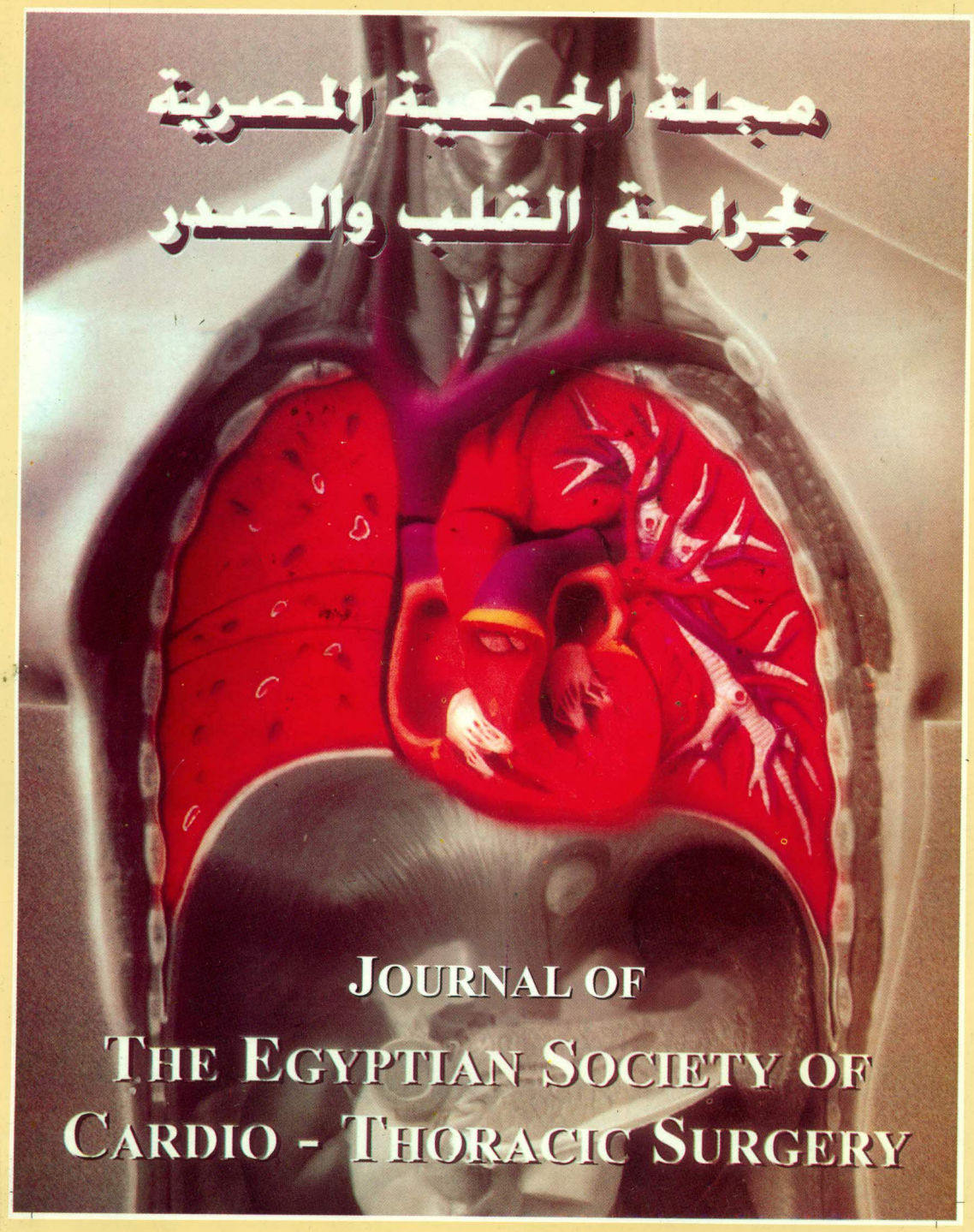
Vol. IV, No 4 September 1996
ISSN 1110-578X
المجلد الرابع عدد رقم ٤ سبتمبر ١٩٩٦



Editor
MOHAMED EL FIKY

الشركة المصرية للتوريدات ش.م.م
Egyptian Company For Supplies S.A.E.

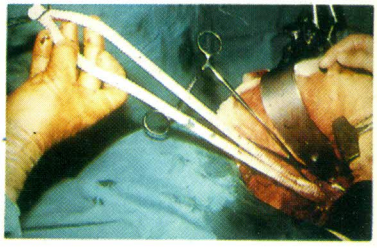
١٠٥ ش عبد العزيز آل سعود - المنيل ت: ٣٦٢٨٩٦١ - ٣٦٣٤٦٩٩ فاكس : ٣٦٢١٧٤٣

105 Abdel Aziz Al Scoud St., Manial, Tel: 3628961 / 3634699 Fax: 3621743

SULZER MEDICA

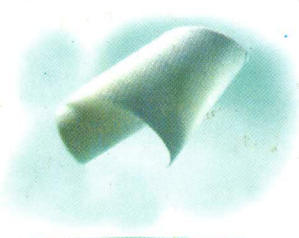
Carotid Patches

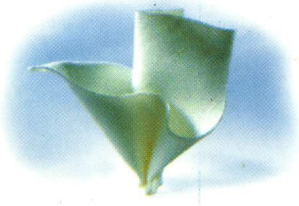
GELSEAL® bifurcate in aorto-bifemoral procedure.

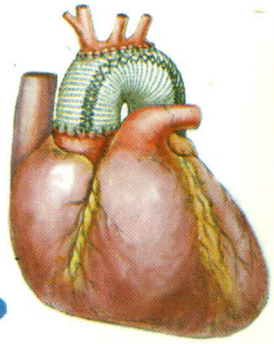


VASCUTEK
A company of SULZER medica

A New Biomaterial For Hernia Repair







Fluoromesh™
Monofilament

Fluorosoft™
Multifilament

Board of the Egyptian Society of Cardio-thoracic Surgery 1996

President	Mohamed El-Fiky
Vice President	Gamal Abou Senna
Secretary General	Hussein Gaafar
Assistant Secretary General	Mohamed Bassiouni
Treasurer	Ibrahim Haggag
Members :	Ahmed Nasr
	Ahmed Boussila
	Aly Seif El din Makled
	Maher Shoeir
	Mohamed Ezz Eldin
	Moustafa Agha
	Moustafa Radwan
	Samir Keshk
	Shaaban Abul-Ela
	Sherif Abd El-Hady

Journal of the
Egyptian Society of Cardio Thoracic Surgery ISSN 1110-578 X

Correspondence to be sent to:
Prof. Dr. Mohamed El Fiky, 79, Ramsis Str., Cairo, Egypt, Post Code 11111

Journal of the
Egyptian Society of Cardio Thoracic Surgery ISSN 1110-578X

Vol. IV, No 4
September 1996

Contents September 1996

Journal of the
Egyptian Society of Cardio Thoracic Surgery ISSN 1110-578 X

EDITOR

MOHAMED EL FIKY.

79, Ramsis Str.
Cairo - Egypt.
Post Code 11111.
Fax (202) 772535

Information for authors

The Journal of the Egyptian Society of Cardiothoracic Surgery [ISSN 1110-578 X] is the official publication of the Egyptian Society of Cardio Thoracic Surgery, a professional society dedicated to promoting scientific knowledge and research in Cardio Thoracic Surgery.

The Journal of the Egyptian Society of Cardiothoracic Surgery, publishes original articles, review articles, leading articles, case report, abstracts from the literature, letters to the editor, special communications and abstracts of papers presented at the Annual Scientific Meeting of the Egyptian Society of Cardio Thoracic surgery. The Journal is published every 3 Months (January, April, June, September). All correspondence should be sent to the Editor-in-Chief at the above address.

The journal is sent free of charge to all members of the Egyptian Society of Cardio-Thoracic Surgery. For other Subscribers, Libraries, Organization, the annual subscription rate is 20 Egyptian Pounds including mailing expenses. For subscribers abroad, the annual subscription rate is $ 30 including mailing expenses. The price of a single number is $8. Back numbers can be obtained, if available at a price which depends on the availability of spare copies.

Three copies of the Manuscripts should be sent to the Editor-in-Chief (at the address given above), type-written on good quarto sized paper, with double spacing and liberal margin (2.5 cms).

The title should be separate and should include: title of paper, Author (s) full names, institution in which the work was carried out complete address, telephone and fax number for mailing purposes. The article should comprise:

1- An Abstract of 150-200 words not exceeding one double spaced page. The abstract should summarize the Material, Methods Results and Conclusions.

2- Introduction, Material, Methods, Results, Discussion and references.

3- Tables and figures should be provided separately; the position of the tables and figures in the text should be marked on the manuscript. Drawings should be with china ink.

References should be given in the Vancouver style. References should be mumbered serially in the text and listed, on a separate sheet, double spaced, at the end of the paper in that order: Author(s) Names & initials, title of article, Journal name, year, volume, number & inclusive pages in that order. List all authors of six or less; when seven or more,

list only three and add et al.

Reprints

Fifty reprints will be furnished to authors at the publication fees (150 Egyptian pounds). Larger quantities could be orderd in advance. The Editor in-Chief can consider excempting special papers & contributions from the fees. Coloured photographs could be published at a rate of L.E. 100 for each page.

Statements and opinions expressed in the articles and communications herein are those of the author(s) and not necessarily those of the Editor and the Editor disclaims any responsibility or liability for such material. The Editor does not, guarantee, warrant, or endorse any product or service advertised in this publication.

An original and two copies of all material, including illustrations, should be submitted. Place author's name and page number in the upper right corner of each page. Use double spacing throughout. Include a covering letter stating that the material has not been previously published or submitted elsewhere for publication. Identify at the letter the name, address, business and home telephone numbers of the author to whom correspondence should be sent.

Illustrations (three Sets of glossy prints) should be numbered in the order of their mention in the text, and marked lightly on the back with the author's name and an arrow to indicate top edge. Original drawings or graphs should be prepared in black India ink or typographic lettering. All lettering must be done professionally and should be in proportion to the drawing, graph, or photograph. Do not send original art work, x-ray films, or ECG strips. Glossy print photographs, 3 by 4 inches (minimum) to 5 by 7 inches (maximum), with good black-and-white contrast or colour balance are preferred. Consistency in size within the article is strongly preferred. Any special instructions regarding sizing should be clearly noted. Suitable legends should be typewritten, double-spaced, and listed on a separate sheet of paper and included at the end of the manuscript.

Tables should be self-explanatory and should supplement, not duplicate, the text. Type on pages separate from the text. Provide a brief title for each. Abbreviations used in Tables should be defined at the bottom of the table.

The Editor-in Chief has the right to make any amendments or abridgment in the articles which he considers necessary to render them suitable for publication in this Journal.

Editorials will be requested to Author (5) by invitation of the Scientific Committee, and should be a maximum of 20 typewritten sheets plus illustrations, graphes and tables.

Morphometric Criteria As a Predictor for the Outcome of Total Correction of Tetralogy of Fallot

ABSTRACT

TOF is one of the most common cyanotic heart disease. A prevalence of 98/336 (29%) was reported in our center during the year 1991, in this disease the magnitude of the pulmonary blood flow is reflected in the development of the pulmonary arteries and the left venticular volume. Severe hypoplasia of the pulmonary artery and the left ventricle may cause excessively high Rvp and heart failure following definitive repair. Since palliative procedures are available for this entity, indication for total correction have to be decided according to many parameters including the method of correction and the surgical skills in each institution. Several methods have been tried to quantify the size of the PA, to determine the surgical outcome. However, standardistion of values in different body sizes and different entities is a problem. PA index of 330 ± 30mm^2/BSA is considered within the normal range. In our series the PA index (PAI) was ranged from 173 to 380 mm^2/BSA (mean 270 ± 50). A PA index of 170 was accepted in our policy as the border line either for shunt or total correction. Determination of left ventricle end diastolic volume index (LVEDVI) provides a reliable index for the severity of the disease, it is considered a good predictor for the stability of post operative hemodynamics. LVEDVI ranged from 30 to 59 ml/m^2 (mean 41 ± 11 ml/m^2) was present in our series The acceptable LEVDVI for total correction in our work was 30 ml/m^2. Outflow tract construction using transannular patch or not will depend upon the size of PA annulus estimated preoperatively and confirmed intraoperatively. Following the previous criteria for total correction a total number of 37 patients had been totally corrected in CUPH from February 1992 till December 1992 (10 months period). Their age ranged from 1.7-12 years with mean of 4 ± 2.1 yrs, and their weight was 8.5-25 kg. with a mean 15 ± 7.8 Kg. 22 cases (59%) necessitated transannular patch. 7 cases monocuspid valve patch (3 pulmonary homograft, 4 pericardial patch) and 15 cases (41%) needed RVOT patching only. A mortality rate of 8.1% (3 cases) had been reported. Evaluation of the haemodynamics was done intraoperatively by measuring RVp, LVp and pressure across pulmonary annulus and O_2 saturation in PA & RA. It is concluded that morphometric criteria (PA index, LVEDVI, PA tree size) are good predictor for the outcome of total correction of TOF following morphometric parameters for choice of patients for total correction (from both Echo, Angio.) besides fulfilment of good understanding of surgical technique and minimising surgical ischaemic time will lead to good results and improve the learning curve of surgical teams.

Tarek El-Khouly, M Sc*, Mohamed Aboul Ezz, MD**, Fadia Mahoud, MD

J. of Egypt. Society of Cardiothorac. Surg. 1996, Vol. IV September No 4

INTRODUCTION

The surgical management of tetralogy of Fallot began with the palliative subclavian pulmonary artery anastomosis 1945 by Blalock and Taussing. Subsequent palliative procedures have included a variety of systemic-pulmonary artery shunts, and a closed palliative operation to reduce the magnitude of pulomnary stenosis. Corrective repair was first accomplished using cross-circulation in 1954 by Lillehei, and using a pump oxygenator in 1955 by

Departments of Cardiology *, Cardiothoracic surgery**, and Pediatrics *** Cairo University .

Kirklin. The following years, since the initiation of these pioneering surgical milestones, have been associated with improved knowledge of the pathologic anatomy of this malformation and it's variants. This was fulfilled by the outbreak development of echocardiographic technology and experience beside the refinement of angiographic methods. Consequently, this improved the decision-making process regarding the application, timing, and techniques of palliative and/or corrective surgical procedures. Despite these refinements, some degree of controversy still surrounds the decision making in the management of this common form of cyanotic heart disease (1) .

The intent of this article is to provide the reader with current opinion concerning diagnostic consideration as well as the indications, techniques, and results of choosing our patients for total correction of tetralogy of Fallot based on our criteria. We followed a quantitative criteria from both echocardiography and angiography, thus minimising the judging by personal impression especially concerning the two important criteria; the capacity of both pulmonary arterial tree and size of left ventricle.

Patients and Methods:

In Cairo University Pediatric Hospital (CUPH) the prevalence of tertralogy of Fallot (TOF) among other congenital heart diseases was 98/336 (29%) during the year 1991. Thirty seven patients diagnosed as a tetralogy of Fallot underwent total correction during the period from February 1992 to December 1992 (10 months). They are prospectively grouped sequentially into one group. Sixteen were females and twenty one were males. Thirty four cases were in situs solitus and 3 cases were situs inversus totalis. Their age ranged from 19 months to 12 years with a mean of 4 ± 2.1 years. Their weight ranged from 8.5 to 25 kilograms with a mean of 15 ± 6.8 kilograms.

On choosing our patients for total correction we followed a quantitative criteria from both echocardiography and angiography.

From Echocardiography. M-mode and two dimensional echocardiography were used in : 1) Detailed anatomical description of RVOT; 2) Assessing the sizes of pulmonary annulus, main pulmonary artery, right and left pulmonary arteries in percentage of their normal values for body surface area ;3) Left ventricle size in percentage of the normal values for body surface area.

From Cardiac catheterization and angiography. 1) Estimation of the pulmonary artery index PAI; 2) Estimation of the left ventricular end diastolic volume index LVEDVI; 3) assessment of the distal run-off of the pulmonary arterial tree. Beside the other angiographic anatomy.

Measurement of the PA - index. All patients were reviewed on an anteroposterior angiocardiogram by measuring the diameter of both the right and left pulmonary arteries immediately proximal to the origin of the first lobar branch. Generally, the size of the pulmonary arteries changes in one cardiac cycle. Then, the diameters that were measured at the maximum and minimum were averaged in order to obtain a mean diameter for each individual (2). The measurements were repeated by two of us independently. It is mandatory to obtain a clear picture of bilateral pulmonary arteries.

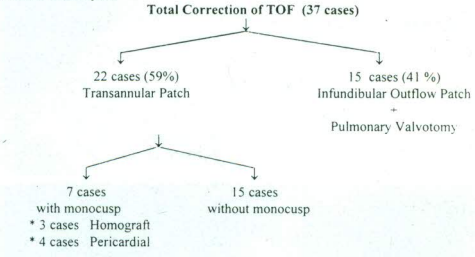
Table 1. Echo Criteria For Total Correction

Criterion	% of Normal
• Pulmonary artery branches	≥ 50 %
• Main pulmonary artery & Pul annulus	≥ 50 %
• Left Ventricle size	≥ 70 %
• Rt PA + Lt PA / descending aorta	> 1.5: 1

Table 2. Angiocardiographic Criteria For Total Correction

Criterion	Value
• PA index	≥ 170 mm^2 / BSA
• LVEDVI	≥ 30 ml/m^2. BSA
• Distal pulmonary run-off	Fair sized peripheral branches

Table 4. Surgical corrective techniques



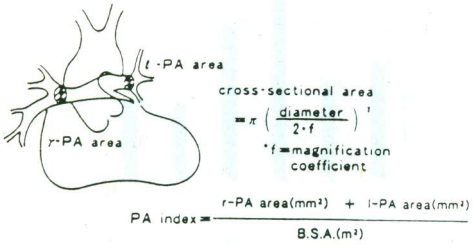


Fig.1: Illustrations of the measurement of PA-index .
Quoted from : Nakata et al, J Thorac Cardiovasc Surg 88:610-619,1984

Table 3. Demographic Data Of The Group

Sex	Age	Weight
16 Female	19 m-12 yrs	8.5-25 Kg
21 Male	mean (4 ± 2.1)	mean (15 ± 6.8)

The cross sectional area of each pulmonary artery was calculated as follows:

$$\text{Cross -sectional area } (mm^2) = \pi \frac{(\text{diameter})}{2f^2}$$

Where f is the corrective coefficient for angiographic magnification and π is equal 3.14. PA-inde was calculated as follows:

$$\text{PA-index } (mm^2/BSA) = \frac{(\text{Rt-PA Cross-sectional area} + \text{Lt-PA Cross - sectional area})}{BSA}$$

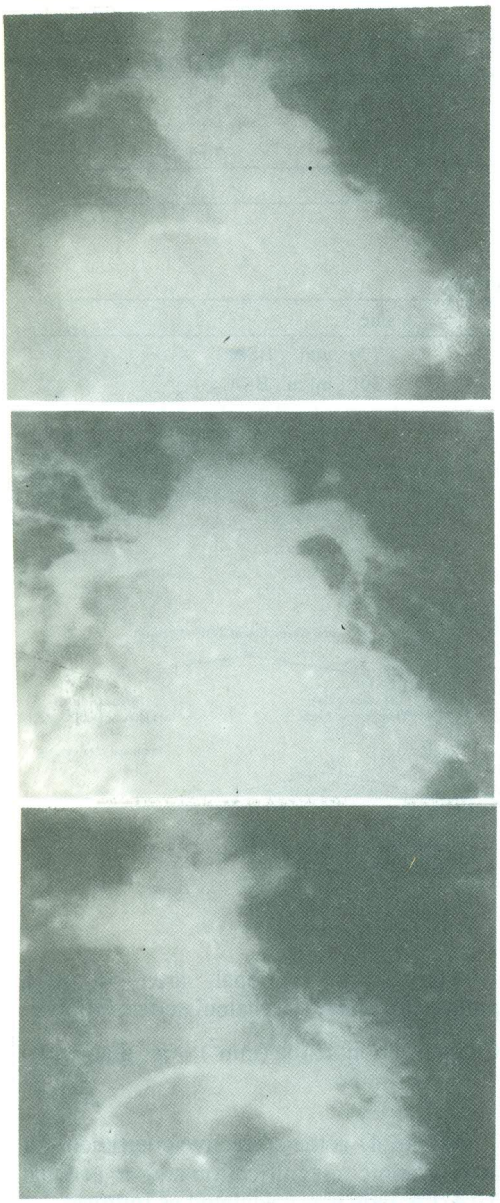


Fig.2:The patient whose angiogram is shown on the upper had a PA-index of 120 mm^2/BSA, the one in the middle angiogram had a PA-index of 170 and the one on the lower had a PA-index of 330 mm^2/BSA .

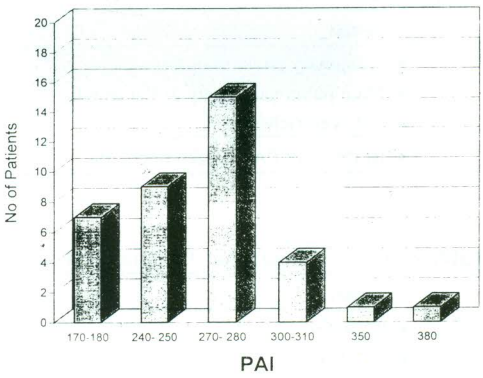


Fig.3: Distribution of Cases According to their PAIFig.4: Distribution of Cases According to their LVEDVI

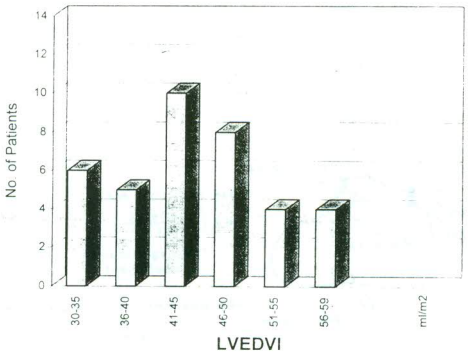


Fig.4: Distribution of Cases According to their LVEDVI

Table 5. Post Operative Course

Post operative course	Duration (Days)	
	Range	Mean
Hospital Stay	9 - 17	12 ± 3
Inotropic support + Afterload reduction	2 - 14	A) 6 ± 2.08
		B) 3 ± 0.68
Ventilatory support Pressure Cycled weaning ⇒ IMV	1-10	4 ± 3

* IMV intermittent mandatory ventilation; A) Patients with transannular patch, B) Patients without transannuluar patch.

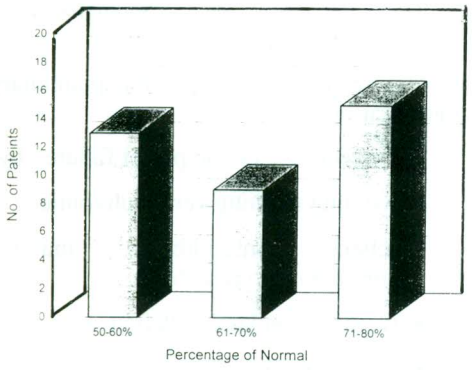


Fig.5: Size of Pulmonary Annulus Obtained by Echocardiography

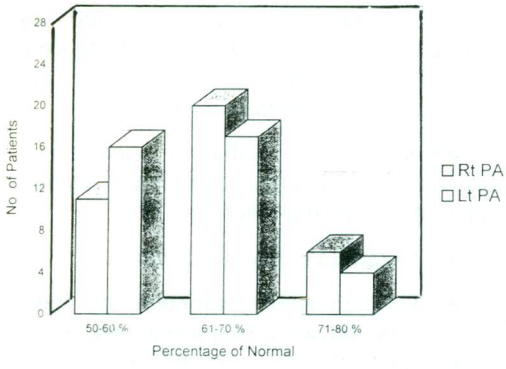


Fig.6: Size of Pulmonary Branches Obtained by Echocardiography

BSA is the body surface area in square meters, the diameters are epressed in millimetres, and the area is expressed in square millimeters (Fig.1). The normal value of PA index is 330 ± 30 mm^2 / BSA (2). Examples of pulmonary arteries with their calculated PAI are shown in Fig.2.

Measurement of Left ventricular volume. Biplane LV angiograms were obtained in long axial projections (RAO 20° in frontal view and RAO 20° cranial angulation in the lateral view) at 60 frames/sec. Special care was taken to avoid extrasystoles and to assure an adequate technical quality for calculating angiographic volumes. Left ventricular diastolic and end systolic volumes were calculated in both end diastolic and end systolic frames excluding extrsystoles and post extrasystolic beats. The ventricular silhouette was considered at the outer most margin of the visible radiographic contrast so as to include trabeculations and papillary muscles within the perimeter. The LV volume was calculated by the following equation assuming that the LV geometry approximated with considerable accuracy by an ellipsoid (3).

$$V = 4/3\ \eta\ (L/2)\ (M/2)\ (N/2) = \eta\ \frac{LMN}{6}$$

Where V is the volume, L is the long axis of LV or the longest line that can be drawn within the ventricular silhouette in either projections, M is the minor axis of LV in one projection (Perpendicular line bisecting long axis), N is the minor axis of LV in the other projection, and η is equal to 3.14. Spheres of diameter 17.5 mm were filmed at mid chest position in each projection and used to correct for X-ray magnification. True volumes were obtained from corrected volumes by applying the regression equation of Graham et al., (4) to correct for overstimation of the LV volume.

$$V\,a = 0.7333\ Vc$$

where Va = actual volume & Vc = calculated volume.

Finally the absolute value for volume was indexed (divided by body surface area) and expressed as ml/m^2. Left ventricular end diastolic volume index (LVEDVI) is calculated by divding the LVEDV by the body surface area.

$$LVEDVI = \frac{LVEDV}{BSA} \quad ml/m^2$$

Normal values is 46 ± 10 ml/m^2 as estimated by Graham et al. (4).

OPERATIVE POLICY

Exclusion Criteria For Total Correction :

1) TOF with criteria less than our chosen figures were candidates for modified Blalock - Taussig shunt (defined as a pulmonary artery index < 170 mm^2/BSA, LVEDVI < 30 ml/m^2 BSA and poor distal run off).

2) Cases with associated cardiac lesion that increase the risk of single stage repair (e.g., atrioventricular septal defect, multiple ventricular defects).

3) Patients with TOF and right ventricular to pulmonary artery discontinuity, who requires a conduit to connect the right ventricle to pulmonary artery.

4) TOF with absent pulmonary valve syndrome (5).

5) TOF with anomalous left anterior descending coronary artery originating from the right coronary artery and crossing the right ventricular outflow tract (6).

When planning primary repair of tetralogy of Fallot we put into consideration that the right ventricle is a compromised chamber which should be preserved and protected by:

1) Avoiding post operative pressure afterload: by appropriate RVOT reconstruction leaving a very minimal gradient if ever across it.

2) Avoiding post operative volume overload: by prompt VSD closure, preserving tricuspid valve function and preventing as much as possible pulmonary regurgitation.

3) Preventing ejection power failure : by

- avoiding too long ventriculotomies.
- incising infundibular muscles (minimal or no resection).
- avoiding conduction deficit.
- gentle handling of myocardium.
- minimising ischemia with good myocardial protection.

Operative Techniques

The same techniques adopted by Castaneda group in Boston in 1990 (5) were applied in our center with little modification to suit our circumstances.

- Standard median sternotomy, cannulation and extra corporeal cirulation under moderate hypothermia (25° C).
- Crystalloid cardioplegic arrest.
- Through right ventriculotomy conal septum is released by partial and septal bands incision with minimal excision if needed.
- VSD is closed by Double Velour Dacron patches using Ethibond 4/0 or 5/0 suture, to ensure complete closure of the VSD, we favour interrupted horizontal mattress sutures reinforced with Teflon pledgets along the posteroinferior margin away from the edge. Once those sutures are placed, they are passed though an appropriate tailored Dacron patch and are tied, then continuos suture is applied to the rest of the defect.
- The right ventricular outflow tract (RVOT) is reconstructed by own Glutaraldehayde treated pericardial patch applied to right ventricular infundibulum

only or crossing pulmonary annulus and/or main pulmonary artery and its branches according to the pathology of the outflow tract.

- If the pulmonary valve is dysplastic, thickened, and cartilaginous in consistency, the valve tissue is excised since it can be a source of residual obstruction.

- Pulmonary annulus size is assessed by Hegar dilators and compared to normal values for body surface area to decide excising the annulus or not (7).

- In cases reconstructed by transannulur patch we fachioned a monocusp for patients with PAI from 170 to 200 mm2/BSA.

Operative results are assessed

1) Immediately in the operating room after coming off bypass and haemodynamic stability by (a) Measuring RV pressure, PA pressure, RA pressure and ascending aortic pressure (= LV pressure). (b) Calculation of $P_{RV/LV}$ and RV/PA pressure gradient. (c) O_2 saturation (mid right atrium and pulmonary artery) to detect residual VSD.

2) Before hospital discharge by echocardiography.

Statistical analysis. Numerical data obtained were expressed as mean ± standard deviation (SD) and non numerical data will be expressed as percentage. Correlation coefficient ® was used to correlate pressure measurements.

Results

Table 6. Postoperative Complications

Complications	Mode	No. Of Patients	Duration in days
Persistent LCO	-Rt.ventricular failure	1	9
Bleeding	-Rt. hemothorax (Rt. SC puncture)	1	first few hours
	-Coagulation problem (medically treated)	1	first few hours
Conduction problems	- AV dissociation	3	6-7 ⇒ SR
	- SR + RBBB	21	
	- SR	4	
Infection	-Chest infection	1	14
	- Mediastinitis	1	5-7
	- Superficial wound infection	5	

LCO: low cardiac output, SC: subclavian vein, AV: atrioventricular, SR: sinus rhythm, RBBB: right bund

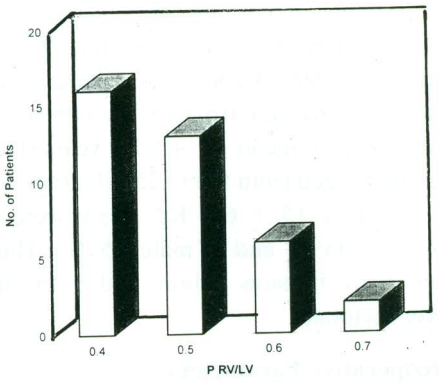


Fig.7: Post repair right ventricular/left ventricular pressure ratio .

Table 7. Conversion Table

McGoon Ratio	0.5	1.0	1.5	2.0	2.5	3.0
Nakata index	25	78	154	249	361	490

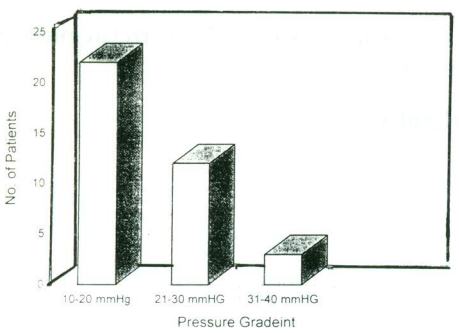


Fig.8: Post repair peak systolic right ventricular-pulmonary artery pressure gradient

At Cairo University Pediatric Hospital 37 patients diagnosed as a tetralogy of Fallot underwent total correction. Table.3 shows the demographic data of the group. Their age ranged from 19 months to 12 years with a mean of 4 ± 2.1 years. Their weight ranged from 8.5 to 25 kilogram with a mean of 15 ± 6.8 Kg. They were 16 females (43%) and 21 males (57%). Thirty four were in situs solitus and 3 in situs inversus totalis.

Preoperative Parameters

•Pulmonary artery index (PAI) as calculated from angiocardiography ranged from 170 to 380 mm^2/m^2 with a mean 270 ± 50 mm2/m2. Among those cases: 7 cases were 170 - 180, 9 cases 240 - 250, 15 cases 270 - 280, 4 cases 300 - 310, one case 350 and one case 380 mm^2/m^2 (Fig.3).

•LVEDVI as calculated from angiography ranged from 30 to 59 ml/m^2 with a mean of 40 ± 9 ml/m^2 Among those cases: 6 cases were 30 -35 ml/m^2, 5 cases 36 - 40 ml/m^2, 10 cases 41 - 45 ml/m^2, 8 cases from 46 - 50 ml/m^2, 4 cases 51 - 55 ml/m^2 and 4 cases 56 - 59 ml/m^2 (Fig. 4).

• Pulmonary artery annulus as estimated from echocardiography was 50 - 80% of normal with a mean of 65 ± 8.7% of normal values, 13 cases were 50 - 60%, 9 cases 61 - 70%, while the rest of the group 15 cases 71 - 80% of the normal (Fig. 5).

•Size of pulmonary branches as obtained from echocardiography were as follows : Right pulmonary artery 11 cases ranged from 50 - 60% of normal values, 20 cases 61 - 70% and 6 cases 71-80%. While the left pulmonary artery 16 cases ranged from 50-60% of normal values, 17 cases 61-70%, and 4 cases 71-80% (Fig. 6).

Operative Techniques

Thirty seven cases underwent total correction of TOF, among those cases 15 cases (41%) needed infundibular outflow patch (Glutaraldehayde treated pericardium) with pulmonary valvotomy. And 22 cases (59%) needed transannular patch, 7 of them with monocusp patch (3 monocuspid patches tailored from aortic or pulmonary homografts and 4 pericardial fashioned monocusps) (Table 4). The ischemic time ranged from 40-70 minutes with a mean of 55±13 minutes.

Post Repair Measurements

a) *Right ventricular - left ventricular pressure ratio ($P_{RV/LV}$).* Sixteen patients had a ratio of 0.4, 13 cases a ratio of 0.5,6 cases a ratio of 0.6 and only 2 cases a ratio of 0.7 (fig. 7&9).

b) Peak systolic right ventricular-pulmonary artery pressure gradient. The gradient as measured postoperativelly was found ranged

from 10-20 mmHg in 22 cases, 21-30 mmHg in 12 cases and in 3 cases from 31-40 mmHg (Fig. 8&9).

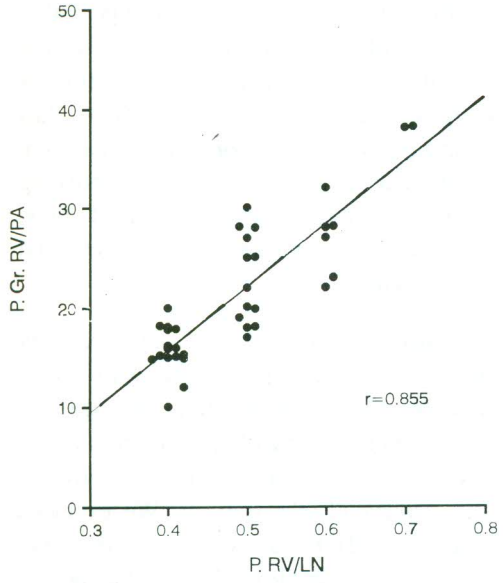


Fig (9). Correlation between P. RV/LV and P.Gr. RV/PA among cases post repair.

c) O^2 saturation. Oxygen step up between samples obtained from mid right atrium and pulmonary artery ranged from 0.1%-3% (mean ± SD of 1.57 ± 0.71), except two patients in whom O_2 step up were 12% 15%, proved by post operative follow-up echocardiography Doppler to have small residual VSDs (0.2-0.3 mm).

Post Operative Course

The average hospital stay for survivors was 9 to 17 days with a mean 12 ± 3 days, The duration of inotropic support and after load reduction regimen (Dopamine, Adrenaline and Tridil or Nipride or Inoxemone) ranged from 2 to 14 days with a mean of 6 ± 2.08 days in patients with transannular patch and 3 ± 0.68 in patients without transannular patch. Patients with transannular patch necessitated high dose of adrenaline (> 1 µg/Kg/min) and longer duration of support (> 5 days). The ventilatory support ranged from one to 10 days with a mean of 4 ± 3 days. Using pressure cycled ventilators, initially on controlled mode and later upon weaning on IMV mode (Table 5).

Complications were listed in (table 6) with no serious complications necessitated prolonged hospitalisation. There were 3 hospital deaths, which represents 8.1%. The first case (No. 3) was a child 9 years old, 23 Kg, suffered from chest problems, prolonged ventilation, prolonged inotropic support and persistent chest infection for 48 days died from septicaemia (Pseudomonas & Staphylococus aureus). The second case (No. 23) was a 6 years old child 18 Kg, suffered from persistent low cardiac output "inspite of increasing the dose of inotropics" and right ventricular failure which lead to death after 5 days due to multi organ failure. The third case (No. 17) was a child 3 years old 12 Kg, suffered from mediastinitis and sternal dehiscence and died on the 7^{th} day from septicemia (staphylococcus epidermis).

Follow-Up Data

EchoDoppler was performed before hospital discharge for every case as a part of our protocol to assess our early results where we found:

1) Small residual VSD (0.2-0.3 mm) in 2 cases.

2) Gradients across ROVT was less or equal to that measured intraoperatively.

3) Pulmonary incompetence grade I-II in patients repaired by transannular patch 22/37 (59%).

4) Tricuspid regurge grade II-III in 5/37 (13.5).

5) Good ventricular functions.

Discussion

Tetralogy of Fallot is commonly encountered among congenital heart disease. A prevalence of 98/336 (29%) was reported in our center during the year 1991. It is generally agreed that definitive repair is needed if the operation can be performed at a low risk and with reasonable expectation of good outcome. The likelihood of successful surgical outcome must be determined by individual institutional status (2).

In TOF, the magnitude of the pulmonary blood flow is reflected in the development of the pulmonary arteries (PAs) and left ventricular volume (LVV). severe hypoplasia of the pulmonary artery and the left ventricle may cause excessively high Rvp and heart failure following definitive repair. Since palliative procedures are available for this entity, indication for total correction have to be decided according to many parameters including the methods of correction and the surgical skills in each institution (3,4).

In order determine the surgical indication based on quantitative evaluation, several methods have been suggested to evaluate the feasibility of performing corrective surgery (3-5). These methods depend mainly on diameter ratios. However, standardisation of values in different body sizes and different pathologies constitute a problem. Therefore, Nakata and associates in 1984 utilised a cross sectional area rather than the diameter to have a better correlation with the capacity of the PAs and the left ventricle, and for the sake of standardisation, divided the resultant value by the body surface area (6).

Reliable methods assessing operability allow early repair of TOF with the advantages of relieving right ventricular outflow tract obstruction (RVOTO), thus aborting the stimulus for pathological right ventricular hypertrophy and establishing early antegrade pulmonary blood flow, which enhance pulmonary angiogenesis and alveologenesis (7).

Since February 1992, our treatment protocol for symptomatic cases with TOF is definite repair, irrespective of age and weight, rather than early palliation followed later by repair if the anomaly is fulfilling our criteria (Table 1 & 2). We excluded cases of TOF associated with other anomalies (complete AV septal defect, multiple VSD, etc.) irrespective of its morphometric parameters due to the fact that this constitute an early burden on our learning curve. This goes in agreement with Rosenkranz and co-workers who concluded that these associated lesions increases much the risk of single stage repair (2).

We believe that the pathological components of TOF which can not be repaired surgically are small sized PAs beyond both pulmonary hila and a small left ventricular volume. Consequently, PAI & LVEDVI beside our echocardiographic criteria are considered good determiinants for operability.

Why PAI?

PAI reprsent the cross sectional areas of the pulmonary arteries measured at both hila. RVOT and pulmonary tree could be enlarged surgically reaching both pulmonary hila, so with good PAI we expect relieving of all the pathway from right ventricle to the lungs.

As regards intrapulmonary tree (i.e. distal pulmonary run-off) as observed from angiography, we observed that it depends on the degree of narrowing of proximal PAs. Cases estimated as fair sized peripheral pulmonary branches found to accommodate well RV output after reconstruction of RVOT denoting its normal texture. This goes in agreement with Castaneda and Groh and their co-workers who stated that most of small pulmonary arteries in TOF once exposed to increased flow, seem capable of enlarging significantly due to the normal elastic contents of their walls (7,8).

The PAI was found to be constant over al wide range of body surface areas from infancy to adolescence, thus, the normal value of 330 ± 30 mm^2/m^2. BSA can be applicable over a wide range of patients (6). Although Nakata and colleagues considered patients with PAI of > 100 mm^2/m^2 BSA can be candidates for total correction we prefer to start operating patients with a PAI of > 170 mm^2/m^2. BSA. Moreover, in patients with PAI below 200 mm^2/m^2 BSA (relatively small PAs), we prefer to use a monocusp if transannular patch is needed to reduce the effect of pulmonary incompetence on RV function early postoperatively.

From Echocardiography although, we used McGoon ratio of ≥ 1.5:1, it was reported that there is some variability among patients in the descending thoracic aortic diameter. So, the use of the descending thoracic aorta as the reference point in judging the size of the pulmonary arteries may lead to a high post repair $P_{RV/LV}$ despite an optimal surgical repair (9). We found that it matches well with PAI and can be considered roughly as a good criterion of PAs size besides other criteria. This was supported by Kirklin and associate who proposed a conversion table correlating between McGoon ratio and PAI (10).

These morphometric criteria concerning pulmonary arteries aize were chosen to suite the early experience of our center and to allow for improving our learning curve by operating on cases having good pathologic anatomy.

Why LVEDVI ?

It is well known that left ventricular voLume (LVV) is small in TOF (11). Inadequate LVV has been reported by many investigators to be a potential cause of death after total correction of TOF. The smaller the LVV, the more severe the post operative LCO syndrome and prolonged high dose inotropic support. The postoperative LVEDV is a major determinant of post operative haemodynamics, so the size of LV should be considered a critical factor in determining the feasibility of intracardiac repair (12,13,14).

Moreover, Nomoto et al in 1986 reported that determinations of left ventricular end diastolic volume (LVEDV) estimated by the equation (Predicted LVEDV = 72.8xBSA) provided a more reliable index of the post operative haemodynamics and the severity of the

disease than the previous morphologic studies of the pulmonary arteries and were useful for selecting candidates for total correction of TOF (15). In our series we calculated LVV more accurately by morphometric parameters and was indexed by dividing it by the BSA (16).

Based on the assessment of pre-operative LVV and post operative hemodynamics, LVEDVI of at least 30 ml/m^2 is required for successful primary repair. Patients with LVEDVI less than 30 ml/m^2, palliation by systemic to pulmonary arterial shunt procedure should be indicated until sufficient LV growth (17). Other investigators reported post operative death of cases having LEVDVI of less than 30 ml/m^2 (26 ml/m^2 & 21 ml/m^2) of severe low cardiac out put without other causes (residual VSD and/or residual RVOT) (3,11).

We chose all our patients to have LVEDVI of $\geq$ 30 ml/m^2 and from echocardiography LVV of $\geq$ 70% of normal which was higher than Nomoto who recommended only 60% of normal value as a safety limit for definitive repair in TOF (13).

Surgical Outcome

After analysing our results we found that our morphometric criteria for choosing candidates for total correction yields good results from the immediate haemodynamic point of view (low $P_{RV/LV}$, acceptable RV/PA pressure gradient (P Gr. RV/PA) and negligigible O_2 step-up in PA) as well as early post operative echo assessment before hospital discharge, allowing us to predict the outcome of future cases depending on the same parameters provided that other variable are constant (anaesthetic management, surgical techniques, postoperative management, etc.).

(a) Post repair PRV/LV & P Gr. RV/PA

They have a good correlation coefficient (r = 0.855) (fig. 9), so whenever we have low post repair $P_{RV/LV}$ we expect no or little gradient across RVOT. Thus, they are considered good parameters in judging successful surgical repair. Reviewing our results revealed that the majority of our cases 29/37 (78%) had $P_{RV/LV}$ between 0.4 and 0.5 and PGr RV/PA between 10 and 30 mmHg indicating prompt VSD closure and relieving RVOTO (Fig. 9). In our series, cases having high $P_{RV/LV}$ usually accompanied by relatively high PGr RV/PA (8/37 21.6%) inspite of the use of transannular patch (Fig. 9). This is may be due to timid RVOT reconstruction. This was also observed by many investigators who added that residual RV hypertension is not always eliminated by transannular patching even when properly extended into the left pulmonary artery. This may be due to a geometric problem of the RVOT resulting in the inability to avoid a gradient between the distal portion of the patch and the pulmonary artery beyond (7,15,17).

However, in case No. 23 where the post repair $P_{RV/LV}$ was high (0.75) and the P Gr. RV/PA was not so high (20 mmHg) had a right ventricular failure and died of persist low cardiac output inspite of inotropic support. We attributed this high pressure in RV & PA probably due to poor distal run-off (i.e. severe hypoplasia of peripheral Pulmonary tree). This is in accordance with Kirklin and Backstone and their co-workers who added that residual post-repair RV hypertension (high $P_{RV/LV}$) is a risk factor for death (5,21).

in PA was insignificant (1.57 ± 0.71%) expect in 2 cases (12, 15%) which were proved later by echocardiography to have small residual VSD. This insignificant step-up attributed to the use of double Velour Dacron patch with some degree of porosity.

Transannular patch

Although nomograms have been generated by cineangiographic criteria for preoperative prediction of the need for transannular patching (7,20,22), in our practice the decision is generally made intraoperatively by direct measurement of the pulmonary annulus by Hegar dilators and according to the comparison with the normal values for BSA we do our adjusted reconstruction. We believe that prediction of transannulur patching before surgery makes no advantage over assessing during surgery.

Transannular patching may predispose to right ventricular failure from pulmonary valve incompetence. This is actually significant when the pathway distally is not sufficient to accommodate right ventricular output. In our study we used monocusps (pericardial or homografts when available) especially when PAI is below 200 mm/m^2 to reduce the effect of pulmonary incompetence over RV function especially in the early critical postoperative period. Although we used transannular patch in 22 cases (59%), we faced no problem of pulmonary incompetence in the post operative period except the use of high dosage (e.g. adrenaline > 0.1 µg/Kg/min) and more duration of inotropic support (e.g. > 5 days).

In our series we encountered 5/37 (13.5%) with tricuspid regurge grade II-III detected by echocardiographic follow-up. This probably due to fixation of the septal tricuspid leaflet by VSD closure stitches in cases with tricuspid-aortic continuity.

Conclusion

Morphometric criteria (PAI, LVEEDI) Beside pulmonary arterial tree size estimated from both angio and echocardiography in choosing cases for total correction of TOF are considered good predictor for the surgical outcome after total correction of TOF provided good understanding of the surgical techniques.

This provides a guiding standards for young surgeons, who have little experience of their own, rather than using personal judgement. From our experience we believe that each center should chose his own criteria, for accepting TOF patients for total correction, which suits its stage of development and experience.

Consequently this protocol will help with time in improving the learning curve of both surgical and medical teams and ultimately yielding good results. Later, protocols can be changed to accept more difficult cases to coincide with the progress of all team members.

REFERENCES

1. Pacifico AD. Introduction. Semin Thorac Cardiovase Surg 1990; 2: (1) 55-60.
2. Rosenkranz ER. Modified Blalock-Taussig shunts in the treatment of tetralogy of Fallot. Semin Thorac Cardiovasc Surg 1990; 2:(1) 27-33.
3. Graham TP, Faulkner S, Bender H, and Wender CM. Hypoplasia of the left ventricle. Rare cause of postoperative mortality in tetralogy of Fallot. Am J Cardiol 1977; 40:454.
4. Kirklin JW, Bargeron LM, and Pacifico AD. The enlargement of small pulmonary arteries by preliminary

T. El-Khouly, M. Aboul Ezz, Fadia Mahoud,

3. Graham TP, Faulkner S, Bender H, and Wender CM. Hypoplasia of the left ventricle. Rare cause of postoperative mortality in tetralogy of Fallot. Am J Cardiol 1977; 40:454.

4. Kirklin JW, Bargeron LM, and Pacifico AD. The enlargement of small pulmonary arteries by preliminary palliative operations. Circulation 1997; 56:612.

5. Blackstone E H, Kirklin J W, Bertranou EG, et al. Preoperative prediction cineangiography of post repair right ventricular pressure in tetralogy of Fallot. J Thorac Cardiovasc Surg 1979; 78:542.

6. Nakata S, Imai Y, Takanashi Y, Kurosawa H, Tezuka K, Nakazawa M, Ando M, and Takao A. A new method for the quantitative standardisation of cross-sectional areas of the pulmonary arteries in congenital heart diseases with decreased pulmonary blood flow. J. Thorac Cardiovasc Surg 1984;88:610.

7. Castaneda AR. Classical repair of tetralogy of Fallot: timing, technique, and results. Semin Thorac Cardiovasc Surg 1990; 2:(1) 70-75.

8. Groh MA, Melione JN, Bove EL, et al. Repair of tertralogy of Fallot in infancy; effect of pulmonary artery size on outcome. Circulation 1991; 84 (Suppll. 1) 111:206.

9. Kirklin JK, Kirklin JW, Pacifico AD. Transannular outflow tract patching for tetralogy: Indication and results. Semin Thorac Cardiovasc Surg 1990; 2: (1) 61-69.

10. Kirklin JW, Blackston EH, Kirklin JK, and Pacifico AD. Predicting the degree of relief of the pulmonary stenosis or atresia after the repair of tetralogy of Fallot. Semin Thorac Cardiovasc Surg 1990;2: (1) 55-60.

11. Naito Y, Fujita T, Yagihara T, et al. Usefulness of left ventricular volume in assessing tetralogy of Fallot for total correction. Am J Cardiol 1985; 56 (4): 356.

12. Kirklin JW and Karp BB. The Tetralogy Of Fallot From Surgical View Point (eds) Philadelphia. W.B. Saunders 1977; 119:153.

13. Nomoto S, Muraoka R, Yokota M, Aoshima, et al. Left ventricular volume as a predictor of postoperative heamodynamics and a criterion for total correction of tetralogy of Fallot. J Thorac Cardiovasc Surg 1984; 88:389.

14. Piehler JM. Danielson GK, McGoon DC, et al. Management of pulmonary atresia with ventricular septal defect and hypoplastic pulmonary arteries by right ventricular outflow tract obstruction (reconstruction). J Thorac Cardiovase Surg 1980; 80:552.

15. Katz NM, Blackstone EH, Kirklin JW, et al. Late survival and symptoms after repair of tetralogy of Fallot. Circulation 1982; 65:403.

16. Graham TP, Jarmakani JM, Canent RV, and Morrow MN. Left heart volume in infancy and childhood. Circulation 1977; 38:826.

17. Kirklin JW. Ventricular septal defects and pulmonary stenosis or atresia. In: Cardiac Surgery (eds). Churchill Livingstone, New York, 1993; pp. 977.

