Notes in Medical Statistics (1)
Some Terminology for Statistics and Sampling

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We aim to give a basic introduction to the main concepts involved in planning and undertaking statistical analysis and to indicate what method of analysis should be used in common situations.

Some Terminology for Statistics

1.Variables

Variable - a measured characteristic that can assume various values or levels.

2.Constants

Constant - has only a single value. A certain characteristic (like grade level) can be a variable in one study and a constant in another study.

3.Quantitative versus qualitative data

Quantitative (numerical) data is numerical and either discrete or continuous.

§ Discrete data i.e. counts, for example, number of cases of certain disease, number of children per family.

§Continuous data : data which assume a continuous uninterrupted range of values e.g. height, weight, age).

Qualitative (categorical) data : data typically in narrative form; gathered by use of observations and interviews; results contextual - unique to individual and setting e.g. sex (male, female),blood groups (A,B,O,AB). Qualitative results are often given as: proportion , percent, ratio ,or rate.

4.Measurement

Measurement - assigning numbers to observations according to rules.

5.Scales of measurement

• **Nominal** (Classificatory) scale - used to label, classify, or categorize data (gender, blood groups).

• **Ordinal (Ranking)** scale - classification function plus observations are ordered, the categories are ranked from the highest to the lowest or vice versa e.g. social classes I, II, III, IV or education level.

• **Interval scale** - equal intervals between adjacent units. There is no zero in this scale or zero does not indicate absence of attribute e.g. body temperature.

• **Ratio scale** – the basic difference between this scale and the interval scale is that the ratio scale has an absolute zero. Most physical measures are at the ratio level of measurement (height, weight, distance, time, pressure).

6.Paired data

Two measurements are paired when they come from the same observational unit: before and after, twins, husbands and wives, brothers and sisters, matched cases and controls. Pairing is determined by a study's design. It has nothing to do with the actual data values but, rather, with the way the data values are obtained. Observations are paired rather than independent when there is a natural link between an observation in one set of measurements and a particular observation in the other set of measurements, irrespective of their actual values.

The tests used for independent samples e.g. t-test and Chi-square test should not be used for paired (not independent, matched) samples instead we should use paired t-test or Mc Nemar ،s χ^2 test or sign test.

7.Descriptive and analytic statistics

•**Descriptive statistics** are a way of summarizing data - letting one number stand for a group of numbers, can also use tables and graphs to summarize data.

• **analytic statistics** - research statistics, a measure of the confidence we can have in our descriptive statistics, the statistics we use to test hypothesis.

8.Parametric and nonparametric statistics

• **Parametric statistics** - used with interval and ratio data and usually with data that were obtained from groups randomly assigned, normally distributed, and with equal variability between groups - preferred statistics to use, they are more "powerful" than nonparametic statistics. Examples, are t-tests, analysis of variance, and Pearson correlation coefficient.

•**Nonparametric statistics** - used with nominal and ordinal data and sometimes with interval and ratio data when other assumptions can not be met. Examples, are the chi-square test and the Spearman rank difference correlation coefficient.

Population and sample

Population – all people living in an area or any collection of individuals or things that we are interested in and their number may be finite or infinite.

Sample - a small group of persons or elements (observations) selected from the total population to find something about this population.

Parameter and statistic

Parameter - a parameter is a characteristic of a population.

Statistic - a statistic is a characteristic of a sample.

The mean of a sample would be a statistic. The mean of a population would be a parameter.

Sampling Methods

There are right and wrong ways of taking a sample. The incorrect way is to allow the researchers to individually select, or to influence the selection of the survey sample(unrepresentative sampling).

A-unrepresentative samples:

1-Haphazard sampling i.e. selection of available number of cases

2-Purposive sampling i.e. planned selection of specific typed of cases.

3-Quota sampling i.e. selection of required numbers in each subgroup of individuals.

B- Random samples:

The basis of random sampling is to try to get, as much as we can, a true representation of the population itself.

•**Simple random sampling** - In simple random sampling, each selected unit has an equal chance of being selected. You could do simple random sampling from tables of random number. For example if you want to select 7 individuals out of 24 . you need first to number all 24 (sampling frame) then randomly you select the needed sample.

•**Systematic random sampling** - Systematic sampling is the process of selecting every nth member of the population arranged in a list. For example you could take every 10th member of a list of people (the population) arranged alphabetically.

•**Stratified random sampling** – The word strata means a group of people whoarerather similar or whoare working or living under similar conditions. A stratified sample is obtained by dividing the population into subgroups and then randomly selecting from each of the subgroups. The number of units selected from each subgroup can be proportional to the groups number in the population or can be equal-sized among the subgroups.

•**Cluster sampling** - In cluster sampling groups are selected rather than individuals. For example select 5 elementary schools from among the 25 elementary schools in the district.

•Multistage sampling – In a cluster sample if people that are present in the cluster are selected randomly instead of being all taken, this will be called a multistage sampling. The random selection of cluster will be called primary sampling and the random selected individuals withinthe cluster will be called secondary sampling units.

Sampling size determination

Sample size determination is depending essentially on the type of the study are going to use.

1-Cross-section descriptive study: In a cross-section descriptive study, our main aim is to determine certain prevalence or percent of occurrence of a certain condition. Therefore, we want to deduce this value with the the smallest error possible. In this case , we need to know: our total populationsize, a guess of the expected prevalence,the power of your test, and the accepted level of error that will give us the best estimate of the true population value.

2-**Analytic study and experimental** study: In analytic study and experimental study, we compare between two groupa according to a certain type of exposure. Our main aim of the study is to find out the difference in the disease occurrence that can be attributed to this specific exposure.In other words, there is certain risk that is responsible for the occurrence of theis condition and we want to quantify this risk. Therefore, in this type of study, we are concerned essentially with the amount of exposure i.e. the presence or absence of the effect of this risk factor or the quantity of the risk that can be attributed to its presence.