18. Castaneda AR, Freed MD, Williams RG, et al. Repair of Tetralogy of Fallot

in infancy. J Thorac Cardiovasc Surg 1997; 74:372.

19. Rowlatt UF, Rimoldi HJ and Lev M. The quantitative anatomy of the normal child. Pediatr clin North Am 1963; 10:449.

20. Kirklin J W, Blackstone E H, Pacifico AD, et al. Risk factors for early and late failure after repair of tetralogy of Fallot and their néutralization. J Thorac Cardiovasc Surg 1984; 32:208.

21. Kirklin JW, Blackstone EH, Jonas RA, et al. Morphologic and surgical determinants of outcome events after repair of tetralogy of Fallot and pulmonary stenosis. J Thorac Cardiovasc Surg 1992; 103:706.

22- Shimazaki Y, Blackstone EH, Kirklin JW, et al. The dimensions of the right ventricular outflow tract and pulmonary arteries in tetralogy of Fallot and pulmonary stenosis. J Thorac Cardiovasc Surg 1992; 103:692.

Ventricular Septal defects with severe pulmonary hypertension: Preoperative, operative and postoperative analysis

ABSTRACT

This work was conducted in Cairo University New Children's Hospital over a period starting from October 1993 till September 1995. It included 30 children suffering from primary ventricular septal defects with a severe degree of pulmonary hypetrension. Their age ranged from 6 to 60 months (28.5 ± 17.9 months) and their weight ranged from 5 to 20 kg (11.2 ± 4.4 kg). Every patient was subjected to preoperative evaluation, operative and postoperative management. All cases were operated upon using open heart technique for of the ventricular septal defect (s). All cases were closed by dacron patch. Operative data included measurement of PASP before and after VSD closure, VSD site and size, O2 saturation difference between blood samples obtained from mid-right atrium and pulmonary artery.

Indwelling pulmonary artery catheter and left atrial line were inserted at the end of operation. Special postoperative management was performed as regards the way of ventilation, sedation, combination of inotropics and afterload reducing drugs. Also preventive measures to avoid the occurrence of postoperative pulmonary hypertensive crisis were taken. Before hospital discharge, postoperative non-invasive investigations were done to all patients, to evaluate the results and detect any postoperative complications.

We found that young age, small weight, severity of preoperative pulmonary artery systolic pressure (haemodynamic data), were important factors affecting the surgical outcome and postoperative course. Postoperative complications included small residual VSD (3.3%), partial right bundle branch block (13.3%), mild tricuspid regurge (6.6%), severe pulmonary infection (3.3%), right sided pleural effusion (3.3%) and acute pulmonary hypertensive crises (6.6%). Postoperative mortality was attributed to pulmonary hypertensive crises with the resultant 2 mortality cases (6.6%). It was concluded that:

- Early primary repair is recommended to interrupt the natural history of VSD before the development of severe pulmonary vascular obstructive disease.

- Young age, small weight and severity of preoperative pulmonary artery systolic pressure are not determinants of postoperative mortality, although they increase the incidence of postoperative morbidity.

- Prophylaxis from postoperative pulmonary hypertensive crises is better than treatment.

- Meticulous and minute-minute postoperative care is mandatory to achieve favourable surgical outcome and postoperative results.

Mohamed Aboul-Ezz* and Ahmed El-Minshawy**

J. of Egypt. Society of Cardio thorac. Surg. September1996, Vol. IV No 4

Departments of Cardiothoracic Surgery, Faculty of Medicine, Cairo University and Faculty of Medicine, Assiut University***

Journal of the
Egyptian Society of
Cardio Thoracic Surgery

Vol. IV, No 4
September 1996

INTRODUCTION

Isolated ventricular septal defect is the most common congenital heart defect. It occurs at a rate of two per 1000 livebirths, and constitutes about 25% of all forms of congenital heart diseases (1).

The closure of simple ventricular septal defects has been perfor ned with a low mortality. The proper time for and type of surgical treatment of large ventricular septal defect with severe pulmonary hypertension have been controversial (2).

The functional disturbance caused by a VSD depends primarliy on its size and the status of the pulmonary vascular bed rather than on the location of the defect. Kimball et al (3). found good positive correlation between symptoms and defect size.

Currently, there is a tendency to repair essentially all large ventricular septal defects except some of those with severe irreversible obstructive pulmonary vascular disease (4).

On the other hand, it has been found that at a certain stage in the evolution of congenital heart disease with left-to-right shunt, pulmonary hypertension is produced, at least in part, by vasoconstriction and therefore is potentially reversible. On this basis, it is important to know whether any of this increased resistance is due to active vasoconstriction, so that, its assessment may be helpful in evaluating the condition of pulmonary hypertension for the surgical correction of the ventricular septal defect (5).

The most significant and detailed classification in the pathologic features of pulmonary vascular disease was described by Heath and Edwards (6) (Table 1) and this classification is still in use (7).

More recently by a new quantitative methods of analysis, additional features of pulmonary vascular changes associated with congenital heart disease have been analyzed by Rabinovitch et al (8).

Children with congenital cardiac defects with high pulmonary artery pressure may die early in the postoperative period after surgical closure (9). Postoperative mortality has been attributed to acute rise in pulmonary artery pressure and resistance, but the aetiology of such pulmonary hypertensive crisis is uncertain and therapy remains empirical (10).

Primary definitive repair of large ventricular septal defects, even in infancy whenever operative intervention is indicated, has been advocated by several groups experienced in open intracardiac surgery in infants and the results have been good (11,12,13,14). Also, late haemodynamic results are excellent and suggest that cure is likely when surgery is performed early in life even when the pulmonary vascular resistance is mildly or moderately elevated (4,15).

The present study aims to clarify and analyze the management of VSDs with severe pulmonary hypertension in infants and children.

Patients and Methods

Patients

This work was conducted in Cairo Univarsity New Children's Hospital over a period starting from October 1993 till September 1995. It included 30 children suffering from primary ventricular septal

defects with a severe degree of pulmonary hypertension. Their age ranged from 6 to 60 months and their weight ranged from 5 to 20 kg.

Table (1): Pathological grading of pulmonary vascular disease

Grade	Description
I	The stage of retention of foetal-type pulmonary vessels.
II	Stage of medial hypertrophy with cellular intimal reaction.
III	Stage of progressive fibrous vascular occlusion.
IV	Stage of progressive generalized arterial dilatation.
V	Stage of chronic dilatation and pulmonary haemosiderosis.
VI	Stage of necrotizing arteritis.

Inclusion criteria:

- All patients with primary VSDs, with severe degree of pulmonary hypertension (pulmonary to systemic pressure ratio Pp/Ps>0.75).

- Patients with VSD associated with minor cardiac anomalies, e.g. patient with ductus arteriosus, atrial septal defect, coarctation of aorta, etc.

Exclusion criteria:

- Any patient with VSD associated with or a part of major cardiac anomalies, e.g. transposition of great arteries, A-V canal or Fallot's tetralogy.

- Any patient with fixed pulmonary/systemic resistance ratio (Rp/Rs) more than 0.75 (haemodynamically inoperable).

Methods

Every patient was subjected to preoperative evaluation, operative and postoperative management, as follows:

1) Preoperative evaluation:

i) Thorough history

ii) Clinical Evaluation: including general and local examination for all patients

(iv) Echo-Doppler study: each patient underwent complete M-mode, two-dimensional, pulsed, continuous and colour flow Doppler-Echocardiographic study.

(v) Cardiac catheterization: it was done for all patients.

Pulmonary artery pressure was recorded, also pulmonary/systemic blood flow ratio (Qp/Qs) and pulmonary/ systemic resistance ratio (Rp/Rs) were recorded.

In cases of elevated pulmonary vascular resistance (i.e., Rp/Rs more than 0.50), all the pressures and oxygen saturations were measured after inhalation of 100% O2 for about 15 minutes, to test for pulmonary vascular reactivity and reversibiility of pulmonary hypertension.

II) Operative management:

All cases were operated upon in Cairo University New Children's Hospital using open heart technique for closure of the ventricular septal defect (s), with the aid of cardiopulmonary bypass, moderate systemic hypothermia (25°C-28°C), cold potassium cardioplegic arrest and topical cooling.

All cases were closed using transatrial route and with good retraction of the anterior and septal leaflets of the tricuspid valve, the defects were well exposed in all cases except in cases, in whom detachment of the septal leaflet was needed for full exposure of the defect (16).

-The defect was closed in all cases with "double velour dacron patch", with mean porosity 3000 cm and nominal thickness 1.4 mm, using interrupted pledgeted 5/0 Ethibond sutures away from the edge of the defect especially in its postero-inferior part,

where the conduction system passes. Operative data included:

i) Direct measurement of pulmonary artery systolic pressure after opening of the pericardium (before closure of VSD).

ii) Description of the VSD site and size of the defect.

iii) Calculation of the total bypass time and aortic cross clamp time (ischaemic time).

iv) Direct measurement of pulmonary artery systolic pressure at the end of operation (after closure of VSD and weaning from bypass).

v) Blood samples were taken from mid-right atrium and pulmonary artery to detect any oxygen step up for detection of significant residual VSD.

vi) Indwelling pulmonary artery catheter was inserted at the end of operation to measure changes in the pulmonary artery pressure after surgery and to help in diagnosis of postoperative pulmonary hypertensive crises, also for direct infusion of pulmonary vasodilators.

vii) A left atrial line was inserted at the end of operation for continuous postoperative left atrial pressure monitoring and drug or fluid infusion if necessary.

Operative drug management:

- Phenoxybenzamine, "an alpha blocker" was administered for all cases (except in the first 2 cases) in the following manner:

* 1 mg/Kg at the start of cardiopulmonary bypass.

* 1 mg/Kg during rewarming.

*Phenoxybenzamine was used as a prophylaxis against postoperative pulmonary hypertensive crises.

- Myocardial inotoropic support during weaning from bypass "if needed" was restricted to the following drugs:

* Dopamine in a dose not more than 8 µg/Kg/min.

* Dobutamine in a dose not more than 10 µg/Kg/min.

* Isoprenaline in a dose of 0.01 - 0.05 µg/Kg/min.

* Adrenaline was avoided to prevent the incidence of postoperative pulmonary hypertensive crises.

III) Postoperative Management (till hospital discharge):

• All patients were transferred after operation for postoperative care in the Paediatric Intensive Care Unit till complete haemodynamic stability and weaning from pharmacologic support (inotroptics and vasodilators), and mechanical ventilation. Patients were discharged to the paediatric cardiac surgery ward for convalescence and evaluation until hospital discharge.

• Special postoperative management was performed as regards the way of ventilation, sedation, combination of inotropics and afterolad reducing drugs.

• Preventive measures to avoid the occurrence of postoperative pulmonary hypertensive crises, were taken:

1. Phenoxybenzamine 0.5 mg/Kg/dose slowly IV every 8-12 hours until weaning from mechanical ventilation.

2. Full sedation with fentanyl 4-8 µg/Kg/hour.

3. Complete muscle relaxation with vecuronium infusion 3 µg/Kg/min.

4. Hyperventilation to maintain PCO2 (3.3 - 4.0 Kpa).

5. Gradual reduction of FiO2 according to blood gases to maintain arterial PO2 (15-20 Kpa).

6. Regarding myocardial inotropic support, only dopamine up to a dose of 8 µg/Kg/min, or isoprenaline in a dose of 0.01-0.05 µg/Kg/min, were used.

7. Tracheal suctioning and other stimulating procedures may precipitate crises. So, full sedation with fentanyl bolus of 25 µg/Kg IV was given. Also, preoxygenation by hand-bagging preceeded every tracheal suctioning. Physiotherapy was not given routinely except after haemodynamic stability.

8. Weaning from mechanical ventilation proceeded from continuous mandatory ventilation (CMV), to intermittent mandatory ventilation (IMV), then continuous positive airway pressure (CPAP), and after that extubation of the patient was done.

• Management of acute postoperative pulmonary hypertensive crisis:

Pulmonary hypertensive crisis may still develop in spite of the preventive measures. The following could be undertaken:

1) Hand ventilation with 100% O2.

2) Complete sedation must be established (boluses of fentanyl 25 µg/kg) may blunt stress response associated with endotracheal suctioning, physiotherapy, or painful procedures such as removal of the chest drains.

3) Sodium bicarbonate (1 mEq/kg IV) can be given as a bolus.

4) Pulmonary vasodilators can be administered directly to the pulmonary artery, e.g. sodium nitroprusside, nitroglycerine, aminophylline or phenoxybenzamine.

5) Direct infusion of inotropics and fluids into left atrial line.

6) When the situation is under control, a period of stability for at least 24 hours is essential.

7) Gradual weaning from mechanical ventilation is done and if the pulmonary artery pressure remains at normal levels of arterial PCO2, then fentanyl and pulmonary vasodilators can be gradually withdrawn.

• Before hospital discharge, all the pre-operative non-invasive investigations, were done to all patients to detect any postoperative complications, especially residual VSD or residual postoperative high pulmonary pressure and/or poor myocardial functions.

Statistical analysis:

Descripitve statistics, i.e. mean, standard deviation, frequencies, percentages, etc. were calculated. Student's t-test was applied to compare two mean values of variables with homogeneous variances. Chi square test was used to compare differences in distribution of frequencies among different groups. A significant p-value was considered when p is less then 0.05.

Results

This study included 30 patients having primary ventricular septal defects with severe pulmonary hypertension.

Table (2): Personal characteristics of all patients

Variable	Range	Mean ±SD
Age (months)	6 - 60	28.5± 17.99
Weight (kg)	5 - 20	11.2± 4.41

Table (3): Age (in months) and sex distribution of all patients

Age	Males (%)	Females (%)	Total (%)
6 - ≤ 24	9 (30%)	8 (26.7%)	17 (56.7%)
> 24 - ≤ 60	7 (23.3%)	6 (20.0%)	13 (43.3%)
Total	16 (53.3%)	14 (46.7%)	30 (100%)

Table (4): Weight and sex distribution of all patients

Weight	Males (%)	Females (%)	Total (%)
5 - ≤ 10 Kg	7 (23.3%)	10 (33.4%)	17 (56.7%)
> 10 - ≤ 20	9 (30.0%)	4 (13.3%)	13 (43.3%)
Total	16 (53.3%)	14 (46.7%)	30 (100%)

4- History and presenting symptoms:

These data are represented in Table (5).

Table (5): History and presenting symptoms.

History and presenting symptoms	No. of patients	(%)
1. Difficulty of breathing on feeding	19	(63.3%)
2. Failure to thrive	30	(100%)
3. Repeated chest infection	30	(100%)
4. Presence of Cyanosis on effort or crying	8	(26.7%)
5. History of previous heart failure	20	(66.7%)
6. Therapeutic history:		
(Digoxin)	29	(96.7%)
(Frusemide)	21	(70.0%)
(Captopril)	10	(33.3%)

8- Preoperative Echo-Doppler findings (Tables 6,7):

Table (6): Preoperative Echo-Doppler diagnosis of VSD number and site

VSD	Number of patients	Percentage
* Single VSD	27	90 %
I. Perimembranous	25	83.3 %
(Inlet)	(13)	(43.3 %)
(Outlet)	(7)	(23.3 %)
(Trabicular)	(5)	(16.7 %)
II. Muscular inlet	1	3.3 %
III. Muscular outlet	1	3.3 %
** Multiple VSDs	3	10.0 %
Total	30	100 %

Table (7): Preoperative Echo-Doppler diagnosis of VSD diameter

VSD diameter		VSD diameter as % of Ao
Range	Mean	(Mean±SD)
1.0 - 2.5 cm	1.4 cm	101.6± 5o.51

9- Cardiac catheterization:

Done to all patients. Their data are represented in Tables (8 and 9)

Table (8): Preoperative cardiac catheterization data

Variable	Range	Mean±SD
PASP	55 - 105 mmHg	83.4±12.1
Pp / Ps	0.78 - 0.97 mmHg	0.89±0.06
Qp / Qs	1.6 - 3.5	2.39±0.60
Rp / Rs	0.25 - 0.50	0.38±0.07

PASP: Pulmonary artery systolic pressure
Pp Ps: Ratio of pulmonary to systemic pressures
Qp Qs: Ratio of pulmonary to systemic blood flows
Rp Rs: Ratio of pulmonary to systemic vascular resistance

Table (9): Preoperative cardiac catheterization diagnosis of degree of pulmonary vascular resistance

Degree of pulmonary vascular rsistance	Rp/Rs range	No.	%
Normal	<0.25	0	0.0
Mild elevation of pulmonary vascular resistance	0.25 - 0.45	18	60.0
Moderate elevation of pulmonary vascular resistance	0.45 - 0.50	12	40.0
Severe elevation of pulmonary vascular resistance	0.75 - 1.0	0	0.0

Table (10): Operative data

	Range	Mean±SD
PASP (1)	50-85 mmHg	75.4±8.83
PASP (2)	23-60 mmHg	38.0±9.73
Pp/Ps (1)	0.71-0.88	0.81±0.05
Pp/Ps (2)	0.20-0.60	0.37±0.10

Table (11): Postoperative inotropics (dose and duration)

Inotropic	Dose	No. of patients	Duration (range)	Duration (Mean±SD)
Dopamine	2-6 µg/Kg/min.	15	12 -160 hours	76.7±62.83
Dobutamine	10 µg/Kg/min.	2	130-136hours	133.0± 4.24
Isoprenaline	0.01-0.05 µg/Kg/min.	10	20 -192 hours	90.6±57.82

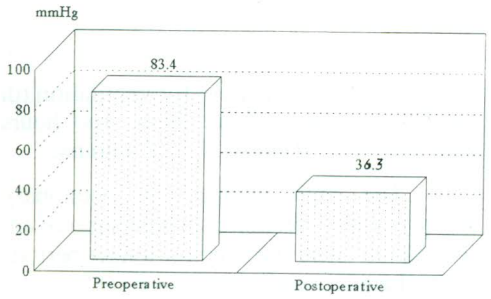


Fig.1: Postoperative drop in pulmonary artery systolic pressure

Results of the study were classified into:

I. Preoperative results.

II. Operative results.

III. Postoperative results "until hospital discharge".

I. Preoperative Results

1. Age:

The age of the patients ranged from 6 - 60 months with a mean of 28.5 ± 17.9 months. Most of the patients were in the first 2 years of life, 17 patients (56.7%), while 13 patients (43.3%) were between 2-5 years of age, Tables (2 & 3).

2- Gender:

Sixteen patients were males (53.3%) while 14 patients were females (46.7%), Tables (3,4).

3- Weigh:

It ranged from 5-20 kg with a mean ± SD of 11.2 ± 4.4 Kg. Most of the patients (17,56.7%) were between 5-10 kg, Table (4).

Table (12): Combination of inotropics in postoperative care

Number of Inotropic agents	Number of patients	%
One	5	16.7 %
Two	18	60.0 %
Three	7	23.3 %
Total	30	100 %

3- Postoperative pulmonary artery systolic pressure (PASP):

Table (13): Postoperative complications

Morbidity	No. of patients	%
Residual VSD#	1	3.3 %
Partial right bundle branch block	4	13.3 %
Surgically induced tricuspid regurge (grades I - II)	2	6.6 %
Severe pulmonary infection needing mechanical ventilation	1	3.3 %
Acute postoperative pulmonary hypertensive crises *	2	6.6 %
Right sided pleural effusion	1	3.3%

 # Closed spontaneously after 3 months ** Could not be saved and eventually died*

Table (14): Postoperative mortality (until hospital discharge)

Cause of death	No. of patients	%	Time of death
Postoperative pulmonary hypertensive crises	2	6.6 %	(1st) 14 hours postoperative (2nd) 72 hours postoperative

II. Operative Results

The intraoperative measurements included the following:

1- Pulmonary artery systolic pressure (PASP):

The intraoperative pulmonary artery systolic pressure (PASP) "before VSD closure", ranged from 50-85 mmHg with a mean 75.4±8.83. These measurements were lower than preoperative measures because intraoperatively the patient is completely relaxed and breathing 100% O2.

After VSD closure and weaning from bypass, (PASP) as measured from the indwelling pulmonary artery catheter ranged from 23-60 mmHg with a mean 38.00 ± 9.73.

2- Oxygen saturation difference "O2 step up"

O2 step up between samples obtained from mid-right atrium and pulmonary artery, ranged from 0.2%-3% (mean ± SD

of 1.22 ± 0.69%), except in one patient in whom O2 step up was 14%, proved by postoperative follow-up Echo-Doppler study to have small residual VSD "0.2 cm".

3-The total pump time (PT) and aortic cross clamp time (Ischaemic time) (IT):

- The total pump time (PT) ranged from 75-120 minutes with a mean of 99.16±15.05.

- The ischaemic time (IT) ranged from 40-80 minutes with a mean 58.33±13.45.

III. Post Operative Results:-

1- Postoperative sedation:

Fentanly was used for sedation in a dose of 4 - 8 µg/Kg/hr.

2- Pharmacologic support:

- Inotropics:

Young age and low body weight showed a significant correlation with the need for more inotropic support (p = 0.019). The doses and duration are represented in Table (11). Most patients needed a combination of more one inotropic drug (Table 12).

3- Postoperative pulmonary artery systolic pressure (PASP):

This was continuously monitored through a pulmonary artery catheter inserted at the end of operation for the first five postoperative days. PASP ranged from 23 to 50 mmHg with a mean ± SD of 36.33 ± 8.12 mmHg. (Fig. 1).

The immediate drop of systolic pulmonary artery pressure measured intraoperatively after VSD closure and weaning from bypass was statistically significant (p = 0.0001).

4 - Postoperative mechanical ventilation:

The duration needed for ventilation till extubation ranged from 26 to 160 hours with a mean ± SD of 62.5 ± 47.4 hours.

- The high preoperative pulmonary artery systolic pressure showed siginificant correlation with the need for longer periods of mechanical ventilation (p = 0.0001).

5- Early postoperative complications:

These are listed in Table (13).

6- Hospital case fatality:

Two out of thirty patients (6.6%) died in the early postoperative period, as shown in Table (14).

It was noted that in these two cases, phenoxybenzamine was not used as prophylaxis against acute postoperative pulmonary hypertensive crises, as the drug was not available during the early time of the study.

Age and weight showed no significant relation with postoperative mortality (p=0.80 and 0.85, respectively. Also, the level of PASP showed no significant relation with postoperative mortality (p = 0.14).

Discussion

Isolated ventricular septal defect is the most common congenital heart defect. It occurs at a rate of 2 per 1000 live births, and constitutes about 25% of all forms of congenital heart diseases (1). The functional disturbance caused by a VSD depends primarily on its size and the status of the pulmonary vascular bed rather than on the location of the defect. Kimball et al.(3) found good positive correlation between symptoms and defect size. Very small infants especially prone to development of severe congestive heart failure if there is

large left-to-right shunt. Furthermore, the present out-patient anticongestive therapies often fail to ameliorate symptoms. So, early primary VSD repair is recommended (4).

In our study, most of the cases (17 patients, (56.7%) presented below two years of age and all had primary closure of their defects, regardless of the age limitation. Operative interference was done based on the criteria that most of the cases below 2 years (15/17 patients) had previous history of congestive heart failure. The clinical findings for all of them (17 patients) were typical for large ventricular septal defects with repeated chest infection and failure to thrive. Also all of them had severe pulmonary hypertension with mild to moderate elevation of pulmonary vascular resistance. Early primary closure without delay was done in accordance with many investigators (17,4,18,19) where they found that patients born with non-restrictive defects have a high probability of needing surgery. Also, early primary closure is now possible with both low mortality and morbidity, and any delay in surgery is no longer indicated. In addition, favourable improvement in postoperative growth after early surgical intervention, supports the policy of early closure of the defect (4).

The other 13 patients (43.3%), presented between 24 to 60 months of age, all of them were suffering from severe pulmonary hypertension (Pp/Ps>0.75) with mild to moderate elevation of pulmonary vascular resistance (RP/Rs = 0.25 - 0.50). Also they had repeated chest infection and growth retardation. The decision for surgical closure was taken promptly as reported by others (17,18,20) who concluded that children with large VSD, first seen at older ages, should be operated upon promptly, especially when there is mild to moderate elevation of pulmonary vascular resistance. However, Kirklin and Barratt-Boyes (21), demonstrated that the younger the child at the time of repair, the better are the child's chances of surviving and having an essentially normal pulmonary artery pressure late postoperatively. Also, the lower the pulmonary vascular resistance at the time of the repair, the better are the chances of having normal pulmonary artery pressure late postoperatively. These two factors, age and preoperative pulmonary vascular resistance, interact in determining late postoperative pulmonary artery pressure.

Age in the present study was not found to be an incremental risk factor for hospital mortality (P = 0.80). This was also reported by other groups (4,22,19) who demonstrated that, the neutralization of young age as an incremental risk factor for hospital death, may be attributable to the demonstrated decrease in fatal human errors. Also, the scientific progress has brought improved preoperative diagnostic accuracy and surgical techniques, together with improved supportive techniques, such as methods of myocardial preservation, and good postoperative care with better handling of infants and young children. However, Cartmill et al.,(20) and Rizzoli et al.(18) found the reverse, probably because it may be the result of their early experience. From other points of view, young age and small weight showed significant correlation with the need for higher doses and longer durations of pharmacological support (p = 0.01), and more ventilatory support (P = 0.003). This significant correlation with increased perioperative morbidity was also clarified by Knott-Craig et al.(22) who found that significant morbidity occurred in 15.5% (16/103) of infants operated on for simple VSDs, with the identification of young age as a risk factor for significant perioperative morbidity (P = 0.001).

Regarding the level of preoperative pulmonary artery pressure, our study demonstrated that no significant relation

between the severity of preoperative pulmonary hypertension and postoperative mortality (P = 0.14), in accordance with others (21,22) who considered the level of preoperative (PASP), and pulmonary vascular resistance are not at present determinats of early postoperative mortality. These findings were in contrast with the earlier results reported by Cartmill et al (20), where there were no deaths in patients with mild or moderate pulmonary hypertension (Pp/Ps < 0.75), but there was a 6% mortality in patients with severe pulmonary hypertension (Pp/Ps > 0.75) with mild elevation of pulmonary vascular resistance (Rp/Rs < 0.45), their mortality reached 17% in cases with (Rp/Rs > 0..75). Similar results were also reported where the combination of young age and increased pulmonary vascular resistance seemed to result in a very high operative mortality rate (23,24). However, results of our study revealed that the high level of preoperative pulmonary artery pressure showed significant correlation with the need for longer periods of postoperative mechanical ventilation (a mean of 62.5 ± 47.4 hours). This observation reflects the significant perioperative morbidity, which occurred in cases of severe pulmonary hypertension, plus the need for meticulous postoperative care, especially in infants with severe pulmonary hypertension (22).

It was observed that the level of PASP measured intraoperatively before VSD closure was slightly lower than that estimated preoperatively for all patients (mean = 75.4 ± 8.8 mmHg, versus 83.4 ± 12.1 mmHg). This is because during anesthesia the patient is completely relaxed and breathing 100% O2 (5).

In the present study, it was observed that there was a striking fall in pulmonary artery pressure and (Pp/Ps) on the operating table immediately after closure of VSD in all patients, and this drop of pressure was highly significant (P = 0.0001). This observation was previously explained by Heath et al.(25), who considered that this drop of pulmonary pressure may be due to the effect of cutting off the increased pulmonary flow and possibly the relief of pulmonary vasoconstriction. However, it was noticed that the drop of pulmonary pressure occurred also in patients of our study who presented with mild to moderate elevation of pulmonary vascular resistance, which indicated that pulmonary vasoconstriction may be an important factor in the findings of many investigators (26,27,28,7,29,5), who found that there was considerable fall in pulmonary pressure on the operating table after VSD closure in patients with mild to modrerate elevation of pulmonary vascular resistance. Also, the significant drop of (PASP) which occurred after VSD closure in all current cases, with severe pulmonary hypertension, supported the assumption that the pathological grade of the pulmonary vasculature did not exceed Heath-Edwards grade II (25). these data correlate with the results obtained by Fried et al. (30), who found that immediate intraoperative drop of (PASP) was significant in nearly all patients with Heath-Edwards grades less than grade II.

We found that haemodynamic criteria for operability (Rp/Rs ≤ 0.50), i.e. mild to moderate elevation of pulmonary vascular resistance, were good predictors of the structural state of pulmonary vascular bed and accurately predicted the expected fall of pulmonary artery pressure immediately after VSD closure on the operating table. Our results supported the work of Mair (29) who stated that cardiac catheterization is still an accurate method of assessing the pulmonary

vascular bed. Also, Frescura et al (27) found that the correlation between pulmonary vascular resistance and lung biopsy is reliable. Moreover, Wilson et al.(5) found that carefully measured pulmonary vascular resistance and ratio (Rp/Rs) were reliable indicators of the structural state of the pulmonary vascular bed, obviating the need for routine lung biopsy. Also, when lung biopsy procedures were used as an isolated procedure, they were more dangerous (20% mortality, 13% morbidity).

This haemodynamic criteria for operability (previously mentioned) were applied in our patients with severe pulmonary hypertension, where there were 18 patients who had mild elevation of pulmonary vascular resistance (Rp/Rs = 0.25-0.45), while the remaining 12 patients had moderate elevation of pulmonary vascular resistance (Rp/Rs = 0.46-0.50), and in those patients, all the readings of cardiac catheterization were repeated after 100% O2 inhalation, and their ratios (Rp/Rs) returned to nearly normal levels (0.10-0.25). This test can be useful in determining the pulmonary vascular reactivity, to rule out fixed pulmonary resistance, and to help in determining operability of the case (26).

For closing VSD, we used a high porosity Dacron patch with the observation that some shunting may occur through the patch for 12 to 24 hours after operation, and this does not necessarily indicate a residual shunting as proved later by Echo. This was detected in our patients from oxygen step up in pulmonary artery samples in the range of (0.2% to 3%), which was due to shunting through the porous patch and not a residual VSD, as also reported by Kirklin and Barratt-Boyes (21).

Children with congenital heart defects associated with severe pulmonary artery pressure may die despite surgery (9). Postoperative mortality has been attributed to acute rises in pulmonary artery pressure and resistance, but the aetiology of such pulmonary hypertensive crises is uncertain, and therapy remains empirical (10).

In our experience with cases of ventricular septal defects with severe pulmonary hypertension, the first two operated patients had acute fatal episodes of postoperative pulmonary hypertensive crises with eventual death. The first patient weighed 8.5 kgs and was 16 months old, with severe pulmonary hypertension (Pp/Ps = 0.95) and mild elevation of pulmonary vascular resistance (Rp/Rs = 0.40) with large left-to-right shunt (Qp/Qs = 2.1). These data suggested that the patient was haemodynamically operable, and immediate fall (PASP) after VSD closure was expected. This was achieved operatively (Pp/Ps = 0.95, down to 0.60). Ths patient was transferred to ICU with no intraoperative or immediate postoperative complications except for a persistently low arterial PO2. This resistant hypoxaemia was present desipte excellent ventilation with an FiO2 of 0.90. A stable haemodynamic state existed for about 12 hours postoperatively, with continuous monitoring of pulmonary arterial pressure together with the systemic radial pressure. Afterwards, and during endotracheal suctioning, the patient showed abrupt deterioration manifested by acute elevation of pulmonary artery pressure which reached suprasystemic, elevated right atrial pressure, and more hypoxaemia, with consequent rapid fall in systemic pressure (all these events occurred in less than 3 minutes). Immediate management was started with pure 100% O2 by manual ventilation. Fentanyl bolus was given in a dose of 25 μg/Kg to ensure full sedation and to suppress the hypertensive pulmonary response to broncho-carinal stimulation. The setting of inotropic support was increased (Dopamine up to 8 μg/Kg/min). together with direct infusion of isoprenaline (0.05 μg/Kg/min.) into the pulmonary

artery catheter, along with other pulmonary vasodilators (aminophylline and sodium nitroprusside). However, the previous measures failed to control the crisis and the systemic pressure continued to fall, so infusion of the inotropic support had been shifted together with fluids to the left atrial line, but no improvement occurred and the patient sustained low cardiac output and died 14 hours postoperatively.

The second patient weighed 15 kgs and 47 months old, with severe pulmonary hypertension (Pp/Ps = 0.90) and mild elevation of pulmonary vascular resistance (Rp/Rs = 0.36) with large left-to-right shunt (Qp/Qs = 2.4). These data also suggested haemodynamic operability together with the expected immediate fall of PASP after VSD closure (Pp/Ps = 0.90, down to 0.30). Then the patient passed a stable haemodynamic state for the first postoperative day, but on the 2nd postoperative day the patient developed an acute episode of pulmonary hypertensive crisis during weaning from mechanical ventilation. Weaning was stopped and a bolus of Fentanyl (25 µg/kg) was given, and vecuronium (3 µg/kg/min.) together with manual hyperventilation with 100% O2. Direct infusion of isoprenaline (0.05 µg/kg/min.) and Sodium Nitroprusside (4 µg/kg/min.) into the pulmonary artery catheter was instituted. Consequently, the crisis was overcomed and the patient was maintained on ventilatory support again. On the third postoperative day, during endotracheal suctioning, a fatal episode of pulmonary hypertensive crisis occurred with resultant severe right-sided heart failure and trials for control as done before failed, with death of the patient 72 hours postoperatively.

From our experience, pulmonary hypertensive crisis was found to be a significant problem in infants undergoing surgery for VSD with pulmonary hypertension. Despite the aggressive approach that had been tried, eventual mortality occurred whenever a major crises took place. This is similar to other experiences (31,10). Though acute pulmonary vasoconstrictive episodes could be reversed initially in the second patient, he eventually died because of protracted right sided heart failure so that prevention of this condition is obviously ideal as concluded by Sumner and Stark (32). We found that monitoring of the pulmonary artery pressure is very important. If only systemic arterial pressure is monitored, all that may be observed (during a crisis) is a decline from normal systemic pressure to catas trophically low in less than 3 minutes. Thus, a "crisis" is a true emergency as death is eminent. This drop of systemic blood pressure without the monitoring of pulmonary artery pressure, may provoke therapies such as intravenous epinephrine or norepinephrine, which could very well aggravate the pulmonary hypertension. So, monitoring of pulmonary artery pressure with the use of indwelling pulmonary artery catheter is mandatory in cases in VSD with severe pulmonary hypertension (31,32).

An important observation in the postoperative care of patients with VSD and severe pulmonary hypertension is that endotracheal suctioning, which was found in the present work to be a strong stimulus for initiating the crises, partly because of the hypoxaemia which occurs during prolonged endotracheal suctioning, and also because of the hypertensive pulmonary response to broncho-carinal stimulation. This necessitates that, before endotracheal suctioning is done, pretreatment with Oxygen hyperventilation and narcotic bolus

with an anesthetic dose of Fentanyl (25 μg/Kg) to blunt the stress response (32).

We used phenoxybenzamine for prophylaxis and treatment of postoperative pulmonary hypertensive crises. This long lasting alpha-adrenergic blocking agent was used in the next 28 patients with severe pulmonary hypertension, together with the other measures for prophylaxis, so that the development of major crises could be prevented, and all of the 28 patients were saved from these fatal episodes. This policy was similar to other workers (33,32).

Early postoperative mortality occurred in the first two operated patients (6.6%). This mortality could be prevented if avoidance of the occurrence of acute postoperative pulmonary hypertensive crises or treatment of the major crises were successful. However, this led to the suggestion that it is probably better to prevent the incidence of the crisis rather than its treatment. Also, if these patients were presented early, and operated upon before the development of severe pulmonary hypertension, they may be saved from this fatal complication. So, it is better to interrupt the natural history of large VSDs with large left-to-right shunt before the development of severe pulmonary hypertension and elevation of pulmonary vascular resistance. However, the incidence of mortality in our cases is in contrast to other reports (17,20,24,34). Cartmil et al.(20) reported a mortality of 17% in cases with pulmonary hypertension and elevated pulmonary vascular resistance. Also, Blackstone et al.(17) reported 9.1% mortality, while John et al.(24) found 22% of mortalities in patients with severe pulmonary hypertension. Stark and Sethia (34) reported a hospital mortality of 11.9%. However, in the current era, Hardin et al.(4) reported no deaths in 23 infants weighing 4 kg or less, compared with one infant (4%) died out of 25 infants weighing more than 4 kg. Also Van-den-Heuvel et al.(19) reported no deaths in 43 patients that had early primary surgical closure of large VSDs. It has been found, in our experience and in others (18,34,19,35) that there is a steady decrease in hospital mortality, and this resulted from scientific progress with improved preoperative diagnostic accuracy, improved myocardial protection, and avoidance of right ventricular incisions together with the increased experience of handling infants and young children subjected to open-heart surgery. Also, meticulous and minute-by-minute postoperative care permits very early time of repair to achieve favourable surgical outcome and postoperative results with the prevention of occurrence of severe pulmonary vascular changes.

Conclusion

Based on results of our work, the following can be concluded:

- Early primary closure of the ventricular septal defects, regardless of age, is now possible with both low mortality and morbidity. Early closure is specially recommended if there is a large left-to-right shunt or mild-to-moderate elevation of pulmonary vascular resistance.

- The younger the child at the time of repair and the lower the pulmonary vascular resistance, the better are the chances of having normal pulmonary artery pressure early and late postoperatively.

- Age was not found to be an incremental risk factor for hospital morality, although young age and small weight showed significant correlation with increased perioperative morbidity.

- The striking fall of pulmonary artery systolic pressure immediately after VSD closure, supported the assumption that the pathological grade of the pulmonary vasculature did not exceed grade II. These

findings indicated that accurate preoperative haemodynamic assessment and carefully measured pulmonary/systemic vascular resistance ratio (Rp/Rs) were raliable indicators of the structural state of the pulmonary vascular bed and obviating the need for routine lung biopsy. However, lung biopsy procedures should be done in borderline cases with fixed severe elevation of pulmonary vascular resistance (Rp/Rs > 0.75).

- Pulmonary hypertensive crisis was a significant problem in young children undergoing surgery for VSD with pulmonary hypertension. Despite the aggressive approach that had been done, eventual mortality occurred whenever major crises took place.

- Monitoring of pulmonary artery and left atrial pressures may be beneficial in early detection and management of pulmonary hypertensive crisis.

- Endotracheal suctioning was a strong stimulus for initiation of the crisis. So, heavy sedation with fentanyl bolus in a dose of 25 µg/kg prior to suction is of vital importance to suppress the hypertensive pulmonary response to broncho-carinal stimulation, especially in patients with signs of reactive pulmonary circulation.

- Prophylaxis from this crisis is obviously ideal, so that, the use of phenoxybenzamine was found to be useful and succeeded in the prevention of major crises in 28 patients.

- Lastly, it is better to interrupt the natural history of large VSDs with large left-to-right shunt before the development of severe pulmonary hypertension and elevation of pulmonary vascular resistance. So, the policy of early primary surgical closure is highly recommended.

References

1. Hoffman JIE (1968): Natural history of congenital heart disease; Problems in its assessment with special reference to ventricular septal defects. Circulation, 37:97.

2. Neutze JM, Ishikawa T, Clarkson PM, Colder Al, Barratt-Boyes BG and Kerr AR (1989) : Assessment and follow up of patients with ventricular septal defect and elevated pulmonary vascular resistance. Am. J Cardiol, 63:327-31.

3. Kimball TR, Danbiels SR, Meyer RA, Hannon DW, Khoury P and Schwartz DC (1991) : Relation of symptoms to contractility and defect size in infants and children with ventricular septal defects. Am. J Cardiol, 67 : 1097 .

4. Hardin JT, Muskeet AD, Canter CE, Martin TC and Spray TL (1992): Primary surgical closure of large ventricular septal defects in small infants. Ann Thorac Surg, 53:397-401.

5. Wilson NJ, Seear MD, Taylor GP, Le Blanc JG and Sandor GGS (1990): The clinical value and risks of lung biopsy in children with congenital heart disease. J. Thorac Cardiovasc Surg 99:460-8.

6. Heath D and Edwards JE (1958): The pathology of hypertensive pulmonary vascular disease: A description of six grades of tructural changes in the pulmonary artery with special reference to congenital cardiac septal defects. Circulation, 18:533.

7. Hoffman JIE, Rudolph AM and Heymann MA (1981): Pulmonary vascular disease with congenital heart lesions; Pathologic features and causes. Circulation, 64 (5): 873-8.

8. Rabinovitch M, Keane JF, Fellows KE, castaneda AR and Reid L (1981): Quantitative analysis of the pulmonary wedge angiogram in congenital heart defects. Correlation with haemodynamic data and morphometric findings in lung biopsy tissue. Circulation, 63:152-64.

9. Wheller J, George BL, Mulder DG and Jarmakani JM (1979): Diagnosis and management of postoperative pulmonary hypertensive crisis. Circulation, 60:1640-4.

10. Jones ODH, Shore DF, Rigby ML, Leijala M, Scallan J, Shinebourne EA and Lincolin JCR (1981): The use of Tolazoline hydrochloride as a pulmonary vasodilator in potentially fatal episodes of pulmonary vasoconstrictive after cardiac surgery in children. Circulation, 64 (Suppl. II): 134-9.

11. Agosti J, Chiariello L, Wagner H and Subramanian. (1976): Intracardiac repair of isolated ventricular septal defect below two years of age. J Cardiovasc Surg, 17:147-154.

12. Arciniegas E, Farooki ZQ, Hakimi M. (1980): Surgical closure of ventricular septal defect during the first twelve months of life. J Thorac Cardiovasc Surg, 921.

13. Laks H, Deren M and Shieh CJ (1979): Surgical treatment of ventriclar septal defects: experience with pulmonary artery banding and primary correction. Clin Res, 27:182 A.

14. McNicholas KW, Bowman FO Jr and Hayes CJ (1978): Surgical management of ventricular septal defect in infants. J Thorac Cardiovase Surg, 75:346-53.

15. Richardson JV, Schieken RM, Lauer RM, Stwart P and Doty D (1982): Repair of large ventricular septal defects in infants and small children. Ann Surg, 199 (3): 318-22.

16. Frencker BP, Olin CL and Bonfim V (1981): Detachment of the septal tricuspid leaflet during transatrial closure of isolated ventricular septal defect. J Thorac Cardiovasc Surg, 82:773-5.

17. Blackstone EH, Kirklin JW, Bradley EL, DuShane JW and Appelbaum A. (!976): Optimal age and results in repair of large ventricular septal defect. J Thorac Cardiovasc Surg, 72:661.

18. Rizzoli G, Blackstone EH, Kirklin JW, Pacifico AD and Bargeron LM Jr (1980): Incremental risk factors in hospital mortality after repair of ventricular septal defect. J Thorac Cardiovasc Surg, 80:494.

19. Van den Heuvel F, Trimmers T and Hess J (1995): Morphological, haemodynamic and clinical variables as predictors for management of isoalted ventricular septal defect. Br Heart J, 73 (1): 49-52.

20. Cartmill TB, DuShane JW, McGoon DC and Kirklin JW. (1966): Results of repair of ventricular septal defect. J Thorac Cardiovasc Surg, 52:486.

21. Kirklin JW and Barratt-Boyes BG (1993): Ventricular septal defect. In: Cardiac surgery, 2nd edition. Kirklin JW and Barratt-Boyes BG (Eds). Churchill Livingstone Inc, Chapter 20, pp. 749-824.

22. Knott-Craig CJ, Elkins RC, Ramakrishnan K, Hartnett DA, Lane MM, Overholt ED, Ward KE and Razook JR (1995): Associated atrial septal defects increase perioperative morbidity after ventricular septal defect repair in infancy. Ann Thorac Surg, 59 (3) : 573-8.

23. Friedi B, Kidd BSA, Mutsard WT and Keith JD (1974): Ventricular septal defect with increased pulmonary vascular resistance. Am J Cardiol, 33:403-409.

24. John S, Korula R, Jairai PS, Muralidaran S, Ravikumar E, Babuthaman C, Sathyamorrthy I, Kirishnaswamy S, Cherian G and Sukumar IP (1983): Results of surgical treatment of ventricular septal defects with pulmonary hypertension. Thorax, 38:279.

25. Heath D, Helmoholz HF Jr, Bruchell HB, Du Shane JW and Edwards JE (1958): Graded pulmonary vascular changes and haemodynamic Findings in cases of atrial and ventricular septal defects and patent ductus arteriosus. Circulation, 18:1155.

26. Davies N, Shinebourne EA, Scallan MJ, Sopwith TA and Denison DM. (1984): Pulmonary vascular resistance in children with congenital heart disease. Thorax, 39:895-900.

27. Frescura C, Thiene G, Franceschini E, Talenti E and Mazzucco A. (1987): Vascular disease in infants with complete atrioventricular septal defect. Int J Cardiol, 15:91-100.

28. Hallidie-Smith KA, Hollman A, Cleland WP, Bentall HH and Goodwin JF (1969): Effects of surgical closure of ventricular septal defects upon pulmonary vascular disease. Br Heart J, 31:246-260.

29. Mair DDD (1979): Effect of markedly elevated haematocrite level on blood viscosity and assessment of pulmonary vascular resistance. J Thorac Cardiovasc Surg, 77:682-4.

30. Fried R, Falkovski G and Newburger J (1986): Pulmonary arterial changes in patients with ventricular septal defects and severe pulmonary hypertension. Paediatr Cardiol. 7:147-54.

31. Hopkins RA, Bull C, Haworth SG, de Leval MR and Stark J (1991): Pulmonary hypertensive crises following surgery for congenital heart defects in young children. Eur J Cardio Thorac Surg, 5:628-634.

32. Sumner E and Stark J (1994): Postoperative Care. In: Surgery for Congenital Heart Defects. WB Saunders Co., Philadelphia, 2nd edn. Ch. II,pp. 193-233.

33. Ogawa K, Yamamoto T, Asada S, Iwai S, Toriyama A, Horikoshi K, Yamaguchi M and Kimura K (1979): The effect of phenoxybenzamine on the pulmonary vascular bed in surgically corrected ventricular septal defect associated with pulmonary hypertnsion. Jap Heart J, 20 (2): 157-61.

34. Stark J and Sethia B (1986): Closure of ventricular septal defect in infancy. J Cardiac Surg, 1:135.

35. Vincent RN, Lang P, Chipman CW and Castaneda AR (1985): Assessment of haemodynamic status in the intensive care unit immediately after closure of ventricular septal defect. Am J Cardiol, 55:526-9.

Redo Valvular Surgery: The Recent Allegheny General Hospital Experience

ABSTRACT

From August, 1991 to December, 1993, a total of 495 cardiac valve replacement operations were performed, 97 of them (19.6%) were redo operations. There were 29 males (29,9%) and 68 females (70.1%). Their age ranges from 30-88.5 years with a mean of 61.4+11.9 years. Indications for re-operation were; prosthetic valve disease in 73 patients (65,8%) and native valve disease in 38 patients (34.2%) with a well-functioning prosthetic valve. There were 7 patients in whom there were both prosthetic and native valve disease. The overall hospital mitral valve replacement was 9% (5 out of 55), for aortic valve replacement 8% (2 out of 25) and for double valve (aortic & mitral) valve replacement it was 26.7% (4 out of 15). Associated surgical procedures were done in 11 patients (11.3%). Repaid of aneurysm of Sinus of valsalva in, one case, Mitral valve repair in 2 cases, triunpid annuloplasty in 4 cases, left atrial thrombectomy in 2 cases & CABG in 2 cases. There were no mortality related to the associated surgical procedures. Univariate analysis shows that: NYHA class IV, congestive heart failure, renal failure, urgent/emergency operation, double valve replacement and the need for intra-aortic balloon are predictors of operative mortality. Mutlivariate analysis by forward stepwise selection shows that renal faillure is the most powerful predictors of operative mortality, with congestive heart failure comes next to it. Close and careful follow-up of patients with prosthetic cardiac valves, with early detection of prosthetic dysfunction and immediate re-operation before clinical and hemodynamic deterioration occurs is strongly recommended.

Mohamed A.F. El Gamal, M.D.*, Richard E. Clark, M.D.** and George J. Magovern, MD ***

J. of Egypt. Society of Cardio thorac. Surg.September 1996, Vol. V No 4

INTRODUCTION

Since the first successful heart valve replacements began in 1960, the results of cardiac valve replacement have improved markedly. (1) With decreased operative mortality, better valve design and improved postoperative follow-up, more patients are surviving following cardiac valve replacement. Despite these improvements, infectious, thromboembolic and durability complications still plague all forms of prosthetic and bioprosthetic valves. 2 Also, some patients with prosthetic cardiac valves may develop lesion in another native valve, requiring re-operation. Thus, re-operative cardiac valve surgery are required in many patients who undergo primary valve replacement regardless of the type of valve used. We reviewed all patients who underwent redo cardiac valve surgery at the Division of Cardiothoracic Surgery, Allegheny General Hospital from August,

* *Lecturer of Cardiothoracic Surgery, Dept. of Cardiothoracic Surgery, Faculty of Medicine, Mansoura University, Mansoura, Egypt.*

** *Director of the Cardiovascular & Pulmonary Research Center, Allegheny General Hospital, Medical college of Pennsylvania, Pittsburgh, PA; U.S.A.*

*** *Chairman, Dept. of Surgery, Allegheny General Hospital, Pittsburgh, Medical college of Pennsylvania, Pittsburgh, PA; U.S.A.*

1991 to December, 1993 to determine the risk factors for operative mortality and to find out ways of improving the results.

Patients And Methods

Table (1): The most frequent clinical findings that were present at the time of admission are listed in table 1.

Clinical finding	*No. of patients*	*%*
Shortness of breath	81	83.5
Paroxysmal nocturnal dyspnea	21	21.6
Orthopnea	29	29.9
Peripheral edema	28	28.9
Syncope	2	2.1
Gallop	9	9.3
Appearance of a new murmur or change of preexisting one	86	88.7
Rales over the lung bases	14	14.4
Atrial fibrillation	42	43.3
Congestive heart failure	31	31.9

The clinical records of all patients who underwent valve replacement operations at Allegheny General Hosital from August 1991 to December, 1993 were reviewed. There total number was 495 patient. Of them 97 patients (19.6%) underwent valve re-operation during the same period. There were 29 males (29,9%) and 68 females (70.1%). The maximum age 88.5; the minimum 30 with a mean of 61.4+11.9 years.

Table 1 shows the most frequent clinical findings in patients who underwent redo cardiac valve surgery, in this series.

The indications for re-operation were 111 in 97 patients. They were divided into three categories: (A) prosthetic valve disease in 66 patients; (B) Native valve disease in 31 patients with a well-functioning prosthetic valve; and (C) Both prosthetic and native valve disease in 7 patients (i.e. 14 indications). Figure 1&2 shows the indications for re-operations for re-operations and the etiology of prosthetic valve dysfunctions in the patients of this series respectively.

The indications for prosthetic valve re-replacement were classified into five groups in accordance with the definitions recommended and reported by the Council of the Society of Thoracic surgeons published in 1988 "Guidelines for reporting morbidity and mortality after cardiac valvular operation (3)

1) Structural dysfunction: patients in this group have deterioration of the prosthetic valve either stenosis and/or regurgitation due to calcification and/or perforation.

2) Non-structural dysfunction: patients having either paravalvular leak or pannus formation. Patients with paravulvular leak secondary to prosthetic valve endocarditis were not considered in this group.

3) Prosthetic valve endocarditis.

4) Prosthetic valve thrombosis.

5) Prophylactic replacement.

Preoperative patient management:

All patienbts with suspected prosthetic valve disease were fully examined clinically and were non-invasively evaluated by echo-Doppler study and in some with transesophageal echocardiography. Twenty eight patients underwent diagnostic cardiac catheterization before surgery. Laboratory investigations were done for all patients.

Table (2) : Univariate analysis of perioperative variables among survivors non-survivors.

Preoperative variable	*Survivors*	*Non-Survivors*	*P Value*
1- Age > 65	32 (37.2%)	7 (63.6%)	0.11
2- Age (Survivors n =86, Non-Survivors n=11)	60.1±12.1	66.7±9.0	0.12
3- Sex Females Males	 60 (69.8%) 26 (30.2%)	 8 (72.7%) 3 (27.3%)	 1.00
4- NYHA Category I II III IV	 16 (18.6%) 19 (22.1%) 32 (37.2%) 19 (22.1%)	 2 (18.2%) 0 2 (18.2%) 7 (63.6%)	 0.02*
5- Renal Failure	10(11.6%)	6 (54.5)	0.002*
6- left Ventricular Ejection Fraction (Survivors n=17, Non-Survivors n=11)	55±17.0	70.7±17.2	0.16
7- Valve Endocarditis	6 (7.0%)	2(18.2%)	0.22
8- COPD	15 (17.4%)	4 (36.4%)	0.22
9- CHF	22 (25.6%)	9 (81.8%)	0.00047*
10- Procedure Status Emergent Urgent Elective	 1 (1.2%) 29 (33.7%) 56 (65.1%)	 0 10 (90.9%) 1 (9.1%)	 0.001*
11- Bypass Time (Survivors n=86, Non-Survivors n=11)	121.9 ±46.8	137.5±34.6	0.09
12- Cross-Clamp Survivors n=86, Non-Survivors n=11)	75.4±30.5	81.2±25.0	0.34
13- Number of Valve Replacements Single Double Survivors n=86, Non-Survivors n=11)	 75 (87.2%) 11 (12.8%)	 7 (63.6%) 4 (36.4%)	 0.06
14- IABP/ECMO Pre-operative Post-operative	 0 4 (4.6%)	 0 5 (45.4%)	 NA 0.00072*

Legend :

These included complete blood picture, hepatic and renal function tests.

Patients presented with acute heart failure were managed medically in intensive care unit with cardiac inotropics, digitalis, diuretics and after load reducing agents till optimal hemodynamics were achieved. Patients with elevated serum creatinine are managed by hemodialysis and/or hemofiltration. Once the patients conditions were stabilized, they were immediately brought to the theater for operation.

Table (3): Reported hospital mortality rates in redo valvular surgery

Medical Center	Period	No. in series	Mortality rate %
Columbia-Presbyterian (USA[12])	1960-1977	89	19
Mayo Clinic, USA[14]	1961-1980	617	9.4
St. Louis, USA[15]	1962-1977	68	41.3
Stanford,. Calif, USA[9]	1964-1978	232	11.6
National Heart, London [4]	1968-1969	50	22
Cambridge, England[5]	1972-1976	43	4.6
Hamburg, Germany[16]	1975-1979	100	3
Brigham & Women's Hospital Boston, Massachusetts, USA[2]	1972-1981	58	14
Humana Heart Institute Kentucky, USA [10]	1968-1987	152	14.2
Centro cardiologico, Milano, Italy[11]	1983-1992	41	17
Allegheny General Hospital Pittsburgh, USA (present series)	1991-1993	97	11.3
Mean	--	--	15.2

Operative technique:

All operations were done by the same surgical group using the same operative technique. The standard approach was through a median sternotomy. In all cases the femoral vessels were exposed in preparation for cannulation should they be needed. The skin incision were placed over the previous one with removal of the excess scar tissue. The sternal wires, once identified, were removed and an oscillating saw is used to reopen the sternum. Meticulous and patient dissection of the dense adhesion between the back of the sternum and the heart, to expose the aorta and right atrium first for arterial and venous cannulation respectively. The venous drainage was obtained either by a single two-stage cannula or double venous cannulae depending on the procedure.

After connection of the patient to the heart lung machine and aortic cross

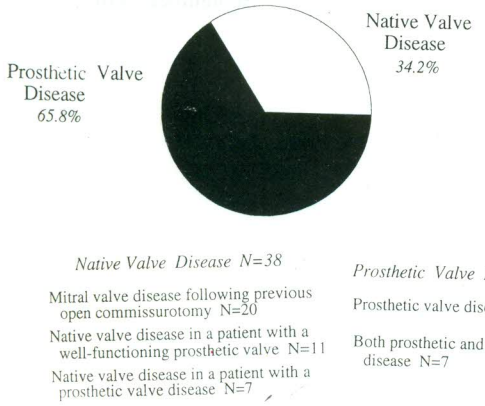


Figure.1:Indications for valve Reoperation N=111

Statistical analysis:

The statistical analysis was done using SPSS statistical software package (SPSS Inc. 444 N. Michigan Avenue, Chicago, Illinois, USA). Univariate and multivariate stepwise. Logistic regression analysis were performed to identify predictors of in-hospital mortality among patients undergoing re-operative valve surgery. The likelihood ratio test was used to determine whether a variable should be removed from the model. The dependent variable, survival, was coded using binary digits, with "1" representing non survivor and "O" representing survivor. Independent variables used to construct the model

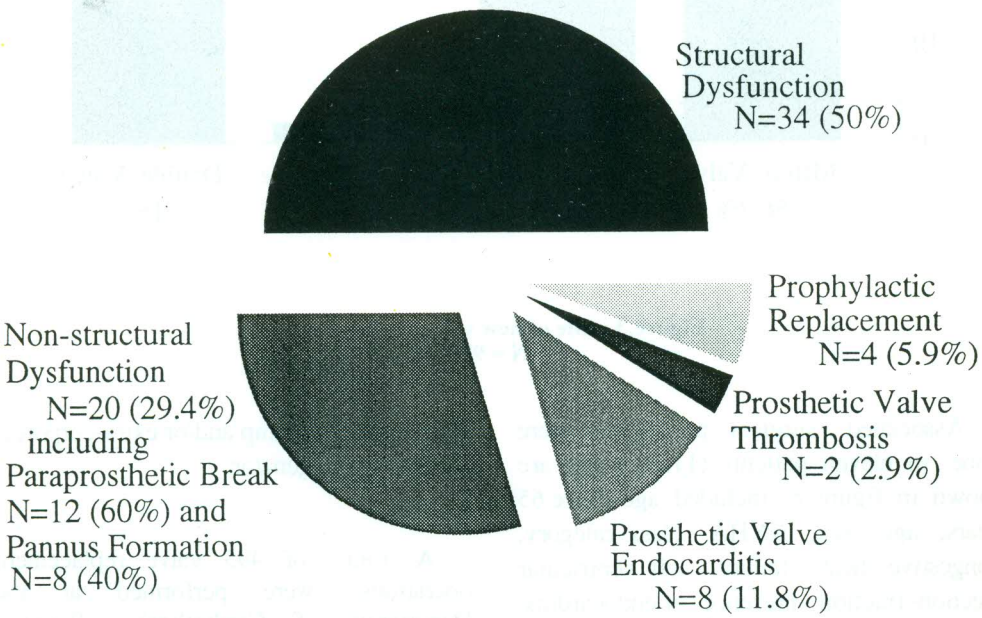


Figure 2: Etiology of Prosthetic Valve Disease N = 68

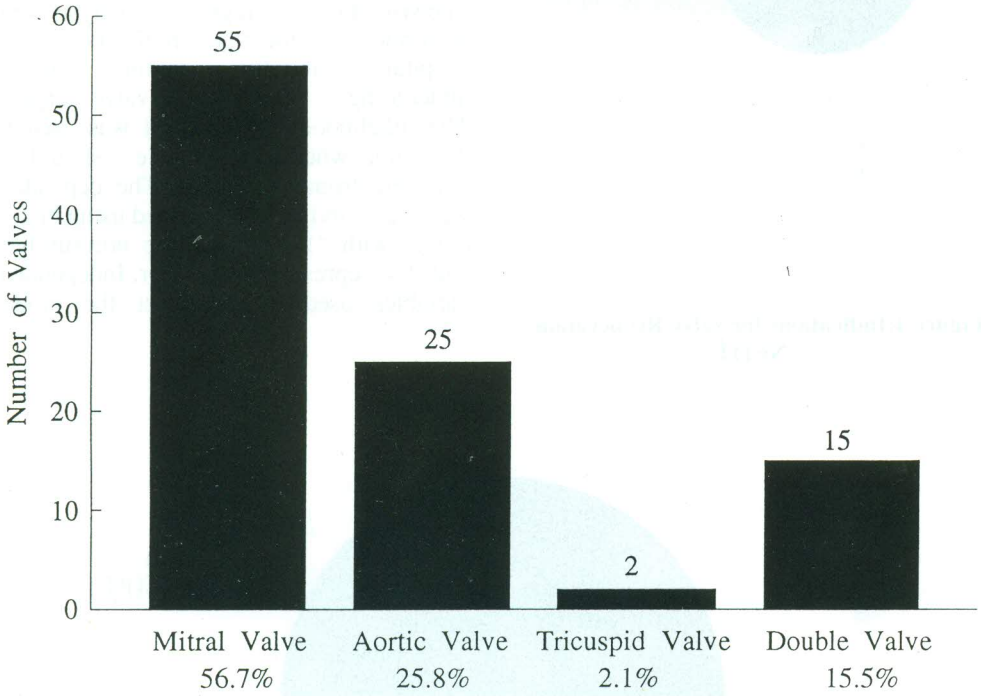
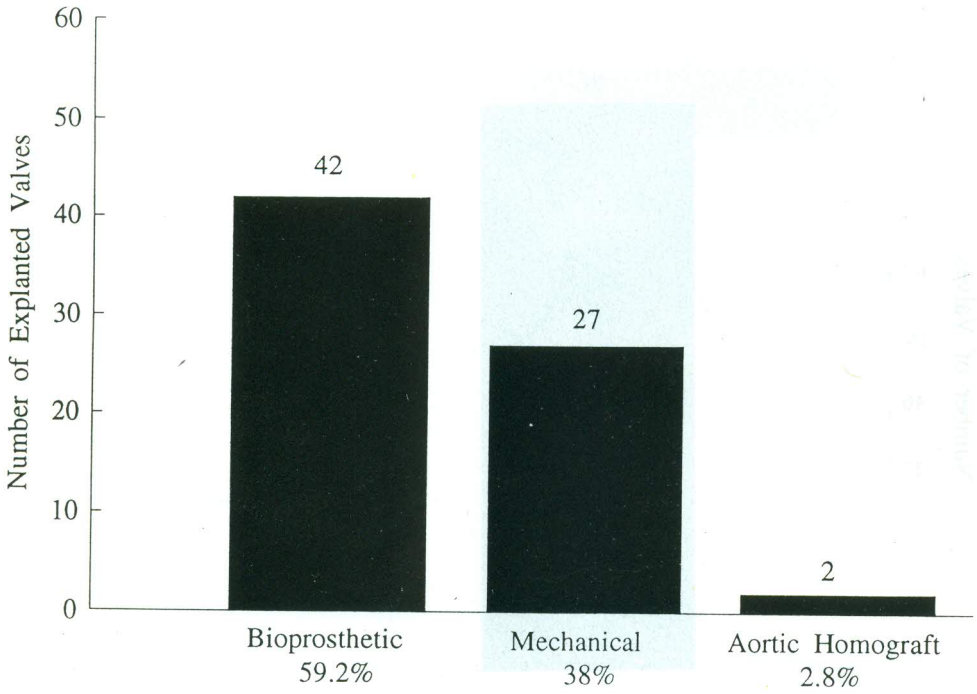


Figure.3 : Site of new valve replacement
N = 97

Associated surgical procedures were done in eleven patients (11.2%) and are shown in figure 6. included: age above 65 years, age, sex, NYHA class category, congestive heart failure, left ventricular ejection fraction, presence of endocarditis, presence of chronic obstructive pulmonary disease, procedure status (urgent-emergent), cardiopulmonary bypass time, cross-clamp time, 24 hours bleeding and the use of intra-aortic balloon pump and/or extra-corporeal membrane oxygenator.

Results

A total of 495 valve replacement operations were performed at the Department of Cardiothoracic Surgery, Allegheny General Hospital, Medical College of Pennsylvania, from August, 1991 to December, 1993. Out of them 97 patients (19.6%) underwent redo valve operations.



[1] A total of 71 prosthetic valves were explanted from 66 patients and 5 patients had dou valves explanted.

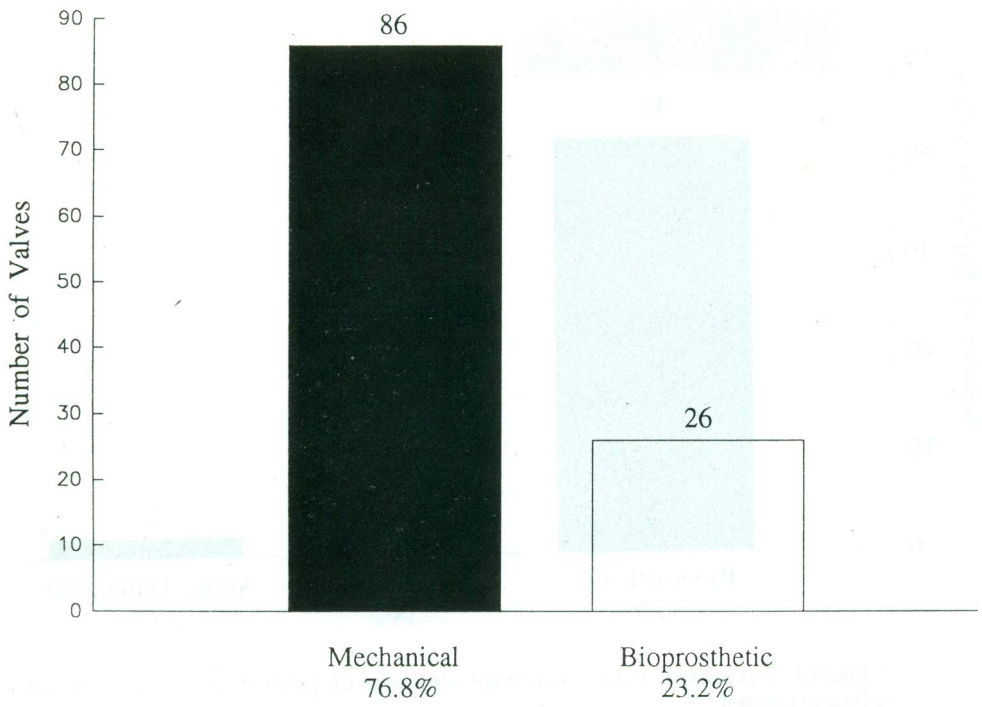
Figure.4: Explanted Valve

N = 66

Figure 3 shows the site of new valve replacement. Figure 4 shows the type of the explanted prosthetic valve. A total of 71 prosthetic valves were explanted from 66 patients as in 5 patients, double valves were explanted. Figure 5 shows the type of the implanted valve. A total of 112 valves were implanted in 97 patients as 15 patients had double valve replacement. Figure 6 shows the associated surgical procedures performed in 11 patients.

The overall operative mortality rate was 11.3% (11 out 97). The operative mortality rate for mitral valve replacement was 9% (5 out 55), for aortic valve replacement it was 8% (2 out 25), for double valve replacement it was 26.7% (4 out 15) and it was zero% for tricuspid valve replacement (0 out 2). There was no operative mortality related to the associated surgical procedures. Although the morality rate for double valve replacement is high it has no univariate significant influence on operative mortality, (P value=0.06).

Causes of operative mortality in 11 patients were ; low cardiac output and



[1] A total of 112 valves were implanted in 97 patients, 15 of which were double valve replacements.

Figure.5: Implanted Valves

N = 97

cardiogenic shock with no response to intra-aortic balloon pump or extra-corporeal membrane oxygenator (IABP/ECMO) in 4 patients, renal failure in 6, and intractable whom required IABP/ECMO for management of low cardiac output developed, also, multiorgan failure.

The pre-operative variables with significant influence on operative mortality, as shown by univariate logistic regression analysis, were: NYHA class category (P=0.02), renal failure (P=0.002), congestive heart failure (P=0.004) procedure status i.e. emergent/urgent versus elective (P=0.001). The intraoperative variables, cardiopulmonary bypass time, cross-clamp time and number of valve replacement all have no significant influence on the operative mortality. The post-operative use of IABP/ECMO had a statistically significant influence on the

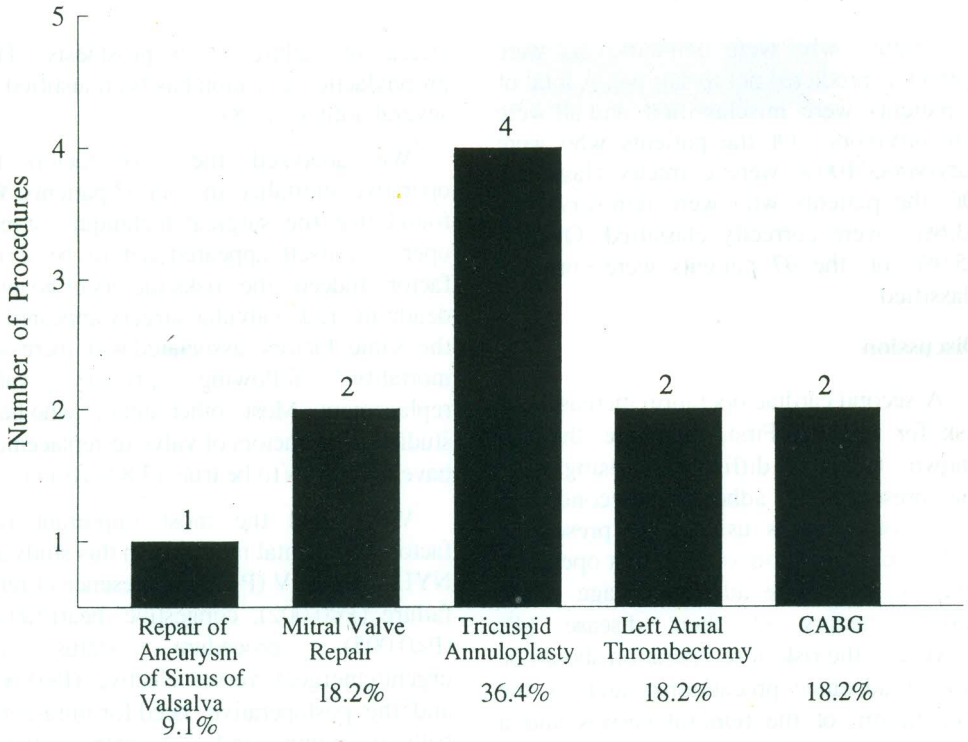


Figure.6: Associated Cardiac Surgical Procedures

Table (4): Reported hospital mortality rates for emergency redo valvular surgery.

Medical Center	Mortality rate %
Columbia-Presbyterian, USA [12]	67.0
St. Louis, USA [15]	41.0
Humana Heart Institute, Kentucky, U.S.A [10]	72.7
Centero Cardiologico, Milano, Italy [11]	38.0
University of Pavoda medical school Italy[17]	57.0
Allegheny General Hospital, Pittsburgh U.S.A. (present series)	90.9
Mean	61.1

operative mortality. Table 2 shows the univariate analysis of the perioperative variables.

When all the previous factors were used to construct a model with multivariate logistic regression analysis by forward stepwise selection, renal failure was the most powerful predictor of in-hospital mortality. Congestive heart failure comes next to the renal failure. This model provided a high sensitivity and specificity, as the classification model demonstrated the 86 patients who survived were correctly predicted by the model to survive. Likewise,

7 patients who were non-survivors were correctly predicted not to survive. A total of 4 patients were misclassified and all were non-survivors. Of the patients who were survivors, 100% were correctly classified. Of the patients who were non-survivors, 63.6% were correctly classified. Overall, 95.9% of the 97 patients were correctly classified.

Discussion

A second cardiac operation increases the risk for reasons. First, there are the well known technical difficulties arising from the presence of adhesions. Second, this group of patients usually are presenting with a complication of the first operation and are at a more advanced stage of the natural history of their disease (4), However, the risk of re-operation should be low if adequate precautions, such as the preparation of the femoral vessels and a careful surgical technique are employed.(5)

In this series, no serious bleeding was encountered on reopening of the sterum, dissection of the heart from the pericardium or cannulation for by pass.

The indications for re-operation in our series are all internationally accepted. We have four partients who had their redo operations for prophylactic indications, three of them were in response to re-call made by the Shiley Incorporated, Irvine, California to explant the convexoconcave Bjork-Shiley valve because of increased incidence of strut fracture. (6) The fourth patient was a young female with a Carpentier-Edwards valve expressed her desire to replace her bioprosthetic valve with a mechanical one because she was afraid of failure of bioprosthesis. This prophylactic indication has been justified by several authors. (7,8).

We analyzed the risk factors for operative mortality in our 97 patients. We found that the surgical technique of redo operation itself appeared not to be a risk factor. Indeed, the risks factors of hospital death in redo valvular surgery appeared be the same factors associated with increased mortality following primary valve replacement. Most other authors who have studied risk factors of valve re-replacement have found this to be true. (7,8,9,10,11)

We found the most important risk factors of hospital mortality in this study are NYHA class IV ($P<0.02$), presence of renal failure ($P<0.002$), congestive heart failure ($P<0.005$), procedure status i.e. urgent/emergent versus elective ($P<0.001$) and the postoperative need for intra-aortic balloon pump and or extra-corporeal membrane oxygenator ($P<0.007$). The results of other studies support our results. Those authors found NYHA class III/IV status, necessity for emergency operation, prosthetic valve endocarditis are important risk factors. (8,9,10).

Syrcase et al. 12 founded that an additional procedure increased the risk of re-operation. Biglioloi et al 11 added longer extra-corporeal circulation time and aortic cross-clamp time as risk factors. A recent report by Houser et al. 13 agreed with our identification of the use of intra-aortic balloon pump as a risk factorsfor hospital mortality in redo valvular surgery.

Multivariate analysis of perioperative risk factors indicated the presence of renal failure and congestive risk factors indicated

the presence of renal failure and congestive heart failure are most powerful predictors of mortality in our patients. Biglioli et al., 1994 11 using multivariate analysis showed the long extra-corporeal circulation time and urgent-emergent status as predictors of hospital mortality in a series of 41 patients, but the considered P,0.1 as significant at logistic regression because of relatively small number of patients. In our series p value of less that 0.05 ($P<0.05$) was considered significant at logistic regression, which is statistically more powerful.

The overall hospital mortality in the present study is 11.3% which falls within range of mortality rates reported in the literature (Table 3). This table shows a great variation in the mortality rates depending mainly on time frame of the study. The report of Mayo clinic (14) showed improvement in the mortality rate between 1960 and 1980. The variation in the reported mortality rates is due to the differences in the patient population of each study, since some series had relatively larger number of emergencies and of patient with NYHA class IV. Table 4 shows the reported mortality rates for emergcy redo valvular surgery by many studies including ours. It varies from 41-72.7%. Our rate is 90.9% in emergency re-operation. This rate is high because many of our emergency re-operation were performed in extremely ill patients, some cases were actually salvage operations.

Every effort should be done to avoid delay in the diagnosis of prosthetic valve dysfunction. Once the diagnosis is established the patient should be operated upon without any hesitation, before the deterioration of the patient's clinical condition. We feel that other risk factors, namely congestive heart failure, renal failure, the need for intra-aortic balloon are all interrelated to NYHA class and emergency operative status, and all are usually the result of delay in diagnosis and sometimes to the reluctance of both the patients and physicians to seek re-operation until the patient's clinical conditions had deteriorated to urgent or emergent status. Thus, earlier operation in patients with all forms of valve dysfunction is recommended. This recommendation have been made, also, by several previous studies. (2,10,11,12)

Whenever a patient with prosthetic heart valve shows clinical signs which suggest a prosthetic dysfunction, it is mandatory to confirm the diagnosis as soon as possible with non-invasive methods such as Doppler echocardiography and eventually transesophageal echocardiography. (18). We used these technique and in 28 patients we used cardiac cartheterization.

When a patient presented in failure, with pulmonary edema and impaired renal function, the patient's general conditions should be optimized first by medications, ultrafilteration or hemodialysis before admission to the operating theater. This critical delayed presentation, which definitely put the patient at the detrimental effect of many perioperative risk factors, points out the importance of continued medical follow up of patients with mechanical or bioprosthetic valve so once dysfunction is documented early re-operation could be conducted before clinical and hemodynamic deterioration (2&13). We feel to re-emphasize that urgent/emergent operative status in redo valvular surgery is associated with a very high mortality, (90.9% in this study).

Conclusion

The surgical technique of redo cardiac valve surgery have not, in itself, been considered a risk factor. Subsequently redo operation should not be deferred solely on the basis of the technical considerations. Hospital mortality following re-operation on prosthetic valves is principally associated with NYHA class IV; congestive heart failure; presence of renal failure; urgent/emergent operative status; and the need for intra-aortic balloon. So, every effort should be done to conduct the re-operation before these factor come in action. In order to establish this, we recommend the following:

1- All patients with prosthetic cardiac valves should be followed-up closely by frequent medical examinations.

2- Whenever a patient with prosthetic heart valve shows clinical manifestation of valve dysfunction, he should be fully investigated by non-invasive diagnostic tools, cardiac catheterization my be needed to confirm the diagnosis.

3- Once the diagnosis had been confirmed, there should be no hesitation in deciding on re-operation. This aggressive approach to the patient in need for neocardiac valvular surgery is strongly supported in the literature. Hesitation and delay invite many risk factor to get in action and negatively affect the outcome.

Acknowledgments

The authors Diane Vido for her expert statistical analysis of the data.

REFERENCES

1. Christakis GT, Weisel RD, David TE, Salerno TA, Ivanov J and the Cardiovascular Surgeons at the University of Toronto: Predictors of operative surgical after valve replacement. Circulation 1988; 78 (suppl I): I-25.

2. Cohen LH, Koster JK Jr., Vande Vanter S and Collins JJ Tr: The in-hospital risk of replacement of dysfunctional mitral and aortic valves. Circulation 1982; 66 (supple I): I-153-I-156.

3. Edmunds LH Jr., Clark RE, Cohn LH, Miller DC and Wiesel RD: Guidelines for reporting morbidity and mortality after cardiac valvular operations. Ann Thorac Surg 1988; 46: 257-259.

4. Wisheart JD, Ross DN and Ross JK: A review of the effect of previous operations on the results of open-heart surgery. Thorax 1972; 27: 137-142.

5. English TAH and Milstein BB: Repeat open intra-cardiac operation. J. Thorac. Cardiovasc. Surg. 1978; 76: 56-60.

6. Lindblom D, Bjork VO and Semb BKH: Mechanical failure of the Bjork-Shiley valve: Incidence., clinical presentation and management J. Thorac. Cardiovasc. Surg. 1986; 92: 894-907.

7. Cohn LH: Valve re-replacement in the asymptomatic patient. Ann. Thorac. Surg. 1991; 51: 357-358.

8. Wideman FE, Blackstone EH, Kirklin JW, Karp RB, Kouchoukos NT and Pacifico AD: Hospital mortality of re-replacement of the aortic valve. J.

Thorac. Cardiovasc. Surg. 1981; 82; 692-698.

9. Rossiter SJ, Miller DC, Stinson EB, Oyer PE, Reitz BA and Shumway NE: Aortic and mitral prosthetic valve re-operations. Arch. Surg. 1979; 114: 1279-1283.

10. Masri Z, Girardet R, Attum A, Barbie R, Yared I and Lansing A: Re-operation for prosthetic heart valve dysfunction. Texas Heart Institute J. 1990; 17: 106-111.

11. Biglioli P, DiMatteo S, Parolari A, Antona C, Arena V and Sala A.: Re-operative cardiac valve surgery: a multivariable analysis of risk factors. C

12. Syrcase DC, Bowman FO and Malm JR: Prosthetic valve re-operations: Factors influencing early and late survival J. Thorac. Cardiovasc. Surg. 1979; 77:343-352.

13. Houser S, Salomon **J.** Carlas N, Hashmi F, Lchmann T and Chawla S: Predictors of perioperative morbidity and mortality in repeat valve replacement: a seven-year experience. Conn, Med. 1993; 57:715-720.

14. Huseby DG, Pluth JR, Plehler JM et al., Re-operation on prosthetic heart valves J. Thorac Cardlovasc. Surg. 1983. 5 86 : 543-552.

15. Sandaza JG, Clark RE, Fergusen TB, Connors JP, Welden CS: Replacement of prosthetic heart valves : A fifteen year experience J., Thorac. Cardiovase. Surg. 1977; 74:864874.

16. Rodewald G, Guntan J, Bantea C et al: The risk of re-operation in acquired valvular heart disease. Thorac. Cardiovasc. Surg. 1980. 28 : 77-88.

17. Bortolotti M 5 Milano A, Mossuto **E,** Mazzaro E, Thiene G and Casarotto D: Early and late outcome after re-operation for prosthetic valve dysfunction: analysis of 549 patients during a 26 year period **J.** Heart Valve Dis. 1994, 3.81-87.

Role of Pediatric Transesophageal Echocardiography in Immediate Evaluation of Interventions for Correction of Congenital Heart Disease

Taher Elkady, MD, FACC., M.El-Gabaly, MD., M. Nawaytou, MD., D.J. Sahn, MD, FACC
A.Abdel Monem, MD, Sherif Abdel Hady, MD & Adel Imam, MD, FACC

J. of Egypt. Society of Cardio thorac. Surg. September 1996, Vol. IV No 4

INTRODUCTION

Increasingly complex cardiac surgical procedures are being performed for correction of congenital heart disease (CHD), and there has been an increasingly growing interest in operations that attempt to preserve rather than replace the patients own native cardiac structure. Because the outcome of these procedures can be uncertain at times, a greater need has evolved to obtain immediate and accurate information about the adequacy of surgical repairs (1) Transophageal echocardiography (TEE) appears uniquely suited to offer such information. TEE has emerged as an important diagnostic tool for use in the adult cardiac population with congenital and acquired heart disease in various outpatient, intraoperative and intensive care setting (2,3).

Implementation of this technology in the pediatric population has been slow, largely because of the mismatch in size between the youngest pediatric patients and available TEE probes. However advances in the minimaturization of TEE probes and an increasing population of adolescents and young adults with repaired CHD have arouesd widespread interest in this technology for the pediatric Cardiac population. This review will focus on our initial experience with intraoperative TEE in evaluation of surgical repair of CHD and some interventional procedure in the young population (4).

National Heart Institute, Cairo-Eypt & UCSD Medical Center, San Diego, CA., U.S.A.

Study Group

During the period between December 1988 and June 1992, we performed intraoperative TEE examination in 84 patients with congenital heart disease ranging in age from 9 months to 12 years and weighing from 2 Kgm, to 55 Kgm who had surgeries for different forms of CHD. Diagnoses in our group included:

VSD: 24, ASD:13,TOF:5,AVSD:8, TGA:5,TAPVD:2Dorv:3,M.R.; 3, Co A:5. Fifty four (54) patients had intraoperative TEE examinations while 17 patients had their TEE done 24 hours before and 48 after the procedure. In 13 children (Age:7-11 years) who had balloon valvuloplasty we performed TEE during the procedure.

Instrumentation and Probe Technology

For children below 15 Kgm (N=28) we used a 5 Mhz single plane TEE probe measuring 6.8 mm in diameter mounted on a flexible 70 cm steerable gastroscope containing 28 elements (ALOKA-COROMETRICS, TOKYO, JAPAN/CT

USA) and interfaced with and ALOKA/CROMETRICS-870 Two-dimensional and color flow imaging echocardiographic instrument. This probe can be anteriory and posterioly angled, but not moved side to side. In a small number of children (9=) we used a biplane pediatric TEE probe (ALOKA) or most children above 15 Kgm (N=12) we used an adult TEE probe (ALOKA) measuring 9mm in diameter interfaced to the same ALOKA 870-Machine mentioned above. This probe can be angulated anteriorly and posterioly rotated and moved side to side using the control Knobs at the base of the endoscope. For bigger children (above 40 Kgm, N=) we used a single plane 5 Mhz interspec TEE (13 mm Diameter) probe interfaced to interspec apogee color Doppler machine.

EXAMINATION PROCEDURE-IMAGING PLANES

Intubation of the TEE probe was performed under general anesthesia by either anesthesiologist or the pediatric Cardiologist performing the study. The endoscope is initially advanced into the esophagus approximatery 15-20 cm from central incisors where it is usually located behind the left atrium. 5 Standard cross sectional views of the heart and off-axis angulated views can be obtained by rotating the endoscope shaft to optimize the image(6).

The first imaging view obtained is the short axis of the base of the heart and at this plane we can visualize aortic valve, prox. PA, LAA, and proximal coronary arteries. Advancing the probe gradually for 1-2 cm yields the LVOT in a long-axis equivalent view including LA,LV and mitral valve. From this view retroflexion yields 4-chamber equivalent view where both atria, both ventricles as well as the entire length of the interatrial and inter-ventricular septae can be visualized. To visualize PVOT/PA and branches we get LVOT plane then we pull the probe gradually backwards with slight rotation and superior angulation. A dvancing the probe into the lower esophagus and passing the gastroesophageal,junction (at approximately 20-35 cm) yielded multiple short axis views of the left ventricle. It should be emph a sized that imaging using the biplane TEE probe, in order to obtain an equivalent view in the vertical plane, we have to pull the probe up for about one cm as the vertical plane crystal is at higher level than the horizontal crystal.

For each procedure we obtained a base line study in the operating room before surgical correction then the study was repeated after repair when the patients has come off the bypass machine. In 17 patients the baseline study was done 24 hour before surgery and then repeated 48 hour after surgery.

TEE EVALUATION OF SURGERY FOR INDIVIDUAL CONG H.DIS

ATRIAL SEPTAL DEFFECT (ASD)

Closing an ASD is now common place, simple and safe. The mortality rate is about 0.5% and should be Zero in children. The defect is usually completely closed but only very rarely there is a residual L-R shunt particularly in large defects close to the IVC in the lower margin and the surgeon may not close this portion adequately and this may result is patients who became blue postoperatively due to a R-L shunt with drainage from IVC to LA. TEE provided a superb image to the entire atrial septum (7-11) and we were able to detect easily ASD and visualized the atrial septal patch in all

our patients (n-13) TEE identified 2 patients with additional sinus venosus ASD which were not detected by surface echocardiogram and dealt with during surgery.

Table I: Indications of Intraoperative TEE in Pediahic Patients

* ADEQUACY OF ASD / VSD CLOSURE
*ASSESSMENT OF RVOT - PA CONDUITS
*IDENTIFICATION OF FLOW THROUGH RE-ROUTED SHUNTS :

Fontan connection, venous flow to common chamber in TAPVR, and B/T shunts

*VISUALIZATION OF INTRAATRIAL BAFFLES
* EVALUATION OF VALVULOPLASTY PROCEDURES
* ASSESSMENT OF LV FUNCTION
* VOLUME STATUS (PRELOAD) & SEGMENTAL ISCHEMIA
* DETECTION OF AIR EMBOLISM

RVOT : right ventricular outflow tract, PA: main pulmonary artery,

B / T : Blalock - Taussig shunt

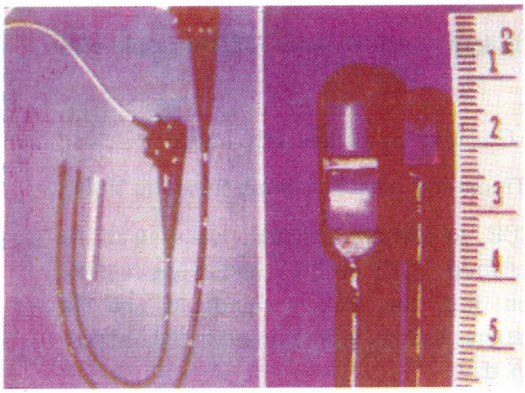


Fig.1: Left : Pediatric (small) TEE probe measuring 8.6 mm in diameter and an adult TEE probe measuring 9 mm .

Table II: Surgical repairs that had been revised intraoperatively on TEE findings.

PROCEDURE	No	REVISED	CAUSE OF REVISION	DECISION
VSD Repair	24	8	significant patch leak in 4 patients Another VSD which was not detected in 1 pt potential LVOT obstruction in 3 patients patch Ajusted	Patch adjusted
AVSD	8	2	Moderately severe MR in pt with small L.V.	Venting of the ASD Patch repair revised (patient died)
MUSTARD	4	1	Systemic venous inflow obstruction	Upper Baffled revised
DORV	3	3	LOVOTO IN 1 PATIENT M.V. straddle in 1 pt.T,V, Involved in the sub. P.S.	Palliative shunt in both Cavopulm shunt
ASD	13	3	significant patch leak in 2 patients sinus verosus ASD was missed in 2 pts.	patch adjusted patch closure

VSD : Ventricula septal defect,*AVSD:* Atrioventriculadr septal defect,*LVOT:* Left ventricular outflow Tract obstruction,*DORV:* Double outlet right ventricle,*MV:* Mitral valve,*TV:* tricuspiud valve,*SUB P.S:* sub-pulmonic stenosis

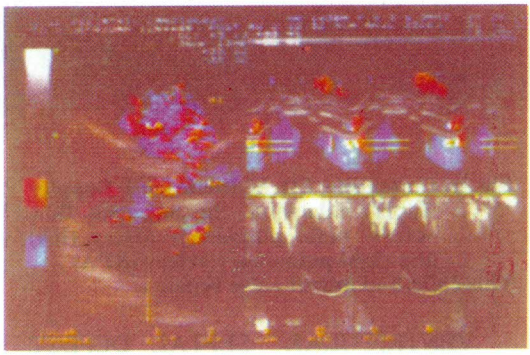


Fig.2: 4-Chamber view in transverse plane TEE.

A composite 2-D, M-Mode and Doppler display showing flow across VSD. Color flow display shows also significant Mitral valve regurgitation in a patient with atrioventriculer septal defect

Table III : Role of transesophageal Echocardiography during BMV

- Localize the site of septostomy puncture
- Guide Catheter
- Immediate estimation of pressure gradient
- Assess shunt across septostomy ASD

Table IV : Future Developments in Transesophageal Echocardiography

Continous wave doppler
Higher frequency probes
Three dimensional reconstruction
Tissue characterization
Myocardial contrast imaging
Multiplane and wider field technology

Fig.3: Composite 2D M-Mode and Doppler display showing homogenous flow across main pulmonary artery (PA) and right pulmonary artery (RPA) . This child had mitral valve repair .

Fig.4(a): Color Doppler TEE in a child with TOF

5-Chamber equivalent TEE image

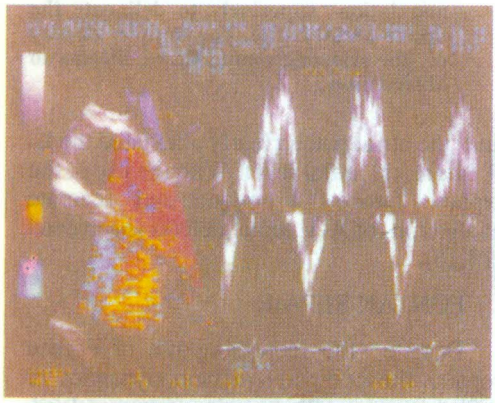
(Transverse plane) showing subaortic VSD

VENTRICULAR SEPTAL DEFECT (VSD)

VSD is the most common congenital cardiac anomaly. It has been reported that a residual L-R shunt is not uncommon (12). These leaks are usually small and should not beer any significance but the importance of detecting these residual leaks early in the immediate post-op period is that these patients are at risk of EC in the later years and should be detected We were able, using TEE, to identify residual, leaks in all the repaired VSD, (100%) and in one case we felt that the leak is significant and the patient had his leak reclosed in the 3rd post op. day.

With a high VSD the aortic valve is very close to the upper rim of the defect and rarely aortic regurge could occur post repair.

B. Composite 2D, color Doppler and spectral display showing flow pattern across VSD



C. Same plane as B. with slight angulation to show small shunt scross small ASD which was not detected by transthoracic Echo

We detected only one case with AR after closure of the VSD. Also TEE provided invaluable information about the patency of LVOT in those with large VSD as sometimes patch insertion may result in LVOT obstruction 13 Also these patients the tricuspid valve may be damaged in the repair of VSD if this was done through a RA incision resulting in TR. Using TEE it was easy to assess degree of TR after repair of large VSD (1,12,13).

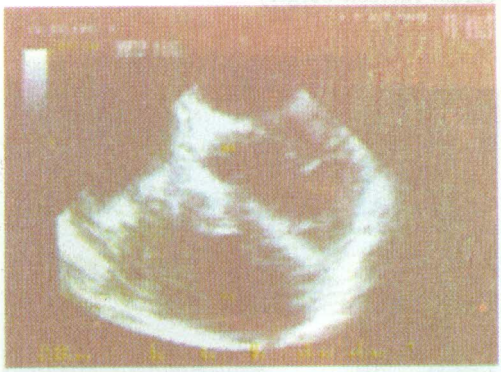
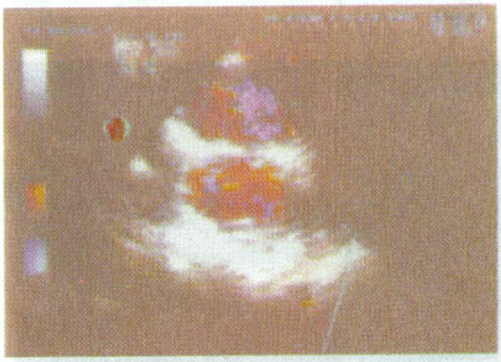


Fig.5 : Pre and Post repair TEE evaluation in a child with TGA

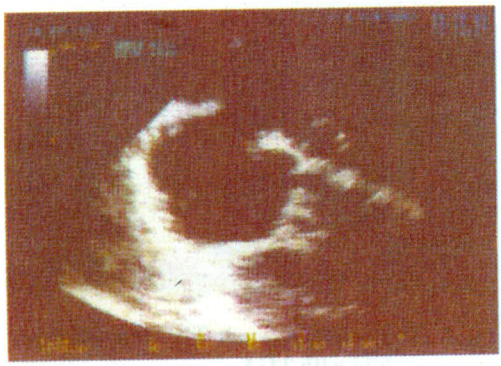
A. 4 Chamber view showing LA, LV, RA, RV, pulmonary artery originating from L.V. The pulmonary cusps are thichened



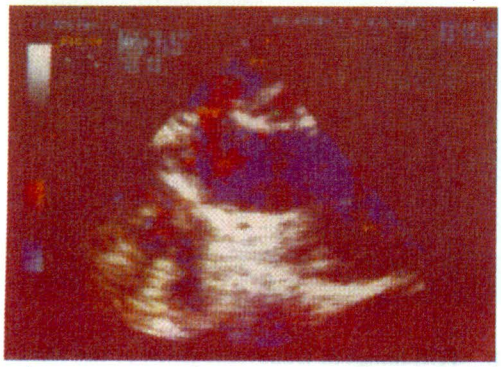
B. TEE image in transverse plane at the level of great vessels (in short axis) showing ventricular -atrial discordance note the posterior relation of pulmonary artery (PA) to aorta (Ao) .

ATRIOVENTRICULAR SEPTAL DEFECT

The central defect in the A-V septum may be associated with an interatrial or interventricular communication or both. A single A-V valve is usually common to both ventricles and may differentially into separate orifice with or without a common bridging anterior leaflet .



C.TEE 4 chamber view in the same patient. The endoscope was angulated to delineate the atrial septum note the large secondum ASD



D. Transverse TEE view at the re-routed pulmonary venous blood into RA.

Homogenous flow pattern is clearly seen without turbulence indicating absence of obstruction

TEE provides a superb image to the crux of the heart. We were able to image nicely the exact anatomy of these defects and we detected common valve leaks in 2 patients as well as patch leak through the VSD patch. In all patients the pre bypass AV valve regurgitation was reduced in severity

E. Same view as in D bu with slight angulation superiorly to delineate the upper atrial baffle. The Doppler display of the systemic venous flow indicates no obstruction .

and the atrial patch clearly alleviated the L-R shunt at atrial level. With the use of the biplane probe a unique and accurate evaluation of A-V septal defects is achieved (14,16).

FONTAN REPAIR

Despite the increasing use of Fontan repair, the comparative hemodynamics of different types of connections are uresolved. Still the use of valved conduits is presently contoversial, and generally their insertion is avoided in the artio-plum anatomosis, TEE provides an invaluable assessment of RVOT/MPA region preoperatively we were able to give reliable information using TEE about the size of main pulmonary artery (MPA) and its branches. TEE also determined the post repair flow patterns through the Fontan connection. We also detected conduit insufficienly in a child with tricuspid atresia and Fontan repair with a valved conduit between RA and PA (21-23)

TRANSPOSTION OF GREAT ARTERIES

The anatomic correction of TGA [arterial switch] is now getting more popular, however the Mustard and Senning type repairs of TGA, although no longer advocated by many, have resulted in an aging population of patients who require regular observation. TEE can provide valuable information about both pulmonary and systemic venous routes of the atrial baffle. Small baffle leaks can easily be demonstrated, baffle obstruction to the pulmonary venous atrium can be identified. In one patient among 4 who had Mustard correction TEE indicated systemic venous inflow obstruction near superior vena caval entry into systemic venous atrium. Accordingly the upper baffle was revised instantaneously. Potential LVOT obstruction from bulging IVS,. or systolic anterior motion of the mitral valve can be easily evaluated by TEE (24). TEE identified one patient with LVOTO and another patient who had mitral valve straddling. This has led to the institution of palliative shunt in both.

The third patient has his tricuspid valve involved in the subpulmonic stenosis and accordingly a cavopulmonary shunt was done.

TERALOGY OF FALLOT (TOF)

The outcome of TOF varies widely depending on the original anatomy and residual defects after repair. These patients must be carefully assessed to rule-out residual RVOT obstruction or significant residual VSD leaks since both are related to poor out-come. We obtained detailed instantaneaous information about patch leaks, RVOT/PA conduits and the degree of tricuspid insufficiency using TEE. As in all VSD repairs we assessed also the patency of LVOT before and after repair (1,19,20).

PULMONARY ARTERY BANDING

PA banding was performed particularly in children having large VSD with high pulmonary blood flow to keep the lung from being flooded with excess blood. TEE was found to be invaluable in answering problems associated with both PA banding and debanding. If the band was put on too loose or too tight and VSD persisted, the blood flow will follow from RV to LV and the valve will open against the band and became thickened or stenotic, or with the other extreme if the band migrated to the bifurcation of PA, then the PA became hypoplastic. TEE provides a high quality image of the RVOT/PA and we were able to determine the width of the band, an important determined in taking down the band in later repairs, as the band will not grow with the growth of the baby and this made for increasingly more progressive pulmonic stenosis (2,15) .

TOTAL ANOMALOUS PULMONARY VENOUS RETURN

TAPVR may involve a very severe cardio-respiratory failure in neonates with the need of urgent surgical repair. The crucial aspect of correction is to create a large shunt between the L.A. and the common chamber with a non obstracted flow through the created shunt. With the infanct TEE probe (6.8 mm) we could image blood flow through the common chamber and visualize the common entry of anomalous veins (1.7.9)

FUTURE DEVELOPMENTS IN TECHNOLOGY

Future technological advanced include the development of smaller probes with improved steerable CW. Doppler

sensitivities (27, Higher frequency probes, 7.5 Mhz should allow the implementation of 64 element arrays within the 7mm probes for use in infants (28) Multiplane (omniplane) probe capabilities would optimize visualization of coronary arteris. (29) Implementation of three dimensional reconstruction may improve our understanding of complex of congenital can be also applied to provide tomographic imaging of mediastinal structures: The panorama- View (31)

SUMMARY

Pediatric TEE is now clinically established and being used in most major pediatric cardiovascular centers, It is capable of providing high quality diagnostic imaging even for small infants. With increasing experience and expanding technology. newer applications will be found for pediatric TEE.

REFERENCES

1. Wintraub R, Shiota T.EL-Kdi T, Golebiovski P, Z, Hang J, Rothman A, Ritter SB and Sahn DJ.: Transesophaageal echocardiography in infants and children with congenital heart disease. Circulation 1992; 86; 3; 711-722.

2. Matsuzaki M, Toma Y, Kusudawa R; Clinical applications of Transesophaageal echocardiography. Circulation 1990; 82; 709-722.

3. Sweard JB, Khandheria BK, Edward WD, OHJK, Freeman WK, Tajik AJ; Biplane Transesophaageal echocardiography Anatomic corrections, Image orienattion and clinical application.

4. Stumper OFW, Elzena NJ, Hess J, Sutherland GR; Transesophaageal echocardiography in children with congenital heart disease, An initial experience JMA. Coll Cardiology 1990; 433-441.

5. Roberson DA, Muhideen IA, Silverman NH, Transesophaageal echocardiography c1990; 6: 699-712.

6. Ritter SB; Transesophaageal echocardiography in children; New peephole to the heart JAM. Coll Cardiol. 1990: 16; 447-450.

7. Sahn DJ, Moises V, caliG. Valdes-cruz LM, Mazzi W, Mitchel M. Important Roles of Transesophaageal color doppler flow studies (TEE) in infants with congental heart disaese (Abstract) JAM coll cardiology 1990; 15; 204 A.