For the calculation of the sample size in such study we need to know the power of the test used to detect the condition, and the accepted error, the percent of occurrence among the groups and the amount of risk that can be attributed to this exposure.

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Experience & Early Results Of Endarterectomy, Extended Saphenous Vein Patching With LIMA Implantation In CABG Surgery For Diffusely-diseased Left Anterior Descending Coronary Artery.

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Background: Coronary artery bypass grafting (CABG) with Coronary Endarterectomy (CE) is claimed to cause increased morbidity and mortality. This study was carried out to evaluate the impact of operative and perioperative management on outcomes after CABG combined with CE.
Patients and Methods: This prospective study was carried out starting from January 2000 until December 2005 in Kasr El- Aini hospitals. Out of 120 CABG patients done during this period, 20 patients (16.6%) were chosen. Those 20 patients (10 men and 10 women), underwent concomitant CABG surgery with LAD Endarterectomy. Criteria of inclusion were presence of single or multi-vessel ischemic heart disease with total or near-total occlusion of LAD. All were submitted to elective surgery for coronary artery bypass graft surgery using cardiopulmonary bypass, moderate hypothermia (28°C) and intermittent blood-cardioplegia.. The mean patient age was 55 ± 2.5 years. Six patients (30%) were in New York Heart Association Functional Class III-IV; with impaired left ventricular function (LVEF ≤ 45 %); and a mean EuroSCORE of 5.5 ± 1.5. All CABG operations were carried out between 2000-2005. Revascularization was done using combined procedures of LAD endarterectomy, extended saphenous vein patching followed by LIMA implantation. Patients were postoperatively followed-up from 2000 till 2005. Ten patients (50 %) agreed to perform postoperative follow-up angiocatheterization.
Results: The 30-day mortality rate was 5 % as one patient died. This 66-year old patient had long-standing systemic hypertension, diabetes mellitus, and poor preoperative myocardial functions (LVEF of 35 %). He died in the 12th. postoperative day due to fulminant mediastinitis. The mean total operative time was 89 ± 26 minutes (range 105-180 minutes). Mean number of grafts done was 2.0 ± 0.8 (range 1-3). The mean cardiopulmonary bypass time was 99 ± 15 minutes (range 34-130 minutes). Mean postoperative ICU stay time was 25 ± 4.5 hours. Patients were extubated after a mean time of 6 ± 4.9 hours. The mean length of hospital stay was 7 ± 3.0 days. A mean of 2 ± 0.5 units of blood were transfused postoperatively, but none of our patients required reexploration for bleeding. Postoperatively, all patients were angina free with only 2 of them (10 %) were in NYHA Class III-IV. Postoperative dysrrhythmias (as Ventricular Tachycardia) occurred in one patient (5 %); and Atrial Fibrillation in another patient (5 %). All were controlled using Amiodarone by IV then oral routes. No patient suffered from postoperative myocardial infarction. Three patients (15 %) (who had preoperative LMS), developed postoperative CHF for which they needed Inotropic and IABCP Support. Neurological manifestations did not occur in any of our patients.
Conclusion: LAD Endarterectomy, combined with extended saphenous vein patching and LIMA implantation was both safe and feasible and

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achieved surgical revascularization in patients with diffuse coronary artery disease, without major short-term complications.

During the past few years, cardiac surgeons started to deal with an increased number of referred patients with diffuse coronary artery disease for consideration for coronary artery bypass grafting (CABG) (1).

Despite the introduction of coronary endarterectomy (CE) 40 years ago [1],[2] as a method of treatment of diffuse coronary artery disease, its wide application remained controversial [3-6]. CE was accused of carrying higher perioperative risks and inducing poorer long-term survival [7-9], in addition to being a technically challenging procedure even when cardiopulmonary bypass (CPB) is used.

For the previous reasons, some surgeons refrained from performing it presumably due to inadequate experience, and this unfortunately lead to incomplete revascularization [4-5].

More recently, although several authors [10-12], have reported better short-term outcome and improved long-term survival, it is still performed in a small proportion of CABG patients, in contrast to earlier decades when it was performed more frequently [7]. Moreover, some surgeons reported using CE while performing Off-Pump CABG (OPCABG) in order to avoid the institution of CPB with its attendant risks of inflammation and global ischemia [13],[14], especially in high-risk patients [15],[16].

Patients and Methods:

This prospective study was carried out starting from January 2000 until December 2005 in Kasr El- Aini hospitals.Revascularization to the LAD was done using combined procedures of LAD endarterectomy, extended saphenous vein patching followed by LIMA implantation at the proximal part of the saphenous vein patch.

Patient population and characteristics :

Of 120 CABG patients done during this period of time , 20 patients (16.6%) were chosen: 10 men (50 %) and 10 women (50 %). Those 20 patients, underwent concomitant CABG surgery with LAD Endarterectomy. The mean patient age was 63.6 ± 9.3 years. Six patients (30%) were in New York Heart Association Functional Class III-IV; with impaired left ventricular function (LVEF ≤ 35 %); and a mean EuroSCORE of 5.5 ± 1.5. Preoperative previous MI (> 1 month duration) was present in 2 patients (10 %); Diabetes mellitus was present in 3 patients (15 %); Hypertension in 11 patients (55 %); Hypercholestremia in 9 patients (45%); LMS disease in 2 patients (10 %). The number of vessels diseased was one vessel in 3 patients (15 %); Two vessels in 6 patients (30 %); and Three vessels in 11 patients (55 %).

Criteria of inclusion:

Were presence of single or multi-vessel ischemic heart disease with total occlusion of LAD (by coronary angiography) supplying a viable myocardial segment (myocardial ischemia is reversible as seen by Thallium study). All were submitted to elective surgery for coronary artery bypass graft surgery using cardiopulmonary bypass, moderate hypothermia (28°C) and intermittent blood-cardioplegia..

Study Methodology:

All clinical data were prospectively collected and entered into a database before being reviewed.

Criteria of exclusion:

Were patient refusal to participate in the research; presence of heart failure; left ventricular ejection fraction of 30 % or less; in addition to presence of any resistant general disease contraindicating surgery. The preoperative Demographic Data of the Study Patients (Table1).

Table (1): Preoperative Demographic Data of the Study Patients

Patient Characteristic	Value ((± SD
- Age (mean in years)	63.6 ± 9.3
- Gender :	
- Males (number)	10 (50 %)
- Females (number)	10 (50 %)
- Male-to-Female ratio	1-1
- NYHA Clinical Class III/IV	6 (30%)

- Previous MI (> 1 month duration) 2 (10 %)
- Diabetes mellitus 3 (15 %)
- Hypertension 11 (55 %)
- Hypercholestremia 9 (45%)
- Impaired LVEF ≤ 45 % 6 (30%)
- LMS disease 2 (10 %)
- Number of vessels diseased
  - One 3 (15 %)
  - Two 6 (30 %)
  - Three 11 (55 %)
- EuroSCORE 5.5 ± 1.5

LVEF: Left Ventricular Ejection Fraction per cent. EuroSCORE: European System for Cardiac Operative Risks Evaluation. LMS: left main stem. MI: Myocardial Infarction. NYHA: New York Heart Association for clinical classification.

Follow-up

All patients were postoperatively followed-up from 2000-till-2005 by clinical examination guided by any needed special investigations. Electrocardiograms were performed in all patients on day 1 and day 4 postoperatively and more frequently if required. Ten patients (50 %) could be convinced to submit themselves for postoperative follow-up coronary angiocatheterization.

Statistics

Preoperative and postoperative data were gathered in table forms, then expressed as means ± SD. The Kaplan-Meier method was used to analyze actuarial survival and freedom from angina. Statistical analysis was performed using SPSS software (release 12.0.1 for Windows; SPSS, Chicago, Illinois).

Clinical Definitions

(1) Myocardial Infarction (MI) :

Was defined as persistent electrocardiographic changes such as new Q waves, loss of R-wave progression, new intraventricular conduction defects, or new echocardiographic evidence of wall motion abnormality.

(2) Indication for LAD Endarterectomy :

The process of decision-making: The final decision to endarterectomize a vessel was made intraoperatively based on the surgeon's own technical considerations. Complete occlusion on angiogram was not considered a definite indication for endarterectomy. Coronary endarterectomy was considered when no adequate segment of a vessel, supplying viable muscle with reversible ischemia, was suitable for grafting. Apparently patent and therefore graftable segment on angiogram was on occasion found unsuitable due to severe narrowing or heavy calcification precluding effective anastomosis. Endarterectomy of the diseased vessel was only performed when the artery was completely or nearly occluded with heavily calcified plaques and long stenotic segments extending distally.

Details of the surgical procedure :

Standard perioperative monitoring techniques were used. Standard CPB circuit was used with aorto-caval cannulation. CPB was performed using moderate hypothermia (28°C) and intermittent warm blood-cardioplegia given at the aortic root. All procedures were performed through a midline sternotomy. After the conduits (internal thoracic arteries, the radial artery, and the saphenous vein) were harvested, heparin was administered to maintain an activated clotting time greater than 400 seconds.

We used the "Open-endarterectomy technique" as follows: The coronary arteriotomy done was usually ranged from 3-8.5 cm in length. A fine dissecting probe was used to develop a distal plane between the adventitia and the atheromatous core. The atheroma was then held with a pair of large blunt forceps in the middle, while gentle sustained traction (17),(18), is applied from the cranial end on the distal segment. Only 1-2 cm of the proximal core was dissected, and the atheroma sharply-divided at this level to avoid inducing the risk of competitive flow between the graft and the native vessel that may compromise flow through the graft in general. In our opinion, complete proximal endarterectomy should be avoided except if it was performed only to release the adventitia distally over tenacious segments using peanut swab dissection or by lifting and picking the external layers, thus enhancing layer separation.

To ensure complete removal of the distal atheroma, intraoperative inspection for the core was done carefully to visualize the smooth distal tapering end as shown in figure (1). If the distal end was irregular, or a residual plaque was felt to remain in the distal vessel, the arteriotomy was enlarged as necessary to allow complete removal of the plaque. The endarterectomized vessel was irrigated was heparanized Plasmalite (Travenol; Baxter) to remove residual small particles. The bypass conduit (Saphenous Vein Graft) was then directly anastomosed to the endarterectomy site after being longitudinally-opened. We considered that presence of some back flow of blood from the distal vessel during the dissection and after complete extraction of the atheroma is a reassuring sign of a successful and satisfactory CE. The distal anastomosis to the endarterectomized vessel was constructed end to side using 7-0 polypropylene sutures using standard techniques with a long arteriotomy, a vein patch was used to reconstruct the anastomosis. The distal anastomosis was then constructed between the conduit and the patch. Antiplatelet agents (baby aspirin 150 mg) were started 6 hours postoperatively in all patients once bleeding had settled in the drains of the retrosternal space and Warfarin was given until 6 months postoperatively.