8. Muhiudeen JA, Roberson DA Silveman NH, Haas G, Turley K, Cahalan MK, Intraoperative echocardiography in infants and children with congenital cardiac shunt lesions; Transesophaageal versus epicardial echocardiography. JAM Coll cardio 1990; 16; 1687-1695.

9. Kobayashi T, Musew N, Benson L; Biplane Transesophaageal echocardiography evaluation of the atrial septal defect in children; implications for Circulation 1990; 82 (suppl II -402.

10. Ho JK Seward JB Khandheria BK<Khanderia BK, Danielson GK, Tajik AJ visualization of sinus venous

atrial septal defect by Transesophaageal echocardiography JAM SOC Echo 1988; 1; 275-277.

11.Kronson I, Tunick PA Glassman E; Transesophaageal echocardiography is superior to Transesophaageal echocardiography in the diagnosis of sinus venous atrial septal defect.

12.Robenson DA, Muhiudeen IA, Gahalan MK, Silverman NH; Intraoperative Transesophaageal echocardiography of ventricular septal defect Echocardiography 1991; 8; 687-697.

13.Stumper O. Elzenga NJ. Sutherland GR; Obstruction of the left ventricular outflow tract in childhood-improved diagnoses by Transesphaageal echocardiography Int J Cardial 1990; 28; 107-199.

14.Streeram N. Stumber OfW. Kaulang R. Hess J. Roclant JR. Sutherland GR; Comparative Value of Transthoracic and Transesophaageal echocardiography in the diagnosis of congenital abnormalities of the atrioventricular junction. J AM Coll cardiol. 1990; 16; 12026-1214.

15.Ritter SB Transesophaageal real-time echocardiography in infants and children with congenital heart disease Nam, Coll Cardiol 1991; 18; 569-580.

16.Roberson DA, Muhiudeen IA Silverman NH, Intraoperative Transesophaageal echocardiography of atrioventricular septal detect. J AM Coll Cardial 1991; 18; 537-454.

17.Penheiro L, Nada NC, Jain H; Transesophaageal echocardiography imaging of the pulmonary veins, Echocardiography 1991; 8; 741-758.

18.Stumber O, Vargas-Barron J, Rijillaarsdam M; Assessment of anomalous systemic and pulmonary venous connection by transeopageal echocardiography in infants and children Br Heart J 1991; 66; 411-8.

19.Kohayash T, Musew NN, Smalhorn JF; Early postoperative Transesophaageal echocardiography evaluation of results of right ventricular out-flow tract reconstruction for congenital heart disease (Abstract) A Am coll cardiol 1991; 17; 257 A.

20.Fyfe DA Kline CH; Transesophaageal echocardiography for congenital heart disease Echocardiography 1991, 8; 573-586.

21.Stumber O, Sutherland GR, Guuesken R. Roelandt JRTC; v in evaluation and management after Fontant procedure. J Am coll cadiol 1991; 17; 1152-1160.

22.Fyfe DA Kline CH; Sade Rm, Green CA Gillette PC; detects thrombes formation not identified by Transthoracic echocardiography After the Fontan operation J Am coll. cadiol 1991; 22; 1403-1415.

23.Fyfe DA Kline CH; Sade Rm, Green CA Gillette PC; The utility of Transthoracic echocardiography during and after Fontan operation in small children. Am coll. cadiol 1991; 22; 1403-1415.

24.Smith FC, Obeid Al Kveseli DA; Transthoracic color flow imaging of venous return after Mustard repair of transposition of the great arteries (Abstract) Circulation 1989-80; (suppl II); II-186.

25.Kronson I, Tunick PA, Glassman E, Stater S;Transthoracic echocardiography

to detect atrial clost in canditates for percutanious transeptal mitral balloon valvuloplasty J Am Soc Echo 1991; 4; 631-635.

26. Kipel G, Arnon R, Ritter S; Transesophaageal echocardiography guidance of balloon atrial septostomy J Am Soc Echo 1991; 4; 631-635.

27. Weintraub A, PANDIAN N, Simonetti J, Calderia M, England M; CW Doppler in Transesophaageal echocardiography allows analysis of high velocity flows and enhances the utility of TEE (Abstract) Circulation 1990; 82 (suppl III-699.

28. Omoto R. Kyo S. Matsumura M; future technical propects in biplane Transesophaageal echocardiography; use of adult and pediatric matri probes Echocardiography 1991; 8; 713-720.

29. Flachkampf FA, Hoffman R, Hanarash p; Experience with a Transesophaageal echo-trancducer allowing a full rotation of the viewing plane; The omniplane probeabstract) J Am Coll Cardiol 1991; 17; 34 A.

30. Von Ramm OT, Ravy HA Smith SW; Real-time three-dimentional echocardiography; The first human images (abstract) Circulation 1991; 84 (suppl II) II-684.

31. Seward Jb, Khandhheria BK, Tajik Wide field Transesophaageal echocardiography tomography. Fesability study Myo clinic proc 1990; 65; 31-37.

Role of Exercise Program in Changing Physical Activity of Patients after Valve Replacement.

ABSTRACT

The necessity, the methodology and clinical benefit of physical training were evaluated in 59 patients after valvular heart surgery at N.H.I. All patients had undergone the exercise test according to Wasserman protocol to determine their maximum aerobic capacity (duration of exercise and estimated VO_2). The preliminary exercise test was performed on the fifth postoperative day and another one on day before discharge.

The 18 patients who assigned as a control group the duration of exercise increased by 47% ±.27, from 3.9±1.3 to 5.8±1.9 min. and the estimated VO_2 increased by 14 ± .1% from 5299 ± 634 to 606.4±100.4 mlO_2.

The studied population were 41 patients assigned randomly into one of two methods of training that is, program I (interval training) of short duration and frequent exercise, and program II (continuous training) of longer duration and less frequently. Both programs increase the duration of exercise significantly, ($P < 0.05$) it increase in program I by 230 ± 128% and in program II by 148±47%. Also, the estimated VO2 increased in program I and II by 90±47% and 67±27% respectively. There was a nonsignificant difference between relative changes of physical work indices occurred in both methods of training. The significant increase in work capacity of studied patients was attributed to (1) reconditioning effect of exercise, (2) promoting the O_2 transport pathway, and (3) psychological benefits of exercise. The final values of OV_2 in all patients were less than the predicted normal value, suggesting that a return to work might be difficult without rehabilitation.

Mostafa Hussein Gadk Ph.D.,* Osama M. Mohsen. MD.,* Abd Elghany M. Abd Elghay, MD. Zeinab Mohamed Helmy, Ph.D.** Diaa Aboshouka. MD.*

J. of Egypt. Society of Cardiothorac. Surg. 1996, Vol. IV September No 4

INTRODUCTION

Mitral and/or aortic valve replacement are among the most frequently performed surgical procedures. The postoperative goals for patients undergoing these operations include a restored or improved symptom-free tolerance for daily functional activities as well as exercise tolerance (1).

Current literature on cardiac rehabilitation for the surgical patient is limited. There is relatively little definitive information on establishing protocols and guidelines for a post-surgical rehabilitation program.

A study of one cardiac rehabilitation program found that patients undergoing coronary artery bypass can safely participate in a low level exercise program 12 to 24 hours after surgery. In that study, low level exercise programs were successful in preventing the deleterious effects of prologed bed rest and in reducing the anexiety and depression that frequently follow surgery (2,3).

It was found that the postoperative exercise programs, have a positive effect on the physical, psychological and economic aspects on patients who have undergoing cardiac surgery (1).

From the National Heart Institute, Imbaba, Giza
*** From Faculty of Physical Therapy, Cairo University, Egypt*

The conditioning exercise program at National Heart Institute (N.H.I) jointly developed by the Department of physical Therapy and Rehabilitation and the Departments of Cardiac Surgery and Cardiology, was designed to accept patients following cardiac surgery. The program offers medically supervised, monitored exercise sessions and educational information.

The staff's common goals for patients after cardiac surgery usually are to : (a) Improve the patient's physical condition (posture, strength and endurance). (b) Improve the patient's and support person (s) confidence in becoming involved in full range of activities of daily living and appropriate exercise activities. and (c) promote independence in maintaining and monitoring the physical condition (2,4).

Our study was aimed to further examine and document the effects of an inhospital exercise program on the physical work capacity of patients after valvular operations and to obtain data which provide a guide line for construction the conditioning exercise program, through compairing between two methods of training.

Method

The study included fifty nine patients had rheumatic valvular heart disease. They had been operated upon by the same anaesthetic and surgical team between January 1995 to December 1995 at National institute (N.H.I). The patients had been classified into 3 groups; group (A), control group, included 18 patients; group (B), interval training included 22 patients and group (C), continuous training included 19 patients. The preoperative clinical charactrestic features and the surgical procedures as well as the pretesting status had been mentioned in tables (1), (2a, b) and (3).

The study was continued from the third to fifth postoperative day until the day before discharge. The duration of training ranged from 15 to 21 days with average of 19±4 days. Preoperative and immediate post operative clinical examination had been done by the same cardiologist. Patients with complication or unfit for post-surgical exercise assessment were excluded.

Contraindications for study participation included (1) resting systolic blood pressure > 120 mmHg or resting diastolic pressure > 100 mmHg. (2) uncontrolled frequent atrial or ventricular arrhythmias. (3) uncontrolled diabetes, and orthopedic problems prohibiting exercise (1).

Test Protocol: At the second day of discharge from ICU, each patient performed incremintal bicycle exercise test described by Wasserman et al (5). The test was performed on a bicycle ergometer (model Corvial 300) with a programmer enabling automatic progression through the preselected exercise program. During exercise the patients were monitored (VISMO) for ECG-lead II- and for noninvasive blood pressure measurement. Each patient pedalled at a constant speed (60-70 rpm) on unloaded ergometer for 3 minutes, then the work load increased automatically 5 Watts every minute. Patients were encouraged to complete as much as possible. The test was immediately terminated for the following reasons (a) symptoms of significant exertional intolerance i.e. (1) dizziness or near

syncope (2) angina, (3) unusual or intolerable fatigue, and (4) intolerable claudication or pain. (b) signs of intolerance i.e. (1) staggering or unsteasdiness, (2) mental confusion (3) facial expression signifying disorders "stained or blank facies", (4) cyanosis pallor" facial or elsewhere", (5) rapid distressful breathing and (6) nausea or vomiting. And / or (C) inproper heart rate or blood pressure response, as well as appearance of major arrhythmia like > 6 PVCs per minute, SVT > 150 / minute or multifocal PVCs6. The heart rate, blood pressure and ECG were monitored before and after test completion for safety in exercise testing. At the day before discharge the exercise test was performed again.

The maximum heart rate (Hrmax) and maximum systolic blood pressure (SBPmax) attainded during the test was recorded, as well as the duration of pedalling the cycle, for each subject.

The maximum oxygen consumption. was estimated from the following equations (5).

Estimated VO_2 (ml/min) = VO_2 unloaded + (10.2 ml/min W x T min - 0.75min) XS

Where, VO_2 unloaded is VO_2 measured after 3 minutes of unloaded pedalling and equall to 150 + (6 X whieght in Kg). T is the total time in minutes of incremental work until maximum VO_2 is reached. 0.75 min. is the time displacement between the start of the linear increase in work rate and S is the slope of the work rate increment in watts per minute.

As well as the predicted normal maximum oxygen consumption was estimated for each subject from nanogram depicted in figure (1).

Fig.1. Mean maximum VO_2 values for sedentary men (A) and women (B) of normal (predicted) weight using the cycle ergometer. To use, locate the patient's height and weight on the horizontal axis. If the patients is underweight (i.e., the patient's actual weight is to the left of that directly above the patient's height), draw a line half-way between the marks vertically to the line that indicates the patient's age, From this intersection draw a line horizontally to the vertical axis and read off the predicted maximum VO_2 in liters perminute. If the patient is over weight (i.e., the patient's actual weight is to the right of that directly above the patient's height), draw a line vertically from the hight marker to the line that indicates the patient's age. From this intersection draw a line horizontally to the vertical axis and read off the preliminary predicted maximum VO_2 in liter per minute. To obtain the actual predicted maximum VO_2 for the obese patient, add 6 ml/min for each kilogram the patient is overweight (5).

The training programs. Program I (Interval training-group B); consists of twice daily exercise session. Each session include five bouts of training, every bout's duration equaled to 60% of the individual's maximal time performed during the exercise test. Enough rest time was allowed between bouts. Program II (continuous training-group C) in which the patient cycled twice daily as much as possible until became exhausted.

Patients in training groups were not restricted by time only but also by their subjective tolerance. Also, the heart rate was used as an index and means of regulating the relative exercise intensity. We used the safe limit recommended for phase I of cardiac rehabilitation in most facilities as an increase in HR not more than 24 bpm above resting and/or 120 bpm as the maximum value7,8.

Table (1) : Preoperative Characteristic of Patients

	Group A	Group B	Group C	P Value
Number	18	22	19	
age (y.)	30.5 ± 9.13	30.2 ± 9.39	29.1 ± 7.32	> 0.05
Sex :				
male	11	15	11	
female	7	7	8	
Weight (Kg)	61.6 ± 13.35	60.4 ± 11.94	59.9 ± 11.65	> 0.05
Height Cm	163.9 ± 8.61	164.36 ± 9.61	161.47 ± 5.89	> 0.05
NYHA				
Class I	-	-	-	
II	-	-	-	
III	10	11	9	
IV	8	11	10	
Diagnosis				
MVD	4	4	5	
MVD + TR	4	5	4	
AVD	3	4	2	
DVD	5	3	5	
DVD + TR	2	6	3	

MVD = Mitral Valve Disease
T.R. = Tricuspid Regurgtation
AVD = Aortic Valve Disease
DVD = Double Valve Disease

Table (2a) Surgical Procedures of Patients

	Group A	Group B	Group C	P Value
Valve Procedure				
MVR	4	4	5	
MVR + T. Rep	4	5	4	
AVR	3	4	2	
DVR	5	3	5	
DVR + T. rep.	2	6	3	
Mean Aortic Clamp Time (min.)	74.2 ± 15.9	76.2 ± 11.7	73.9 ± 12.4	> 0.05
Mean Total Bypass Time (min.)	10.5 ± 17.1	109.1 ± 14.9	102.1 ± 11.8	> 0.05
Cardic Support				
Pharmacological	5	7	7	
Mechanical	3	4	2	

Table (2b) Shows Immediate post operative complications

Immediate post operative complication	Group A	Group B	Group C	P Value
- I.C.U lenght of stay				
less than 48 hours	15	18	16	> 0.05
More than 48 hours	3	4	3	> 0.05
- Rexploration for surgical bleeding.	1	2	-	> 0.05
- Neurospychatric complications				
Phrenic nerve paralysis	1	-	-	> 0.05
Neuropsychatric changes	-	2	1	> 0.05
- Cardiovascular complications				
Low CO	2	3	1	> 0.05
Arrhythmias				
- Supraventricular	1	1	2	> 0.05
- Ventricular	-	1	-	> 0.05
- Pacer dependent	1	-	1	> 0.05
- Respiratary complications				
Prolonged artifical ventilation (more than 48 hours)	2	2	1	> 0.05
Pneumania	1	1	-	> 0.05
Pneumothorax	-	1	-	> 0.05
- Renal failure				
Oliguria	1	1	-	> 0.05
- Endocrinal and/or metabolic complication.				
Stress diabetes	1	1	2	> 0.05
Metabolic acidosis	2	2	1	> 0.05

CO = cardiac output

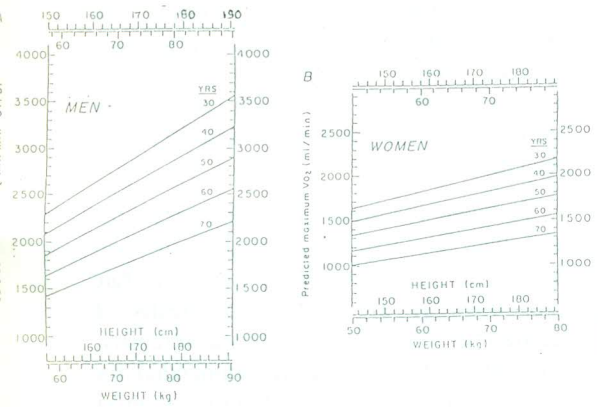


Fig.1: Nanogram to predicte normal VO_2 max

Table (3) : Postoperative Characteristics of Patients in all groups

	Group A	Group B	Group C	P value
NYHA				
I	-	-	-	
II	14	18	16	
III	4	4	3	
IV	-	-	-	
Resting HR (bpm)	90.59 ± 7.74	86.92 ± 4.59	88.57 ± 10.65	> .05
Resting SBP (mmHg)	116.36 ± 11.8	117.69 ± 10.95	119.96 ± 11.37	> .05
Resting DBP (mmHg)	77.38 ± 9.3	77.36 ± 10.36	75.92 ± 8.69	> .05
Predicted Normal VO_2 max ($ml.O_2$)	2173.4 ± 447.6	2312 ± 631.4	2228.9 ± 744.6	> .05

Table (4) : Comparative Statistical Analysis of all Parameters Among The Three Groups

Variable	Control Group (A)			Interval Training Group(B)			Continous Training Group(C)		
	Pre	Post	P value	Pre	Post	P value	Pre	Post	P value
HR rest (bpm)	90.6 ± 7.7	92.1 ± 3.5	> .05	89 ± 7	86.9 ± 6	> .05	90.5 ± 5.4	88.4 ± 7.5	> .05
HR max (bpm)	126.9 ± 11.9	135 ± 7.1	> .05	122.2 ± 11	137.7 ± 4.6	> .05	125.3 ± 9.2	135.7 ± 13	> .05
SBP rest (mmHg)	116.36 ± 11.8	120.5 ± 13.6	> .05	117.7 ± 10.9	119.7 ± 10.8	> .05	120.8 ± 7.7	123.4 ± 16.1	> .05
SBP max (mm Hg)	135 ± 18.7	145.3 ± 18.9	> .05	138 ± 20.9	143.8 ± 16.2	> .05	148.3 ± 17.5	152.1 ± 15.4	> .05
Duration of Cycling (min)	3.9 ± 1.3	5.8 ± 1.9	< .05	4 ± .95	12.2 ± 3.9	< .0001	4.2 ± .92	10.9 ± 2.6	< .0001
Estimated $VO_{2\ max}$ ($ml.O_2$)	529.9 ± 63.4	606.4 ± 100.4	< .05	514.3 ± 88	936.9 ± 238	< .0001	523.3 ± 80.8	846.27 ± 171.6	< .0001

HR rest (bpm) = resting heart rate in beat per minute
HR max (bpm) = maximum heart rate in beat per minute
SBP rest mmHg. = resting systolic blood pressure in millimeter mercury
SBP max mmHg. = maximum systolic blood pressure in millimeter mercury.

The data were analyzed using a paired t test for the mean pre-to post training changes whithin each group. analysis of variance (ANOVA) was used to test the significance of mean pre to post-treatment changes (relative changes) among the three groups. The 0.05 level was chosen to evaluate the statistical significance of mean differences found. Scheff-F test specified where significant differences between groups occurred in the ANOVA.

Results

There was a nonsignificant diference (P > 0.05) between the three groups as regard for the preoperative clinical features, surgical procedure and the pretesting status as shown in tables (!),(2) and (3).

Table (5) : Mean and Standard Deviation of Relative Changes in Duration of Cycling and Estimated $VO_{2\ max}$ Among all Groups

Variable	Control Group (A)	Interval Training Group (B)	Continu Training Group (C)
Duration of Cycling. min.	47 ± .27%	230 ± 1.28 %	148 ± .47
Estimated $VO_{2\ max}$ $ml.O_2$	14 ± .1%	.90 ± . 47 %	.67 ± .27 %

Table (6) : Comparison Between Physical Work Indices Among all Group

Variable	Comparison Between Groups	Scheff-F Test	P - Value
Duration of Cycling (min.)	Control vs. Interval Tr.	14.79	< .001
	Control vs. Continuous Tr.	4.46	< .001
	Interval tr. vs Continuous Tr.	3.00	> .05
Estimated $VO_{2\ max}$ ($ml.O_2$)	Control vs. Interval Tr.	18.63	< .001
	Control vs. Continuous Tr.	9.19	< .001
	Interval tr. vs Continuous Tr.	1.65	> .05

The mean values of all parameters measured before and after conditioning exercise, represented in table (4) and figure (2).

The cardiac performance parameters, that is, the HR and the SBP measured during rest and at the end-point of exercise did not changes significantly (P > .05), in all groups. While the indices of physical work capacity (duration of cycling and estimated $VO_{2\ max}$) increased significantly in all groups. The mean value of duration of cycling in control group increased significantly (P < .05) from 3.9±1.3 to 5.8±1.9 min. The patients who participated in interval training program could increased the cycling duration significantly from 4±.95 to 12.2±3.9 min. (P < .0001). The average value of duration of cycling in continuous training group increased significantly (P < .0001) as a result of exercise intervention from 4.2±.92 to 10.9±2.6 min. The mean value of estimated $VO_{2\ max}$ improved significantly (P < .05) in control group, it was 529.9±63.4 $ml.O_2$ and 606.4±100.4, before and after the period of the study respectively. The estimated $VO_{2\ max}$ of patients in interval training group increased siginificantly (P < .0001) from 514.3±88 to 936.9±238 $ml.O_2$ after performed the exercise program. The continuous training group had an average value of estimated $VO_{2\ max}$, 523.3±80.8 ml. O_2 before training and 846.27±171.6 $ml.O_2$, after training with significant difference (P < .0001).

In spite of increasing in the estimated $VO_{2\ max}$ for all group. It did not reache the relative predicted normal value its ratio to the relative predicted normal $VO_{2\ max}$, they were 27.9% 40.5% and 37.9% in control, interval and continuous training group, respectively.

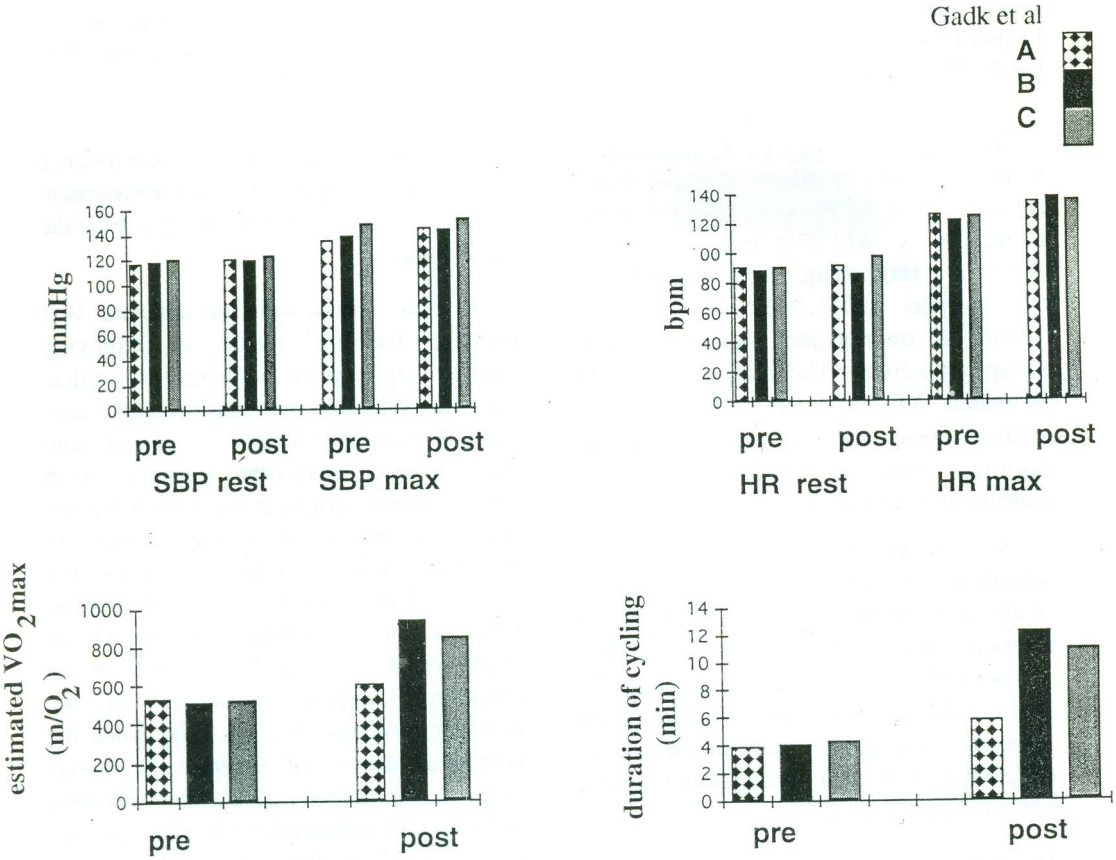


Fig.(2) : Mean of all parameters among the three groups

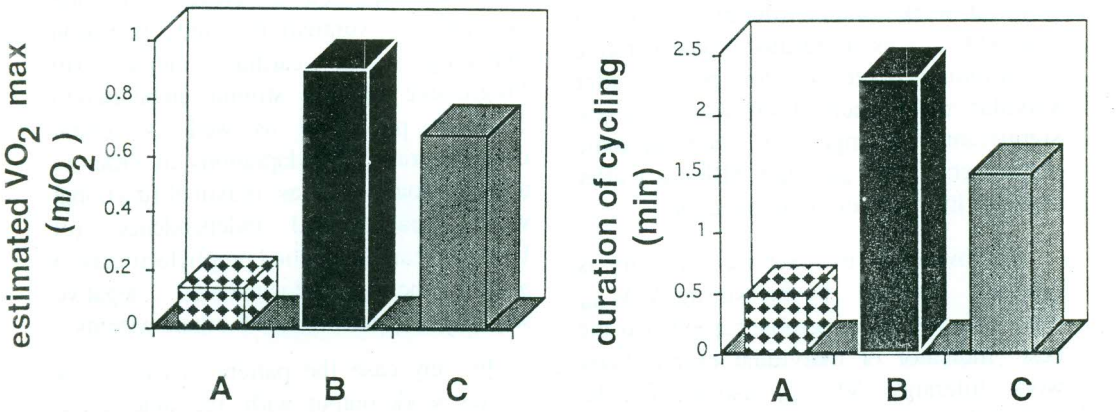


Fig.(3) : Relative change in duration of cycling and estimated VO_2 max

Table (5) and figure (4) depicted the relative changes in indices of physical work capacity. The duration of cycling in minute increased by 47±.27% in control group. While the ratio of increasing in duration of cycting was 230±1.28% and 148±.47% within the interval and continuous training group respectively. The relative improved in estimated $VO_{2\ max}$ was 14±.1% for the control group, 90±.47% for the interval training group and.67±27% for the continuous training group.

As shown in table (6), there was significant difference in indices of physical work capacity between control group and interval training group ($P < .001$), as well as, with the continuous training group ($P < .001$). While both training programs intervention could not induced a significant difference ($P > .05$) in duration of cycling nor estimated $VO_{2\ max}$.

Discussion

The principal finding of the present study was a significantly greater increase in physical work indices (duration of cycling and $VO_{2\ max}$) as a results of postoperative conditioning exercise for patient after valvular replacement. There was also a non significante change in hemodynamic parameters ($HR_{\ max}$ and $SBP_{\ max}$.) after exercise intervention in all patients.

Improvement in exercise capacity is typically assessed by measuring $VO_{2\ max}$ (also referred to as aerobic capacity) as the best indicator of individual exercise and work tolerance. $VO_{2\ max}$ also reflects the maximal capacity of the cardiovascular system to deliver O_2 to exercising muscles (9). As well as, the duration of performance of the exercise was a reliable measurment for reevaluation of the work capacity of the subject (1).

It has been well decumented that exercise training results in improving aerobic capacity in postoperative cardiac patients. Whether this improvement takes place to the some extent in patients who have suffered, myocardial infarction as in other patients after cardiac surgery has not been extensively studied. Although an enhanced $VO_{2\ max}$ does not necessarily reflect improvement in contral cardiac function, it is related to either an improvement in cardiac output or an enhanced oxygen extraction in the peripheral tissues (10). In other word; the beneficial effects of exercise on various steps in the oxygen transport pathway have been well documented to take place at three distinct levels with respect to achieving the overall goal of optimising oxygen transport (11) . That is (a) Acute effects of exercise can be exploited to enhance alveolar ventilation, ventilation and perfusion matching and cardiac output. (b) Progressive exercise stimuli can be used to optimise peripheral as well as central oxygen transport adaptations in order to achieve goals such as maximal functional work capacity and independence. (c) Exercise can be applied prophylactically to avert the well-documented negative sequelae of inactivity on all organ-systems.

In any case the patient is capable of greater work output with the same or less cardiac work, indicating a greater reserve of heart rate at submaximal work loads (11).

If the beneficial effects of exercise training are to take place, the training must be of sufficient stimuli i.e. the intensity, duration (of each session) and frequency per week to indefinite time. Recommendations of the American College of sport Medicine include the following: (1) Frequency-3 to 5 days a week. (2) intensity 60% to 90% of HR_{max} or 50% to 85% of $VO_{2\,max}$ and (3) duration-15 to 60 min. depending on the intensity of the activity (12) . So our finding the exercise programes used in the present study had insufficient stimulus to induce significant changes in HR and SBP.

The increase in work capacity reported in our patients who did not involve in exercise groups was attributed to spontaneous recovery after surgery and to early ambulation. Carstons et al (13), showed a generally good exercise performance after cardiac surgery although haemodynamic remained abnormal. Many investigators demonstrate the benficial effects of early ambulation after cardiac surgery (14,15). IT was shown that early mobilization alone is an effective in returing airflow and lung volumes toward preoperative values in patients after cardiopulmonary bypass. Furthermore, Jenkins et al (15) found that early ambulation was an effective in improving lung function and prevent postoperative complication in men recovering from coronary artery bypass grafting.

Comparing the physical work of patients who participated in conditioning programs with patients in control group, revealed that postoperative conditioning program results in great improvement in physical work capacity. Unfortunately, there was scantly studies evaluate the value of postoperative training. One study (1), evaluates the postoperative exercise program on the physical status. All patients were tested preoperatively and before discharge. On assessment of the functional activity at discharge, patients in training group increase their performance in test of distance walking than preoperatively. While most of the patients in control group (no training) were walked shorter than preoperatively (1). Similar to our study, the benefit of physical training (4 weeks) were evaluated in patients with valvular replacement. Exercise program increase $VO_{2\,max}$ significantly without any complication. In 19 patients who served as controls undergoing no physical training, no spontaneous improvement in exercise capacity was observed (16). In our study the control group exhibited a significant increase in estimated $VO_{2\,max}$ which may be due to early ambulation protocol used in our institution. In a prospective study on children with congenital heart defects, to evaluate the impart of a postoperative training program on physical exercise capacity. Children who completed a simple, home exercise program during the first 3 postoperative months achieved a normal level of physical fitness. These benefits were maintained up to 5 years postoperatively without further intervention (17).

It was evident that the improvement in $Vo_{2\,max}$ after training depending upon the initial (pretraining level. The training program may cause the $VO_{2\,max}$ in physically active subject to increase by 4% explain the dramatic increase in work capacity reported in our study, which was 90% and 67% for the participants in the interval and continuous training program respectively.

A common finding following physical conditioning is an increase in work capcaity

as measured by total body O_2 consumption. Increase in $VO_{2\ max}$ in the coronary patient reflect enhanced O_2 extraction by trained muscles, resulting in a widened ($A\text{-}VO_{2\ max}$) arteriovenous difference(12). In contrast normal individuals improve $VO_{2\ max}$ by increasing both the cardiac output and A-VO2 max difference (12). However, we attributed the improvement in work capacity of patients involved both training programs to the following.

(1) Reconditioning Effect of Exercise:

The functional capacity of normal subjects confined to bed for three weeks decreased approximately 33%18. Multiple factors may contribute to a lower maximal exercise capacity after bed rest. These include to a lower maximal exercise capacity after bed rest. These include hypovolemia resulting in a decrease in venous return and preload preventing adequate rise in stroke volume and cardiac output during maximal exercise and a deconditioning effect characterized by a decrease in mitochondrial respiratory capacity of the skeletal muscle, leading to a lower O_2 extraction during exercise following bed rest. The orthostatic intolerance observed following bed rest is manifested by orthostatic hypotension and compensatory tachycardia and is probably the result of relative hypovolemia equivatent to 700 to 800 ml of blood. loss. Autonomic dysfunction may also contribute to orthostatic hypotension (19,20,21). The most serious consequences of immobility and recumbency are those resulting from the effects on the cardiopulmonary and cardiovascular systems and hence on oxygen transport (4). Thus, the upright exercise is essential to maximize lung volumes and flow rates and this the only means of optimizing fluid shifts such that the circulating blood volume and the volume regulating mechanisms are maintained16. It was suggested that conditioning exercise program avert the negative consequence of recumbency, so it enhance the spontaneous recovery.

(2) Promote the Oxygen Transport Pathway:

A restrictive ventilatory defect demonstrated by a fall in total lung capacity (TLC), functional residual capacity (FRC) and the subdivisions of vital capacity (VC) accompanies cardiac surgery. The changes described reach a maximum between 48 and 72 hours post-operatively. The volume at which airways close in dependent lung regions is known as the closing volume (CV). When CV exceeds FRC, airway closure occurs during tidal breathing and gas exchange is impaired (22). Relatively low intensities of exercise can have a direct profound effect on oxygen transport in patients after cardiopulmonary bypass (14,23). The resulting exercise hyperpnoea, i.e. the increase in minute ventilation VE, is affected by an increase in tidal volume and breathing frequency. In addition, ventilation and perfusion matching is augmented by the distension and recruitment of lung zones with low ventilation (and low perfnsion spontaneous). Spentaneous exercise induced deep breaths are associated with improved flow rates and mobilization of pulmonary secretions, these effects elicit spontaneous coughing (24). When exercise is performed in the upright position, the anteroposterior diameter of the chest wall assumes a normal configuration compared with the recumbent position. In addition, diaphragmatic

excursion is favoured, flow rates augmented and coughing is mechanically facilitated (25,26). We concluded that conditioning exercise programe resulting in reduced the postoperative pulmonary complication and hence augmented the oxygen transport pathway.

(3) Psychological Benefits of Exercise Training:

Anxiety and depression frequently accompany heart disease, especially in patients after cardiac surgery, and may contribute to the decrease in exercise tolerance and a heightened perception of breathlessness (27). It was reported that systematic physical activity of patients after acute myocardial infarction, enhanced cardiac function and improved work capacity. The authors attributed that, to the psychological benefits of participation in physical training (28). Gilliss et al (20) suggested that a low-intensity physical activity intervention can promote self-efficacy expectations for wailing in recovery and is associated with more self-reported walking and lifting behavior after cardiac surgery (20). The improved in physical work capacity noticed in this study was due, in part, to the positive psychological effect of training.

Comparison of interval versus continuous exercise training program showed no significant difference in work capacity indices. Similer finding was reported by Toyomasu et al (16). They stated that both exercise programs similarly increased VO2 max in patients with valvular heart disease.

Contradicted to our finding, Meyer et al (29) reported that physical performance on bicycle ergometer increased significantly in interval training group than the contniuous. one This study involved patients who had undergone coronary bypass surgery 24 and/or 26 days before the training started.

The present study revealed that estimated VO2 max for all patients was less greatly than expected normal values, even after performed conditioning exercise program. Many investigators confirmed this finding (13,16,29). At one study, pre-and post operative exercise examination on 46 patients undergoing mitral valve replacement, 19 undergoing aortic and mitral valve replacement and 17 undergoing mitral valve reconstruction. Their postoperative evaluation generally found marked improvement in exercise performance (13). Disturbed haemodynamics persisted 6 months after surgery with elevated pulmonary artery pressures at rest which rose further during exercise and a low cardiac output at rest which failed to increase normally with exertion. The ability to exercise was generally significantly less than that of age matched sedentary control subjects ()29.

It was concluded that patients after valvular replacement surgery could benefit physically from inhospital conditioning exercise program and improve their work capacity without a negative effect on either moratlity or morbidity. The significant increase in work capacity of studied patients was attributed to (1) reconditioning effect of exercise, (2) promoting the O2 transport pathway, and (3) psychological benefits of exercise. Our finding prompt us to recommend that exercise should play an important part in the physical therapy management of patients after valvular replacement. Furthermore a longer-term slow incremental exercise programme is indicated for patients following valvular surgery because of their reduced functional ability postoperatively.

REFERENCES

1. Ungerman P, Pemis A, Siebens A: Exercise program for patients after cardiac surgery. Arch. Phys, Med. Rehabil 1986, 67:463-466.

2. Certo CM: History of cardiac rehabilitation. Phys. Ther. 1985, 65:1793-1795.

3. Dion WF, Grevenow P, Pollock ML, Squires RW, Foster C, Johnson WD, Schmidt DH: Medical problems and physiological responses during supervised inpatient cardiac rehabilitation: patients after coronary artery bypass grafting. Heart Lung, 1982, 11: 248-255.

4. Bray CE: Cardiopulmonary Transplantation. IN Webber BA, Pryer JA, (eds), Physiotherapy for respiratory and cardiac problems. Edinburgh, Churchill Livingstone. 1993, PP 343-356.

5. Wasserman K, Hansen, Sue D, Whipp BJ, Casaburi R: Principles of Exercise testing and Interpretation, 1994, 2 nd ed. Lea & Febiger, Philadelphia, A Waverly Company.

6. Astrand PO, Rodahi K: Textbook of work physiology: Physiological bases of exercise, 3 rd. (ed.). NY, Mc Graw - Hill Inc. 1989.

8. Dubach P, Litscher K, Kuhn M, Laske P, Buser P, Muller P, Ratti R, Myers J : Cardiac rehabilitation in Switzerland: Efficacy of the residential approach following bypass surgery. Chest, 1993, 103:611-615.

9. Hertanu JS, Davis L, Focseneanu M, Lahman L: Cardiac rehabilitation exercise program : Outcome assessment. Arch. Phys. Med. Rehabil. 1986, 67:431-435.

10. Hartung GH, Rangel R: Exercise training in post-myocardial infarction patients: Comparison of results with high risk coronary and post-hypass patients. Arch. Phys. Med. Rehabil. 1981, 62:147-150.

11. Dean E, Ross J: Discordance between cardiopulmonary physiology and physical therapy:toward a rational basis for practice. Chest. 1992, 101:1694-1698.

12. Ehsani AA: Cardiac rehabilitation, Cardiology Clincs, 1984, 2:63-69.

13. Carstens V, Bethrenbeck DW, Hilger HH: Exercise capacity before and after cardiac valve surgery. Cardiology, 1983, 70:41-49.

14. Dull JL, Dull WL : Are maximal inspiratory breathing exercises or incentive spirometry better than early mobilisation after cardiopulmonary bypass ? Phys. Ther. 1983, 63:655-659.

15. Jenkins SC, Soutar SA, Loukota JM, Johnson L: Physiotherapy after coronary artery surgery: are breathing exercises necessary? Thorax, 1989, 44:634-639.

16. Toyomasu K. Nishiyama Y, Yoshida N: Physical training in patients with valvular heart disease after surgery. Jpn. Circ. J. (abstract), 1990, 54:1451-1458.

17. Longmuir PE, tremblay MS, Goode RC: Postoperative exercise training develops normal levels of physical activity in a group of children following cardiac

surgery. Pediat. Cardiol. 1990, 11:126-130.

18. Convertino V, Hung J, Goldwater D, DeBusk R: Cardiovascular responses to exercise in middle - aged men after 10 days of bedrest. Circulation 1982, 65:134-140.

19. Davidson DM, Maloney CA : Recovery after cardiac events. Phys. Ther. 1985, 65:1820-1827.

20. Gilliss CL, Gortner SR, Hauck WW, Shinn JA, Sparacino PA, Tompkins C: A randomized clinical trial of nursing care for recovery from cardiac surgery. Heart and Lung, 1993, 22:125-133.

21. Hahn-Winslow E: Cardiovascular consequences of bed rest. Heart and Lung 1985, 14:236-246.

22. Jenkins SC, Soutar SA, Moxham J: The effects of posture on lung volumes in normal subjects and in patients pre-and post-coronary artery surgery. Physiotherapy, 1988, 74:492-496.

23. Ross J, Dean E: Integrating physiological principles into the comprehensive management of cardiopulmonary dysfunction. Phys. Ther. 1989, 69:255-259.

24. Wolff RK, Dolovich MB, Obminski G, Newhouse MT: Effects of exercise and eucapnic hyperventilation on bronchial clearance in man. J. Appl. Physiol 1977, 43:46-50.

25. Blomqvist CG, Stone HL: Cardiovascular adjustments of gravitational stress. In Shepherd JT, Abboud FM (eds), Handbook of physiology, Section 2: circulation, 1983, PP 1025-1063. American Physiological Society. Bethesda.

26. Dean E: Effect of body position on pulmonary function. Phys. Ther. 1985, 65:613-618.

27. Dracup K, Moser D, Marsden, Taylor SE, Guzy PM: Effects of a multidimensional cardiopulmonary rehabilitation program on psychosocial function. Am. J. Cardiol., 1991, 68:31-34.

28. Hoskins TA, Habasevich RA: Cardiac rehabilitation: an overview. Phys. Ther. 1978, 58:1183-1190.

29. Meyer K, Lehmann M, Sunder G, Keul J, Weidemann H: Interval versus continuous exercise training after coronary bypass surgery: a comparison of training - induced acute reactions with respect to the effectiveness of the exercise methods. Clin. Cardiol. 1990, 13:851 - 861.

Surgical Treatment of Discrete Subaortic Stenosis : Operative Technique as a Predictor of Recurrence .

ABSTRACT

The preferred operative approach for discrete subaortic stenosis (DSS) remains controversial. This study was performed to evaluate the beneficial effect of combining septal myomectomy to membranectomy on the rate of recurrence and further need for reoperation.

From January 1987 through December 1996, 80 patients were operated upon for relief of DSS. Forty-five patients benefited from simple membranectoy (Group 1; 56.3%), while septal myomectomy was additionally performed in the other 35 patients (Group 11; 43.7%). Both methods of operation were performed contemporarely and at no time was one technique used to the exclusion of the other.

The peack systolic pressure gradient (PSPG) of all patients had significantly decreased from 79.1 ± 5.4 mm Hg (mean ± SEM) to 16.9 ± 1.3 mm Hg (P<O. 00 1) with no significant difference between the means of the difference calculated for Group 1 and II patients (- 67.4 ± 6.9 and -55 ± 4.8 mmhg; respectively). The 78 hospital survivors were followed-up for a mean period of 43.4 ± 3.8 months (range: 6-125 months, total: 282 patient-year) with an overall 10-years actuarial reccurence-free rate of 79.5 ± 9.5 % and a significantly higher rate in Group II as compared to Group 1 patients (100% vs 52.4 ± 18.9 %; respectively. P= 0.03). The 4 cases of recurrence (5.1%), all belonging to Group 1 patients (9.3%), had occured after 42, 48, 60 and 72 months. Their mean early postoperative PSPG (25 ± 2 mmhg) was significantly higher than that of the other patients (16.1 ± 1.4 mmhg ; P<0.02).

These results suggest that complete relief of the obstruction as well as the routine combination of septal myomectomy to membranectomy may significantly help in decreasing the recurrence of DSS.

Sh. Azab, MD ,A. Hassouna, MD , A. El Keradany, MD, Kh. Mansour, MD

J. of Egypt. Society of Cardiothorac. Surg. 1996, Vol. IV July No 4

INTRODUCTION

The results after operative treatment of DSS have been generally good. Two issues mainly still address some controversy: the timing of surgical interference and the technique used for resection. We have reviewed our experience at Ain-Shams University Hospitals, in order to compare the results of membrane resection alone and resection combined to myomectomy; with respect to long term freedom from recurrence of subaortic stenosis.

Department of Cardiovascular and Thoracic Surgery, Ain-Shams University Hospital, Cairo, Egypt .

Methods

In the period from January 1987 to September 1996, 38 males and 42 female patients underwent surgical correction of

DSS. At the time of surgery, the patients' age had ranged from 2.5 to 25 years with a mean age ± SEM of *10.5* ± 0.7 years. Patients with hypertrophic obstructive cardiomyopathy or complex muscular subaortic stenosis that were primarily treated with Kono procedure, were excluded from this study.

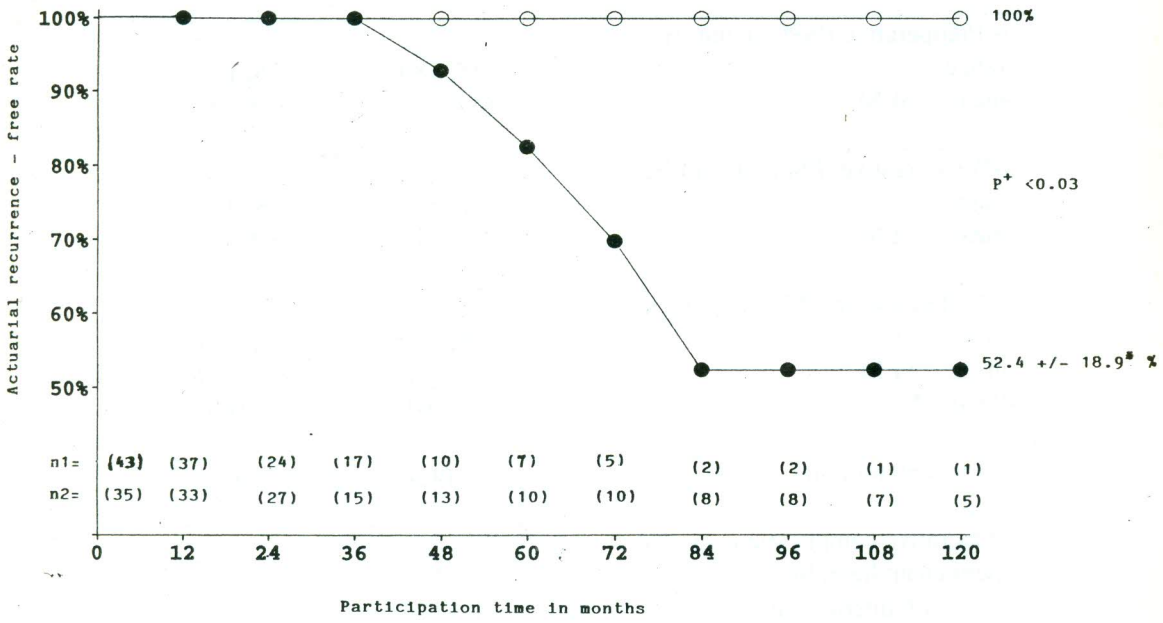
The main presenting symptoms were exertional dyspnea (25 patients; 31.2%), palpitation (24 patients; 30%) and easy fatiguability (10 patients; 12.5 %). The condition was otherwise discoverd during a routine clinical examination (21 patients; 26.2%). In all patients, the diagnosis was confirmed by complete echocardiographic study including M-mode and two dimensional echocardiography with Doppler flow studies. The peak systolic pressure gradient (PSPG) measured across the left ventricular outflow tract (LVOT) was used to quantify the degree of obstruction. It ranged from 30 to 185 mm Hg with a mean value of 79.1 ± 5.3 mm Hg. In asymptomatic patients, surgery was indicated in the presence of a PSPG of 30 mmhg or higher. Forty-eight patients (60%) had an associated aortic valve incomptence: The degree of incompetence was judged to be mild in 36, moderate in 8 and severe in 4 patients. Other associated cardiovascular anomalies were present in 17 cases (21.2%) and necessitated cardiac catheterization in 10 patients. They included a ventricular septal defect in 7 patients, a patent ductus arteriosus in 3, valvular aortic stenosis in 3, an atrial septal defect in 2, Fallot's tetralogy in 1 and Shone's syndrome in another patient.

Surgery was routinely conducted through an oblique aortotomy extending towards the non-coronary cusp. After careful inspection of the aortic cusps, they were retracted and the membrane was carefully excised with combined sharp and blunt dissection. In Group 11 patients, septal myotomy or wedge myomectomy was additionally performed below the commissure between the right and left coronary cusps. In these patients, septal muscle excision was primarily performed to remove the source of the fibromuscular membrane rather than to relief a residual obstruction after membranectomy. In all patients, utmost care was taken not to injure the aortic cusps, conduction system, anterior mitral valve leaflet or create a ventricular septal defect. The aortic valve was replaced in the 4 cases presenting with severe aortic incomptence. Associated cardiac anomalies were treated simultaneously. This included patch closure of a ventricular septal defect in 7 patients, direct closure of an atrial septal defect in 2, aortic valvotomy in 3, ligation of patent ductus arteriosus in 3, repair of Fallot's tetralogy in 1 patient and repair of Shone's syndrome in another patient.

Before hospital discharge, survivors benefited from a full echocardiographic and Doppler study in order to assess the residual PSPG, degree of aortic valve incomptence, success of repair of associated anomalies as well as the presence of any iatrogenic defects.

Patients were then followed up at the outpatient clinic. The echocardiographic study was repeated in symptomatic patients or otherwise on a regular 6-months interval. Reccurence was considered whenever the PSPG reaches 60 mm Hg. Patients were then rescheduelded for surgery.

Statistical analysis: The significance of the postoperative drop of PSPG was assessed by the paired Student test. The differences between both groups were compared by Wilcoxon test. The latter was also used to compare the postoperative PSPG of cases showing recurrence of DSS to that of other patients. The actuarial reccurence-free rates calculated for the patients' groups were compared by the logrank test.



-●- = Group I patients undergoing membranectomy,
-○- = Group II patients undergoing membranectomy and myomectomy,
n1 = number of Group I patients living at the begining of the interval,
n2 = number of Group II patients living at the begining of the interval,
* = Standard error of cumulative probability,
\+ = Logrank test.

Fig. (1): Actuarial recurrence - free rate of discrete subaortic stenosis.

Table (1): Distribution of selected variables between the patient's groups.

Variable	Group I (n= 45)	Group II (n= 35)
1- Age	10.9 ± 1	9.9 ± 1
2- Sex: female : n, (%)	22, (48.8)	20, (57.1)
3- Preoperative PSPG in mm Hg		
-range:	38, 180	35, 129
-mean + SEM:	85.4 ± 7.9	70.5 ± 6.2
4-Postoperative PSPG in mm Hg		
-range:	6, 50	5, 35
-mean + SEM:	18. ± 1.8	15.4 ± 1.8
5- Difference of PSPG in mm Hg		
-range:	-26, -155	-21, -95
-mean + SEM:	-67.4 ± 6.9	-55 ± 4.8
-P value*:	>0.001	>0.001
6-Hospital mortality: n, (%)	2, (4.4)	0
7-Operative complications: n, (%)		
- permenant heart block	1, (2.2)	0
- injury of anterior mitral leaflet	1, (2.2)	0
- iatrogenic VSD	0	1, (2.8)
- total	2 (4.4)	1, (2.8)
8- Postoperative SBE: n, (%)	1, (2.2)	0
9-Reccurence: n, (%)	4, (9.3)	0
10-Late mortality: n, (%)	1, (2.3)	0

Group I = patients undergoing membranectomy,
Group II = patients undergoing membranectomy and myomectomy,
SBE = subacute bacterial endocarditis,
n = number of patients,
* = paired "t" test.

Results

As shown in table 11, there was no statistically significant difference as regarding age, sex distribution or preoperative PSPG between the patients' groups. Postoperatively, the PSPG had significantly dropped from a mean value of 79.1 ± 5.4 mmHg to a mean value of 16.9 ± 1.3 mmHg (mean of the difference - 62.2 ± 4.6 mmHg; P<0.001). The significance was maintained per patient group and was insignificantly different between both groups of patients. Surgery was uneventfull in 74 patients. We had 2 hospital mortalities (2.5%) from irreversible ventricular fibrillation; both belonged to Group 1 patients (4.41/o). We faced 3 operative complications: 1 patient developed complete heart block (1.3%) which necessitated the implantation of a permenant pace-maker. In 2 more patients, an iatrogenic defect (2.5%) - a VSD in 1 patient and a small injury of the anterior mitral valve leaflet in another patient - was discovered and succesfully repaired intraoperatively. A last patient developed postoperative subacute bacterial endocarditis resistant for antibiotic therapy. The inflamed aortic valve was replaced by a St. Jude mechanical prosthesis, 3 weeks after the primary surgery. The distribution of these complications between both groups was insignificantly different.

The 78 hospital survivors were followed-up for 6 - 125 months with a mean of 43.4 ± 3.8 months and a total follow-up period of 282 patient-year. One patient, initially belonging to Group 11, required reoperation for progressive aortic valve insufficiency during the 5th postoperative year. Intraoperatively, no recurrence of of subaortic stenosis was noted and the aortic valve was uneventfully replaced with a mechanical St. Jude prosthesis. On the other hand, recurrence was noted in 4 cases (5. 1 %) at 42, 48, 60 and 70 months *(55.5* ± 6.6 months) postoperatively. They all belonged to Group 1 patients (9.3%; P>0/05). Their postoperative PSPG (25,20,30 and 25 mmhg with a mean of 25 ± 2 mmhg) of recurrent cases was significantly higher than that of other patients (16.1 ± 1.4 mmhg; P<0.02). Reoperation included reexcision of the subaortic membrane and myomectomy in the first 3 patients and aortoventriculoplasty by means of Kono procedure in the last patient. This patient however, died intraoperatively from severe low cardiac output status. The other 3 patients survived reoperation and have had no additional recurrence of subaortic stenosis during 48, 30 and 12 months follow-up period; respectively. The overall actuarial reccurence-free rate was 86.2 ± 7.6 % and 79.5 ± 9.5 % at 5 and 10 years; respectively. As shown in figure 1, Group 11 patients had a significtantly higher (P<0.03) actuarial reccurence free-rate as compared to Group 1 patients; whether calculated at 5 years (100% vs. 69.8 ± 15.2%) or at 10 years (100% vs 52.4 ± 18.9 %) postoperatively ; respectively .

Discussion

Discrete subaortic stenosis is a membranous or fibromuscular diaphragm that extends from 180 degrees to a complete ring around the subvalvular left ventricular outflow tract. The disease

that is thought to be acquired due to abnormal motion, growth or hypertrophy of the LVOT (1); tends to be progressive with increasing muscle hypertrophy and ventricular dysfunction (2). The resulting poststenotic turbulence predisposes to aortic leaflet thickening and valve insufficiency; and is a nidus for infective endocarditis (3). Consequently, surgery is actually advised even for asymptomatic patients with gradients as low as 30 (1), or 20 mm Hg (4). In this series however, patients have been operated upon for a gradient of at least 30 mmhg or with the new onset of aortic valve insufficiency regardless the gradient.

Surgical resection has been reported as being a safe and effective procedure. The hospital mortality is low, most of the postoperative complications are nonfatal and the pressure gradient drops dramatically (2,5-8). Our hospital mortality was 2.5% and the postoperative complications (5%) were those commenly reported (5-7,9) due to injury of adjascent structures (aortic cusps, Hiss bundle and left bundle branch, ventricular septum and mitral valve) or bacterial endocarditis. In this series, neither the hospital mortality and morbidity nor the signfficant postoperative pressure drop were statistically related to the applied technique. Effective prudent resection and postoperative prophylaxis against endocarditis is expected to give good early postoperative results.

This work was originally addressed to study the main point of concern: i.e. recurrence of DSS after an apparentely "satisfactory resection". The factors that predispose to recurrence of obstruction have not been clearly defined. Several hypotheses have been advocated that included: incomplete resection (6,7, 1 0), regrowth of tissue from the region of the septum that gave rise to the initial fibromuscular obstruction (6) and scar tissue formation from the original excision, fixing the diameter of the left ventricular outflow tract and limiting its growth (11). Dynamic outflow obstruction (2), on the other hand, was thought to contribute to any of these factors.

In our study, both methods of operation - i.e. membranectomy alone (Group 1) and membranectomy with myomectomy (Group II) - were performed contemporanesly during the time period of this study. At no time was one technique used to the exclusion of the other. Our overall recurrence rate was *5. 1* % with an actuarial reccurence-free rate of 86.2 $\pm$ 7.6 % and 79.5 $\pm$ 9.5% at 5 and 10 years; respectively. None of our Group II patients has undergone reoperation for recurrent DSS. On the other hand,' 4 out of the 43 patients (9.3%) who survived membrenectomy showed recurrence of obstruction and were reoperated 3.5 - 6 years after the primary procedure. The postoperative PSPG of these 4 patients was significantly higher than that of the remaining 74 hospital survivors ($P<0.001$). Moreover, Group II patients had a significantly higher ($P<0.03$)

actuarial reccurence free-rate as compared to Group I patients; whether calculated at 5 years (100% vs. 69.8 ± 15.2%) or at 10 years (100% vs 52.4 ± 18.9 %) postoperatively; respectively. In concordance to other studies (6,7,10), the elimination of the gradient at the initial operation reduced recurrence. Our data showed, in addition, the beneficial effect of myomectomy (6,12). Myomectomy is thought to decrease recurrence by changing the LVOT geometry and turbulence (6,13) and by excising the region of septum that gave rise to the initial fibromuscular obstruction (6). This was based on the morphological similarity between the fibromuscular diaphragm found during reoperation and that observed at the initial operation (6). Noting the same phenomena in our recurrent cases, has encouraged us to routinely remove the underlying septal muscle.

We conclude that as DSS is a progressive disease , it should be emphasized that all surgically treated patients should be followed up closely by repeated clinical and echocardiographic examination and for many years to detect any recurrence or complications. Although simple membranectomy or membranectomy with muscle excision appears to be equally safe and effective in improving the patients immediately after surgery, yet the long term follow up of our patients has shown that elimination of the gradient at the initial operation and combining myomectomy to membrane excision has significantly decreased the risk of reoperation for recurrence. For this reason we advocate routine myomectomy for all patients with discrete subaortic stenosis undergoing operative treatment.

REFERENCES

1- Somerville J, Stone S, Ross D. Fate of patients with fixed subaortic stenosis after surgical removal. Br Heart J 1980; 43:629-47.

2- Wright GB, Kaene JF, Nadas AS, Bernhard WF, Castaneda AR. Fixed subaortic stenosis in the young: medical and surgical course in 83 patients Am. J Cardiol. 1983; 52: 830-5.

3- Shem-Tov A, Scheneeweiss A, Motro M, Neufeld HN. Clinical presentation and natural history of mild discrete subaortic stenosis. Follow up of 1-17 years. Circulation 1982; 66:509-12.

4- De Laval M: Surgery of the left ventricular outflow tract. In: J Stark & M De Laval eds. Surgery for congenital heart defects. Philadeiphia, WB Saunders, 1994: 511-37.

5- Brown J, Stevens L, Lynch L, et al. Surgery for discrete subvalvular aortic stenosis: actuarial survival. hemodynamic results and acquired aortic regurgitation. Ann Thorac Surg 1985; 40:151-5.

6- Lupinetti FM, Pridjian AK, Callow LB, Crowley DC, Beekman RH & Bove EL. Optimal treatment of discrete subaortic stenosis. Ann Thorac Surg 1992; 54: 467-71.

7- Ashraf H, Cotroneo J, Dhar N, et al. Long-term results after excision of

fixed subaortic stenosis. J Thorac Cardiovasc Surg 1985; 90: 864-71.

8- Douville EC, Sade RM, Crawford FA Jr, Wiles HB. Subvalvular aortic stenosis : timing of operation. Ann Thorac Surg 1990; 50:29-34.

9- Kirklin JW, Barrat-Boyes BG. Congenital discrete subaortic stenosis. In: Kirklin JW, Barrat-Boyes BG eds. Cardiac surgery. New York, John Wiley, 1986: 988-1001.

10- Stellin G, Mazzucco A, Bortolotti K, Tiso E, Daliento L, Maraglino G, Milano A, and Gallocci K : Late results after resection of discrete and tunnel subaortic stenosis. Eur J Cardiothorac Surg 1989; 3: 235-40.

11- Stewart JR, Merrill WH, Hammon JW Jr, Grahain TP Jr, Bender JW Jr. Reapraisal of localised resection of subvulvular aortic stenosis. Ann Thorac Surg 1990; 50:197-203.

12- Cerini E,, Festa P, Bottura C, Gaioni L, Frigiola A. The surgical treatment of fixed aortic subvalvular stenosis. Pediatr Med Chir 1994; 16 (5): 497-8.

13-Oztunc F, Ozme S. Ozkutlo S, Saraclar M, Bilgic A, Ozer S. Fixed subaortic stenosis in childhood. Medical and surgical course in 90 patients. Jap Heart J 1992; 33 (3): 327- 30

Completion Pneumonectomy Indications and Early Results

ABSTRACT

Completion pneumonectomy refers to an operative procedure in which the surgeon removes what is left of a preveiously partially resected lung. The present study included 13 patients operated upon during the period from January 1985 to January 1996 for malignant disease in seven patients and benign lung disease in six patients. The aim of this work is to outline the causative factors that lead to the second surgery and demonstrate the surgical approaches adopted and the precautions followed during completion pneumonectomy. the median interval between the first pulmonary resection and completion pneumonectomy was 37.15 months. The intrapericardial approach was utilized in four patients due to frozen hilum, while bronchus first technique was adopted in the rest of patients.

Only one patient died after six weeks (7.14%) and morbidity occurred in seven patients (53.84%). Completion pneumonectomy for benign infective conditions was associated with higher morbidity.

Due care should be given during the first surgery to good dissection of the bronchial stump and exact site of bronchial sectioning, proper hemostasis to avoid bleeding and secondary infection and the use of absorbable suture material to avoid stump granuloma, so the chance for completion pneumonectomy will be less.

Ahmed Saleh*, Moustafa El-Hamami*, Abd El-Meguid Ramadon And Essam Gouda**

J. of Egypt. Society of Cardiothorac. Surg. 1996, Vol. IV September No 4

INTRODUCTION

Completion pneumonectomy refers to an operative procedure in which the surgeon removes what is left of a previously partially resected lung (1).

The indications for completion pneumonectomy have greatly increased with the wider use of bronchoplastic techniques, the management of early lung cancer with limited resection, and the increasing demand for pulmonary metastasectomy (2). The range of indications of completion pneumonectomy covers both benign and maliganant disease (3). Completion pneumonectomy for benign disease is bronchiectasis after lobectomy, or required when superinfection occurs in a destroyed lung, such as relapsing complication of the conservative cancer treatment (bronchostenosis after sleeve lobectomy or radionecrosis). Indications in malignancies include primary bronchogenic cancer after lobectomy for benign disease, metachronous bronchogenic cancer and resectable local recurrence. Additionally relapsing metastases may be amenable to completion pneumonectomy (3).

The aim of the present study is to:

1. Outline the causative factors in the first surgery which resulted in complection pneumonectomy, so, they can be avoided later on.

2. Demonstrate the surgical approaches used in completion pneumonectomy and the specific precautions to be considered.

From Cardiothoracic Surgery, And Chest Departments***
Faculty of Medicine, University of Alexandria

Table I: Data of the first pulmonary resection and complications that lead to completion pneumonectomy

Indication	Type of resection	No.	Pulmonary pathology	Complication
Bronchogenic carcinoma	Rt upper lobectomy	2	Squamous C. carcinoma	Local recurrence
	Rt middle and lower lobectomy	2	Squamous C. carcinoma and adenocarcinoma	Primary tumor Local recurrence
	Rt lower lobectomy	1	Squamous C. carcinoma	Local recurrence (Lymph nodes)
	Lt upper lobectomy	1	Undifferential carcinoma	Primary tumor
	Lt lower lobectomy	1	Adenocarcinoma	BPF
Bronchiectasis	Lt lower lobectomy and lingulectomy	2	Bronchiectasis	Stump granuloma
	Lt lower lobectomy	1		Continuation of bronchiectasis
	Rt lower lobectomy	1		Continuation of bronchiectasis BPF
Bronchial adenoma	Rt lower lobectomy	1	Bronchial adenoma	Recurrence
Chronic lung abscess	Rt upper lobectomy	1	Tuberculosis	Primary bronchogenic carcinoma

Table II: Data of completion pneumonectomy

Complication of first resection	No.	Time interval between two resections	Type of resection (completion pneumonectomy)
Local recurrence	4	1.5 year	Rt middle and lower lobectomy
		2 years	Rt middle and lower lobectomy
		2 year	Rt upper lobectomy
		2.5 year	Nodal resection - Rt upper and middle lobectomy
		4 year	Rt upper lobectomy
Primary tumor	3	3 year	Lt upper lobectomy and lingulectomy
		6 year	Rt middle and lower lobectomy (previous Rt upper lobectomy for tuberculous cavity)
Bronchopleural fistula	2	3 months	Lt lower lobectomy and lingulectomy
		8 months	Rt upper and middle lobectomy
Bronchiectasis	2	3 year	Lt upper lobectomy
		5 years	Lt upper lobectomy and lingulectomy
Stump granuloma	1	9 month	Lt upper lobectomy
Recurrent adenoma	1	7 year	Rt upper and middle lobectomy

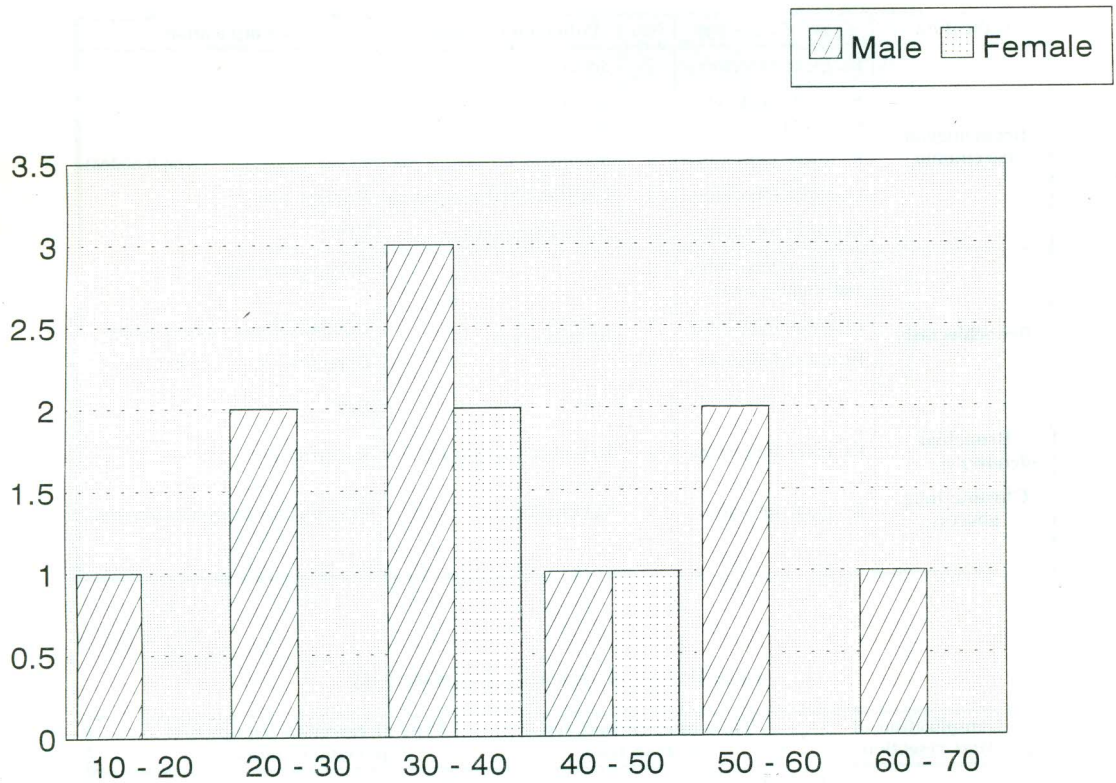


Figure 1: Age and sex distribution

Initial Pulmonary Resection:

Lobectomy was performed in 9 patients, Bilobectomy in two, and in two patients left lower lobectomy and lingulectomy was done, there was no wedge resection performed in any patients. The resection was on the right side in eight patient and on the left in five (Table I).

In the malignancy group (n = 7), four patients were post-surgically classified as stage I, three as stage II. All patients had single resection before completion pneumonectomy, and all operations done for lung cancer were considered complete on the basis of removal of all gross tumour, a disease-free bronchial resection margin and nodes free of tumour. Pathological study of such patients showed that, four of them had squamous cell carcinoma, two adenocarcinoma and one had anaplastic carcinoma (Table I).

Results

The median interval between the first pulmonary resection and completion

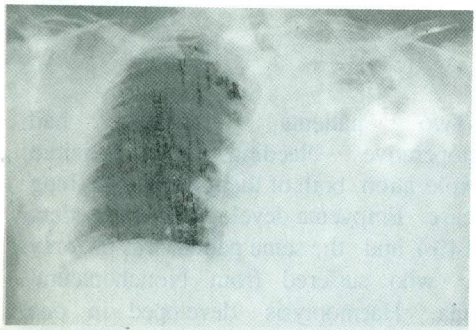


Figure 2: Bronchiectasis involving the left upper lobe and lingula 5 years after left lower lobectomy for the same disease.

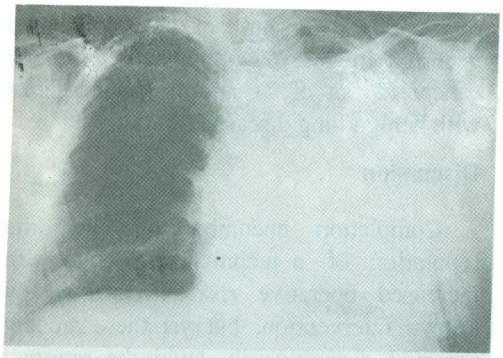


Figure 3: Completion pneumonectomy (left upper lobectomy and lingulectomy) for the same patient in **Figure 2**.

pneumonectomy for the 13 patients was 37.15 months and ranged from three months to seven years. The median interval was less than one year in three patients, one to five years in eight patients, and more than five years in two patients. The median interval was 28.71 months for patients with prior lung tumour (range 3 months to 72 months), and 47 months for patients with prior benign disease (range 8 months to 79 months) (Table II).

Table III: Complications of completion pneumonectomy

Variable	Lung cancer (n = 7)	BLD (n = 6)
No. of patients (n = 7)	3	4
Total complications (n = 14)	4	10
Operative		
Excessive bleeding	1	2
Post operative		
Arrhythmias	2	1
Haemoptysis	1	-
Empyema	-	1
Re-exploration	-	2*
Wound infection	-	2
Chest wall sinus	-	1
BPF	-	1

BLD = Benign lung disease
BPF = Bronchopleural fistula
* Post operative bleeding

Operative technique: All operations were done by reopening the previous thoracotomy incision to its full length. In four cases, the fifth (3 cases) or the sixth (one case) rib was removed to provide easier access to the pleural space. To prevent excessive bleeding from the chest wall, mobilization of the lung was done through the intrapleural plane in nine patients. Once the lung was freed, we tried to isolate and divide the bronchus first and then ligate the pulmonary blood vessels. The bronchus was transected as close to the tracheal bifurcation as possible. In four patients with benign condition, the hilum was frozen and the intrapleural plane could not be dissected, so extrapleural dissection as well as intrapericardial ligation of the vessels were done. If the pericardial cavity was completely obliterated, we tried to isolate and divide the bronchus first and then ligate the pulmonary blood vessels.

The resection performed at completion pneumonectomy was lobectomy in four patients, and bilobectomy in nine patients. complection pneumonectomy was on the right in eight patients and on the left in five

(Figure 3). In one patient, thoracoplasty was performed two months after completion pneumonectomy for post pneumonectomy empyema.

Fourteen complications both intraoperative and postoperative, occurred in seven patients (53.84%) (Table III). Of patients with benign lung disease, 66.66% (4 of 6) had complications compared with 42.86% (3 of 7) for those with lung cancer.

We encountered dense pleural and perihilar adhesions in ten of our patients (71.42%), more adhesions were noted in patients with benign lung disease, and only three cases were performed without difficulty.

Intraopertive cardiac or great vessel injury occurred in two patients (pulmonary artery and left atrium, in one patient each). Excessive intraoperative blood loss was more in the two patients with bronchiectasis and there were no increased bleeding after a previous upper lobe resection, compared with lower lobe resections. There was no intraopertive moratlity.

A single patient died postopertively six weeks after the procedure with operative mortality rate of (7.14%). This occurred in 35 years old man who had a right upper lobectomy done for a tuberculous cavity, five years later he developed bronchiectasis of the lower lobe, completion pneumonectomy was done and extensive adhesions encountered during the procedure, re-exploration was done postoperatively to stop bleeding, patient developed later post-pneumonectomy empyema and bronchopleural fistula that was managed by tube drainage and thoracoplasty, multiple organ failure developed later leading to his death.

Two patients (14.28%) had postoperative bleeding that required reexploration, both of them had benign lung disease. Empyema developed in one patient (7.14%) and the same patient was the only one who suffered from bronchopleural fistula. Haemoptysis developed in one patient eight months after completion pneumonectomy, bronchoscopy revealed stump granuloma that responeded well to endoscopic laser.

Arrhythmia was recorded in 23.08% of our patients (3 out of 13), arrhythmia occurred in 28.57% of patients with lung cancer (2 out of 7) and 16.6% of patients with benign lung disease (1 out of 6).

Discussion

Completion pneumonectomy has the reputation of a technical challenge with increased operative risk. It is a widely known intervention, but yet there are few reported discussing in detail the rational, indications and the results of the operation. In 1988, McGovern et al (1). reported a series of 113 consecutive cases who underwent completion pneumonectomy for lung cancer (n = 64), pulmonary metastasis (n = 20), and benign lung disease (n = 27). There were 14 operative deaths (operative mortality 12.4%), and the 5-year acturial survival for all 113 patients was 28.4%. In 1990, Oizumi and associates (7) reported a series of 29 patients who had completion pneumonectomy, these operations were done for lung cancer (n = 21), complications of the initial operation (n = 7), and pulmonary arterial injury during a second operation (n = 1). The operative mortality was 13.8% and the 5-year survival was 32.9% for patients with lung cancer.

Completion pneumonectomy has become a more frequent therapeutic option in the field of thoracic surgery, the procedure may be indicated for a new primary carcinoma, which is expected to occur in about 5% to 10% pf patients having had a complete resection before (2), local recurrent tumour, pulmonary metastasis, complication of a previous operation, or recurrent inflammamtory disease of the lung. The indications for completion pneumonectomy have increased demand for pulmonary metastasectomy and the longer survival of the patients with early lung cancer have tendency to develop a second primary lung cancer after a 5-year disease-free interval (9). The complications of sleeve resection include stricture and dehiscence, which can occur in up to 13.1% of cases requiring completion pneumonectomy (10).

Completion pneumonectomy is a technically difficult operation which proved on many occasions to be a challenging procedure which calls for careful planning of the operative strategy. Deslauriers (3) recommended that the first task of the surgeon operating is to carefully read the surgical report of the patient's previous procedure. Not only will he learn about important problems that may have been encountered at that time, but also if the first operation was done extrapleurally, we expect a lot more difficulties in mobilizing the lung and excessive blood loss. Besides, Gregoir et al.(11) emphasize the importance of reading the report of the previous procedure to know if the first operation was done extrapleurally, alerting the surgeon to the potential injuries to important structures such as the superior vena cava, diphragm, esophagus, and the thoracic duct. Some authors described that they open the chest a space above or below the previous thoracotomy, to avoid the major adhesions at the site of thoracotomy (12). We and others (3,11) prefer to reopen the previously used thoracotomy incision to its full lengh, and in some cases, it is best to excise the fifth or the sixth rib. To prevent excessive bleeding from the chest wall, mobilization of the lung should be done through the intrapleural plane whenever possible (13). When the intrapericardial cavity has not been obliterated by previous radiotherapy or inflammation, control of lung pedicle and ligation of pulmonary blood vessels intrapericardially is often advisable (11). If the pericardial cavity is obliterated, intrapericardial dissection is precluded. In these situations, Deslauriiers (3) recommends bronchus first before the pulmonary artery and vein. On the other hand, Utley (12) chose not to explore the pericardial space because of concern that it might spread the infection to the pericardial cavity, and recommended resection of the lung after securing the hilum en bloc with transfixing matterss sutures. One should try to ligate the pulmonary vessels intrapericardially in cases of frozen hilum to lesson chances of intraoperative bleeding.

The use of non-absorbable suture material in closing the hilar stump in one of the leading causes of stump infection and stump granuloma (14). In order to avoid this complication, many surgeon shifted to the use of synthetic absorbable sutures.

In our series, mortality and morbidity clearly varied with the indication for completion pneumonectomy. The associated morbidity occured mainly in those who underwent completion pneumonectomy for benign disease (4 of 6). Dense inflammatory adhesions, due to the long standing benign disease, hilum full of inflammation or fibrosis and presence of infection in the

pleural space add greatly to the technical problems of completion pneumonectomy in those patients and contributed to a less favorable outcome. This agree with the results obtained by Goldstraw et al.(12) Where six out of seven patients who underwent completion pneumonectomy for benign disease had complications. This also compares with results by McGovern (1), where complications recorded in over half of his patients with benign disease, but in only 5% of patients with lung metastases. These data also agree with these of Conlan et al.(15)

Bleeding is a major postoperative complication and every effort should be made to secure hemostasis before closure. Intraoperative bleeding is a major threat which accounted for one intraoperative and one early postoperative death in series done by Massard et al.(13) This compares with 6 of 113 and of 60 reported by other authors.(1,3) Median operative blood loss in 1000 ml in Massard (13) experience, which is comparable to the 1500 mL reported by Gregoire and his colleagues.11 Re-operation for bleeding may occur in 5% to 10% of patients (.3) In our series re-operation was needed in two patients (14.28%), both of them were in the benign group.

The association of cardiac arrhythmia with pneumonectomy has been well documented. In our series, arrhythmia occurred in three patients (23.08%) two of them were in the malignant group (28.57%) and one was in the benign group (16.6%). This figure is similar to the 22% incidence noted by Krowka and associates (16) in 236 consecutive patients undergoing pneumonectomy. In the study done by McGovern1, overall incidence of arrhythmia was 17.7% being the commonest complication; it occurred in 25.0% of this patients with lung cancer, in 13.8% of patients with benign lung disease, and in none of patients with pulmonary metastasis. Why arrhythmia should be highest in patients with lung cancer is probably related to an older age, longer smoking history and presence of both coronary artery disease and/or chronic obstructive lung disease.

Post-pneumonectomy empyema and bronchial stump fistula occurred in one patient (7.14%) of the benign lung group, and it was the cause of the single mortality in our series. Infective complications are more common in patients with benign lung disease and it could be life threatening. This coincides with the results obtained by McGovern et al (1) who had 9.3% empyema and 3.1% fistula in patients with malignancy, while he had 20.7% empyema and 17.2% fistula in patients with benign lung disease .

Utley (12) recommended that, in cases in which empyema carries a higher risk, such as in elderly patients with infective pathologic conditions, additional procedures might be advisable. Limited thoracoplasty or the use of omental or muscle flap to fill the hemithorax at the time of the operation can reduce this risk. Those maneuvers may prevent some complications, but in our opinion, would add substantial operative trauma to an already major operation.

Morality varied with the indication for completion pneumonectomy. McGovern and colleagues (1) reported overall

mortality of 12.4%, mortality rate in cancer patients of 9.4 with %, and that in benign conditions of 27.6%. Jansik (17) and his colleagues reported 14.3% mortality rate. In our series, we had only mortality (7.14%), the patient belonged to the benign group with mortality rate within this group of 16.66%. Those results are similar to that reported by Ginsberg and associates with the Lung Cancer Study Group (18) who showed that the 30-day mortality for simple or radical standard routine pneumonectomy was 6.2% with a wide variations among centers (0 to 17.5%) and hospitals (0 to 25%) whithin the Lung Cancer Study Group. The difference in mortality between cancer and benign group lies mainly in that the indication for completion pneumonectomy in the benign patients was either a complication of the initial lung resection, e.g. (fistula or stenosis) or persistence of residual pulmonary disease (bronchiectasis or lung abscess) that showed extensive hilar inflammatory reaction which add to the major intraoperative difficulties and risk of the procedure. On the other hand, Gregoire and colleagues (11) reported low mortality rate in benign group of 5.3% versus 12.2% in the cancer group, with overall mortality rate of 10%.

To conclude, due care should be given during the first surgery in the form of good dissection of the bronchial stump and exact site of bronchial sectioning, proper hemostasis to avoid bleeding and secondary infection and the use of absorbable suture material to avoid stump granuloma, so the chance for completion pneumonectomy will be less. Completion pneumonectomy for benign infective problems is associated with higher morbidity and a greater level of preoperative fitness and careful preoparation are necessary to keep the operative risk acceptable. With careful selection of patients undergoing completion pneumonectomy, an operative risk and mortality similar to that of standard pneumonectomy can be achieved. The procedure should be done under circumstances in which there is sufficient pulmonary reserve to tolerate loss of the remaining ipsilateral lung and in which the patient's general condition can tolerate the surgical intervention. Intraoperative selection of the surgical procedure is mandatory and should be planned according to the existing adhesions and due care should be experienced in control of bleeding and avoding injury to important strutures.

REFERENCES

1. McGovern EM, Trastel VF, Pairolero Pc, Payne WS. Completion pneumonectomy: indication, complications and results. Ann Thorac Surg 1988; 46:141-6.

2. Al-Kattan, Goldstraw P. Completion pneumonectomy: Indications and outcome. J Thorac Cardiovasc Surg 1995; 110:125-29.

3. Deslauriers J. Indications for completion pneumonectomy. Ann Thorac Surg 1988; 46:133.

4. American Joint Committee for Cancer Staging and End Results. Reporting: Manual for staging of cancer. Chicago, American Joint Committee, 1977, 174 pp.

5. Martini N, Ghosen P, Melamed MR. Local recurrence and new primary carcinoma after resection. In: Delarue NC, Eschapasse H, eds. International treands in general thoracic surgery. Vol 1, Philadelphia: WB Saunders, 1985:164-9.

6. Martini N, Melamed MR. Multiple primary lung cancers. J Thorac Cardiovase Surg 1975; 70:606-12.

7. Oizumi H, Naruke T, Watanabe H et al. Completion pneumonectomy, a review of 29 cases. Nippon Kyobu Geka Gakkal Zasshi 1990;38:72-7.

8. Pairolero PC, William DE, Bergstahi EJ, Piehler JM, Bernatz PE, Payne WS. Post-surgical stage I bronchogenic carcinoma morbidity implications of recurrent disease. Ann Thorac Surg 1984; 38:331-8.

9. Thomas PA, Rubinstein L. Lung Cancer Study Group. Malignant disease appearing late after operation for TI NO non-small-cell lung cancer. J Thorac Cardiovasc Surg 1993; 106:1053-8.

10. Van Schil PE, Brutel de la Riviera A, Knaepen PJ, Van Swieten HA, Defauw JJ, Van den Bosch JMM. Completion pneumonectomy after bronchial sleeve resection: incidence, indications and results. Ann Thorac Surg 1992; 53:1042-5.

11. Gregoire J, Deslauriers J, Guojin L, Rouleau J. Indications, risk and results of completion pneumonectomy. J Thorac Cardiovasc Surg 1993; 105:918-24.

12. Utley JR. Completion Pneumonectomy and thoracoplasty for bronchopleural fistula and fungal empyema. Ann Thorac Surg 1993; 55:672-6.

13. Massard G, Lyons G, Wihlm J, Fernoux P, Dumont P, Kessler R, Roeslin N, Morand G. Early and long term results after completion pneumonectomy. Ann Thorac Surg 1995; 59:196-200.

14. Hsieh CM, Tomita M, Ayabe H, Kawahora K, Hasegawatt, Yoshida R. Influence of suture on bronchial anastomosis in growing puppies. J Thorac Cardiovasc Surg 1988; 95:998-1002.

15. Conlan AA, Lukanich JM, Shutz J, Hurwitz SS. Elective pneumonectomy for benign lung disease: Modern-day mortality and morbidity. J Thorac Cardiovasc Surg 1995; 110:1118-24.

16. Krowka MJ, Pairolero PC, Trastek VF et al. Cardiac dysarrhythmia following pneumonectomy: Clinical correlates and prognostic significance. Chest 1987; 91:490.

17. Jansik RJ, Faber LP, Kittle CF, Meng RL. survival following resection for second primary bronchogenic carcinoma. J Thorac Cardiovasc Surg 1981; 82:658-62.

18. Ginsberg RJ, Hill LD, Eagan RT. Modern thirty-day operative mortality for surgical resection in lung cancer. J Thorac Cardiovasc Surg 1983; 86:654-8

Video Assisted Thoracoscopy for The Management of Malignant Pleural Effusion

ABSTRACT

Malignant pleural effusion is a commonly encountered clinical condition which may present significant diagnostic and therapeutic challenges. Video-assisted thoracic surgery is a new modality that allows visualization of and access to the intraoracic organs without making a thoracotomy incision, 21 patients with malignant pleural effusion were operated upon by this technique. In order to evaluate the role of videoassisted thoracoscopy in the management of malignant pleural effusion; its diagnostic sensitivity, morbidity and mortality were studied. In 15 patients thoracoscopy was done to diagnose the etiology of pleural effusion and induce pleurodesis, while in 6 patients it was done to confirm an established diagnosis and induce pleurodesis. Non malignant pleural effusions proved by thoracoscopy were excluded form the study.

The thoracoscopic findings varied between nodules 1-5 mm in diameter in 8 patients, polypoid lesions in five patients, localized tumoral masses in three patients and lumpy pleural thickening in five patients. Pleural fluid aspirated ranged between 1,200 ml to four liters with a mean of 1,900 ± 350 ml.

Talc poudrage by insufflation was used to induce pleurodesis in all patients. Hospital stay ranged between 2 to 11 days with a mean of 58 ± 17 hours. Recurrence of pleural effusion occurred only in one patient (4.76%).

Ahmed Saleh Abou El-Kassem

J. of Egypt. Society of Cardiothorac. Surg 1996, Vol. IV September No 4

INTRODUCTION

Malignancy is the most common cause of exudative pleural effusions in middle-aged or elderly patients(1). These patients often develop symptoms of cough, pain or dyspnea requiring relief of the effusion.

Pleural drainage and the installation of a sclerosing agent is the preferred treatment in most cases, and a wide variety of potential sclerosants exist.

Thoracoscopy was introduced more than 80 years ago for the diagnosis of pleural disease(2), and had a high diagnostic yield.(3) Also may be used to facilitate instillation of sclerosants under vision into the pleural cavity. (4)

The use of this technique, however, was limited until recent advances allowed thoracic surgeons to have greater visualization and manipulation within the chest(5). The advent of miniaturized video cameras, placed on the tip of the thoracoscope, has enabled multiple persons to simultaneously view the procedure via television with excellent resolution (6).

The aim of this work is to evaluate the role of video assisted thoracoscopy in the

Assistant Professor of Cardiothoracic Surgery Faculty of Medicine, Univarsity of Alexandria

management of malignant pleural effusion by assessing its diagnostic sensitivity, morbidity and mortality in terms of hospital stay, chest tube duration, perioperative complications and procedure failure.

Patients and Methods

Video assisted thoracoscopy was performed on 21 patients between January 1994 and June 1996. There were 12 males and 9 female patients ranging in age from 17 to 65 years (median age 42 years) (Figure 1). The study included two different groups of patients. The first group included 15 patients with recurrent pleural effusion to diagnose its etiology after failure of other modalities of diagnosis such as thoracocentesis in all patients, bronchoscopy in 11 patients, pleural biopsy (Abram's needle) in eight patients and CT guided needle biopsy in seven patients. The second included six patients with malignant pleural effusion secondary to carcinoma of the breast in three patients, bronchial carcinoma in two patients, and carcinoma of the stomach in one patient. Thoracoscopy was done for confirmation of the diagnosis and pleurodesis.

All proceduress were performed under general anesthesia with a double-lumen endotracheal tube. The patients were placed in the lateral position for all procedures and skin was widely prepared to allow maximum flexibility for access in case conversion to an open thoracotomy becomes necessary. Mechanical ventilation to the ipsilateral lung is discontinued. A 10 mm trocar was then inserted through the seventh intercostal space mid - axillary line to create access for the thoracoscope and camera. A 10 mm, 0 degree rigid telescope and camera attached to a video monitor was then inserted. Exploratory video thoracoscopy was then performed to identify any pulmonary, pleural, or mediastinal pathology, and appropriate sites for additional trocar placement were selected. Most frequently, additional trocars were placed one interspace higher in the anterior or posterior axillary lines. Pleurodesis was done by talc poudrage instilled into the pleural cavity by insufflation through one of the trocar sites. A chest tube was inserted under direct visualization through one of the trocar sites. The remaining trocar sites were closed with absorbable sutures. Postoperatively, patients were returned to a hospital room and not routinely placed in an intensive care unit except in two patients, because they were seriously ill preoperatively.

All patients in this study were followed up paying attention to chest tube duration, hospital stay, perioperative complications, and procedure failures. According to a system originally proposed by Clavien et al.(7) there are a total of five grades of complications:

Grade I:

Minor, non-life-threatening complications. No residual disability.

Grade IIa:

Potentially life-threatening. No residual disability.

Operation not required to manage complications.

Grade IIb:

Potentially life-threatening (include intraoperative complications). No residual

disability. Operation required to manage complications.

Grade III: Associated with residual disability.

Grade IV:

Death as a result of a complication.

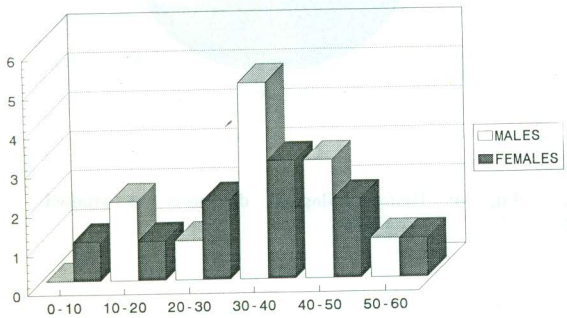


Fig. (1): Distibution of stuied patients by age and sex.

Table I: Different modlities of diagnosis of recurrent pleural effusion and their sensitivity.

Diagnostic modality	No. of patients	No. of diagnosed patients	Sensitivity (%)
Thoracocentesis	15	2	13.33
Bronchoscopy	11	1	9.1
Abram's needle	8	1	12.5
CT guided needle biopsy	7	1	14.28

N.B. Thoracoscopy was positive in these 15 patients.Patients proved by thoracopy to have non-malignant pleural effusion were excluded from the present study.

Results

Thoracoscopy was done in 21 patients; to diagnose the etiology of the recurrent pleural effusion after failure of other modalities such as thoracocentesis, fine needle biopsy (Abram's needle), CT guided needle biopsy and bronchoscopy (Table I) in 15 patients, and in six patients to confirm the diagnosis and induce pleurodesis. Patients proved to have nonmalignant pleural effusion by thoracoscopy were excluded from this study (tuberculous pleural effusion in two patients).

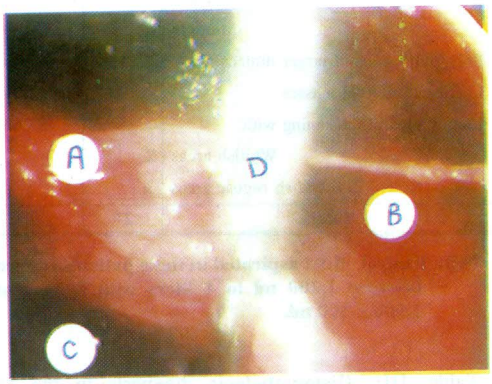


Fig. 2: Thoracoscopic findings shows:
A) Solitary pleural nodule.
B) Mediastinal lymph node enlargement.
C) Pleural effusion.
D) Biopsy forceps.
Histopathology; lymphoma.

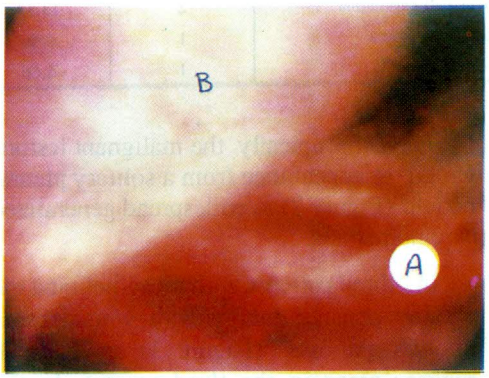


Fig. 3: Thoracoscopy findings. Lumpy thickening of the parietal pleura (A). With whitish areas covering the thickned visceral pleura (B). Histopathology; mesothelioma.

Table II: Thoracoscopic findings in the 21 patients of the present study.

Thoracoscopic findings	No.	%
- Nodules 1 - 5 mm in diameter	8	38.95
Solitary	2	
Multiple	6	
- Polypoid lesions of larger dimensions	5	23.63
- Localized tumoral masses	3	14.09
- Lumpy pleural thickening with:	5	23.63
Whitish areas	2	
Reddish rugose areas	3	
Total	21	

N.B: Pleural fluid aspirated in these patients ranged between 1,200 ml to 4 liters with a mean of 1,900 ± 300 ml.

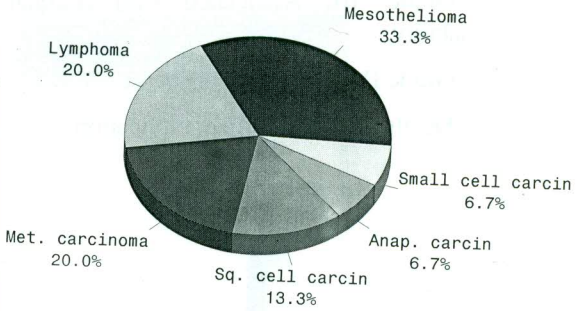


Fig. 4: Histopathological diagnosis of studied patients.

Table III: Histopathologic diagnosis in the 15 patients of malignant pleural effusion (diagnosed by thoracoscopy).

Histopathological diagnosis	No. of patients	%
Mesothelioma	5	33.33
Lymphoma	3	20.00
Metastatic adenocarcinoma	3	20.00
Squamous cell carcinoma	2	13.33
Anaplastic carcinoma	1	6.66
Small cell carcinoma	1	6.66

Thoracoscopically the malignant lesions varied in appearance from a solitary pleural nodule (Figure 2) to widespread generalized carcinomatosis.

In three patients with mesothelioma the pleura appeared lumpy with whitish areas in two patients (Fagure 3) and reddish rugose areas in the third patient. In the remaining two patients of mesothelioma the parietal pleura was studded with multiple small nodules. Table II shows the thoracoscopic findings in the 21 patients.

Table IV: Perioperative complications of video-assisted thoracoscopic surgery according to the modified classification by Clavien et al.

Complication	No. of patients	%
Grade I		
Persistent air leak (>3 days)	2	22.22
Intercostal neuralgia	2	22.22
Superficial wound infection	1	11.11
Grade IIa		
Bleeding	2	22.22
Re-expansion pulmonary edema,	1	11.11
Grade IIb		
Persistent air leak (>10 days)	1	11.11
Grade III		
Port site recurrence	0	
Grade IV	0	
Death		
Total	9	

Table III shows the histopathological diagnosis of the 15 patients with recurrent undiagnosed pleural effusion to whom thoracoscopy was done (Figure 4).

No perioperative mortality occurred. Three patients developed persistent air leak for a period ranging from 2 to 11 days. In two patients bleeding form the chest tube occurred postoperatively and was controlled conservatively without a thoracotomy (Table IV).

The chest tube was removed usually on the second postoperative day. In the three patients with persistent air leak, it was removed on the seventh day in two patients and on the eleyenth day in the third one. Hospital stay ranged between two to eleven days with a mean of 58 ± 17 hours. The follow up period ranged from eleven weeks to two years with recurrence of the pleural effusion in one patient (4.76%).

Discussion

Almost since the advent of thoracoscopy, physicians and surgeons have recognized its potential for evaluating and treating pleural diseases. Its initial use for therapeutic lysis of adhesions and induction of artificial pneumothorax (8) waned with the discovery of adequate chemotherapy for tuberculosis. During the 1950s it became popular again. This time thoracoscopy was proposed for the evaluation and management of pleural effusions of unclear etiology (9). Since then interest in this technique again waned until the modernization of thoracoscopy with improved optics and video assiatance (10). Many authors have demonstrated the capability of thoracoscopy to fully examine the pleura, lyse adhesions, and produce a therapeutic pleurodesis (11).

Patients with late-stage malignancy have significantly shortened life spans. When an effusion develops, it is most often due to the primary malignancy. It may be secondary to increased production of fluid from pleural metastasis or secondary to decreased absorption because of lymphatic obstruction with metastatic tumor. In the former, pleural fluid is often positive for malignant cells. In the latter, the fluid is often negative. Other causes are unlikely but always possible in these patients and include primary cardiac or renal failure and viral illnesses(12). Regardless of the cause, the shortened life expectancy of these patients makes prolonged diagnostic attempts a moot point. Permanent symptom relief is of paramount importance in these individuals(12).

Although cure would be the ideal therapeutic option, this is not always possible. Many of these patients are debilitated or have significant impairment secondary to metastatic disease elsewhere. Under these circumstances, palliation is the pragmatic goal. The definition of palliation is the relief of symptoms. In terms of pleural effusion this relatively easy to measure (12,13) .

The most common indication for diagnostic thoracoscopy is an exudative effusion that remains undiagnosed after the following work-up, one or more thorough biochemical, bacteriologic, and cytologic analyses of pleural fluid, one or two pleural biopsy attempts using a biopsy needle (Abrams, Vim-Silverman, or Cope); microbiologic and cytologic sputum analysis; intradermal testing using tuberculin, as well as fungal antigens in endemic areas; bronchoscopy; and a thorough clinical and radiologic assessment (14) .

In a series of 1000 effusion that were surveyed four or more weeks (15), the usual procedures failed to discover the cause in 215 patients.

Thoracoscopy was thus indicated in this (20%) group. It was diagnostic in 131 of the total 150 malignancies not yet diagnosed. Only 4% of pleural effusion remained idiopathic after thoracoscopy. So, thoracoscopy is the best method of making a histological diagnosis in patients with pleural effusions. Thus we can obtain a definitive diagnosis more frequently than with other methods (Table III). It is essential to have a free pleural cavity in order to perform thoracosopy. The existence of a latge pleural effusion confirms that the pleural cavity is free from adhesions. When there is a bilateral effusion we first aspirate the smaller effusion and then perform thoracoscopy on the contralateral side. Thoracoscopy is contraindicated when thick adhesions are present. Advenced age and respiratory insufficiency are usually not contraindications. In these patients local anaesthesia is used (16).

Several therapeutic options are available for the management of recurrent pleural effusion (17).

1. Pleurectomy.
2. Mechanical pleural abrasion.
3. Talc poudrage.
4. Pleuroperitoneal shunt.
5. Tube thoracostomy and pleurodesis.

The most invasive method would be open pleurectomy. Although quite effective, significant metastatic pleural involvement often leads to major blood loss and moderate-to-severe pain, in addition to the debility of a thoracotomy (18).

At the other end of the spectrum is tube thoracostomy and chemical sclerosis. Because these chemical agents work best at high concentrations, tubes are traditionally left in the patient until the daily output stops, this varies from patient to patient and may require as little as three days or as long as two weeks. As these work by producing an intense pleural reaction that eventually results in fusion, apposition of the visceral and parietal surfaces is essential (19). Thus, after instillation of the agent, tubes usually remain in place for an additional 24 hours. Although shorter regimens are used, this gives the best chance for adequate pleurodesis but leads to a prolonged hospital stay (minimum five days). Video--assisted thoracoscopy offers an excellent alternative to these approaches (20). It can be performed on a short in-hospital stay basis under either local or general anaesthesia. All of the pleural fluid can be completely drained and the pleural cavity inspected for adhesions. By lysing adhesions, the surgeon can eliminate loculated pockets of fluid.(21)

Talc produces an intense reactive pleuritis that is highly effective in producing a chemical pleurodesis. When instilled directly onto the pleural surface via poudrage, talc is effective in colse to 100% of cases (22). In the past, this approcah was used with a rigid thoracoscope under local or general anaesthesia. The rapid evolution of techniques of video-assisted thoracoscopic surgery have made this approach much easier to perform. (23) Webb and colleagues (24) described a method for instilling a talc suspension through the chest tube that gave excellent short-term results.