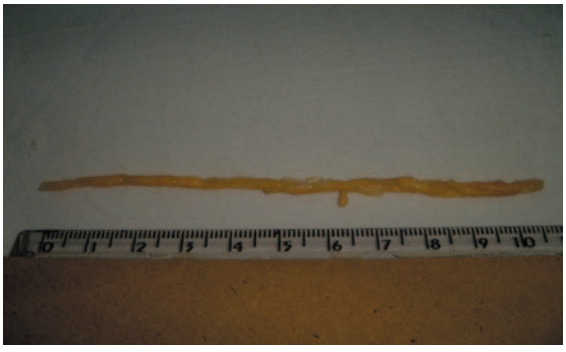

Figure (1): The atheroma after endartrectomy of the LAD

Results

Intraoperative and Surgical Data:

The mean total operative time was 89 ± 26 minutes (range 105-180 minutes). Mean number of grafts done was 2.0 ± 0.8 (range 2-5). The mean cardiopulmonary bypass time was 99 ± 15 minutes (range 34-130 minutes). The Intraoperative and Surgical Data (Table 2).

Table (2): Intraoperative and Surgical Data

Variable	Value (± SD)
(1) Total Operative time (in minutes)	
- Range	105-180
- Mean	89 ± 26
(2) CPB Time :	
- Range	34-130
- Mean	99 ± 15
(3) Grafts performed (number per patient):	
- Range	2-5
- Mean	2.0 ± 0.8

CPB : Cardiopulmonary Bypass. SD .: Error of Standard Deviation

Postoperative Data and Events

Mean postoperative ICU stay time was 25 ± 4.5 hours (range 17-80 hours). Patients were extubated after a mean time of 6 ± 4.9 hours (range 3-15 hours). The mean length of hospital stay was 7 ± 3.0 days (range 5-13 days). A mean of 2 ± 0.5 units of blood were transfused postoperatively (range 1-4 units). None of our patients required reexploration for bleeding. Postoperative dysrrhythmias (as Ventricular Tachycardia) occurred in one patient (5 %); and Atrial Fibrillation in another patient (5 %). All were controlled using Amiodarone by IV then oral routes. Three patients (15 %), who had preoperative left main disease, developed postoperative CHF for which they needed Inotropic and IABCP Support.

Early 30-days mortality

The 30-day mortality rate was 5 % as one patient died. This 66-year old patient had long-standing systemic hypertension, diabetes mellitus, and poor preoperative myocardial functions (LVEF of 32 %). He died in the 12th. postoperative day due to fulminant mediastinitis.

Mid-term Follow-up Data

No patient suffered from postoperative myocardial

infarction. Neurological manifestations did not occurr in any of our patients. For a mean of 2 years postoperatively (range 1.4 -4.5 years), all patients were angina free and only 2 of them (10 %) remained in NYHA Class III-IV. The postoperative Characteristics of the Study Patients (Table 3).

Table (3): Postoperative Data and Events of the Study Patients

Variable	Value (± SD)
(1) Hours of Mechanical Ventilation:	
- Range	3-15
- Mean	6 ± 4.9
(2) ICU Stay time	
- Range	17-80
- Mean	25 ± 4.5
(3) Hospital Stay Time	
- Range	5-13
- Mean	7 ± 3.0
(4) Blood requirements in units per patient	
- Range	1-4
- Mean	2 ± 0.5
(5) Reoperation for Bleeding	None
(6) Postoperative Dysrrhythmias	2 (10 %)
- Ventricular Tachycardia	1 (5 %)
- AF	1 (5 %)
(7) Inotropics + IABCP support for CHF	3 (15 %)
(8) Postoperative Neurological Complications	None
(9) Postoperative MI	None
(10) Early 30-day mortality	1 (5 %)

AF: Atrial Fibrillation. IABP: Intra-Aortic Balloon Counterpulsation
ICU: Intensive Care Unit. MI: Myocardial Infarction.

Discussion

Coronary endarterectomy (CE) was introduced for treating severe atherosclerotic coronary artery disease approximately 45 years ago (1), even before coronary artery bypass grafting (CABG) became the standard operative treatment of myocardial ischemia (2). CE was shown to relieve angina symptoms, but early experiences reported high postoperative morbidity and mortality (2). However, ultimately CE found its role as an adjunct to CABG, mainly in patients with diffuse coronary artery disease, to afford more complete revascularization (3). Most studies on coronary CE report on the right coronary artery (4).

Today many surgeons are still reluctant to use coronary CE primarily because of increased mortality and myocardial infarction (MI) rate postoperatively compared with CABG alone (5). This has been especially the case for CE of the left anterior descending artery (LAD), because of the obvious importance of the LAD with its many branches that need to be addressed during CE (6).

With advances in percutaneous coronary interventions, many patients now referred for CABG present with more complex coronary pathologic conditions and diffuse disease. This shift makes complete revascular-

ization more challenging. At the same time newer treatments such as transmyocardial laser revascularization (7) and angiogenic growth factor therapy (8) have been studied to offer a therapeutic alternative to patients with diffuse coronary artery disease who are not amenable for surgical treatment. In some patients, transmyocardial laser revascularization may be considered as an option, but there are still many unanswered questions regarding the indications and long-term results of this treatment (9). Transmyocardial laser revascularization should be considered complementary to CE and remain in the armamentarium of surgeons treating diffuse coronary disease together with the angiogenic growth factor therapy which is still experimental (10).

Many patients with diffuse LAD disease are currently considered inoperable (10). This is in contrast to patients in whom the LAD is deemed graftable by angiography but not other targets and the referring physicians and surgeons may wish to undertake CABG because of the presence of a graftable LAD (11). The principal finding in this study is that patients with diffuse coronary artery disease may safely undergo LAD-CE as an adjunct to CABG with favorable early and 2-year (mid-term) outcome.

Indications and Techniques for Left Anterior Descending Coronary Endarterectomy

In our study, LAD-CE was performed because in certain group of patients, conventional CABG alone was not possible. Our indications for LAD-CE were clear and strict: coronary arteriotomy revealed an occluded LAD with no graftable vessel in a viable myocardium when a 1-mm probe could not be passed. Our indications were also adopted by other surgeons like Loop et al (1986) (13); Beretta et al (1992)(14); and Vohra et al (2006) (15).