The recurrence rate reported after talc pleurodesis has been low. This reflects the

ability to visualize the whole pleural cavity with single-lung anaesthesia and break down any pleuropulmonary adhesions under direct vision. Talc can then be delivered to the whole lung surface, ensuring the best chance of success. Performing the procedure under a general anaesthetic not only permits excellent access but minimizes the pain to the patient from a chemical pleurodesis.(25)

The safety of thoracoscopic talc poudrage has been questioned.(26) Although talc poudrage has been found safe in our patients and in thousands of cases reported abroad (26,27), significant concerns remain. Rinaldo et al. (28) found adult respiratory distress syndrome in three patients after instillation of a large-dose talc slurry (10 g) in 250 ml of saline solution. Other complications have been detailed (29) or published in abstract form (30), but they appear to have been related to surgical manipulation rather than talc insufflation per se. These accounts and another by Bouchama et al (22). suggest that talc suspensions may have properties quite different from insufflated talc.

There has been a paucity of discussion of complications after thoracoscopy in the literature. Persistent air leaks remain the most common complication. Any definition of "persistent air leaks" is arbitrary[31] Timing for further intervention depends on the suspected cause of the air leak and the expected hospital course if no further treatment is given (32). We normally would not consider further surgical intervention unless the leaks last for more than two weeks. Our three patients who had a protracted air leak had undergone biopsy of lung that was covered in a thick visceral pleura infiltrated by metastatic carcinoma.

Strategies to minimize this complication include the use of pericardial buttress to reinforce the staple line when transecting emphysematous lung (32), avoidance of argon beam coagulation on apical bullae, avoidance of endoscopic graspers on lung (the conventional sponge-holding forceps are ideal in handling lung tissue), and use of two or more endo-loops to ligate isolated small apical bullae to avoid slipping (33).

The risk of infection appears to be low, with only five infections recorded in a collected series of 1,145 patients (34), it is not our practice to administer prophylactic antibiotics to patients undergoing thoracoscopy. Patients with malignancies of the pleural cavity are at risk of development of tumor seedling at the site of the thoracoscopy incision, a finding present in 6 of 215 patients discussed by Boutin and colleagues.(15) In a smaller series in which 2 of 30 patients had this problem, it was successfully palliated with radiotherapy.(35) In the series of Boutin and co-workers(15), five deaths (2.3%) were recorded within 30 days of thoracoscopy. However, the authors stated that death was not due to thoracoscopy but to advanced disease. In our patients, no mortality occurred within three weeks of operation.

Port site recurrence is a known complication when thoracoscopy is applied to manage intrathoracic malignancy(35). How one can best minimize this is uncertain, although gentle tissue handling during dissection and proper wound protection are likely to be important factors. Whether the use of tumoricidal agent can minimize this complication remains to be investigated.(36)

When video-assisted thoracic operations are performed, major muscles are not divided, ribs are not spread, dislocated, or broken and ligaments, nerves and blood

vessels are not severely damaged. The avoidance of these adverse effects will lead to an accelerated recovery. The number of intercostal incisions or even the length of the incisions do not seem to contribute to postoperative disability or pain so long as the rib cage is not traumatized and remains intact. Because of video technology, lighting sources, and magnification, visualization is generally superior to that in open procedures. With rapid improvements in endoscopic instrumentation and surgical ability, the facility with which thoracoscopic surgical procedures can be performed increases. Video-assisted thoracoscopic surgery has been remarkable in reducing the severity and duration of postoperative pain and allows patients to move and ambulate without difficulty the night of operation.(32) Only small doses of analgesics have been required, and most patients no longer require admission to the intensive care unit. Hospitalization has been shortened for many patients, and most of these patients have returned to preoperative levels of activity after anywhere from 10 to 14 days.

Video-assisted thoracoscopic surgery has been supported by pulmonologists, oncologists, and internists.(34) Patients who were not referred to a thoracic surgeon, when a thoracotomy was the only technique available, are now being referred with enthusiasm. Young, active patients and elderly, debilitated patients, who have been known to refuse a thoracotomy in the past, are now readily accepting video-assisted thoracoscopy (37). This is not a new surgical technique, but rather a different approach using standard, basic principles of thoracic surgery. Trained thoracic surgeons have quickly and easily mastered this new modality and have selective used it as another available option for performing thoracic surgical procedures. (37)

Based on our early experience with thoracoscopy, and the results we report here, we believe the following conclusions are warranted; Thoracoscopy may become the preferred procedure for the definitive diagnosis of idiopathic exudative pleural effusion that have eluded less invasive attempts at diagnosis as well as for the management of known malignant pleural effusions. It appears as if the more complete drainage of the pleural space and attainment of pleural symphysis with thoracoscopy can decrease the rate of recurrence. In addition, large quantities of tissue can be easily obtained for the definitive diagnosis of the undiagnosed pleural-based mass.

REFERENCES

1. Anderson C, Philpott G, Ferguson. T. The treatment of malignant pleural effusions. Cancer 1974; 33:916-22.

2. Jacobeus HC. The practical importance of thoracoscopy in surgery of the chest. Surg Gynecol Obstet; 1922; 34:289-96.

3. Mestiz P, Purves MJ, Polland AC. Pleural biopsy in the diagnosis of pleural effusion. Lancet 1958;2:1349-452.

4. Hucker J, Bhatnagar NK, Al-Jilaihawi AN, Forrester-Wood CP. thoracoscopy in the diagnosis and management of recurrent pleural effusions. Ann Thorac Surg 1991; 52:1145-7.

5. Miller JI Jr. Therapeutic thoracoscopy; new horizons for an established

procedure. Ann Thorac Surg 1991; 50:786-90.

6. Menzies R, Charbonneau M. thoracoscopy for the diagnosis of pleural disease. Ann Intern Med 1991; 141:271-6.

7. Clavien PA, Sanabria JR, Strasberg SM. Proposed classification of complications of surgery with examples of utility n cholecystectomy. Surgery 1992; 111:518-26.

8. Jacobaeus HC. The cauterization of adhesions in artificial pneumothorax treatment of pulmonary tuberculosis under thoracoscopy control. Proc Soc. Med 1923, 16:45-62.

9. Donahue RF, Katy S, Mathews M. Pleural biopsy as an aid in the etiologic diagnosis of pleural effusion: review of the literature and are part of 132 biopsies. Ann Intern Med 1958; 48:344-64.

10. Alony Y, King R, Boutin C. Thoracoscopic talc poudrage pleurodesis for chronic recurrent pleural effusions. Ann Intern Med 1991; 115:778-82.

11. Daniel TM, Tribble CG, Rogers BM. Thoracoscopy and talc poudrage for pneumothoraces and effusions. Ann Thorac Surg 1990; 50:186-9.

12. Lo Cicero J. Thoracoscopic management of malignant pleural effusion. Ann Thorac Surg 1993; 56:641-3.

13. Weissberg D, Kauffman M, Zurkowski Z. Pleuroscopy in patients with pleural effusion and pleural masses. Ann Thorac Surg 1980; 29:205-8.

14. Sahn SA. The pleura. Am Rev Respir Dis 1988; 138:184-234.

15. Boutin C, Viallat JR, Cargnino P, Farisse P. Thoracoscopy in malignant pleural effusion. Am Rev Resp Dis 1981; 124:588-92.

16. Canto A, Blasco E, Casillas M, Zarza AG, Paris F. Thoracoscopy in the diagnosis of pleural effusion. Thorax 1977; 32:550-554.

17. Petrou M, Kaplan D, Goldstraw P. Management of recurrent malignant pleural effusions. The complementary role talc pleurodesis and pleuroperitoneal shunting. Cancer 1995; 75 (3): 801-5.

18. Keller SM. Current and future therapy for malignant pleural effusion. Chest; 1993; 103:63S-67S.

19. Miller KS, Sahn SA. Chest tubes: Indications, technique, management and complications. Chest 1987;91:258-264.

20. Fenton KN, Richardson JD. Diagnosis and management of malignant pleural effusions. Am J Surg 1995; 170 (1): 69-74.

21. Rusch VW, Mountain C. Thoracoscopy under regional anesthesia for that diagnosis and management of pleural disease. Am J Surg 1987; 154:274-8.

22. Bouchama A, Chastre J, Gaudichet A, Soler P, Gibert C. Acute pneumonitis with bilateral pleural effusion after talc pleurodesis. Chest 1984; 86:795-97.

23. Colt HG. Thoracoscopy. A prospective study of safety and outcome. Chest 1995; 108 (2) :324-9.

24. Webb WR, Ozmen V, Moulder PV, Shabahang B, Breaux J. Iodized talc pleurodesis for the treatment of pleural effusions. J Thorac Cardiovasc Surg 1992; 103:881-6.

25. Daniel T, Tribble C, Rodgers B. Thoracoscopy and talc prudrage for pneumothoraces and effusions. Ann Thorac Surg 1990; 50:186-89.

26. Heffner JE, Unruh LC. Tetracycline pleurodesis: adios, farewell, idieu (editorial). Chest 1992; 101:5-7.

27. Aelony Y, King R, Boutin C. Thoracoscopic talc poudrage pleurodesis for chronic recurrent pleural effusions. Ann Intern Med 1991; 115:778-82.

28. Rinaldo J, Owens G, Rogers R. Adult respiratory distress syndrome following intrapleural instillation of talc. J Thorac Cardiovasc Surg 1983; 85:523-26.

29. Youmans CR, Williams RD, McMinn MR, Derrick JR. Surgical management of spontaneous pneumothorax by bleb ligation and pleural dry sponge abrasion. Am J Surg 1970; 120:644-48.

30. Todd TRJ, Delarus NC, Ilves R, Pearson FG, Cooper JD. Talc poudrage for malignant pleural effusion (abstract). Chest 1980; 78:542-43.

31. Adebonojo SA. How prolonged to "prolonged air leak"? (Letter). Ann Thorac Surg 1995;59:54950.

32. Jacovici R, Lazdunski L, Pons F, Cador L, Azorin J. Complications of video-assisted thoracic surgery: A five-year experience. Ann Thorac Surg 1996;61:533-7.

33. Yim AP, Liu HP. Complications and failures of video-assisted thoracic surgery: experience from two centers in Asia. Ann Thorac Surg 1996; 61:538-41.

34. Ohri SK, Oswal SR, Townsend ER, Fountain SW. Early and late outcome after diagnostic thoracoscopy and talc pleurosedis. Ann Thorac Surg 1992; 53:1038-41.

35. Davidson AC, George RJ, Sheldon CD, Sinha G, Corrin G, Geddes D. Thoracoscopy: assessment of a physician service and comparison of a flexible bronchoscope used as a thoracoscope with a rigid thoracoscope. Thorax 1988; 43:327-32.

36. Yim AP. Port site recurrence following video assisted thoracoscopic surgery. Surg Endosc 1995; 9:1133-5.

37. Lewis RJ, Caccavale R, Sisler GE, Mackenzie JW. One hundred consecutive patients undergoing video-assisted thoracic operations. Ann Thorac Surg 1992; 54:421-6.

Prevention and Treatment of Mediastinitis and Sternum Separation Following Open-Heart Surquery

ABSTRACT

From a series of 1372 patients requiring median sternotomy for open heart surgery, 32 (2.3%) had deep sternal wound infections and dehiscence. Most of these infections were associated with a number of predisposing factors: re-exploration for the control of hemorrhage or tamponade, prolonged ventilatory support, prolonged CPB (Cardiopulmonary bypass) and low cardiac output, obesity, and external cardiac massage. The highest incidence of deep sternal wound infection and dehiscence was among patients having mitral and aortic valve replacement. Most of these infections were caused by staphylococcus (more than 60% of cases). Surgical debridement of the sternum and mediastinum with reclosure followed by mediastinal irrigation via drainage tubes with 0.5% povidone-iodine solution was used for 26 patients (group A). While debridement and immediate closure with pectoral musculocutaneous flap was used in 6 patients (Group B). Four patients in group (A) required reoperation for persistent infection. The mortality for sternal wound dehiscence and mediastinitis in this report is high (10 cases i.e. 31%). This high mortality call for continuous effort for the prevention of serious sternal infections by a combination of proper preopertive preparation, attention to minute details at the time of operation and recognition of variables predisposing to wound complications. Also, reducing the mortality from this grave complication by early recognition of mediastinitis and adequate and radical wound debridement.

Samir-Adballah MD, Ahmed Farag MD*

J. of Egypt. Society of Cardiothorac. Surg. 1996, Vol. IV September No 4

INTRODUCTION

Median sternotony has become the standard approach to the heart and great vessels in most cardiac procedures. It has gained application for pulmonary resections in patients with bilateral lesions or poor pulmonary function. Indications for operation in both cardiac and pulmonary operations have been extended to include older and higher risk patients with osteoporosis, malnutrition, chronic lung disease, obesity, low cardiac output. Major wound complications, including major wound abscesses, chronic osteomyelitis, costal chondritis, sternal dehiscence, and mediastinitis occur in 0.97% to 1.86% of cases (1,2). These complications have a mortality rate of 19% to 39% (1,2,3,4) .

Although, sternal dehiscence occurs infrequently, it may present a dilemma with regard to optimum clinical management. Minor instability is usually treated conservatively with bed rest and chest binders. Associated soft tissue wound seromas, fat necrosis, or infections are opened and treated locally. Appropriate systemic and local antibiotics are employed. This approach is usually successful if only a portion of the sternal closure is unstable(5). On the other hand several approaches have

Department of Cardio therapg & General Surgery .

been described to treat patients with major sternal dehiscnces and mediastinitis. These include: (1) Debridement, dressing changes, and closure by secondary intention (3,6). (2) Debridment, sternal reclosure and closed irrigation (3,7). (3) Debridement, open dressing changes, and delayed closure with muscle flaps (2,8) .

Aim of the Study

The aim of this study is first to assess our experience in dealing with deep sternal wound infections following median sternotomy for open heart surgery.

Second to set a guideline for reducing the incidence and hastening the resolution of sternal infection and dehiscence following open heart surgery.

Material and Methods

Clinical Data:

The study is carried out at the cardiothoracic surgical department, Kasr El Aini University Hospitals, during a 4 year period from June 1992 to June 1996. Patients included in this study are those having deep sternal wound infection and mediastinitis with partial or complete sternal dehiscence following median sternotomy for open heart surgery. Patients with superficial localized infection of subcutaneous tissues or isolated infection of sternal wire and patients with stable sternum are excluded from this study.

General management of patients undergoing open heart surgery:

Prophylactic antibiotic therapy by one of the parenteral cephalosporin, quinolone and/ or aminoglycosides and aztreonam (azactam) was used. Antibiotics were given before induction of anesthesia and continued for 5 to 7 days post operative. Shifting to oral antibiotic from the 5th post operative day. In the presence of a spiking fever antibiotics were continued until 2 days after control of fever. A bubble oxygenator and roller pump were used for extracorporeal circulation, with a perfusion rate of approximately 2 to 2.5 L/min/m2 and a mean arterial pressure of 50 to 70 mmHg. Sternal closure was done with five to seven No. 5 stainless steel wires; two were placed through the body of the manubrium, and the others were used to encircle the body of the sternum at different interspaces. Great care was always made to avoid placing sutures in any cartilage (9) overlying soft tissues were closed in two layers with absorbable sutures.

Diagnosis:

The presence of erythema, drainage from either a sternal wound or chest site, increased pain and sternal instability together with any sign of infection (fever, leukocytosis, positive blood culture) prompted careful periodic evaluation of the wound with a high index of suspicion concerning the possibility of an evolving sternal infection. unit PA (when possible) or AP chest radiographs. The presence of a lucent midsternal strip should alert the possibility of the development of sternal dehiscence (10). (fig. 1).

A computed axial tomographic scan of the mediastinum was employed only infrequently; it was not found particularly helpful in estabilishing the diagnosis (Fig.2).

Methods of Treatment:

Once the diagnosis has been confirmed, all 32 patients with sternal infection underwent reoperations by one of two methods:

I) Closed technique (dèbridement, closed wound irrigation and systemic antibiotics) this was used for 26 patients (Group A); where re-exploration of the mediastinum and local débridement of visibly affected areas of soft tissue and bone was done. Specimens of bone and infected material were obtained for culture. Exposed prosthetic conduits and pledgets especial for valve or patch fixation were left intact. Then the wound is irrigated with one or two litres of warm saline, this decreases the bacterial count per gm of tissue. Two tubes for subsequent irrigation and drainage of the retrosternal space were inserted one 14FG for inflow in the upper part and the other one 30FG in the lower part of the wound. To achieve sternal stability reclosure of the sternum was done by one of the following methods:

1) A heavy thread of wire is passed parasternally around the cartilages "in and out" and "in and out" until it reaches the lower most point, were we turn around and pass it again parasternally along the edge of the sternum "out and in" and "out and in". The same is done on the other side of the sternum.

The wire sutures which are to hold the sternum together are passed laterally from these two parasterna wire lines. This makes "cutting through" of the wire suture a near impossibility (fig. 3). This method was first described by Robicsek in 1977 for the prevention and treatment of sternum separation (11).

This technique is modified and only one wire is used on each side of the sternum, and fewer is used on each side of the sternum, and fewer circumferential wires are needed (12).

Also, to avoid direct perpendicular shearing forces of the wire figure-of-8 suture technique was used for reclosure of the sternum(13).

Postoperatively, the mediastinum was irrigated with povidone-iodine (Betadine 10%) solution diluted 1.20 (0.5%) in normal saline at a rate of 2-3 L/day for approximately 7 to 10 days. The irrigation was stopped, culture from effluent fluid is taken, and the tubes gradually removed over the next 2-3 days.

During the last two years 6 patients (Group B), with sternal wound infections and mediastinitis, were treated by debridement and immediate closure with pectoral musculocutaneous flap (14). Flaps were created by using electrocautery to elevate both pectoralis muscles from their sternal insertions. Perforating branches from the internal mammary artery (IMA) were ligated. Blunt dissection was performed along the avascular plane between the muscle and the anterior wall. The dissection extended from the clavicle to the inferior ribs and from the medial insertion of the sternum to the anterior axillary line. The humeral attachment of the muscle was preserved. Closed suctions drains were placed under the flaps and the mid-line. The overlying skin was left attached to the pectoralis major muscle and the flaps closed over the sternal defect in two layers with absorbable sutures. The sternal edges were not reapproximated and, other than suction, no attempt was made to obliterate dead space (14). Appropriate systemic antibiotic therapy supplemented both method of treatment.

Results

A total of 32 deep sternal wound infections occurred among a 1372 ptients requiring median sternotomy for open-heart surgery, operated by the cardiothoracic surgical team of Kasr El Aini Univarsity

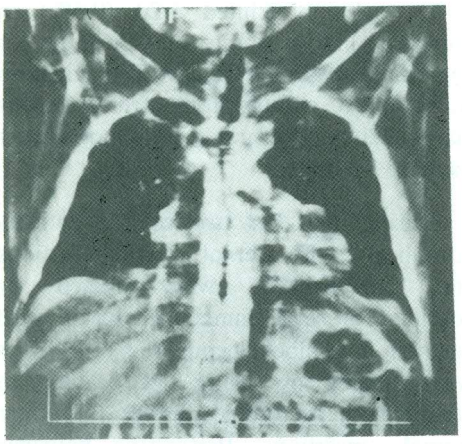


Fig.(1) : A lucent midsternal strip in a patient with sternal dehiscence after open heart procedure .

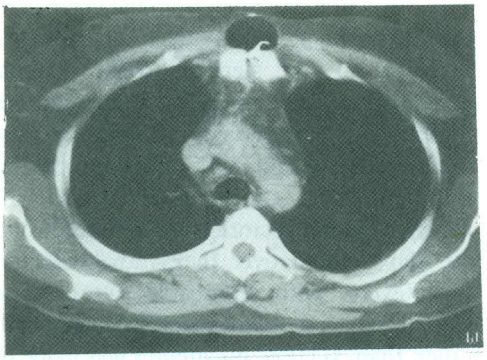


Fig.(2) : CT scan of the same patient in fig.1 demonstrating loose wire and sternal dehiscence .

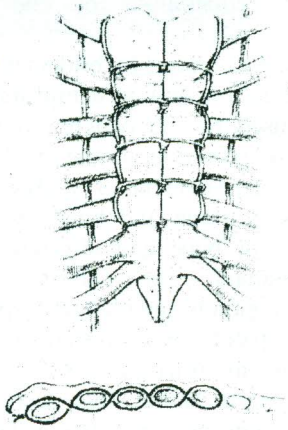


Fig.(3): Sternal weave technique for the prevention and treatment of sternal separation (after Robicsek 1977) (11).

Table (1): Cardiac surgical procedures and incidence of deep sternal wound infections.

Table (1): Cardiac surgical procedures and incidence of deep sternal wound infections

Procedure	No. of procedures	(%)	No. of deep sternal wound infections	Incidence of infections (%)
CABG*	175	12.8%	5	2.85%
Total valve procedure	667	48.6%	25	3.75%
• Mitral	436	65.4%	15	3.4%
• Aortic	104	15.6%	2	2%
• Mitral & aortic	111	16.6%	8	7.2%
• Aortic root replacement	16	2.4%	--	--
CHD**	530	38.6%	2	0.4%
Total	1372	100%	32	2.3%

* CABG = Coronary artery bypass grafting.

** CHD = Congenital heart disease.

Hospital during a 4 year-period (overall incidence of deep sternal wound infections and dehiscence 2.3 percent). There were 23 males and 9 females, their age ranged from 18 to 58 years (mean 34 years). The interval between the initial sternotomy and the re-exploration for infection ranged from 7 days to 58 days (mean 18 days).

In 20 patients infection occurred before two weeks and only in 4 patients after one month.

The number and types of operation performed among the 1372 procedures are shown in table (1).

Cardiac valve procedure is the commonest open-heart procedure in this group, while CABG (coronary artery bypass grafting) is the least common.

Combined mitral and aortic valve least common. Combined mitral and aortic valve replacement resulted in the highest incidence of sternal wound infections (7.2%) among this group, while the least incidence was among patients with CHD (congenital heart disease) (0.4%).

Operative findings confirmed the presence of mediastinitis. Partial sternal dehiscence was present in 20 patients, while complete dehiscence in 12 patients. In all cases, intra-operative cultures from the mediastinum were positive. Organisms cultured from debridement material included, Staphylococcus epidemidis in 12 patients, Staphylococcus aureus in 8 patients, Pseudomoneus aeruginosa in three, E. Coli in two and seven patients had multiple infecting organisms.

Risk factors for development of sternal wound complications were found in 26 patients. These are re-exploration for bleeding or tamponade (n = 8 casaes), prolonged ventilatory support (more than 48 hours) n=4 cases), prolonged CPB and low cardiac output (n=4), obesity (n=4) and external cardiac massage (n=3).

Two methods of treatment were used: Group (A) (n=26 patients) were treated by radical debridment and closed irrigation with 0.5% povidone iodine. Group (B) (n=6 patients with déridement and immediate colsure with pectoral musculocutaneous flap as previously described by Jeevanadam et al., (1990) (15). All ptients in group B started treatment after more than 3 weeks of the initial procedure.

The clinical condition of the patients among both groups varied widely due to the difference in the initial procedures and the time that elapses from the presence of infection and the initation of treatment. There were 10 deaths (31%). The mortality, however, was not significantly different among the two groups i.e. 8 deaths (31%) in group A and two deaths (33%) in group B.

Most deaths resulted from problems in multiple-organ systems, especially the heart, kideny, brain and respiratory system.

Persistent infection required another operation in four patients, all from group A and in all of them re-exploration was delayed to be done after more than 3 weeks from the initial operation. Only two of these patients eventually recovered while the other two died from sepsis.

The length of hospitalization for patients in group A ranged from 20 to 115 days (average 46 days); while for group B, ranged from 18 to 40 days (average 26 days).

Discussion

Despite careful preoperative preparation, adequate hemostasis, and good surgical technique, mid-line sternotomy infection occurs in a small subset of patients undergoing cardiac procedures (16).

Superficial infections are treated by simple incision, drainage and open dressing changes. Deep sternal wound infections, the object of this discussion, are harder to

manage. Several approaches have been used to treat this major complication.

The technique of débridement and sternal reclosure followed by mediastinal antibiotic irrigation, has been used since Shumacker and Mandelbaum report of two cases in 19637.

We have used this closed technique of débridement, primary closure and irrigation for 26 patients with sternal infection and mediastinitis. Povidone-iodine 10% diluted in normal saline 1:20 (0.4%) was the irrigating solution 16, rather than antibiotic as described by Grossi et al. (3) and Culliford et al. (9) as some reports indicated that antibiotic irrigation may allow fungal overgrowth and fungal mediastinitis (17,18), which has an unusually high morbidity and mortality (19). However, povidoneiodine should be used with caution in the pediatric age group. Toxic symptoms, that is fever, agitation, skin eruption and some transient neurological findings (iodine toxicity) have been observed in one child by Kaiser (20) when this technique has been used to treat mediastinitis. Therefore, for the pediatric age group, if this method is to be used alteration both in volume and concentration of the solution should be considered; together with careful monitoring of the serum iodine level (normal range 4.5 to 0.9 micro-grams/DL)(21).

None of the patients in this study developed symptoms related to iodine toxicity, also serum iodine level was not monitored as none of the patients in this report were in the pediatric age group .

Satisfactory results were obtained using this technique. However, 4 patients required reexploration for persistent infection (failure rate 4/26, 15%). Recurrence probably reflects inadequate debridement, due either to inability to reccognize diseased tissue or to surgical caution regarding the degree of soft tissue defect that would result. Also, when operation is postponed and the infectious process spreads, a different pathological problem evolves, sternal osteomyelitis or infection of the wires around the sternum and adjacent cartilages occur. Once osteomyelitis is established, closed drainage is far less effective and probably should rarely be used, even in association with radical debridement. Following radical debridement, the operating surgeon decided whether to employ closure of the sternum with closed irrigation or open packing of the wound which may be followed by muscle flap closure; there is no fixed guidelines (3). Open packing technique needs frequent dressing changes with antibiotic-soaked gauze in combination with systemic antibiotics, which places substantial physical and psychological stress on the patient. In addition, reoperation is necessary in a quarter of patients for persistent infection or failure of the wound to adequately close. The mortality rate is high (22%), with hospital stay averaging 49 days (3,6) .

Successful treatment of sternal wound infection with muscle flaps was described by Jurkiewicz and associates (8), who reported cures in nine of 12 patients unresponsive to debridement and antibiotic irrigattion. Their report led to a dramatic increase in use of muscle or omental flaps (22,23). The flaps are primarily used on

clean wounds after initial debridement and dressing changes have allowed for ingrowth of granulation tissue. Infection is resolved in more than 90% of patients and average hospitalization decreased to a range of 19 to 42 days. Although clearly effective, there is a need for a second procedure, which exposes the patient to increased anesthesia risk (24-26).

In an attempt to simplify management, an approach using immediate pectoralis major muscle, musculocutaneous flap closure after debridement was described by Jeevanandam and associates (14). In their reports hospital stay was reduced from 42 days (range 19 to 88 days) when debridement and closed antibiotic irrigation was used, to 18 days (range 6 to 43 days). When muscle flaps technique was used to treat sternal wound infections. The mortality rate for this later technique was 13% (four patients out of 31 patients). In all four patients the musculocutaneous flaps were intact, and none died of sternal sepsis.

Muscle flaps are thought to work by two basic methods. Chang and Moathes (27) have shown that musculocutaneous flaps demonstrate ability to survive a bacterial inoculation and control infection. The muscle flaps bring a rich network of blood supply to an area of bone that is infected and poorly vascularized. The bactericidal effect of the muscle, along with appropriate antibiotics, promote sterilization of the wound. Especially impresive was the ability to resolve infection in the presence of foreign material such as conduits or pledgets (14).

We have used this technique of single stage debridement and pectoralis musculocutaneous flaps reconstruction in six patients with mediastinitis and sternal wound dehiscence treated after more than 3 weeks of the initial procedure. The technique was used when after complete debridement of the mediastinum and sternum, primary closure of the sternum was not feasible. Apparently, the chest wall is fixed to underlying tissues to such an extent that minimal respiratory paradox occurs. The opposing pectoral muscles are sutured firmly together. This tends to aid in chest wall stability. The sternum is not rewired.

Chest wall mechanics were of concern, in as much as the sternum is debrided and not reapproximated . However, most patients were extubated in the operating room or within 24 hours postoperatively. There has been no evidence of mechanical pulmonary insufficiency in our four surviving patients from group B, and all have good chest wall stability. These results are similar with other reports of preserved respiratory function after sternectomy (14).

Hospital stay was reduced from 46 days (range 20 to 115 days) for patients in group A treated by closed debridement and povidoneiodine irrigation, to 26 days (range 18 to 40 days) for patients in group B treated by pectoral musculocutaneous flaps. However, the mortality was still high for both groups (31% for group A and 33% for group B).

This high mortality appeared to be from hesitancy on our part to utilize aggressive treatment early in the course of mediastinitis. Treatment solely with antibiotics in the presence of sepsis, even though the sternum initially appears stable, is clearly hazardous and ineffective (3).

Of interest is the high incidence of deep sternal infection following open heart

surgery (2.3%) in this report. Post operative mediastinitis developed in 47 out of 1240 patients undergoing open heart surgery (3.79%), in other centre in Egypt, however only 25 patients had sternal dehiscence and deep infection (2%) (28).

Bacterial infections after operations with cardio-pulmonary bypass (CPB) have been reported in 12 to 41% of adult patients (29,31). However, the reported frequency of major wound infection following median sternotomy ranges from 0.5 to 3% with most series 2% or less (19,32,33).

Both patient and operation related factors are involved in the pathogenesis of sternal complications. Patient factors include: obesity, malnutrition, osteoporosis, diabetes mellitus, corticosteroid use, chronic obstructive pulmonary disease, and history of radiation therapy to the chest. Technical errors in opening the sternum, reoperation for bleeding or tamponade, prolonged operative time, low cardiac output, and need of prolonged postoperative ventilatory support, all increase the probability of wound breakdown (9,13,33,34,35). Bilateral IMA harvest also has been reported to be a risk factor (13). However. prospective evaluation with multivariable analysis has shown that increases the rate of sternal dehiscence only in diabetics (33).

The high incidence of sternal wound infection compared to other centers abroad can be partly explained by different patients population undergoing open heart surgery than those abroad. The commonest cardiac operation in Egypt is valve procedure (in this series represent 48.6% of the total open heart procedure while CABG procedure represents (12.8%). In New York university medical centre, for example the commonest cardiac operation was CABG, representing 47.5%, while valve procedure represents 19.2% of the total open heart operation (7949 operative procedures from 1976-1984) (3). The highest incidence of deep sternal wound infection was among patients with multiple valve procedure in this report. Compromised host resistance, was found a significant factor for development of infection in patients with cardiac valve diseases (36). Preoperatively attenuated responsiveness of lymphocytes to stimulation with phytohemagglutinin was reported in patients with mitral and aortic valve disease (37).

In our series, reoperation for bleeding is the commonest risk factor for mediastinitis (8 cases out of 32 i.e. 25%). Reoperation increases the risk by longer operative times, by more tissue traumatization, and probably being performed on more critically ill patients. In addition, more blood transfusion usually needed for these patients. Blood transfusion perse could hamper immunological competence. Transfusion of washed erythrocytes was found to diminish the response of lymphocytes to phytohemagglutinin, to other mitogens and to a mixture of antigens (38).

A gram-positive organism, usually staphylococci caused the sternal infection in more than 60% of patients, a finding similar to that in other reports (6,7). However, there is some difference as regards to other causes of sternal infection such as gram-negative organisms, polymicrobial cultures, or fungi. These differences may reflect variations in the

bacterial spectrum that exist in the environments of different hospitals.

In approximately half of the patients with sternal infection, the organism isolated was sensitive to the prophylactic antibiotic that had been given, wheres in the other patients, the organism was not sensitive. It is obvious that determining the sensitivty of the organism with respect to the prophylactic antibotic is very important. Infection occurring from an organism sensitive to the prophylactic antibiotic suggests that the drug was incorrectly used in regard to such aspects as dosage, intramuscular versus intravenous administration, or frequency of administration. On the other hand, infection from organisms that prove resistant to the prophylactic antibiotic administration indicates an appropriate choice of antibiotic (3).

Summary and Recommendation :

The high mortality due to severe infections after open heart operations justifies continued efforts to reduce their incidence.

The prevention of serious sternal infection depends on a combination of :

1) Proper preoperative preparation of the patient : Adequate preoperative and intraoperative skin preparation is the first step in prevention of sternotomy infection. Skin shaves should be postponed until the morning of the day of surgery. The rate of infection when shaving with razors was performed in the 24 hours prior to surgery was double the rate when shaving with razors just prior to surgery (7.1% vs. 3.1%)(39).

Antibiotic prophylaxis should be routinely used preoperatively and continued until surgical wounds are adequately sealed and the majority of monitoring lines and intravenous catheters are removed. Since the commonest offending organisms are staphylococci, the use of specific antistaphylococcus drugs (oxacillin, cephalosporin or quinolone) is imperative. Frequent surveillance of hospital flora to determine effective prophylactic antibiotics should be employed .

2) Attention to details of operative technique is mandatory. Accurate mid-line sternal division avoids cartilagenous injury or exposure and facilitates mechanically secure closure. Efforts should be made to shorten total operative time. Whenever, mobilization of one or both internal mammary arteries for CABG is performed, careful hemostasis in the mammary bed prevents the excessive postoperative bleeding and hematoma formation which often precede a serious sternal wound infection.

As the most important factor in preventing the major complications, particularly sternal dehiscence and mediastinitis, after open heart surgery, is a stable sternal approximation. Hence, a special reinforced method of sternal closure should be applied in the following cases : Obesity, reoperation, diabetes, sternal dehiscence, bone fracture, bilateral mammary artery dissection for bypass grafting, anticipated postoperative low cardiac output, anticipated prolonged respiratory assistance (40). Many innovative techniques have been proposed to achieve a stable sternotomy wound; such as the Robicsek weave (11) or its modification (12), interlocking figure-of-8 (41) and others .

4) Finally, two important corner stones of therapy for postoperative mediastinitis emerge, regardless of technique. These are; First early diagnosis before infection spread to bone, leading to osteomylitis which is difficult to be treated. Second; is adequate and radical wound debridement; the sternal edges are debrided to bleeding cancellous bone to provide a clean edge for sternal reapproximation. Muscle flap closure can be used for chronic infection, or whenever sternal reapproximation is not feasible.

REFERENCES

1. Breyer RH, Mills SA, Zhudspeth AS, et al. A prospective study of sternal wound complications. Ann Thorac Surg 1984; 37:412-6.

2. Scully HE, Leclerc Y, Martin RD et al. Comparison between antibiotic irrigation and mobilization of pectoral muscle flaps in the treatment of deep sternal infections. J Thorac Cardiovasc Surg 1985; 90:523-31.

3. Grossi EA, Culliford AT, Kreiger KH, et al. A survey of 77 major infectious complications of median sternotomy: a review of 7,949 consecutive operative procedures. Ann Thorac Surg 1985; 40:214-23.

4. Nagashinta T, Stephens M, Reitz B, Polk BF. Risk factors for surgical wound infection following cardiac surgery. J Infect Dis 1987;156:967-73.

5. Bowen TE, Brott WH, Green DC et al. Thoracic traction for median sternotomy dehiscence. Ann Thorac Surg 1987; 26:148-9.

6. Gromliez PF, Barner HH, Willman VL, Kaiser GC: Major complications of median sternotomy. Am J Surg 1975; 130:679-81.

7. Shumacker HB Jr, Mandelbaum J. Continuous antibiotic irrigation in the treatment of infection. Arch Surg 1963; 86:384-7.

8. Jurkiewicz MJ, Bostick J, Hester TR, et al. Infected median sternotomy wound : successful treatment by muscle flaps. Ann Surg 1980;191:738-44.

9. Culliford AT, Cunnigham JN Jr, Zeff RH, et al. Sternal and costochondral infections following open-heart surgery. J Thorac Cardiovasc Surg 1976; 72:714-26.

10. Escorvitz ES, Okulski TA, Lapajowker MS. The midsternal strip : A sign of dehiscence following median sternotomy. Radiology 1976; 121:521-24.

11. Robicsek F, Daugherty HK, Cook JW. The prevention and treatment of sternum separation following open heart surgery. J Thorac Cardiovasc Surg 1977; 73:267-68.

12. Sutherland RD, Martinez HE, Guenes WA. A rapid, secure method of sternal closure. Cardiovasc Dis Bull Tex Heart Inst 1981; 8:45-5.

13. Taber RE, Madaras J. Prevention of sternotomy wound disruption by use of figure-of-eight pericostal sutures. Am Thorac Surg. 1969;8:367-9.

14. Jeevanandam V, Smith CR, Rose EA, et al. Single-stage management of sternal

wound infections. J Thorac Cardiovasc Surg 1990;99:256-63.

15. Majure JA, Albin RE, O'Donell RS, et al. Reconstruction of the infected median sternotomy wound. Ann Thorac Surg. 1986;42:9-12.

16. Serry C, Black RC, Jowid H, et al. Sternal wound complications : management and results. J Thorac Cardiovasc Surg 1980;80:861-7.

17. Thurer RJ, Bognolo D, Vargas A, et al. The management of mediastinal infection following cardiac surgery: an experience utilizing continuous irrigation with povidone iodine. J Thorac Cardiovasc Surg 1974;68:962-8.

18. Engelman RM, Williams DC, Gough TH, et al. Mediastinitis following open-heart surgery. Arch Surg 1973;107:772-8.

19. Glower DD, Douglas JM Jr, Gaynor JW, et al. Candida mediastinitis after a cardiac operation. Ann Thorac Surg 1990;49:157-63.

20. Kaiser GA [Discussion of (16)].

21. Glick PL, Guyliclimo BJ, Tranbaugh RF, Turley K. Iodine toxicity in a patient treated by continuous povidone-iodine mediastinal irrigation. Ann Thorac Surg 1985;39:478-80.

22. Ringelman PR, Vander-kolk CA, Cameron D et al. Long term results of flap reconstruction in median sternotomy wound infections. Plast Reconstr Surg 1994;93:1208-14.

23. Pairolero PC, Arnold RG, Harris JB. Long term results of pectoralis major muscle transposition for infected sternotomy wounds. Ann Surg 1991;213:583-9.

24. Nahai F, Morales L, Bone DK, et al. Pectoralis major muscle turnover flaps for closure of the infected sternotomy wound with preservation of form and function. Plast Reconstr Surg 1982;70:471-4.

25. Heath BJ, Bagnoto VJ: Poststernotomy mediastinitis treated by omental transfer without postoperative irrigation or drainage. J Thorac Cardiovasc Surg 1987;94:355-60.

26. Pairolero PC, Arnold PB. Management of infected median sternotomy wound. Ann Thorac Surg 1986; 42:1-2.

27. Chang N, Mathes SJ: Comparison of the effect of bacterial inoculation in musculocutaneous and random pattern flaps. Plast Reconstr Surg 1982; 70:1-9.

28. Bassiouny M, El-Saegh MM, Ali MA, Shoeb A. A new approach for management of postoperative mediastinitis. The Egyptian Journal of Surgery 1988; 7-25-8.

29. Goodman JS, Schaffner W, Collins HA, et al. Infection after cardiovascular surgery: clinical study including examination of antimicrobial prophylaxis. N Eng J Med 1968; 278:118.

30. Bell DM, Goldman DA, Hopkins DA, Hopkins CC, et al. Unreliability of fever and leukocytosis in the diagnosis of infection after cardiac valve surgery. J Thorac Cardiovasc Surg 1978; 75: 87-91.

31. Wells FC, Newson SWB, Rowlands CH. Wound infection in cardiothoracic surgery. Lancet 1983; 2:1209-14.

32. Demmy TL, Park SB, Leibler GA, et al. Recent experience with major sternal wound complications. Ann Thorac Surg 1990; 49: 458-62.

33. Loop FD, Lytle BW, Cosgrove DM, et al. Recent experience with major sternal wound complications after isolated coronary artery bypass grafting: early and late mortality, morbidity, and cost of care. Ann Thorac Surg 1990; 49:179-87.

34. Shafir, Weiss J, Herman O, Cohen N, et al. Faulty sternotomy and complications after median sternotomy. J Thorac Cardiovasc Surg. 1988; 96:310-3.

35. Hendrickson SC, Kogers KE, Morea CJ et al. Sternal plating for the treatment of sternal non union. Ann Thorac Surg 1996; 62: 512-8.

36. Miholic J, Hudec M, Domanig E, et al. Risk factors for severe bacterial infections after valve replacement and aortocoronary bypass operation. Analysis of 246 cases by logistic regression. Ann Thorac Surg 1985; 40: 224-28.

37. Park SK, Cody JI, Wallace HA, Blackmore WS. Immunosuppressive effect of surgery. Lancet 1971; 1:53-6.

38. Fischer E, Lenhard V, Seiffert L, et al. Blood transfusion induced suppression of cellular immunity in man. Hum Immunol 1980; 3; 187-91.

39. Seropian R, Reynolds BM: Wound infections after preoperative depilotory versus razor preparation. Am J Surg 1971; 121:251-54.

40. Scovotti CA, Ponzone CA, Leyro-Diaz RM. Reinforced sternal closure. Ann Thorac Surg. 1991; 51: 844-5.

41. DiMarco RF, Lee MW, Bekoe S, et al. Interlocking figure-of-8 closure of the sternum. Ann Thorac Surg. 1989; 47:927-9.

Comparative Effects of enoximone and Nitroprusside after Mitral Valve Replacement in Patients with Chronic Pulmonary Hypertension

ABSTRACT

Pulmonary hypertension may result in acute right ventricular failure in the early post-operative period following mitral valve replacement. This complication can be prevented or treated by the use of pulmonary vasodilators. In this study, 2 groups of patients were treated by 2 different vasodilators. Enoximone through its inotropic and vasodilator properties (phosphodiesterase III inhibitor) resulted in improved overall myocardial functions with very high significant increase in cardiac index.

Nitroprusside through its direct vasodilator properties resulted in improvement of right ventricular function but inotropic support was needed in some cases.

Kawther Taha Khalil

J. of Egypt. Society of Cardio thorac. Surg. 1996, Vol. IV September No 4

INTRODUCTION

Mitral valve replacement surgery may be complicated by right ventricular failure in the early postoperative period especially in patients with poor preoperative right ventricular function or those with high pulmonary vascular resistance (Camara et al., 1992).

Right ventricular failure is usually manifested by low cardiac output difficulties in weaning from cardiopulmonary bypass, and from ventilation support in the postoperative period.

Treatment of acute right ventricular failure include the use of inotropic agents (dopamine or dobutamine) that increase myocardial contractility, but, in some instances, can increase pulmonary and peripheral vascular resistance (Camara et al., 1992) (1).

Assistant Consultant of Anaesthesia
National Heart Institute Imbaba-Cairo

On the basis of the pathophysiology of this complication, drugs that produce pulmonary vasodilatation would be the treatment of choice for patients with this type of right ventricular failure (Flaherty et al., 1982) (2).

Vasodilator agents that have been used for either the acute or the chronic treatment of pulmonary hypertension include:

Oxygen, hydralazine, phentolamine, diazoxide, nifedipine, isoproterenol, prostacyclin, tolazoline, verapamil, captopril, nitroglycerin, nitroprusside, and recently enoximone and inhaled nitric oxide (Brauwald, 1992) (3).

Enoximone (MDL 17,043), a recently synthesized imidazolone derivative, has been investigated in both experimental and clinical conditions and has been shown to be a non glycosidic, non sympathomimetic cardiotonic agent, acting mainly by inhibition of phosphodiesterase III (Braunwald, 1992) (3).

In animals and man, enoximone exert a potent inotropic as well as a direct vasodilatory action [Indolator] (Dage et al., 1987) (4).

The present work assess the comparative hemodynamic effects of Enoximone and Nitroprusside on pulmonary artery pressure early after mitral valve replacement in patients with mitral valve disease complicated by chronic pulmonary hypertension.

Patients and Methods

The study was done on thirty adult patients of both sexes, scheduled for mitral valve replacement. All patients had rheumatic heart disease diagnosed preoperatively by ECG, echo-cardiography and cardiac catheterization. The mean pulmonary artery pressure was above 35 mmHg in all patients. Mitral valve replacement were done using standard cardiopulmonary bypass with the use of hyperkalemic cold cardioplegia solution for myocardial protection.

Pulmonary artery pressures and cardiac output were measured by insertion of Swan-Ganz catheters and thermodilution technique using ARROW cardiac output computer 7350.

During weaning from cardiopulmonary bypass the patients were classified into two groups: Group I (Enoximone group) 15 patients received Enoximone (Perfan injection, Merrell Dow pharmaceuticals) 0.5 mg/kg as a loading dose over a period of 10 min, followed immediately by an infusion of 10 mg/kg/min via central venous line . Group II (Nitroprusside group) 15 patients received nitroprusside as an infusion of 1 mg/kg/min via central line.

The study was conducted approximately 120 min. After termination of the cardiopulmonary bypass, when the patients were in the I.C.U. During the study period, all patients were ventilated using controlled mandatory ventilation. Blood pH, PaO_2, and Pa Co_2 were kept within normal limits.

Full hemodynamic data were recorded following induction of anaesthesia, following mitral valve replacement, after 15,30,60 and 120 min after drug administration.

The following hemodynamic parameters were recorded :-

1. Heart rate (HR, beats/min).

2. Systolic, diastolic, and mean arterial pressure (MAP, mm Hg).

3. Central venous pressure (CVP, mmHg).

4. Systolic, diastolic and mean pulmonary artery pressure (MPAP, mm Hg).

5. Pulmonary capillary wedge pressure (PCWP, mmHg).

6. Cardiac output (Co,L/min).

From these hemodynamic data. The following derived data were calculated:-

1- Cardiac index (CI) = Co/body surface area (BSA) (L/min/m2).

2- Systemic vascular resistance (SVR) - MAP-CVP/CO x 80 (Dyn-S/cm $^{-5}$)..

3- Pulmonary vascular resistance (PVR) = MPAP - PCWP /Co x 80 (DYN-s/CM $^{-5}$).

4- Stroke volume (SV) = Co/Hr (mf).

5- Stroke volume index (SVI) = SV/BSA (ml /m^2).

6- Stroke index (SI) = CI/HR (MI/Beat/L/min/m^2).

7- Left ventricular stroke work index (LVSWI) = SI/BSA x (MA0-PCWP) x 0.0136 (gm/m/m^2).

8- Right ventricular stroke work index (RVSWI) - SI/BSA (MPAP-CVP) x 0.0136 (gm/m/m^2).

Statistics :-

Statistical analysis was done using analysis of variance (ANONA) with repeated measurements (Statview 4.0, Abacus Incorporation). Mean values ± SE are quoted. P>0.05 was considered significant.

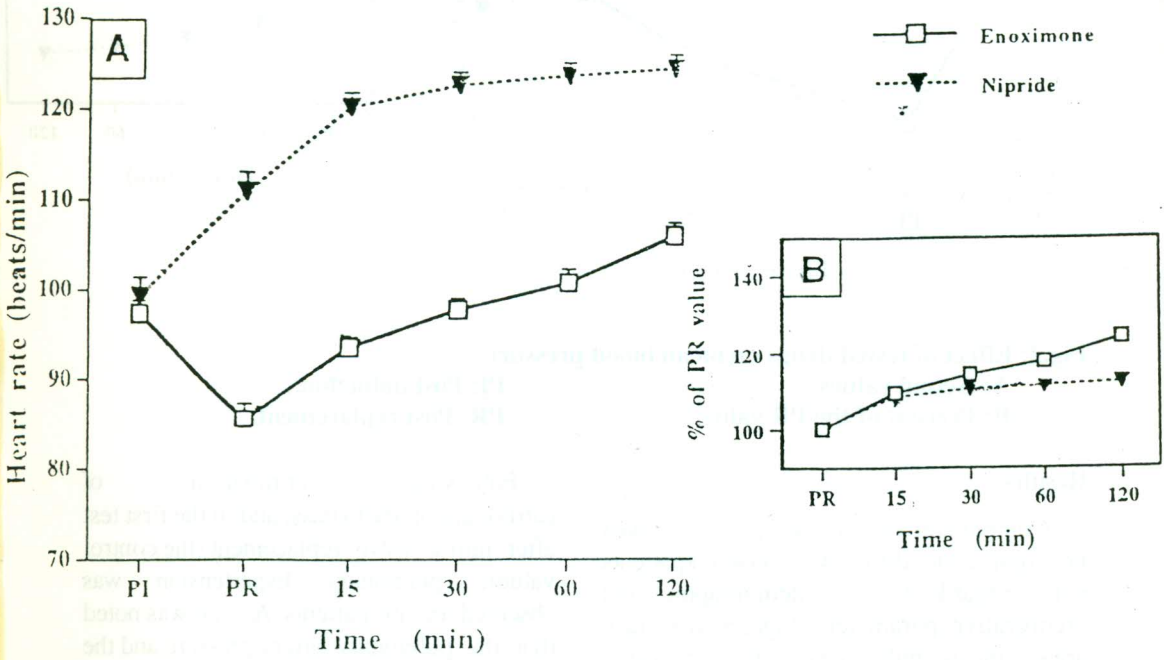


Fig.1: Effect of tested drugs on heart rate.
A: Actual values.
B: Perecent of the PR value.

PI: Post induction.
PP: Post replacement.

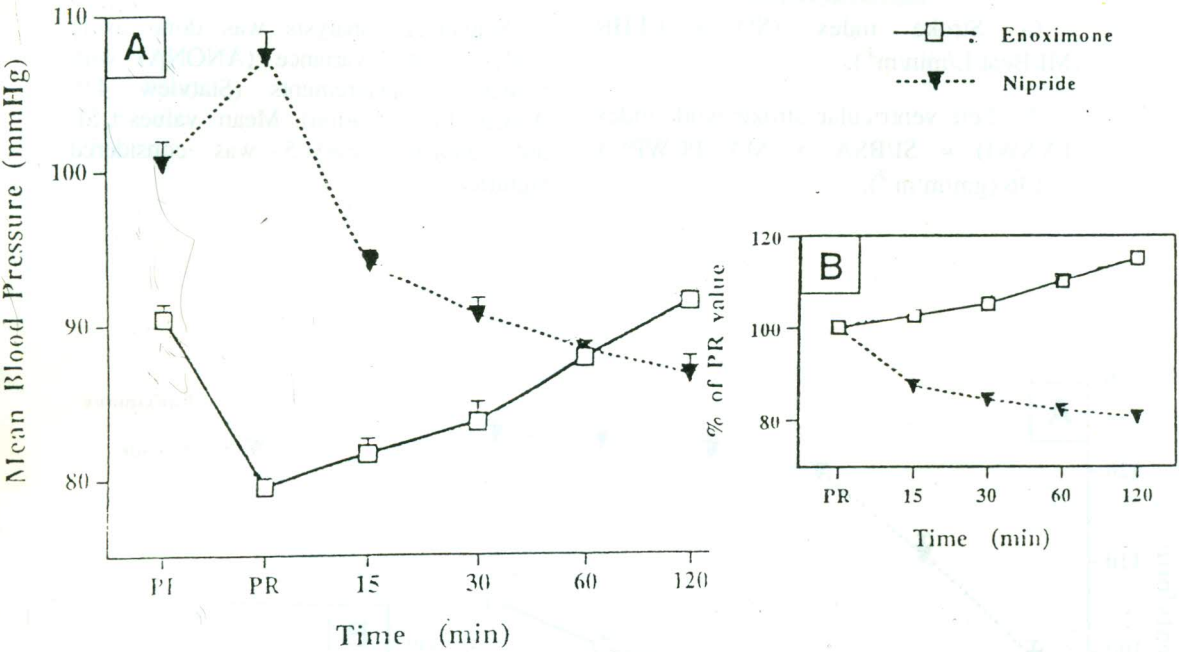


Fig.2: Effect of tested drugs on mean blood pressure
A: Actual values. **PI: Post induction.**
B: Percent of the PR value. **PR: Post replacement.**

Results

Comparison of the two groups showed no significant differences between patients with regard to the demographic and preoperative parameters (age, body surface area, mean pulmonary artery pressure, fractional shortening, and ejection fraction) or the intraoperative factors (type of operation, cross clamp time, and bypass time) (Table 1).