Previously, the internal mammary artery (IMA) has been used cautiously as a conduit to an endarterectomized vessel because of concerns regarding mismatch of luminal diameter (10). Following certain procedures (as Off-pump CABG), several authors have now reported equal satisfactory early and late clinical outcomes and luminal patency of endarterectomized vessels grafted with either saphenous vein or mammary artery (25-27).

In this study, we preferred the long arteriotomy technique for CE. It is our belief, as well as others (14-28-29) that it is the most reliable technique that offers the advantage of ensuring total plaque removal, despite the misfortune that it requires a longer aortic cross-clamp time because of the need to sew the vein patch to the LAD-CE bed. Although the small arteriotomy technique has the advantage of a shorter cross-clamp time, the surgeon must be sure that the entire plaque is removed with proper distal tapering. If distal tapering is not observed, then the arteriotomy should be extended to ensure complete plaque removal. In our series, we used the long arteriotomy technique in conjunction with saphenous vein graft over the endarterectomized LAD vessel, as we found it relatively technically-easier and also to its reported reasonable postoperative patency as proved by the postoperative coronary angiography examinations that was performed in 10 of our patients.

Operative Mortality, Early and Mid-term Survival

This study demonstrated the feasibility to perform combined CABG + LAD-CE with a low operative mortality rate (5%) and hence reasonable early and mid-term survival. This operative mortality rate is similar to the 2-6% reported in other institutions performing combined CABG + CE (4-12).

The relatively-low operative mortality rate in our study reinforces the trend seen in recent studies on CE (4-11), as well as other areas of cardiac surgery, in which declining morbidity and mortality have been documented in several high-risk patient groups. The reasons are probably due to many factors: Advances in patient selection, surgical technique, myocardial protection, and intensive care unit management probably explain the improved operative mortality rates. Our 2-year survival rate is in agreement with previous reports that have shown an early and a mid-term survival rate between 71% and 92% (10),(12). These results probably account for the presence of more-advanced coronary artery disease in patients who required LAD-CE compared with those who undergo conventional myocardial revascularization and the presence of more risk factors for worse early and late outcomes (3).

Anticoagulation and Platelet Inhibition

The anticoagulation protocol that we used in our patients is by using 2 tabs of the 75-mg baby aspirin daily after a meal together with Warfarin for 6 months postoperatively. Some surgeons (14),(15), reported that (before 1999), they gave their CABG+ CE patients at least 3 months of warfarin treatment together with a life-long aspirin treatment. We still use heparin infusion at 500 U/h on the day of the surgery, and it is started only when the chest tube output is less than 50 mL for 2 con-

secutive hours to be followed by the oral aspirin dose. This strategy has not resulted in problems with postoperative bleeding, supported by the fact that none of our patients required surgical reexploration to stop bleeding. Large-scale comparative studies on anticoagulation protocols after combined CABG+CE are not yet available (15). Our postoperative anticoagulation protocol of initial heparin followed by aspirin and Warfarin has partially been based on studies on thrombosis after CE (16). Several studies have documented that more than aspirin alone is required to maintain long-term patency in culprit vessels in the setting of disturbed coronary endothelium (3-7).

Perioperative Myocardial Infarction:

In our study, none of our patients developed MI. Our rate is less than rates reported by other surgical groups like 3% by Ivert et al (1989)(12); 2.5 % by Djalilian et al (1995) (10); and 5 % by Shapira et al (1999)(11), and this may partly be due to the lesser number of our study cases. More-recent coronary CE studies have reported lower MI rates, similar to ours (13),(14). This discrepancy may also be related to the definition used for MI in each study. We included patients with enzymatic definition of MI with concomitant electrocardiographic or echocardiographic changes in the LAD territory. Some reports (16),(17), have shown an increased risk in perioperative MI when an LAD-CE is performed, in contrast to when CE of the right coronary artery is performed (18),(19). The increased risk in MI in the LAD territory seems to be correlated with the probability of blocking off small septal and diagonal branches when LAD-EA is performed (16). Our opinion, as well as others (17-19), that if the LAD-CE specimen is delivered intact, the likelihood of MI is low. In these patients, the alternative is incomplete revascularization, transmyocardial laser revascularization, or angiogenic growth factor therapy. We concur with previous reports that performing multiple endarterectomies causes a greater risk factor for early death as well as yielding poor long-term outcomes (20-22).

ICU and Hospital Stay Times:

Mean postoperative ICU stay time and was 25 ± 4.5 hours (range 17-80 hours). The mean length of hospital stay was 7 ± 3.0 days (range 5-13 days). Patients were extubated after a mean time of 6 ± 4.9 hours (range 3-15 hours). The previous mean times recorded in our series were in agreement with the figures reported in other series (11-14) and hence were considered satisfactory.

Postoperative Data and Events :

A mean of 2 ± 0.5 units of blood were transfused postoperatively (range 1-4 units). None of our patients required reexploration for bleeding. Postoperative dysrrhythmias (as Ventricular Tachycardia) occurred in one patient (5 %); and Atrial Fibrillation in another patient (5 %). All were controlled using Amiodarone by IV then oral routes. Three patients (15 %), who had preoperative left main disease, developed postoperative CHF for which they needed Inotropic and IABCP Support. The undesired postoperative events of morbidity recorded in our study was also reported by other surgical groups (16-22) in similar rates of occurrence. Being reversible without serious long lasting effects, we considered them acceptable.

Clinical improvement of Symptoms :

Symptomatic relief and clinical step-up of the NYHA clinical class was accomplished in almost all patients. Except for the mortality case, only two patients (10 %) remained in NYHA class III-IV but free from any cardiac event of deleterious haemodynamic consequences requiring hospital admission during the 2-years postoperative follow-up. Rates similar to ours were reported in other series. Djalilian and coworkers (10), reported a 91% freedom from angina at 3 years' follow-up. Asimakopoulos and associates (23), reported a 74.5% postoperative freedom from angina at 21 months' follow-up; whereas a rate of freedom from angina lower than 92% was reported by Sergeant and associates (24), in a study of 9,600 patients undergoing coronary artery revascularization. It is, however, in agreement with previous reports on CE. The differences in recurrence of angina between patients undergoing CE and those undergoing simple CABG may be related to the presence of severe diffuse coronary artery disease.

The final clinical impression reached by our results are important because many patients with diffuse LAD disease are currently considered inoperable. This is in contrast to patients in whom the LAD is deemed graftable by angiography but not other targets and the referring physicians and surgeons may wish to undertake CABG because of the presence of a graftable LAD.

The Study Limitations :

A limitation of this study is the lack of a control group. However, comparison versus such a group is not practical because conventional CABG was, by definition, not possible in these patients.

Conclusion: LAD Endarterectomy, combined with extended saphenous vein patching and LIMA implantation was both safe and feasible and achieved surgical

revascularization in patients with diffuse coronary artery disease, without major short-term complications.

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Postoperative Bleeding after Myocardial Revascularization in patients on Clopidogrel

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BACKGROUND:Clopidogrel (CL) is a potent inhibitor of platelet aggregation; it has become the standard of care to prevent thrombotic complications following cardiological interventions. Platelet dysfunction is one of the major reasons of postoperative bleeding following coronary artery surgery. The aim of this study was to evaluate the effect of Clopidogrel on bleeding and the use of blood and blood products after coronary artery bypass grafting (CABG).

METHODS: Data were prospectively collected on 286 consecutive patients who underwent isolated conventional CABG (with cardiopulmonary bypass) and compared two groups: group (1), those who had the drug discontinued more than 7 days prior to surgery or were never on it (n = 201), to those with clopidogrel exposure up until 72 hours prior to surgery (group 2, n = 85). The duration of the study covered the period between April 2004 and March 2006. Preoperative patient characteristics, intraoperative variables, and postoperative outcomes were prospectively collected and recorded in the cardiac surgery database.

RESULTS:Chest tube drainage was significantly increased during the first 24 hours following CABG in the group of patients who had clopidogrel treatment (1392 ± 212 vs.785.29 ± 145). These patients also required more transfusion of packed red cells (4.23± 2.3 vs. 2.21± 1.5). Platelets (4.1 ± 1.2 vs. 0.2 ± 0.6), and fresh frozen plasma (3 ± 0.9 vs. 1.5± 1.1)
Overall re-exploration rate due to bleeding was significantly higher in the clopidogrel group (5.88% vs. 1.8%).

CONCLUSIONS:Patients using Clopidogrel 3 days or less prior to CABG surgery have a significantly increased risk of postoperative bleeding, with increased need for surgical re-exploration as well as risks of transfusion with blood and blood products after coronary artery bypass surgery. Platelets transfused before chest closure had a beneficial effect on preservation of the hemostasis.

Clopidogrel is an acetate derivative of ticlopidine and is an inhibitor of platelet aggregation that works by irreversible blockage of adenosine diphosphate (ADP) mediated platelet activation ([1]). It has several advantages over other antiplatelets, including more rapid onset of action, more potent antiplatelet effect, and lower incidence of severe neutropenia and thrombotic thrombocytopenic purpura([2]). The antiplatelet effect of clopidogrel is time and dose dependent. Maximal inhibition of platelet aggregation of 50% to 60% can be achieved with a dose of 75 mg daily (without a loading dose) within 4 to 7 days, or more rapidly with a loading dose of 300 to 600 mg within 4 to 24 hours. Platelet function recovers completely 7 days after stopping clopidogrel in healthy volunteers. ([3],[4])

The cause of early postoperative bleeding following CABG may be mul-

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tifactorial; insufficient surgical hemostasis, disorders of the coagulation system due to hemodilution, platelets dysfunction as well as negative effects of increased cardiopulmonary bypass time, concomitant procedures, and urgency status, are the most common causes for impaired hemostasis and postoperative bleeding.([5])

Platelet function is integral to hemostasis in the early postoperative period. Preoperative antiplatelet agents have the potential to deliver an additional insult to already dysfunctional platelets. These agents should be discontinued at the appropriate time to ensure adequate platelet function at time of surgery ([6]). However, ongoing ischemia may necessitate continuation of these antiplatelet agents. Although controversial, preoperative aspirin may have a small effect to enhance postoperative bleeding but it does not affect transfusion rates. (7) Due to the advantages and superior action of clopidogrel compared to other antiplatelet agents it is now common practice for cardiologists to give patients both clopidogrel and Aspirin at the time of coronary angiography for possible coronary stent implantation for maximum antiplatelet activity at the time of stent placement. This results in patients with severe coronary artery disease requiring CABG during the same admission to present for surgery with significant platelets' function inhibition. (8)

The aim of this work is to analyze the effect of clopidogrel on postoperative bleeding and blood products transfusion requirements in patients who underwent isolated myocardial revascularization

Patients and Methods

Data were collected prospectively on 286 consecutive patients who underwent isolated CABG with CPB. Exclusion criteria included concomitant valvular procedures, off pump CABG, and bleeding disorders identified preoperatively and patients with impaired renal function. All patients were receiving aspirin, 81 mg/day. Patients receiving clopidogrel were on a maintenance dose of 75 mg daily or receiving the loading dose of 300 mg /day just before surgery.