There were no deaths and no major complications in patients studied ..

Following termination of cardiopulmonary bypass, and in the first test after mitral valve replacement (the control value), pulmonary hypertension was observed in all patients. Also, it was noted that the pulmonary artery pressure and the pulmonary vascular resistance were increased significantly ($P<0.05$) from the post induction reading in all patients.

Mean pulmonary artery pressure increased from (38.8 mmHG) to (40.2 ± 8 mmHg) and pulmonary vascular resistance.

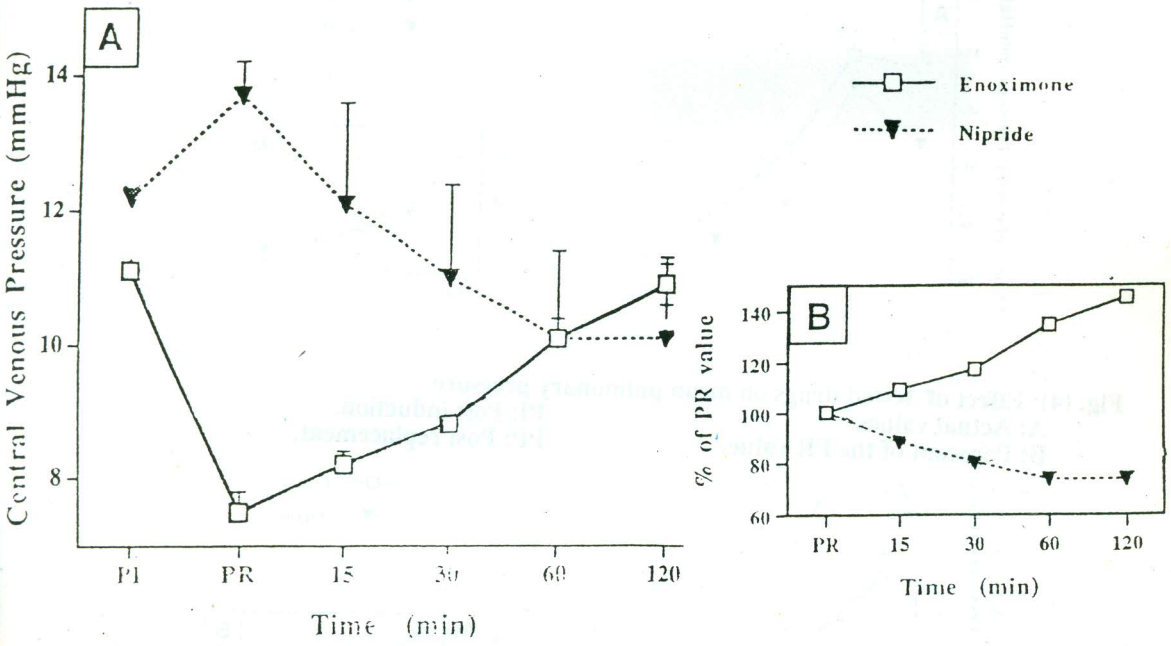


Fig.3: Effect of tested drugs on central venous pressure.
A: Actual values. **PI: Post induction.**
B: Perecent of the PR value. **PR: Post replacement.**

Increased from (384 ± 14 Dn/S/Cm $^{-5}$) to (429 ± 15 Dn/S/Cm $^{-5}$). These changes were matched with the effects of stress of surgery and anaesthesia, events of cardiopulmonary bypass period especially ischemic time during aortic cross clamping, and methods of myocardial preservation on the pulmonary circulation and the right ventricular function.

The hemodynamic effects of the two tested drugs on the different parameters are shown in tables 2 and 3.

Following administration of the tested drugs, the comparative effects of these drugs, on different hemodynamic parameters are illustrated in 2 figures for each parameter: Figure (A) represents the actual values from the post-induction reading, and Figure (B) is the percent changes from the post replacement reading which was considered the control reading (100) for the effect of each drug. (Fig 1) to (Fig.13).

Hemodynamic Changes Following Administration of the Tested Drugs:

In the present study, there was but slight significant rise in heart rate in both groups being 9.5-24% in group I and 8.5-12.3% in group II ($P<0.05$) (Table 4) (Fig.1).

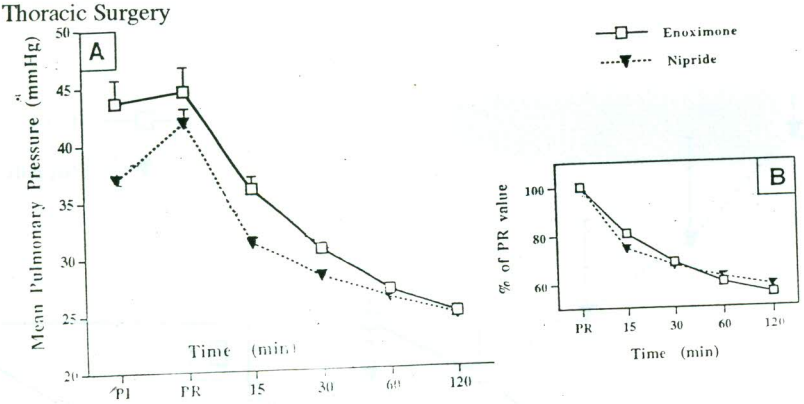


Fig. (4): Effect of tested drugs on mean pulmonary pressure
A: Actual values.
B: Perecent of the PR value.
PI: Post induction.
PP: Post replacement.

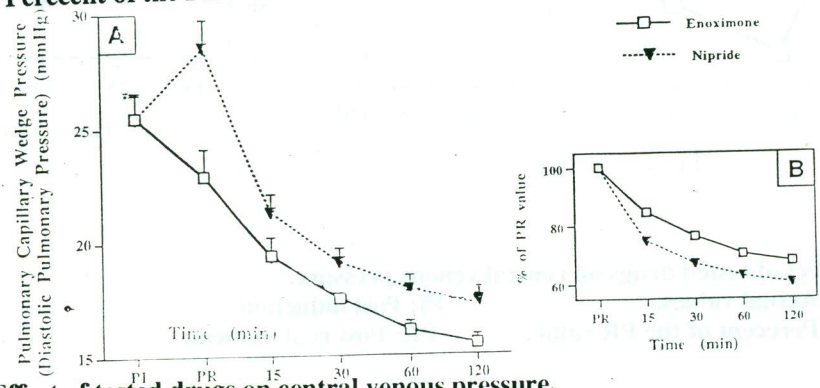


Fig.5: Effect of tested drugs on central venous pressure.
A: Actual values.
B: Perecent of the PR value.
PI: Post induction.
PR: Post replacement.

Enoximone resulted in a slight rise in mean arterial blood pressure ranged from 2-6% -15% but Nipride resulted in significant reduction in mean arterial blood pressure ranged from -12.7 to 19.4% (Table 5) (Fig 2).

The mean pulmonary pressure and pulmonary pressure and pulmonary capillary wedge pressure were reduced significantly in both groups : In group I (-19.3 -32.3%) and in group II (-25.3 -39.6%) (P<0.001) (Table 7,8) Fig 4,5).

There was a very high significant increase in augmented cardiac output (CO) and cardiac index (CI) in group I (65-100%) from the control value (P<0.0001), but the increase in CO and CI in group II was (4.8 - 28.6%) which was also significant (P<0.05) (Table 9,10) Fig.6,7).

The systemic vascular resistance was reduced in group I (-39-45.4%) (P<0.0001) and in group II (-15.7-35.1) (P<0.001) (Table 11) (Fig.8).

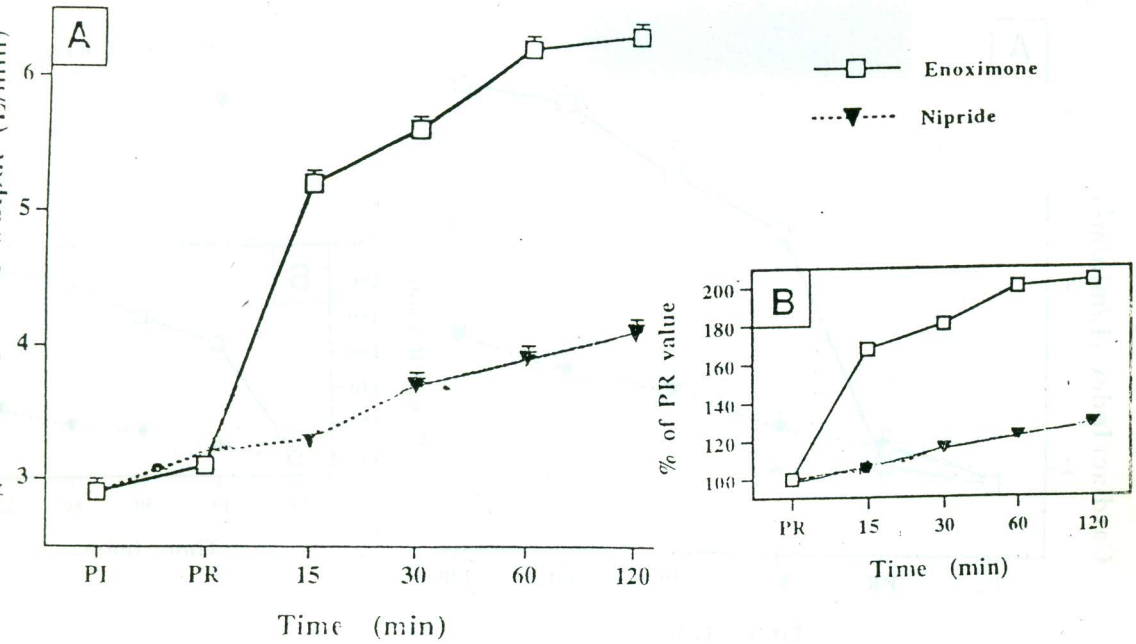


Fig.6: Effect of tested drugs on augmented cardiac output.
A: Actual values. PI: Post induction.
B: Perecent of the PR value. PR: Post replacement.

The pulmonary vascular resistance was reduced in group I (-54.2-79%) (P<0.0001) but in group II (-29-55.9%) (P<0.001) (Table 12) (Fig.9).

The stroke volume and stroke volume indeÿ were increased in group I (52.8-64.8%) which was highly significant (P<0.001) but in group II the increase in SV and SVI was less significant ranged from (-4.7+ 12%) (P<0.05) (Table 13,14) (Fig 10,11).

Following administration of drugs, there was a highly significant increase in LVSWI in group I ranged from (69.2-119.7%) (P<0.001) but on the other hand in group II LVSWI decreased by (12.1-1.4%) at the end of infusion (Table 15) (Fig.12).

In group I there was an initial rise in RVSWI to about 14.5% which declined gradually until reaches -38.2% in the 120 minutes reading, this drop was statistically significant (P<0.05). In group II RVSWI was decreased significantly from the start to the end of infusion (-34-42%) (P>0.05) (Table 16-Fig.13).

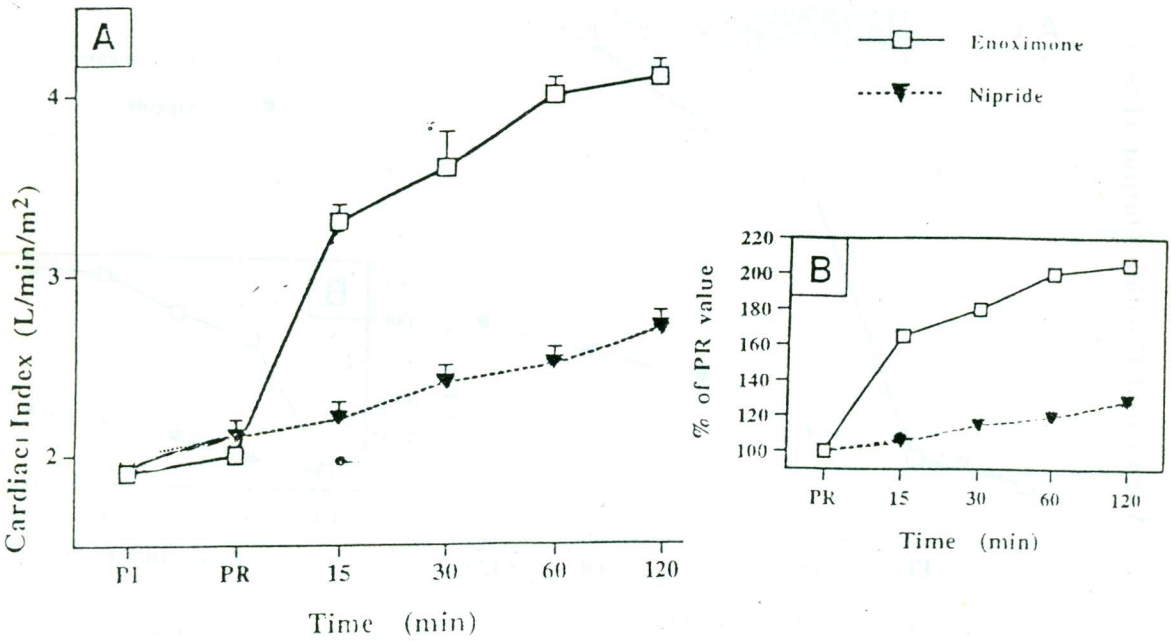


Fig.7: Effect of tested drugs on cardiac index.
A: Actual values. PI: Post induction.
B: Perecent of the PR value. PR: Post replacement.

Table 1: Details of patients demographic data, cardiopulmonary bypass time and aortic cross-clamp time.

Item	Group I (Enoximone)	Group II (Nipride)
Age (Years)	28.8 ± 2.0	30 ± 2.2
Sex (Males / Females)	11/4	9/6
Weight (Kg)	55.7 ± 3.1	55.6 ± 3.8
Height (cm)	161. ± 1.9	160.4 ± 3.1
Body surface area (m2)	1.6 ± 0.1	1.6 ± 0.1
Fractional shortening (%)	33.4 ± 1.4	33.9 ± 1.5
Ejection fraction (%)	55.3 ± 1.5	55.6 ± 2.1
Mean pulmonary pressure (mm Hg)	43.7 ± 2.0	37.0 ± 1.2
Aortic cross - clamp time (min)	50.0 ± 3.1	74.3 ± 3.0
Bypass time (min)	94.3 ± 2.3	107.7 ± 3.3

Number of patients in each group (n) is 15.
Values (excepl sex) are presented as mean ± S.E.

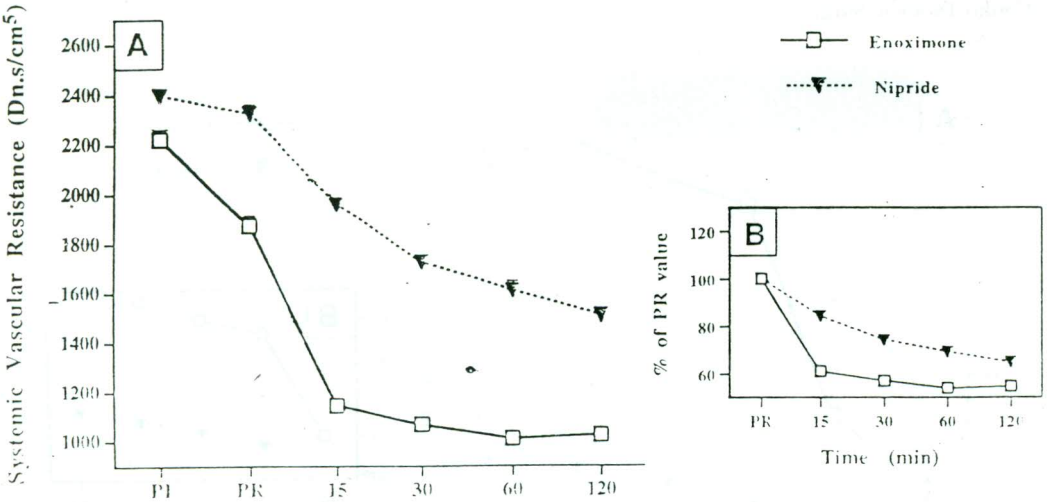


Figure (8): Effect of tested drugs on systemic vascular resistance.

A: Aetual valaes. **PI: Post induction.**

B: Percent of the PR value. **PR: Post replacement.**

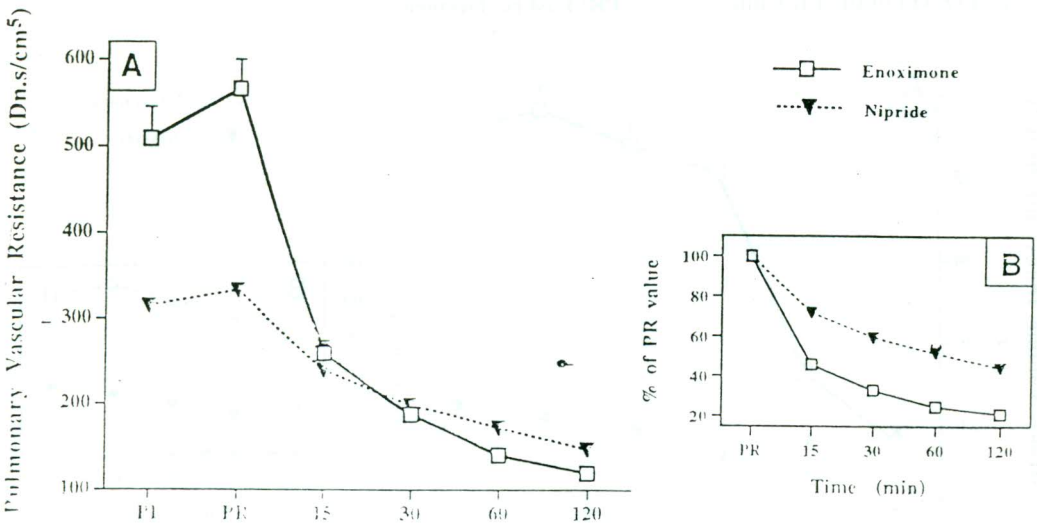


Figure (9): Effect of tested drugs on pulmonary vascular resistance.

A: Aetual valaes. **PI: Post induction.**

B: Percent of the PR value. **PR: Post replacement.**

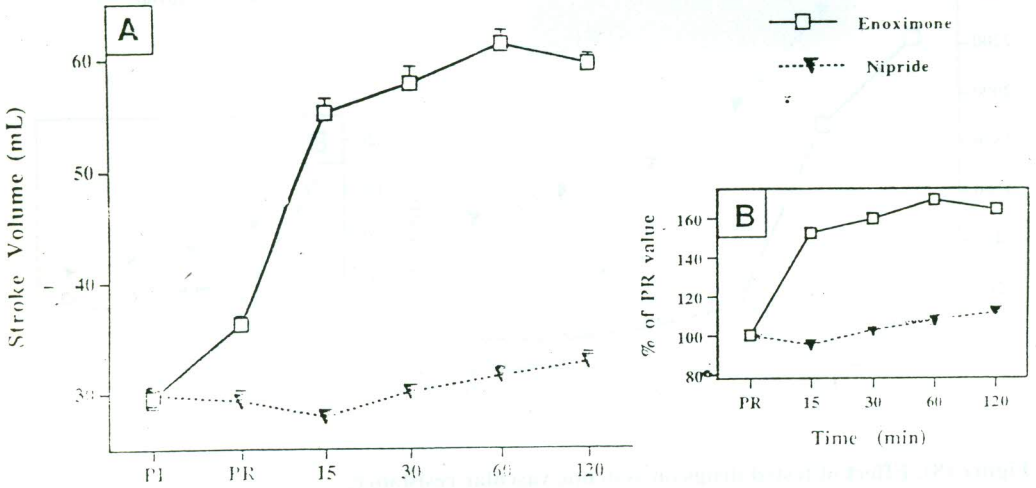


Figure (10): Effect of tested drugs on stroke voulme..
A: Aetual valaes. **PI: Post induction.**
B: Percent of the PR value. **PR: Post replacement.**

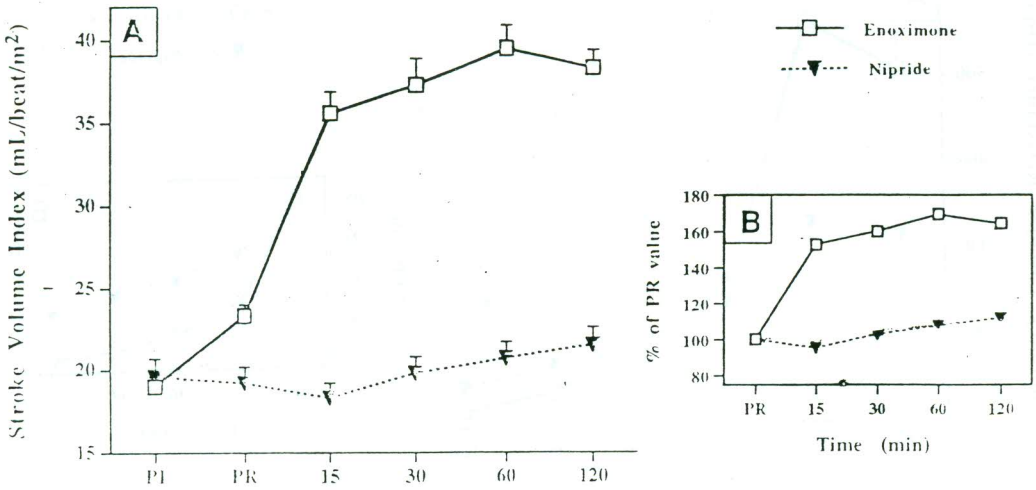


Figure (11): Effect of tested drugs on stroke voulme index.
A: Aetual valaes. **PI: Post induction.**
B: Percent of the PR value. **PR: Post replacement.**

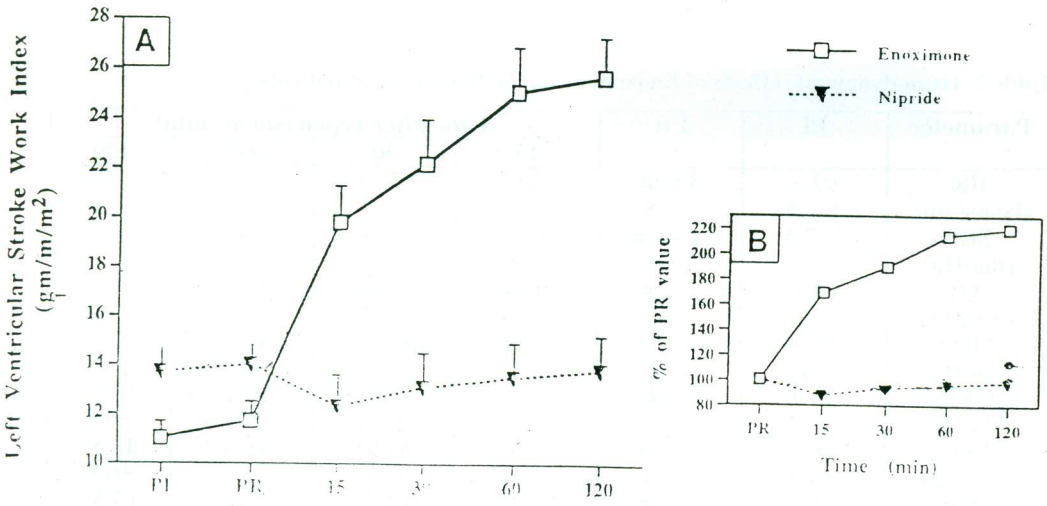


Figure (12): Effect of tested drugs on left ventricular stroke worke index.
A: Aetual valaes. **PI: Post induction.**
B: Percent of the PR value. **PR: Post replacement.**

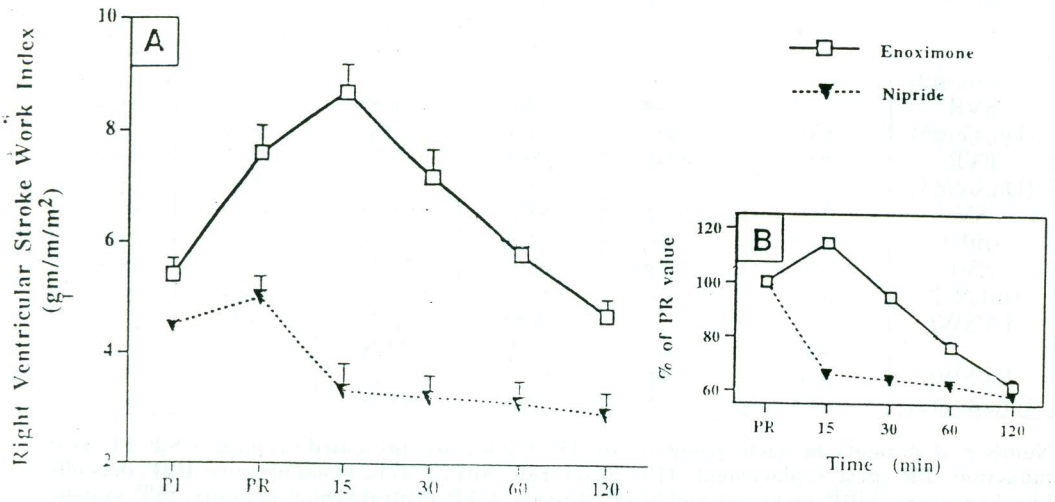


Figure (13): Effect of tested drugs on right ventricular stroke worke index.
A: Aetual valaes. **PI: Post induction.**
B: Percent of the PR value. **PR: Post replacement.**

Table 2: Hemodynammic effects of Enoximone on the first group of patients.

Parameter	PI	PR	Time after replacement (min)			
			15	30	60	120
IIR	97.3	85.5#	93.6*	97.7*	100.7*	106*
(beats/min)	± 1.5	± 1.8	±1.2	±1.3	±1.6	±1.5
SBP	117.5	104.1#	108.1	111.3*	116.6*	119.4*
(mmHg)	±1.3	±1.5	±1.6	±1.7	±1.8	±1.7
DBP	76.8	67.2#	68.4	69.8	73.2*	77.4*
(mmHg)	±1	±1.3	±0.9	±1.2	±1.1	±1.2
MBP	90.4	79.5#	81.6*	83.6*	87.7*	91.4*
(mmHg)	±1	±1.2	±1	±1.3	±1.2	±1.3
CVP	11.1	7.5#	8.2*	8.8*	10.1*	10.9*
(mmHg)	±0.4	±0.3	±0.2	±0.3	±0.3	±0.3
SPP	80	88.1#	69.3*	56.9*	48.4*	43.5*
(mmHg)	±4.3	±4.4	±2.2	±0.9	±1	±0.9
DPP	25.5	22.9#	19.4*	17.5*	16.1*	15.5*
(mmHg)	±1	±1.2	±0.8	±0.7	±0.4	±0.4
MPP	43.7	44.6	36*	30.6	26.9*	24.8*
(mmHg)	±2	±2.1	±1.1	±0.6	±0.5	±0.5
PCWP	25.5	22.9#	19.4*	17.5*	16.1*	15.5*
(mmHg)	±1	±1.2	±0.8	±0.7	±0.4	±0.4
ACO	2.9	3.1#	5.2*	5.6*	6.2*	6.3*
(L/min)	±0.1	±0.1	±0.1	±0.1	±0.1	±0.1
CI	1.9	2#	3.3*	3.6*	4*	4.1*
(L/min/m2)	±0.1	±0.1	±0.1	±0.2	±0.1	±0.1
SVR	2222	1874#	1144*	1068*	1010*	1024*
(Dn.s/em5)	±55	±41	±19	±18	±18	±14
PVR	509	566#	259*	187*	140*	119*
(Dn.s/em5)	±37	±34	±11	±6	±5	±3
SV	29.6	36.2#	55.2	57.8*	61.3*	59.5*
(mL)	±0.5	±0.8	±1.3	±1.5	±1.2	±0.9
SVI	19	23.3#	35.6*	37.3*	39.5*	38.3*
(mL/m2)	±0.6	±0.7	±1.3	±1.6	±1.4	±1.1
LVSWI	11	11.7	19.8*	22.2*	25.1*	25.7*
	±0.7	±0.8	±1.5	±1.8	±1.8	±1.6
RVSWI	5.4	7.6#	8.7*	7.2	5.8	4.7*
(gm/m/m2)	±0.3	±0.5	±0.5	±0.5	±0.3	±0.3

Number of patients in each group (n) is 15. Values are presented as mean ± S.E. PL. post induction. PR, post replacement. HR, heart rate. SBP, systolic blood plessure. DBP, diastolic blood pressure. MBP, mean arterial blood pressure. CVP, central venous pressure. SPP, systolic pulmonary pressure. DPP, diastolic palmonary pressure. MPP, mean arterial pulmonary blood pressure. PCWP, pulmonary eapillary wedge pressure. ACO augmented cardiac output. CI eadiac index. SVR systemic vascular resistance. PVR, pulmonary vascular resistance. SV, stroke volume. SVI, stroke volume index. LVSWI, left ventricular stroke work mdex. RVSWI, right ventricular stroke work index.

 # = Significant change from the corresponding PI value ($p < 0.05$).

*** = Sighnificant change from the corresponding PR value (< 0.05).**

Table 3: Hemodynammic effects of Nipride on the first group of patients.

Parameter	PI	PR	Time after replacement (min)			
			15	30	60	120
IIR	99.3	110.9#	120.3*	123.7*	123.7*	124.5*
(beats/min)	± 2.1	± 2.1	±1.6	±1.4	±1.4	±1.5
SBP	136.6	145#	119.5*	116.3*	114.7*	113.9*
(mmHg)	±1.6	±2.2	±1.4	±1.6	±1.5	±1.6
DBP	82.4	88.5#	80.9*	77.7	74.9*	72.9*
(mmHg)	±1.6	±1.5	±1.1	±1.1	±1.1	±1.2
MBP	100.5	1.7.4#	93.8*	90.6*	88.2*	86.6*
(mmHg)	±1.5	±1.6	±1	±1.3	±1.1	±1.2
CVP	12.2	13.7#	12.1*	11*	10.1*	10.1*
(mmHg)	±0.4	±0.5	±1.5	±1.4	±1.3	±1.2
SPP	60.1	68.6#	51.1*	46.4*	42.9*	39.4*
(mmHg)	±1.3	±1.5	±0.7	±0.7	±0.9	±0.9
DPP	25.5	28.2#	21.3*	19.1*	17.9*	17.2*
(mmHg)	±1.1	±1.2	±0.8	±0.7	±0.6	±0.6
MPP	37	41.9	31.2*	28.2*	26.2*	24.6*
(mmHg)	±1.2	±1.2	±0.6	±0.5	±0.6	±0.7
PCWP	25.5	28.9#	21.3*	19.1*	17.9*	17.2*
(mmHg)	±1.1	±1.2	±0.8	±0.6	±0.6	±0.6
ACO	2.9	3.2#	3.3*	3.7*	3.9*	4.1*
(L/min)	±0	±0.1	±0.1	±0.1	±0.1	±0.1
CI	1.9	2.1#	2.2*	2.4*	2.5*	2.7*
(L/min/m2)	±0.1	±0.1	±0.1	±0.1	±0.1	±0.1
SVR	2399	2326#	1961*	1728*	1612*	1510*
(Dn.s/em5)	±26	±36	±42	±34	±38	±31
PVR	315	333#	239*	189*	172*	147*
(Dn.s/em5)	±7	±10	±7	±6	±5	±5
SV	29.9	29.3#	27.9	31.1*	31.5*	32.7*
(mL)	±0.8	±1	±0.7	±0.7	±0.8	±0.9
SVI	19.6	19.2	18.3*	19.8*	20.7*	21.5*
(mL/m2)	±1.1	±1	±0.9	±1	±1	±1.1
LVSWI	13.7	14#	12.3*	13.1	13.5*	13.8*
	±1.5	±1.5	±1.3	±1.4	±1.4	±1.4
RVSWI	4.5	5#	3.3	3.3	3.2	3.1*
(gm/m/m2)	± 0.5	±0.5	±0.5	±0.5	±0.4	±0.4

Number of patients in each group (n) is 15. Values are presented as mean ± S.E. PL. post induction. PR, post replacement. HR, heart rate. SBP, systolic blood plessure. DBP, diastolic blood pressure. MBP, mean arterial bllod pressure. CVP, central venous pressure. SPP, systolic pulmonary pressure. DPP, diastolic palmonary pressure. MPP, mean arterial pulmonary blood pressure. PCWP, pulmonary eapillary wedge pressure. ACO augmented cardiac output. CI eadiac index. SVR systemic vascular resistance. PVR, pulmonary vascular resistance. SV, stroke volume. SVI, stroke volume index. LVSWI, left ventricular stroke work mdex. RVSWI, right ventricular stroke work index.

 # = Significant change from the corresponding PI value ($p < 0.05$).

*** = Sighnificant change from the corresponding PR value (< 0.05).**

Table (4): Effects of the tested drugs on heart rate (beats / min).

Drug used	PI	PR	Time after replacement			
			15	30	60	120
Enoximone [Group 1]	97.3 ±1.5	85.5 ±1.8	93.6 ±1.2	97.7 ±1.3	100.3 ±1.6	106 ±1.5
Nipride [Group2]	99.3 ±2.1	110.9 ±2.1	120.3 ±1.6	122.7 ±1.4	123.7 ±1.4	124.5 ±1.5

Number of patients in each group (n) is 15.
Values are presented in each group as mean ± S.E.
PI = POST INDUCTION PR = POST REPLACREMENT

Table (5): Effects of the tested drugs on mean arterial blood pressure (mmHg).

Drug used	PI	PR	Time after replacement			
			15	30	60	120
Enoximone [Group 1]	90.4 ±1	79.5 ±1.2	81.6 ±1	83.6 ±1.3	87.1 ±1.2	91.4 ±1.3
Nipride [Group2]	100.5 ±1.5	107.4 ±1.6	93.8 ±1	90.6 ±1.1	88.2 ±1.1	86.6 ±1.2

Number of patients in each group (n) is 15.
Values are presented in each group as mean ± S.E.
PI = POST INDUCTION PR = POST REPLACREMENT

Table (6): Effects of the tested drugs on central venous pressure (mmHg).

Drug used	PI	PR	Time after replacement			
			15	30	60	120
Enoximone [Group 1]	11.1 ±0.4	7.5 ±0.3	8.2 ±0.2	8.8 ±0.3	10.1 ±0.3	10.9 ±0.3
Nipride [Group2]	12.2 ±0.4	13.7 ±0.5	12.1 ±1.5	11 ±1.4	10.1 ±1.3	10.1 ±1.2

Number of patients in each group (n) is 15.
Values are presented in each group as mean ± S.E.
PI = POST INDUCTION PR = POST REPLACREMENT

Table (7): Effects of the tested drugs on mean pulmonary pressure (mmHg).

Drug used	PI	PR	Time after replacement			
			15	30	60	120
Enoximone [Group 1]	43.7 ± 2	44.6 ±2.1	36 ±1.1	30.6 ±0.6	26.9 ±0.5	24.8 ±0.5
Nipride [Group2]	37 ±1.2	41.9 ±1.2	31.2 ±0.6	28.2 ±0.5	26.2 ±0.6	24.6 ±0.7

Number of patients in each group (n) is 15.
Values are presented in each group as mean ± S.E.
PI = POST INDUCTION PR = POST REPLACREMENT

Table (8): Effects of the tested drugs on pulmonary capillary wedge pressure (mmHg).

Drug used	PI	PR	Time after replacement			
			15	30	60	120
Enoximone [Group 1]	25.5 ±1	22.9 ±1.2	19.4 ±0.8	17.5 ±0.7	16.1 ±0.4	15.5 ±0.4
Nipride [Group2]	25.5 ± 1.1	28.5 ±1.2	21.3 ±0.8	19.1 ±0.6	17.9 ±0.6	17.2 ±0.6

Number of patients in each group (n) is 15.
Values are presented in each group as mean ± S.E.
PI = POST INDUCTION PR = POST REPLACREMENT

Table (9): Effects of the tested drugs on augmented cardiac output (L/min.).

Drug used	PI	PR	Time after replacement			
			15	30	60	120
Enoximone [Group 1]	2.9 ± 0.1	3.1 ±0.1	5.2 ±0.1	5.6 ±0.1	6.2 ±0.1	6.3 ±0.1
Nipride [Group2]	2.9 ±0.1	3.2 ±0.1	3.3 ±0.1	3.7 ±0.1	3.9 ±0.1	4.1 ±0.1

Number of patients in each group (n) is 15.
Values are presented in each group as mean ± S.E.
PI = POST INDUCTION PR = POST REPLACREMENT

Table (10): Effects of the tested drugs on cardiac index {L/(min*m2)}.

Drug used	PI	PR	Time after replacement			
			15	30	60	120
Enoximone [Group 1]	1 9 ± 0.1	2 ± 0.1	3.3 ± 0.1	3.6 ± 0.2	4 ± 0.1	4.1 ±0.1
Nipride [Group2]	1.9 ± 0.1	2.1 ±0.1	2.2 ±0.1	2.4 ±0.1	2.5 ± 0.1	2.7 ± 0.1

Number of patients in each group (n) is 15.
Values are presented in each group as mean ± S.E.
PI = POST INDUCTION PR = POST REPLACREMENT

Table (11): Effects of the tested drugs on systemic vascular resistance (Dn.s/cm^5).

Drug used	PI	PR	Time after replacement			
			15	30	60	120
Enoximone [Group 1]	2222 ± 55	1874 ± 41	1144 ± 19	1068 ±18	1010 ±18	1024 ±14
Nipride [Group2]	2399 ± 26	2326 ± 36	1961 ± 42	1728 ± 34	1612 ± 38	1510 ± 31

Number of patients in each group (n) is 15.
Values are presented in each group as mean ± S.E.
PI = POST INDUCTION PR = POST REPLACREMENT

Table (12): Effects of the tested drugs on pulmonary vascular resistance (Dn.s/cm^5).

Drug used	PI	PR	Time after replacement			
			15	30	60	120
Enoximone [Group 1]	509 ±37	566 ±34	259 ±11	187 ± 6	140 ± 5	119 ±3
Nipride [Group2]	315 ±7	333 ±10	239 ± 7	198 ± 6	172 ±5	147 ± 5

Number of patients in each group (n) is 15.
Values are presented in each group as mean ± S.E.
PI = POST INDUCTION PR = POST REPLACREMENT

Table (13): Effects of the tested drugs on stroke volume (mL).

Drug used	PI	PR	Time after replacement			
			15	30	60	120
Enoximone [Group 1]	29.6 ± 0.5	36.2 ±0.8	55.2 ±1.3	57.8 ±1.5	61.3 ±1.2	59.3 ±0.9
Nipride [Group2]	29.9 ± 0.8	29.3 ±1	27.9 ± 0.7	30.1 ± 0.7	31.5 ±0.8	32.7 ± 0.9

Number of patients in each group (n) is 15.
Values are presented in each group as mean ± S.E.
PI = POST INDUCTION PR = POST REPLACREMENT

Table (14): Effects of the tested drugs on stroke volume index {mL/(beat*m^2)}.

Drug used	PI	PR	Time after replacement			
			15	30	60	120
Enoximone [Group 1]	19 ±0.6	23.3 ±0.7	35.6 ±1.3	37.3 ±1.6	39.5 ±1.4	38.3 ±1.1
Nipride [Group2]	19.6 ±1.1	19.2 ±1	18.3 ±0.9	19.8 ±1	20.7 ±1	21.5 ±1.1

Number of patients in each group (n) is 15.
Values are presented in each group as mean ± S.E.
PI = POST INDUCTION PR = POST REPLACREMENT

Table (15): Effects of the tested drugs on left ventricular stroke work index {gm/(min*m^2)}.

Drug used	PI	PR	Time after replacement			
			15	30	60	120
Enoximone [Group 1]	11 ±0.7	11.7 ±0.8	19.8 ±1.5	22.2 ±1.8	25.1 ±1.8	25.7 ±1.6
Nipride [Group2]	15.7 ±1.5	14 ±1.5	12.3 ±1.3	13.1 ±1.4	13.5 ±1.4	13.8 ±1.8

Number of patients in each group (n) is 15.
Values are presented in each group as mean ± S.E.
PI = POST INDUCTION PR = POST REPLACREMENT

Table (16): Effects of the tested drugs on right ventricular stroke work index {gm/(min*m^2)}.

Drug used	PI	PR	Time after replacement			
			15	30	60	120
Enoximone [Group 1]	5.4 ±0.3	7.6 ±0.5	8.7 ±0.5	7.2 ±0.5	5.8 ±0.3	4.7 ±0.3
Nipride [Group2]	4.5 ±0.5	5 ±0.5	3.3 ±0.5	3.2 ±0.4	3.1 ±0.4	2.9 ±0.4

Number of patients in each group (n) is 15.
Values are presented in each group as mean ± S.E.
PI = POST INDUCTION PR = POST REPLACREMENT

Discussion

Pulmonary hypertension poses a threat to outcome of operations for mitral valve disease. Although it was shown that an acceptable operative mortality and excellent long-term results can be obtained in patients with severe pulmonary hypertension (Camara et al., 1988 (5), right ventricular failure in the early postoperative period is not uncommon, especially in patients with impaired right ventricular function preoperatively (Camara et al, 1992).

Therapy for right ventricular failure includes the use of inotropic agents and most recently, specific pulmonary vasodilators. A number of new drugs, reported to have combined inotropic and vasodilator effects, have recently been evaluated in right ventricular failure. One such drug is enoximone, available in intravenous as well as oral forms, which has been shown to have significant inotropic and vasodilator effects (Tarr et al.,1990)(6).

Enoximone is a newly developed selective Phosphodiesterase III (PDE III) inhibitor, available already in various countries.

Selective PDE II inhibitors are a new class of drugs that selectively inhibiting PDE III enzyme activity and thereby inhibiting the degradation of intracellular CAMP. These class of drugs has been developed as an alternative or synergistic therapeutic tool in management of congestive heart failure. It has been termed inodilators due to its inotropic and vasodilating properties (Boldt et al., 1989)(7).

Amrinone was the first available drug of this new class of cardiotonic compounds.

However, its inotropic quality has been questioned and its beneficial effects in patients with congestive heart failure was speculated to result from peripheral vasodilation alone. Moreover, amrinone has been associated with severe side effects, such as thrombocytopenia, even after single

dose (Grossman et al., 1992) (8). This limits its clinical use in cardiac surgery, where extracorporporeal circulation may already embarrass hemostasis.

Recently, Tarr et al. (1990), (6) reported the efficacy of enoximone in the management of low cardiac output state following cardiac surgery and concluded that enoximone in comparison to other inotropic agents, fulfills the requirements of hemodynamic support of patients to be weaned from cardiopulmonary bypass in terms of magnitude and duration of effects.

In the present study, it was found that intravenous administration of enoximone in the mentioned dose regimen resulted in a significant improvement in ventricular function reflected by a significant increase in CO, CI ($P<0.001$), SV, SVI ($P<0.001$), a significant reduction in MPAP and PCWP ($P<0.001$), reduction in SVR ($P<0.001$) and PVR ($P<0.0001$).

These improvements was associated with very slight increase in HR ($P<0.05$). Similar hemodynamic effects of enoximone have been reported by Tarr et al., (6) 1992, Vincent et al., 1988 (9), and many others.

The drug used in group II was Nitroprusside, a well known direct acting vasodilator that is used for controlled hypotension.

Following administration of nitroprusside there was a reduction of MAP by 19.4% at the end of infusion with concomitant reduction in MPP by 39.6% in the same reading. There was also a reduction in C.V.P., PCWp, LVSWI and RVSWI ($P<0.05$). The effect of nitroprusside on SVR and PVR was very significant $P<0.001$ with a significant increase HR, CO and CI ($P<0.05$). The dose of nitroprusside used in this study was 1-2 ug/kg/min, and all patients of this group , a higher dose of nitroprusside was not given because the peak dose resulted in significant decline in arterial blood pressure. The results of this study were comparable with the results of Installe et al., 1987 (10) Amin et al.1985(11) and many other investigators.

Intravenous nitroprusside is the most commonly used vasodilator to treat acute severe low-Co states since it acts rapidly and has a balanced effect, dilating both arterioles and veins (Kaptan et al.,1993) (12). The hemodynamic effects of nitroprusside in congestive heart failure are characterized by significant increases in CO and SV along with decreases in PVR, PCWP, C.V.P., SVR Aand PVR.

Amin et al., 1985 (11) compared the effects of intravenous sodium nitroprusside and enoximone in refractory congestive heart ffailure and concluded that while both sodium nitroprusside and enoximone produced salutary acute hemodynamic effects, certain differences were noted. Thus enoximone compared to nitroprusside produced a higher increase in cardiac index (3.3 ± 0.5 vs 2.6 ± 0.4 L/min/m^2, $P>0.05$), stroke volume index (39 ± 9 vs 32 ± 7 ml/beat/m^2, $P>0.05$_, stroke work index (31 ± 17 vs 24 ± 10 mg-m/m^2, $P>0.05$) and mean arterial pressure (75 ± 16 vs 69 ± 14 mmHg, $P>0.01$). These differences in pump function were noted despite reduction of SVR to comparable levels (956 ± 235 vs 1118 ± 306 dynes-sec-cm^{-5}, p=NS). There were no significant differences between nitroprusside and enoximone with respect to changes produced in PCWP, CVP, PAP, SVR or PVR, and arteriovenous oxygen differences (Amin et al., 1985) (11).

In this study.,inotropic support of 4 patients was needed in this group, one patient received adrenaline 0.05 ug/kg/min and 3 patients received dobutrex 5 ug/kg/min to combat the drop of systemic blood pressure and for further support of the myocardial functions.

Conclusion

It was concluded that enoximone in dose of 0.5 mg/kg as a single intravenous bolus dose followed by an infusion of 10 ug/kg/min produces favorable responses and can be a clinically useful drug to enable weaning from cardiopulmonary bypass in those patients who require pharmacological support. Through its inotropic and vasodilator effects, it is preferable than other drugs because it reduces left ventricular filling pressure (preload) as well as pulmonary and systemic vascular resistance (after load). At the same time, it produces a significant and sustained increase in cardiac output and cardiac index.

It was also concluded that low dose infusion of nitroprusside results in beneficial effects on hemodynamics as a result of an increase in cardiac index mainly through pulmonary vasodilation, but in some cases additional inotropic therapy is often necessary. Nitroprusside in doses of 1 mg/kg/min is effective in reducing pulmonary artery pressure and improving myocardial functions. It is especially of value in patients with severe systemic hypertension.

REFERENCES

1. Camara ML, Aris A, Paro JM, Alvures J, and Caralps JM. (1992): Hemodynamic effects of prostaglandin E, and isoproterenol early after cardiac operations for mitral stenosis. J.Thorac. Cardiovasc. Surg. 6, 103:1177-1185, 1992.
2. Flaherty JT, Magee PA, Gardner TL, Potter A, McAlister NP (1982): Comparison of intravenous nitroglycerin and Sodium nitroprusside for treatment of hypertension developed after coronary bypass surgery. Circulation 65:1072-1081, 1982.
3. Braunwald E. (1992): Valvular Heart Disease in Braunwald Heart Disease 4 th ed pp:1007-1077, 1992.
4. Dage RC, Kariya T, Hsieh CP, Roebel LE, Cheng HC, Schmettler RA and Grisar M. (1987): Pharmacology of Enoximone. Am.J. Cardiol, 60:10c-14c, 1987.
5. Camara ML, Aris A, Paro, JM, Caraps JM. (1988): Long term results of mitral valve surgery in patients with severe pulmonary hypertension. Ann. Thorac. Surg., 45:133-136, 1988.
6. Tarr TJ, Jeffrey RR, Kent AP, Cown ME (1990): Use of Enoximone in weaning from cardiopulmonary bypass following mitral valve surgery. Cardiology 77 (suppl 3): 51-57, 1990.
7. Boldt J, Dieterich A, Kling D. (1989): Hemodynamic effects of enoximone in cardiac surgery patients. J. Cardiovasc. Pharmacol 14 (Supp I) : 550, 1989.
8. Grossman W, Braunwald E. (1992): Pulmonary Hypertension in Braunwald Heart Disease 4 th ed. pp:790-816, 1992.

9. Vincent JL, Carlier E, Berre J, Armistead C, Kahan RJ, Coussaert E, and Cantraine F.(1988): Administration on Enoximone in cardiogenic shock. Am. J. Cardiol., 1:419-423, 1988.

10. Installe E, Gonzalez M, Jacquemart JL, Collard P, Roultte F, Pourbaix S, and Tremouroux J (1987) : Comparative effects on hemodynamics of enoximone (MDL 17 - 043), Dobutamine and Nitroprusside in severe congestive heart failure. Am.J. Cardiol, 60:46c-52c, 1987.

11. Amin DK, Shah PK, Hulse S, and Shellock F.(1985): Comparative acute hemodynamic effects of intravenous sodium nitroprusside and MDL-17, 043, a new inotropic drug with vasodilator effects in refractory congestive heart failure. Am. Heart.J. 109:1006, 1985.

Does Topical Application of Vancomycin and Povidone-Iodine Reduce Sternal Wound Infection?