Preoperative patients' parameters, intraoperative variables, and postoperative outcomes including blood loss in the first 24 hours, and transfusion requirements in the first 24 hours postoperatively, re-exploration for bleeding, and length of ICU and total hospital stays, were prospectively collected and recorded in a cardiac surgery database.

The patients were divided in two groups: group (1) those in whom clopidogrel was discontinued more than 7 days prior to surgery or were never taking it. (n = 201) to those with clopidogrel exposure up until 72 hours prior to surgery (group 2, n = 85) from April 2004 to March 2006.

The main indications for clopidogrel treatment were prior percutaneous coronary intervention, unstable angina and patients with critical coronary artery disease needing surgery within the same hospital admission.

Anesthesia's technique, heparin, and protamine management were standardized for all patients in whom systemic temperature was kept between 30°C and 32°C. Myocardial protection was achieved by using intermittent anterograde hyperkalemic cold blood cardioplegia.

Patients were transferred to the intensive care unit (ICU) and managed according to the ICU protocols. They were extubated following our usual criteria of hemodynamic stability and no excessive bleeding (Less than 3-5ml/kg/h), normothermia, and full consciousness. All patients underwent a routine coagulation screening. Transfusion of red blood cells was performed when hematocrit value was less than 24%. Platelets were transfused when the total count less was than 50,000/μL or there was excessive post-operative bleeding. The decision for re-exploration was taken when bleeding exceeded 500 ml in the first hour, more than 200ml /h during next 3 hours, or more than 1 liter over 8 hours despite normalized coagulation profile.

Statistical Analysis

Statistical analysis was carried out using analysis of variance (ANOVA), Fisher's exact tests and t test. P value of 0.05 or less was considered statistically significant.

Results

There were no clinically or statistically significant differences in age, gender, risk factors, or other main profiles of the patients between both groups (table1).

The intraoperative data are presented in table 2 in which there were no statistically significant differences between both groups. Chest tube drainage was significantly increased during the first 24 hrs. following CABG in the group of patients who had clopidogrel treatment (1392 ± 212 vs. 785.29 ± 145), this was demonstrated in figure 1.

Those patients who received clopidogrel also required more transfusion of packed red cells, (4.23± 2.3 vs. 2.21± 1.5), Platelets (4.1 ± 1.2 vs. 0.2 ± 0.6) and fresh frozen plasma (3 ± 0.9 vs. 1.5± 1.1) $p < 0.001$ (table3). Re-exploration for postoperative bleeding was significantly higher and required in five (5.88%)

patients of the CL group, while it was four (1.8%) in the non CL group. After re-exploration, no specific sources were identified and bleeding was thought to be secondary to coagulopathy in all patients. The median ICU and hospital stay were longer in CL. group (Table 4). We had hospital mortality of 4 patients (1.3%) from low cardiac output including both groups.

Table (1): Preoperative patient data.

P value	Group 2	Group 1	
	85	201	No. of patients
NS	57.83 ± 10.6	59.38 ± 10.71	Age
NS	M: 78.83% F: 21.17%	M: 76.62% F: 23.38%	Gender
NS	2.27 ± 0.76	2.43 ± 0.88	NYHA class
NS	42.38 ± 10.71	41.33± 8.55	EF%
NS	2.3±0.85	3.2±0.67	Angina class
NS	52.11	55.12	Previous myocardial infarction
HS	31.8%	9%	Left Main

NS: non significant.
HS: highly significant.

Table(2):Intraoperativedata.

P value	Group 2	Group 1	
NS	48 ±	46 ±	Cross clamp time
NS	81 ± 11	7 7 ± 16	Bypass time in min.
NS	3 . 9 ± 0.4	3 . 6 ± 0.4	Number of coronary anastomoses

Figure (1): Postoperative blood loss

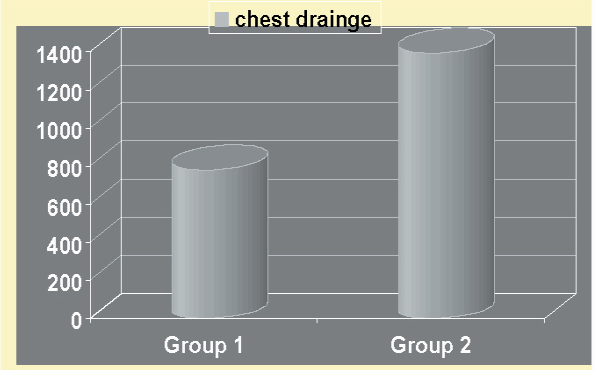

Table (3): Transfusion requirements:

P value	Group 2	Group 1	Blood products transfused
P < .001 HS	4.2 ± 2.3	2.21 ± 1.1	Packed Red cells
P < .001 HS	3 ± 0.9	1.5 ±1.1	FFP
P < .001 HS	4.1 ± 1.2	0.2 ± 0.6	Platelets

Table (4): Postoperative outcome:

P value	Group 2	Group 1	Outcome Variables
P < .001 HS	5 pts. (5.88%)	4 pts. (1.99%)	Re-exploration
P < .001 HS	65.4 ± 7.2	40.3 ± 8.1	ICU stay (hours)
NS	9.3±2.1	7.8±2.0	Hospital stay (days)

Discussion:

Acquired platelet dysfunction is one of the most commonly encountered haemostatic defects in patients undergoing cardiac surgical procedures. The main factors that may affect bleeding and transfusion requirements in these patients are: presence of risk factors for bleeding, as well as, appropriate heparin dosing and protamine reversal, but excess dose of protamine should be avoided in these patients due to its adverse effects on coagulation factors and platelets. (9, 10)