ABSTRACT

In a prospective study of 474 patients having cardiac operations performed through a median sternotomy incision, topical vancomycin was applied to the cut sternal edges in 179 patients (group V), while povidone iodine was topically applied in 166 patients (group P). These two group were compared with a non treated control group (group C) that involved 129 patients. All patients received prophylactic systemic antibiotics for 3 days. Sternal infection occurred in 2 patients in group V (1.1%), 3 patients in group P (1.8%) and in 7 patients in the control group (5.4%). Male sex, lack of topical vancomycin or povidone iodine and repeat operation were positively correlated with sternal infection. Staphylococcus species was the most common organism cultured from our patients (9 out of 12 patients i.e 75%).

We concluded that topical application of vancomycin or povidone iodine to the cut sternal edges reduces the risk of post operative sternal infection.

Mohamoud A. El-Batawy M.D., Ehab A. Wahby M.D.* A. Frigiola M.D.**, L.Menicanti M.D.**

J. of Egypt. Society of Cardiothorac. Surg. 1996, Vol. IV September No 4

INTRODUCTION

Sternal or mediastinal infection after cardiac surgery occurs infrequently but carries a high cost in money, morbidity and mortality (1). The biology of wound infection is an interaction between factors of local and systemic host resistance and bacterial contamination. Host resistance is decreased locally by devascularizition of the tissues, frank tissue destruction by electrocautery and the presence of foreign material such as bone wax (2). Systemic factors contributing to local wound infections include lowering of host resistance by factors such as age, diabetes, poor nutritional status and exogenous steroids (3).

The aim of this work is to study the effect of topical application of vancomycin and povidone iodine to the cut sternal edges on the incidence of sternal infection .

Cardiothoracic Surgery Departments at Cairo and Tanta Universities, and San Donato Hospital in Milano, Italy***

Patients and Methods

The material of the present study included 474 patients who had heart operations performed through a median sternotomy incision in San Donato hospital, Milano, Italy, Except for emergency operations, patients were shaved the night before the operation. All patients received preoperative systemic antibiotics (Cefamandol 1gm I.V. every 6 hours) that were continued for 72 hours post-operatively. Patients were divided into two groups according to the material topically applied to the cut edges of the sternum before inserting the sternal retractor. Group (V) included 179 patients where 500 mg Vancomycin hydrochloride dissolved in 10 ccs distilled water was applied over a gauze on the sternal edges, and group (P) that involved 166 patients where a gauze soaked in povidone iodine was applied to the sternal edges.

Table (1) : Patients characteristics in the 3 groups.

	Group V N = 179	Group P N = 166	Group C N = 129	Probability
Age	58.5	59.2	58.7	N.S
Sex (male)	128(71.5%)	116(72.5%)	90(69.8%)	N.S
Operation time (min)	260.3	256	249	N.S
lung infection	5(2.8%)	4(2.4%)	3(2.3%)	N.S
Urinary tract infection	8(4.5%)	8(4.8%)	5(3.8%)	N.S
leg infection	1(0.6%)	2(1.2%)	1(0.8%)	N.S
diabetes	40(22.3%)	42(25.3%)	26(20.1%)	N.S
CABG	138(77%)	130(78.3%)	104(80.6%)	N.S
Internal mammary artery	122(68%)	118(71%)	90(69.8%)	N.S
Repeat operation	21(11.7%)	20(12%)	8(6.2%)	0.01
Sternal/mediastinal infection	2(1.1%)	3(1.8%)	7(5.4%)	0.02
Mortality	3(1.7%)	2(1.2%)	1(0.8%)	N.S

C.A.B.G. : Coronary artery bypass grafting

N.S. : Not significant

Wounds were assessed daily after operation and rechecked after one month. Late infections were included in the results. Infections were graded as superficial (necessitating only opening of the skin incision) and sternal or mediastinal that necessitated a major reoperation).

Closed irrigation was used for treating most patients (11 patients) where the devitalized sternal edges and soft tissues were debrided and closed over an irrigation system consisting of 16 F red rubber catheter and a retrosternal chest tube. Bacitracin and neomycin solution irrigation

was introduced until the irrigation effluent was sterile for a minimum of 3 consecutive days. Intravenous antibiotics were administered for 2-3 weeks. In one critically ill patient the wound was more radically debrided and left open, with dressing changes three times daily. Subsequent soft tissue closure using pectoralis muscle flap was done in collaboration with the plastic surgeon.

The following variables were recorded: age, sex, operation, operative time, use of topical vancomycin and povidone iodine, the presence of concomitant infection (lung, urinary tract or leg incision), use of internal mammary graft, previous heart operation necessitating repeat operation, diabetes and the outcome. Discontinuous variables were compared with Fisher's exact test and continuous variables with a T test.

Results

As shown in table (1) the characteristics of the patients treated with topical vancomycin, povidone-iodine and those in the control group were indistinguishable except that repeat operations were more prevalent in the treated groups (11.7% and 12% in the treated groups versus 6.2% in the control group).

Table (II): reveals the infection percentages among discontinuous variables

Variable	No. Infected	Percent infected	Probability
Male (sex)	10/334	3%	0.05
Female	2/140	1.4%	
Diabetics	3/108	2.8%	0.15
Non diabetic	9/366	2.4	
Topical vancomycin	2/179	1.1%	0.02
Topical povidone iodine	3/166	1.8%	0.03
Non treated group	7/129	5.4%	
Repeat operation	4/49	8.1%	0.04
First operation	8/425	1.9%	
Internal mammary artery graft use	9/330	2.7%	0.10
No internal mammary artery graft use	3/144	2%	

Also, the rate of sternal or mediastinal infection was higher in the control group than in the treated groups (5.4% versus 1.1% and 1.8% respectively).

The overall incidence of sternal infection in our study was 2.5% (12 patients out of 474).

The overall hospital mortality rate was 1.3% (6 out of 474 patients).

The etiologic micro-organism in the majority of infections (9 patients 75%) was a member of the staphylococcus species.

Staphylococcus epidermidis was responsible in 7 patients while staph, aureus in 2 patients. Pseudomonas and Enterobacteriaceae were the causative agents in the remaining 3 patients (25%). No complications were observed from topical use of vancomycin or povidone iodine.

Discussion

The incidence of mediastinal infection after median sternotomy has been reported to range from 0.4 to 5.1% with wide variance within these limits (4). Cartain medical conditions put the patient at increased risk for mediastinal infection include chronic obstructive pulmonary disease, obesity, diabetes mellitus, chronic debilitative state and long term corticosteroid therapy (5). Inadequate use of preoperative antibiotics, inporoper aseptic skin preparation in the operating room and prolonged cardiopulmonary bypass are predisposing operative factors (6). In the post operative period, the need for closed chest cardiac resuscitation, re-exploration for bleeding, the development of low cardiac output state with long periods of hypotension, prolonged mechanical ventilation, the necessity for tracheostomy and the development of pneumonia has been associated with increased incidence of sternal and mediastinal infection (7).

Little information is available about the use of topical antibiotics with median sternotomies. However, both animal experiments and clinical trials in non-cardiac operations revealed over-whelming evidence of reduced rates of infection with the use of topical antibiotics.

Randomized prospective studies by groups headed by Noon (8) (gastrointestmal perforations), Mountain (9) (appendectomies), Stone (10) (contaminated emergency laparotomies), Pitt (11) (high risk biliary surgery) and Evans (12) (contaminated wounds) all showed a decreased rate of infection with the use of topical antibiotics. Heisterkamp and colleagues (13) also reported a reduced infection rate with topical antibiotic use in Vietnam war wounds.

Again Halasz (14) mentioned that topical antibiotics especially in a dry or powdered form achieve much higher local wound concentrations than do systemic antibiotics and this high concentration persists for several hours after closure of the incision.

The overall incidence of sternal infection among our patients was 2.5% (12 patients out of 474). However, the study demonstrated that the prevalence of sternal infection was reduced by topical application of vancomycin to 1.1% and Povidone-iodine to 1.8% versus the non treated group

(5.4%). In comparing the infected group with the non infected group (table II), it reveals that male sex, lack of topical vancomycin or povidone-iodine and repeat operation were positively correlated with infection. However, sternal infection was just shy of statistical correlation with diabetes ($p = 0.15$) and internal mammary artery use ($p = 0.10$).

In a similar study made by Vander Salm et al.1 vancomycin was applied in a hemostatic paste of topical thrombin and powdered absorbable gelatin to the cut sternal edges. They reported a significant reduction in the incidence of sternal infection in the treated group (0.45%) versus the non treated group (3.6%). They concluded that topical vancomycin and shorter operative time independently predicted reduced infection rates.

Internal mammary artery use was not a significant risk factor in sternal infection in our study ($P = 0.10$). This may be explained by our meticulous pin point electrocautery use on the wound. This is in agreement with the study made by loop et al. (15), who reported a low infection rate of 1% in patients with vein grafts versus 0.9% in patients with a single internal mammary artery graft, and 1.7% when bilateral internal mammary artery grafts were used.

However, Grossi et al (3) demonstrated a significant increase in the incidence of sternal infection with internal mammary artery grafts increasing from a frequency of 0.8% without I.M.A. grafts to a frequency of more than 11% in diabetic patients with double I.M.A. grafts. This was attributed to the degree of devascularization of the sternum and local tissue destruction produced during I.M.A. harvesting and extensive use of the electrocautery. He also stated that the pedicle width and method of sternal wire placement are other contributing factors.

The results obtained by topical application of vancomycin and povidone iodine were nearly identical. Each of these substances has reduced the incidence of sternal infection to a minimum (1.1% and 1.8% respectively) when added to the cut sternal edges. No complications were observed from their topical use.

Although these results must not be constructed as allowing laxity in sterile technique, reduced operating room traffic and optimum air flow patterns in the operating room or elimination of systemic antibiotics, they do show an incremental adventage to their topical use.

Due to the relative high cost of vancomycin, we recommend the topical use of povidone-iodine especially in a country like ours.

REFERENCES

1. Vander Salm T.J.; Okike O.N.; Pasque M.K.; Pezzella A.T.; Lew R.; Traina V. and Mathieu R.: Reduction of sternal infection by application of topical vancomycin. J.Thorac Cardiovasc Surg. 1989; 98:618-622.

2. Galbut D.L.; Traad E.A.; Dorman M.J. et al.: Seventeen years experience with bilateral internal mammary artery grafts. Ann. Thorac. Surg. 1990; 49:195-201.

3. Grossi E.A.; Esposito R.; Harris L.J.; Crooke G.A.; Galloway A.C.; Colvin S.B.; Culliford A.T., Baumann F.G.; Kathy Yao B.A. and Spencer F.C.: Sternal wound infections and use of internal mammary artery grafts. J. Thorac. Cardiovasc Surg. 1991; 102:342-347.

4. Hugo N.E.; Sultan M.R.; Ascherman J.A.; Patsis M.C.; Smith C.R. and Rose E.A.: Single stage management of 74 consecutive sternal wound complications with pectoralis major myocutaneous advancement flap. Plastic Reconster. Surg 1994; 93:1433-1441.

5. Miller J.I. and Nahai F.: Repair of the dehisced median sternotomy incision. Surgical Clinics of North America 1989; 69:No 5 Pag. 1091.

6. Starr M.G.; Gott V.L. and Townsend T.R. Mediastinal infection after cardiac surgery. Ann. Thorac Surg. 1984; 38:415.

7. Fairchild P.G. and Gantz N.N.: Mediastinal and sternal infections. Cardiac Surgery; State of Art Rev. 2; 407, 1988.

8. Noon G.P.; Beal A.C Jr; Jordan G.L. Jr; Riggs S., DeBakey M.E.: Clinical evaluation of peritoneal irrigation with antibiotic solution. Surgery 1967; 62:63-78.

9. Mountain J.C. and Seal P.V.: Topical ampicillin in grid-iron appendicectomy wounds. Br J. Clin. Pract. 1970; 24:111-115.

10. Stone H.H.; Hester T.R. Jr: Incisional and peritoneal infection after emergency celiotomy. Ann Surg. 1973; 177:669-678.

11. Pitt H.A.; Postier R.G.; Gadacz T.R.; Cameron J.L.: The role of topical antibiotics in high risk biliary surgery. Surgery 1982; 91:518-524.

12. Evans C.; Pollock A.V.; Rosenberg I.L: The reduction of surgical wound infections by topical cephaloridine; a controlled clinical trial. Br. J. Surg. 1974; 61:133.

13. Heisterkamp C. III; Vernick J.; Simmons R.L.; Matsmoto T.: Topical antibiotics in war wounds; a re-evaluation. Milit Med. 1969; 13-18.

14. Halasz N.A.: Wound infection and topical antibiotics. The surgeon's dilemma. arch Surg. 1977; 112:1240-1244.

15. Loop F.D.; Lytle B.W.; Cosgrove D.M. et al.: Sternal wound complications after isolated coronary artery bypass grafting : early and late mortality, morbidity and cost of care. Ann. Thorac. Surg., 1990; 49:179-187.

Comparative Study of Four Different Thromboplastins in Monitoring of Oral Anticoagulant Therapy

ABSTRACT

Plasma samples from 326 patients with cardiac valves prostheses on oral anticoagulant treatment, coming to the National Heart Institute for oral anticoagulant monitoring were submitted to quadriple PT ratio and INR value determination, using four commercial thromboplastin reagents with variable ISI values. We studied if the application of the INR system can reduce the variability of the PT ratios obtained with the different thromboplastins used.

Results : For the PT ratio, there was a marked variation in the percentage of patients in each group of anticoagulation between the four thromboplastins used, especially with sub and supratherapeutic group of anticoagulation. 45.4% in the supratherapeutic group with the reagent of low ISI value and from 0.6% to 11.3% with the three reagents of high ISI value. 23.6% in the supratherapeutic group with the reagent of low ISI value and from 51.8% to 62.9% with the three reagents of high ISI value. Applying the INR system made the percentage of patients in each group of anticoagulation closer between the four thromboplastins.

For each sample separately, there was still a discordance of INR values obtained between the reagent of low ISI value and each thromboplastin with high ISI value with variable extent.

Conclusion : The high ISI value of a commercial thromboplastin can influence the INR value obtained, with variable discordance rates between the results obtained with a thromboplastin of low ISI value (near to 1) and those with high ISI values (> 1.5). So using a sensitive thromboplastin with low ISI value in monitoring oral anticoagulant therapy is preferred to obtain precise and accurate INR over a wide range, although it might be more expensive

Azza Abdel Monem Mansy, MD.

J. of Egypt. Society of Cardio thorac. Surg. 1996, Vol. IV September No 4

INTRODUCTION

Oral anticoagulants are widely used for prophylaxis and treatment of venous thrombosis and in the prevention of embolic arterial episodes particularly in relation to mitral valve disease and prostheses. Oral anticoagulants antagonise the action of vitamin K, by inhibiting the production in the liver of four procoagulant clotting factors (II, VII, IX and X), they also depress the blood concentration of protein C which with its cofactor protein S has an anticoagulant action.

Oral anticoagulant treatment must be regularly and frequently controlled by laboratory tests to ensure adequacy of treatment without over- anticoagulation since the anticoagulant response to fixed doses varies among individuals (1&2).

The prothrombin time is the most popular method of laboratory control and is still the most extensively used since it is

National Heart Institute, Imbaba, Cairo Egypt

responsive to a reduction of three vitamin K-dependent clotting factors (II, VII and X). The lack of standardisation of its methodology, particularly in relation to the type of thromboplastin reagents vary in their responsiveness to warfarin induced reduction in clotting factors, a variability that depends on their method of preparation (3).

There are different methods of expression of prothrombin time results e.g. the prothrombin time in seconds, the prothrombin concentration from dilution curves in percentage, the prothrombin ratio (the prothrombin time of the patient : the prothrombin time of the control).

As a result, divergent results may be obtained for the same plasma sample depending on the thromboplastin reagent used, this may lead to inappropriate anticoagulant monitoring (4).

The need to standardize reporting of PT results obtained from thromboplastins of varying sensitivities led to the development of the INR (international normalized ratio).

The INR was approved by the Expert Committee on Biological Standardization of the World Health Organization (WHO) 1983, to provide more uniform, safer and more effective anticoagulant therapy.

The INR corrects the PT ratios obtained with different thromboplastins with different degrees of responsiveness to the warfarin -induced vitamin. K coagulation factors deficiency by converting the PT ratio observed with a local thromboplastin to a reference standard thromboplastin.

I SI

INR = (observed PT ratio)

ISI : the international sensitivity index for the thromboplastin used . The INR is the PT ratio which should be obtained if the international reference thromboplastin was used. The lower the lSl, the more sensitive the reagent and the closer the derived INR to the observed PT ratio references.

Materials and Methods

Plasma samples :

This study was done in the Haemostasis laboratory at the National Heart Institute, Imbaba.

Control plasma samples were obtained from 12 healthy adults males and females receiving no medications, with no history of bleeding of thrombotic problems to be used as a pool.

Plasma samples from 326 patients on warfarin therapy for more than 6 weeks with different degrees of anticoagulation, coming monthly for regular oral anticoagulant monitoring, all having cardiac prostheses after valve replacement. We excluded patients receiving recent anticoagulant treatment (less than 4 weeks) and patients with frequent dose adjustment.

The plasmas were obtained from specimens submitted to the Haemostasis laboratory for routine prothrombin time testing .

Samples for control and patient plasma were routinely collected by drawing 1.8 ml blood by clean venipuncture into a glass tube containing 0.2 ml sodium citrate 3.8%. The blood was centrifuged at 1000 g for 10 minutes and the PT testing was performed on the platelet poor plasma (PPP) obtained within four hours of blood collection .

Thromboplastin reagents :

The four thromboplastin reagents used in this study are referred to as reagents A,B,C,D. Reagent A (lot no. 505609) human placental thromboplastin calcium chloride, ISI: 1.1. Reagent B (lot no. 3005.22B1) rabbit brain thromboplastin with calcium chloride, ISI: 1.77.Reagent C (lot no. 280684/686124) rabbit brain thromboplastin with calcium chloride, ISI:2.15 Reagent D (est no. 6148) rabbit brain thromboplastin with calcium chloride , ISI .

All measurements were performed using the four thromboplastin reagents. A single lot of each reagent was used throughout the study period.

Prothrombin time and INR determination

Prothrombin time for both plasma control and patient samples were determined on a ST 888 ball coagulometer (STAGO, FRANCE), according to the manufacturers' instructions, we have used the same instrument throughout the study, to exclude instrument- thromboplastin ISI relationship.

The PT is measured by adding a thromboplastin reagent to a citrated plasma and recording the time for clotting to occur after recalcification. The geometric mean PT of the 12 haemostatically normal persons was 12.1 seconds for reagent A, 12.2 seconds for reagent B, 12.8 seconds for reagent C, 14.2 seconds for reagent D.

The geometric mean = the sum of the 12 PT determinations in seconds divided by 12.. The PT ratio was calculated by dividing the patient' PT in seconds by the geometric mean of the pool in seconds.

The PT ratios were converted to INR by raising the PT ratio to the power of the thromboplastins' ISI given by the manufacturer corresponding to the instrument used for each reagent used.

To allow the comparison between reagents, quadriple PT determination were performed on each sample using the four reagents.

Statistical analysis

Two regression lines representing the INR/INR plot and the INR/PT ratio were plotted for each thromboplastin . The discordance rate was defined as the number of samples giving one INR value out of the defined therapeutic range with one reagent and an INR value in the therapeutic range with the other reagent divided by the total number of samples with at least one INR in the therapeutic range with the two reagents in comparison .

Results

Comparison of the PT ratio and corresponding INR for each thromboplastin separately :

Reagent A:

The regression lines representing the INR/INR plot and INR/PT ratio plot, were very near to each other with a perfect correlation (slope = 0.838) fig. (1). (that is with the sensitive thromboplastin the PT ratio was very close to the INR value).

Reagent B:

The regression lines representing the INR / INR plot and the INR / PT ratio plot showed considerable divergence (slope = 0.283) fig.(3).

Reagent D:

The regression lines representing the INR / INR plot and the INR / PT ratio plot showed considerable divergence (slope = 0.268) fig.(4).

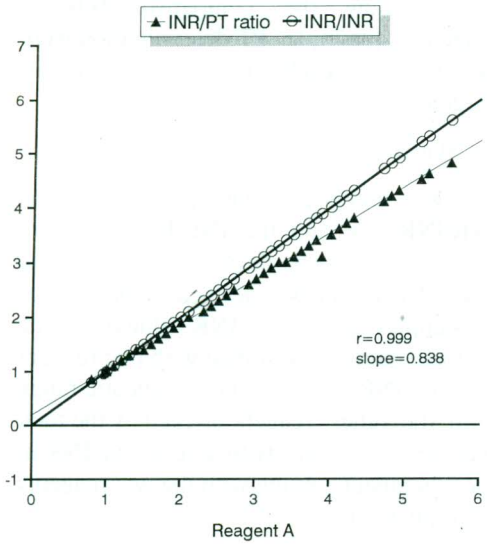


Figure 1: Correlation between PT ratio and INR with reagent A

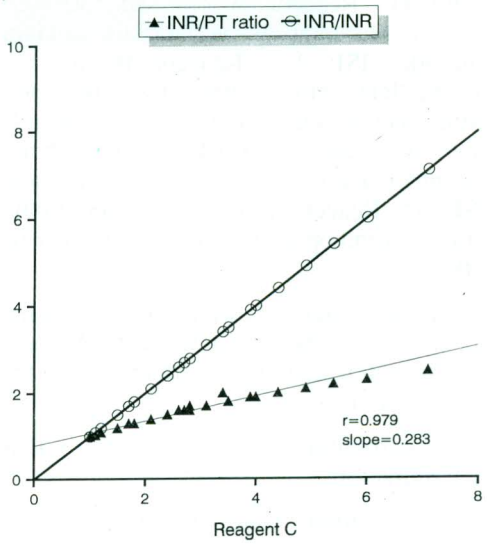


figure 3: Correlation between PT ratio and INR with reagent C

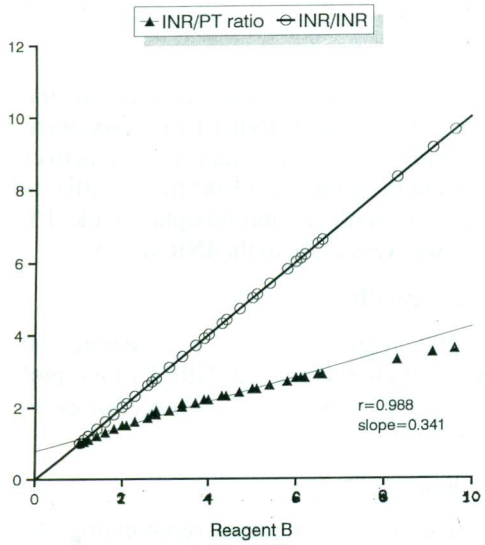


Fig.2:

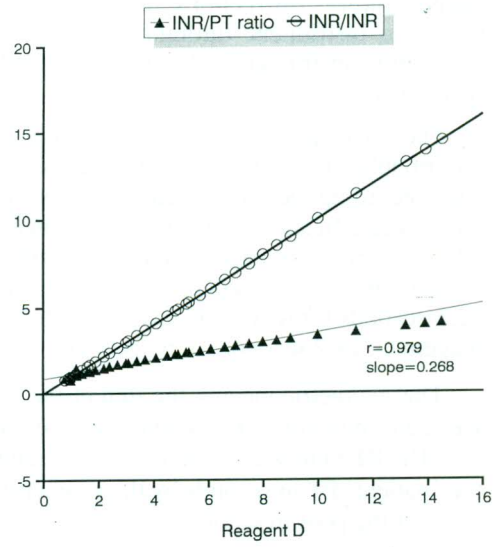


figure 4: Correlation between PT ratio and INR with reagent D

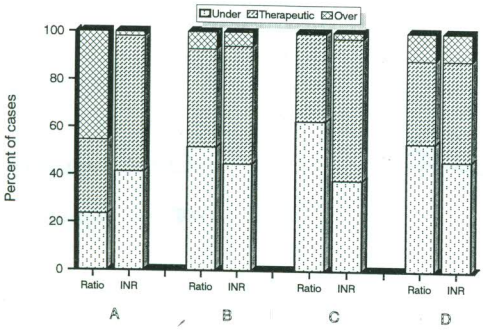


Figure 5: The effect of INR application in minimizing the difference in the percentage of patients in each group of anticoagulation between the four reagents.

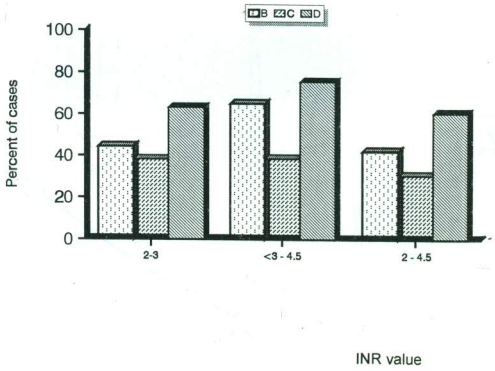


Figure 6: INR discordance rate in relation to reagent A.

Table1: Classification of PT ratio as subtherapeutic, therapeutic (low and high intensity), supratherapeutic.

PT ratio	Reagent A	Reagent B	Reagent C	Reagent D
Sub 1 - 1.5	23.6	51.8	62.9	53.7
Therapeutic >1.5 - 2.2	31.0	41.1	36.5	34.0
Supra > 2.2	45.4	07.1	00.6	11.3

shows the percentage of patients in each group of anticoagulation with the four reagents according to the PT ratio

Table 2: Classification of INR values as subtherapeutic, therapeutic (low and high intensity) and supratherapeutic.

INR value	Reagent A	Reagent B	Reagent C	Reagent D
Sub 1- 2	41.1	44.8	38.0	46.3
Therapeutic >2 - 4.5	56.7	49.4	59.5	42.3
Supra > 4.5	01.8	05.8	02.5	11.4

shows the percentage of patients in each group of anticoagulation with the four reagents according to the INR value

With reagents B,C and D, the values of the PT ratio were considerably lower than the INR values especially with increasing degree of anticoagulation.

Classification of PT ratio as subtherapeutic, therapeutic (low and high intensity), supratherapeutic (table 1):

Reagent A:

23.6% of our patient population had subtherapeutic PT ratio values, 31% had therapeutic PT ratio values and 45.4% of had supratherapeutic PT ratio values.

Most of the patients were in the supratherapeutic group.

Reagent B:

51.8% had subtherapeutic PT ratio values, 41.1% had therapeutic PT ratio values and 7.1% had supratherapeutic PT ratio values.

Most of the patients were in the subtherapeutic group .

Reagent C:

62.9% had subtherapeutic PT ratio values, 36.5% had therapeutic PT ratio values and 0.6% had supratherapeutic PT ratio values. Most of the patients were in the subtherapeutic group.

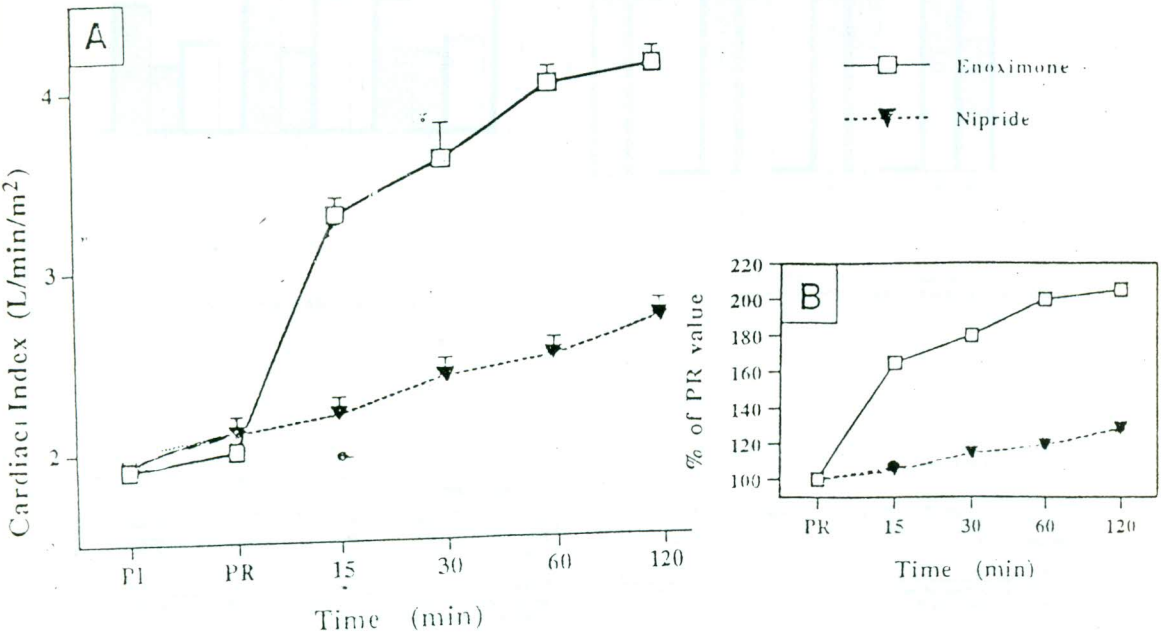


Figure (7) : Effect of tested drugs on cardiac index.
A: Actual values.
B: Percent of the PR value.
PI: Post induction.
PR: Post replacement.

Reagent D:

53.7% had subtherapeutic PT ratio values, 34.0% had therapeutic PT ratio values and 11.3% had supratherapeutic PT ratio values. Most of the patients were in the subtherapeutic group . There was a marked variation between the four thromboplastins in the percentage of patients in the suptherapeutic and the supratherapeutic PT ratio groups.

Classification of INR values as subtherapeutic, therapeutic (low and high intensity) and supratherapeutic (table 2):

Reagent A:

41.1% had subtherapeutic c INR values, 56.7% had therapeutic INR values and 1.8% had supratherapeutic values.

Most of the patients were in the therapeutic group.

Reagent B:

44.8% had subtherapeutic INR values, 49.4% had therapeutic INR values and 5.8% had supratherapeutic INR values.

Most of the patients were in the therapeutic group

Reagent C:

38% had subtherapeutic INR values, 59.5% had therapeutic INR values and 2.5% had subtherapeutic INR values.

Most of the patients were in the therapeutic group.

Reagent D:

46.3% had subtherapeutic INR values, 42.3% had therapeutic INR values and 11.4% had supratherapeutic INR values.

Most of the patients were in the subratherapeutic group .

With the three reagents B, C and D used between 38% to 46.3% had subtherapeutic INR, from 42.3% to 59.5% had therapeutic INR and 2.5% to 11.3% had supratherapeutic INR. With reagent A, the INR values obtained with the three groups of anticoagulation were close to those obtained with reagents B,C and D.

It is evident that on applying the INR system there is minimal variation in the percentage of patients in each group of anticoagulation between the four thromboplastins (as shown in fig.5).

Comparison of discordant INR values between the sensitive thromboplastin and the three standard thromboplastins :

A question of clinical interest is what percentage of plasma samples gives discordant INR values between the thromboplastin of the lowest ISI value (reagent A) and the three thromboplastins with a higher ISI value (reagents B,C, D) in the defined therapeutic INR range of oral anticoagulation.

We have calculated the discordance rate (as mentioned in the statistical analysis) between reagents A and B, A and C and finally A and D as mentioned in the statistical analysis.

For the INR range (2-3), the reagent C performed the best with a discordant rate of 38.2% of samples showing discordant INR values between reagent C and A.

For the same INR range (2-3), the discordance rate of reagents B and D were significantly higher 44.4% and 63.1% respectively.

A similar relationship between reagent performance was noted with the INR range (3-4.5), reagents B and D showing much higher discordance than reagent C (65%, 75.5% and 38.5% respectively).

For the therapeutic INR range as a whole (2-4.5), the same relationship was observed (as shown in fig.6).

Discussion

Oral anticoagulants are still the most widely used prescribed drugs for the prophylaxis and treatment of venous and arterial thrombosis. In the early days of oral anticoagulation 1940s, most laboratories employed in their prothrombin time tests home made thromboplastin reagents of human brain origin and later on commercial thromboplastins of human origin. These were responsive to the reduction of coumarin-dependent clotting factors. The American Heart Association recommended a therapeutic range for oral anticoagulant therapy of 2.0- 2.5 prothrombin ratio based on these reagents.

This situation continued until 1986 when human brain was withdrawn from many laboratories because of fears of transimission of human deficiency virus and replaced by a variety of animal tissue reagents. This introduction was not accompanied by a change in the therapeutic PR 2.0 - 2.5 (6), and since most of animal tissue reagents were less responsive than reagents of human origin of the anticoagulant-induced coagulation defect, clinicians gave larger doses of warfarin to achieve the target therapeutic PR, (7), and the incidence of haemorrhage with oral anticoagulants became relatively higher.

Then, the World Health Organization had approved the adoption of INR on the recommendations of the international scientific committees 1983 (8). The aim was to provide more uniform, safer and more effective oral anticoagulant therapy. The INR is a modified reporting method based on the correction of the different responsiveness of individual thromboplastin to the warfarin-induced coagulation defect. The correction factor was termed the International Sensitivity Index (ISI).

Thromboplastin reagents have different ISI values which range from 1.1-2.8 . Responsive thromboplastin reagents have ISI values close to 1.0. For many reasons, a low ISI value between 1.0-1.2 is preferable. With increasing ISI there is loss of precision of PT testing (5), poor discrimination of normal from coumarin treated patients's prothrombin times and a narrower therapeutic window for warfarin dosage.

Although the ISI compensates for the major differences in PTs between the test system, INR disagreement can be observed between test systems (reagent / coagulometer combination) (9 & 10) . The different INRs should not be regarded as an indictment of the system, but a demonstration of the presence of local variables in PT tests which were not quantifiable before the use of INR, like the method of blood collection, the time and speed of centrifugation and clot detection technique manual or using a coagulometer, Van Rijn et al (1989) (11) investigated the effect of two different thromboplastins and three different coagulometers on the INR, the systematic differences observed were related to the use of different instruments.

With the increasing use of the INR to monitor warfarin therapy, a number of problems have been identified that have led some physicians to question the reliability of the INR, (12 & 13). Some potential solutions to these problems were proposed (14), like good calculation of each laboratory to the normal mean prothrombin time, ensuring the reliability of the ISI value assigned by the manufacturer and using a sensitive thromboplastin for PT determination especially with automated instruments and in the early stages of warfarin therapy.

In our study, were excluded the variables that can affect our Prothrombin time determination, by determining the method of blood collection, time and speed of sample centrifugation, the length of time the samples were maintained prior to testing, we used the same coagulometer all over the study , the same lot number of each reagent, the ISI corresponding to the instrument used.

In this study, we compared the results of monitoring the degree of oral anticoagulation in patients receiving oral anticoagulation therapy with four thromboplastins of different ISI values.

We have found that although the three standard reagents gave lower PT ratios than the sensitive one with great number of patients in the subtherapeutic range of PT ratio. The sensitive reagent gave higher PT ratios with great number of patients in the supratherapeutic range of PT ratio. The application of the INR system made the percentage of patients above , below and in the therapeutic range of INR closer between the three standard reagents and the sensitive one for the patient population as a whole . Our results were comparable to that reported with other trials using thromboplastins with different sensitivities (15).

Then we studied in the therapeutic range of INR ((2-4.5), if there was a discordance of the INR value obtained for the same sample between the sensitive thromboplastin and every standard reagent separately. This issue is important because it represents a situation in which the physician treating the patient would make a different clinical decision depending on which reagent was used to determine the INR.

Actually we observed a discordance of the INR value of the same sample between the standard reagents and the sensitive one with different degrees. The observed high discordance rate between A and B, A and C, A and D may be due to the low sensitivity of thromboplastins with right ISI values since with low sensitive thromboplastins the instrument effect is more obvious and any intrinsic error in the PT determination is greatly magnified with the large exponent of the ISI value (9 &16).

Conclusion

In fact the application of the INR system can reduce the interlaboratory variation of PT ratio value due to the different sensitivity of the different commercial thromboplastins. But the laboratory physician can allow the clinician to achieve a safe and effective anticoagulation by optimising as much as possible the conditions of blood sample handling, calculation of the mean normal plasma, the choice of the thromboplastin used in PT determination, a reagent of low ISI value is preferable and respecting the strict reagent / instrument relationship.

REFERENCES

1. Hirsh J. Oral anticoagulant drugs. Engl. J. Med. 1991: 324; 1865-1875.

2. Hirsh J, Dalen JE, Deyken D et al. Oral anticoagulants: mechanism of action, clinical effectiveness, and optimal therapeutic range. Chest. 1992:102; 312-326.

3. Poller L. The effect of the use of different tissue extracts on one stage prothrombin times. Acta. Haematol. 1964:32;292-298.

4. Hirsh J. Substandard monitoring of warfarin in North America: time for change. Arch. Intern. Med. 1992:152;257-258.

5. Taberner DA, Poller L, Thomson JM, Darby KV. Effect of international sensitivity index (ISI) of thromboplastins on precision of international normalized ratios (INR). Clin. Pathol. 1989:42;92-96.

6. Hirsh J, Poller L, Deykin D et al. Optimal therapeutic range for oral anticoagulants. Chest 95:5S-11S, 1989.

7. Poller L, Taberner DA. Dosage and control of oral anticoagulants:: an international survey. Br J Haematol 51:479-485, 1982.

8. WHO Expert Committee on biological standardization 33 rd Report. Geneva, Switzerland: World Health Organization: 1983. Technical Report Series No.687.

9. Poggio M, Van den Besselaar AMPH, Van der Velde EA, Bertina RM. The effect of some instruments for prothrombin time testing on the international sensitivity index (ISI) of two rabbit tissue thromboplastin reagents. Thromb. Haemost. 1989:62; 868-874.

10. Ray MJ, Smith IR. The dependence of the internathional sensitivity index on the coagulometer used to perform the prothrombin time. Thromb. Haemost. 1990:63;424-429.

11. Van Rijn JLML, Schmidt Nico A, Rutten W. Correction of instrument and reagent based differences in determination of the INR for monitoring anticoagulant therapy. Clin Chem 355:840-843, 1989.

12. Triplett D, Brandt J. International normalized ratios: Has their time come? Arch. Pathol. Med. 1993:117;590-592.

13. Gottfried EI, Ng VL, Levin J, Corash L. Problems with the international normalized ratio. Blood. 1992:80;2690-2691.

14. Hirsh J & Poller L. The International Normalized ratio. A guide to understanding and correcting its problems. Arch. Intern. Med. Vol. 154, Feb. 14, 1994.

15. Altmann P, Rouvier J, Gunfinkel E et al. Comparison of two levels of anticoagulant therapy in patients with substitute heart valves. N Engl. J Med. 1990:322;428-432.

16. Starr H, Rhoades P, Lam-Po-Tang PRLC, Archer GT. Prothrombin times: an evaluation ,of four thromboplastins and four machines. Pathology 1980:12;567-574.

Scoring an ACE in cardiovascular remodeling

1 tablet daily

COVERSYL® 4 mg

PERINDOPRIL

in hypertension and heart failure...

...cardiovascular remodeling is a key pathogenic feature. Coversyl 4 mg actively combats cardiovascular remodeling by correcting the structural and functional alterations of the heart and artery.[1-4]

Coversyl 4 mg is a true once daily ACE inhibitor with guaranteed antihypertensive efficacy right up to 24 hours post dose.[5]

In heart failure, Coversyl 4 mg (half-a-tablet) offers a safer start to treatment thanks to an absence of significant hypotensive first-dose response.[6]

With its original properties, Coversyl 4 mg is a high-performance ACE inhibitor in both its indications.

1. SIHM I et al. *Eur Heart J.* 1993; 14(suppl) : 63 - 2. LEVY BI et al. *Circ Res.* 1988; 63 : 227-239 - 3. ASMAR RG et al. *J Hypertens.* 1988; (suppl 3) : S33-S39 - 4. MICHEL JB et al. *Circ Res.* 1988; 62 : 641-650
5. MORGAN TO et al. *Am J Hypertens.* 1993; 6 : 116 A - 6. MAC FADYEN RJ et al. *Br Heart J.* 1991; 66 : 206-211.

Coversyl is a long-acting ACE inhibitor. **International nonproprietary name** : Perindopril. **Indications :** Essential hypertension. Congestive heart failure (adjunctive therapy). **Dosage and administration :** *Hypertension* : 4 mg once a day in the morning. If necessary, the dose may be increased to 8 mg after one month of treatment. Coversyl should be taken before food. *Congestive heart failure* : Coversyl should be started under close medical supervision at a starting dose of 2 mg in the morning. This may be increased to 4 mg once blood pressure acceptability has been demonstrated. *Elderly patients* : start treatment at 2 mg daily. **Contraindications :** Children. Pregnancy. Lactation. Patients with a history of hypersensitivity to Coversyl. **Precautions :** Assess renal function before and during treatment where appropriate. Renovascular hypertension. Surgery/Anesthesia. Renal insufficiency : the dose should be cautiously adjusted in accordance with the creatinine clearance *(refer to complete data sheet)*. Symptomatic hypotension is rarely seen, but is more likely in volume-depleted patients, those receiving diuretics, or with the first two doses. In diuretic-treated patients, stop the diuretic 3 days before starting Coversyl. A diuretic may later be given in combination if necessary; potassium-sparing diuretics are not recommended. Combination with neuroleptics or imipramine-type drugs may increase the hypotensive effect. Serum lithium concentrations may rise during lithium therapy. **Side effects :** Rare and mild, usually at the start of treatment. Cough, fatigue, asthenia, headache, disturbances of mood and/or sleep have been reported. Less often, taste impairment, epigastric discomfort, nausea, abdominal pain, and rash. Reversible increases in blood urea and creatinine may be observed. Proteinuria has occurred in some patients. Rarely, angioneurotic edema and decreases in hemoglobin, red cells, and platelets have been reported. **Composition :** Each tablet contains 4 mg of the tert-butylamine salt of perindopril. **Presentation :** Packs of 30 tablets of Coversyl 4 mg (scored). *Refer to data sheet for complete prescribing information.*

SERVIER

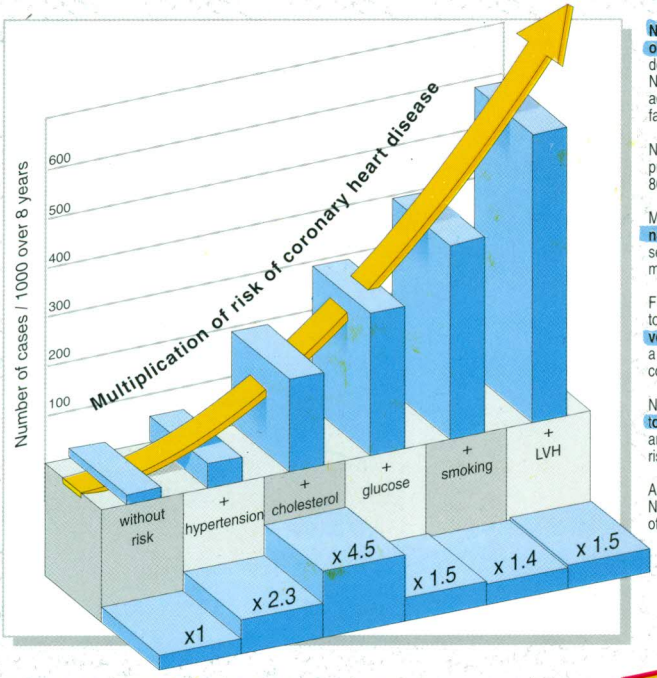
Les Laboratoires Servier, 45520 Gidy - France. Correspondent : **Servier International,** 6, place des Pléiades, 92415 Courbevoie Cedex - France.

NATRILIX®

INDAPAMIDE 2.5 mg

1 tablet daily

THE REFERENCE DIURETIC FOR OPTIMAL CARDIOPROTECTION



As shown in a reference epidemiological trial,[6] when other risk factors coexist with hypertension, the risk of coronary heart disease increases dramatically.

Natrilix is the reference diuretic for optimal cardioprotection: specifically designed for treating hypertension, Natrilix is the only diuretic that addresses all the cardiovascular risk factors of the hypertensive patient.

Natrilix is **highly effective** on blood pressure readings,[1] normalizing up to 80% of hypertensive patients.

Moreover, Natrilix is **metabolically neutral:** Natrilix does not compromise serum cholesterol[2] or glucose metabolism[3].

Furthermore, Natrilix has been proven to **consistently reduce left ventricular hypertrophy,**[4] a recognized critical and independent coronary risk factor.

Natrilix has also been demonstrated **to reduce microalbuminuria,**[5] another independent cardiovascular risk factor in the diabetic hypertensive.

All these major advantages make Natrilix the reference diuretic in terms of cardioprotection.

HYPERTENSION

Treats hypertension without replacing one risk factor by another

1. Abbou CB et al. *Curr Med Res Opin.* 1985; 9 (7): 494-499.
2. Leonetti G et al. *Am J Cardiol.* 1990; 65 (17): 67-71.
3. Raggi U et al. *Hypertension.* 1985; 7 (6) (Part II): 157-160.
4. Raftery EB et al. *J Cardiovasc Pharmacol,* 1993; 22 (suppl 6): 106-110.
5. Flack JR et al. *J Cardiovasc Pharmacol.* 1993; 22 (suppl.6): 75-77
6. Kannel WB. *Am J Hypertens.* 1991; 4: 283-287

Composition: Each coated tablet contains 2.5 mg of 1-(4-chloro-3-sulfamyl-benzamidol)-2-methylindoline (or indapamide hemihydrate). **Indication:** Essential hypertension. **Contraindications:** Severe hepatic insufficiency, recent cerebrovascular accidents. Drug combinations to be avoided: tienilic acid, lithium, fenoxedil, lidoflazine, prenylamine, vincamine. **Combination treatments:** Natrilix may be combined with all nonthiazide antihypertensive agents, with beta-blockers, calcium channel blockers, and ACE inhibitors. **Precautions:** Pregnancy. Lactation. Monitoring of potassium and uric acid serum levels is recommended, especially in subjects with a predisposition or a sensitivity to hypokalemia and in patients with gout. Although no allergic manifestations have been reported during clinical trials, patients with a history of allergy to sulfonamide derivatives should be closely monitored. **Adverse effects:** Hypokalemia, fatigue, orthostatic hypotension, allergic manifestations. **Dosage and administration:** One tablet daily. **Overdosage:** Symptoms of overdosage would be those associated with a diuretic effect; electrolyte disturbances, hypotension, and muscular weakness. Treatment should be symptomatic, directed at correcting the electrolyte abnormalities. Refer to data sheet for complete prescribing information.

Les Laboratoires Servier - 45520 Gidy - France. Correspondent: **Servier International** - 6, place des Pléiades, 92415 Courbevoie Cedex - France

SERVIER

ARTEM - 96 NX 275 IA

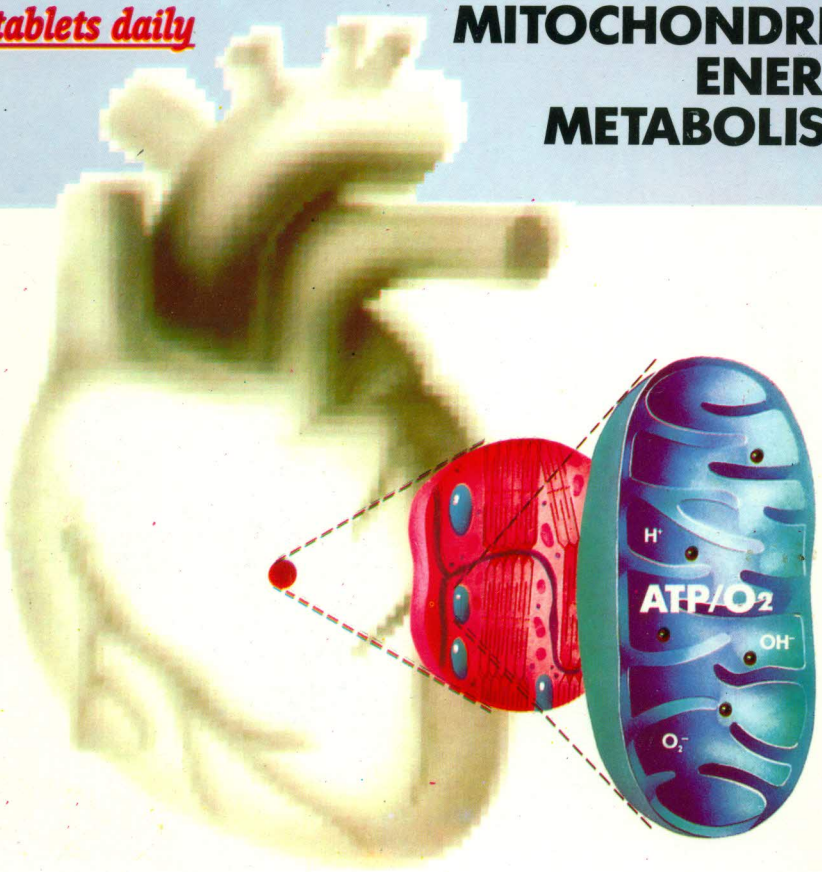
AT THE HEART OF THE ISCHEMIC CELL

VASTAREL® 20

Trimetazidine

OPTIMIZES MITOCHONDRIAL ENERGY METABOLISM[1-3]

3 tablets daily



providing all coronary patients with

- **permanent myocardial cytoprotection**[4]
- **major antianginal efficacy**[4-6]

Indications: Ischemic heart disease (angina pectoris, sequelae of infarction).
How supplied: Box of 60 tablets, each containing 0.02 g trimetazidine dihydrochloride.
Dosage: 3 tablets per day in three divided doses, with meals.
Les Laboratoires Servier · 45520 Gidy · France.
Correspondent **Servier International**
6, place des Pléiades · 92415 Courbevoie Cedex · France.

SERVIER

1. Guarnieri C et al
Biochem Pharmacol. 1988; 21: 128-135.
2. Aussedat J et al.
J Cardiovasc Pharmacol. 1993; 21: 128-135.
3. Fantini E, Grynberg A.
J Mol Cell Cardiol. 1994; 26: 949-958.
4. Detry JM et al.
Br J Clin Pharmacol. 1994; 37: 279-288.
5. Dalla Volta S et al.
Cardiovasc Drugs Ther. 1990; vol 4 (suppl 4): 814-825.
6. Monpère C et al.
Cardiovasc Drugs Ther. 1990: 4 (suppl 4): 824-826.

VASTAREL® 20
Trimetazidine
3 tablets daily