Differentiating between postoperative bleeding due to coagulopathy and surgical bleeding that should be corrected with re-exploration is not always straightforward in the early postoperative period. The differentiation becomes more difficult in the face of preoperative clopidogrel administration which is becoming more popular with cardiologists.(11,12) Our study has demonstrated that exposure to clopidogrel before CABG increased the amount of postoperative blood loss and the number of blood units transfused, supporting the previous findings by Yende and Wunderink(7)who reported their experience with 247 patients, out of which 51 received clopidogrel. Hongo and colleagues (13) prospectively compared 224 patients of whom 59 had preoperative clopidogrel exposure within 7 days before surgery, undergoing non-emergent CABG and observed for postoperative outcome of those with and without clopidogrel exposition. They found that chest tube drainage (1485cc) was significantly increased during the first 24 h following CABG in the group of patients who had clopidogrel treatment. These patients also required more transfusion of packed Red cells Platelets, and fresh frozen plasma. Overall re-exploration rate due to bleeding was significantly higher in the clopidogrel group. Similar results were reported by Ray et al. (14) The potent inhibition of platelet function achieved by the combination of aspirin and clopidogrel has been reported to prolong bleeding time with an increased risk of major hemorrhage. Moreover, the combined antiplatelet effect of clopidogrel and aspirin might be amplified by CPB-related platelet dysfunction. This finding was also supported by Englberger and associates. (8) Who reported increased bleeding and platelet and fresh frozen plasma transfusion in patients receiving clopidogrel within 3 days of surgery? However, Karabulut etal.(6) showed no increase in bleeding and transfusion requirements after preoperative use of clopidogrel and the cause in their series is not clear.

Our study has also demonstrated a significantly increased ICU and postoperative hospital stay in clopidogrel recipients, similar to a study by Chu and coworkers (17). These patients stayed an average of 13.7 hours and 1.9 days longer than non recipients, respectively. Increased ICU and hospital stay significantly impacts on the cost of CABG and will also expose patients to potential hospital stay-related complications. (18)

One of the limitations to the present study, which deserve to be mentioned, is that we did not perform an analysis comparing on-pump to off-pump patients because of the small numbers of patients enrolled in the off-pump group.

In conclusion Bleeding after cardiac surgery is a multifactorial problem and it can often be difficult to eliminate all of the confounding factors. However, our data show that clopidogrel within 3 days of operation is associated with increased bleeding in the first 24 hours and thus an independent risk factor for increased transfusion requirements and prolonged hospital length of stay. One must exercise caution when prescribing clopidogrel to the preoperative cardiac surgery patient, weighing the risk of further myocardial ischemia against the risk of postoperative blood loss and its sequelae.

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Perioperative Intra Aortic Balloon Pump Support For Coronary Artery Bypass Surgery. Five Years Experience.

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Objective: Evaluation of the effect of Intra-Aortic Balloon Pump (IABP) support in the perioperative period in patients undergoing coronary artery bypass grafting (CABG).

Methods: Between February 1999 and February 2004, five hundred fifty six patients underwent coronary artery bypass graft surgery (CABG), fifty seven of them received perioperative intra aortic balloon pump support. Twenty eight high risk patients having 2 or more of the following criteria: preoperative Left ventricular ejection fraction (LVEF) ≤ 40%, left main coronary artery stenosis ≥ 70%, reoperation and/or unstable angina despite maximum medical treatment received preoperative IABP (group 1), and 29 patients received postoperative IABP due to hemodynamic instability (group 2). Cardiac index as a parameter of cardiac performance was measured pre- and post operatively by Swan-Ganz catheter.

Results: Mean age was 52 years and all patients were men. The preoperative LVEF was lower in group (1) 33% versus 45% (P < 0.001). It improved in group (1) in the immediate postoperative period to 37% versus 42% (P < 0.01), yet it was still lower in group (1). The cardiopulmonary bypass time was shorter in group (1), 102 minutes versus 127 minutes (P = 0.02). Cardiac index rose significantly at 4 hours postoperatively in group (1) (P < 0.008). It continued to rise 12 and 24 hours postoperatively (P < 0.002), and (P < 0.001) respectively. In group (1) patients, the duration of IABP support time was less 21.6 hours versus 34.7 hours in group (2) with The (P < 0.0001). The preoperative IABP supported patients had a shorter surgical intensive care unit stay 2 days compared with group (2) 4.7 days (P < 0.001) as well as a shorter hospital stay 11.8 days versus 14.8 days (P < 0.03). There were no hospital deaths in group (1), but one death occurred in group (2).

Conclusions: this study has demonstrated the efficacy of preoperative IABP treatment in high-risk patients undergoing CABG. The preoperative IABP therapy has improved cardiac performance pre- and postoperatively and was associated with a lower incidence of postoperative low cardiac output, a lower hospital mortality rate and less postoperative morbidity, as well as a shorter need for SICU and hospital stay. Early postoperative application of IABP before the deterioration of hemodynamic status of the patient had helped to lower mortality rate in our patients compared to other studies. These findings suggest that early and low threshold of use of the IABP is advisable in high-risk patients.

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The Intra Aortic Balloon Pump (IABP) is usually the first mechanical device used for perioperative cardiac failure [1]. It is the most commonly used device for mechanical circulatory support in cardiovascular surgery today. Major indications for IABP use include intractable cardiac failure after cardiopulmonary bypass, pre-operative stabilization of refractory unstable angina pectoris or severe left

ventricular dysfunction and complication of myocardial infarction (MI) refractory to pharmacologic therapy [2,3,4].

The main effects of IABP are reduction of ventricular afterload, improvement of diastolic coronary perfusion by diastolic pressure augmentation, and enhancement of subendocardial perfusion. It reduces the energy requirement of the left ventricle and maximizes coronary perfusion by diastolic augmentation. Previous studies have demonstrated that the augmented diastolic pressure results in a redistribution of coronary blood flow towards ischemic areas of the myocardium [5].

The first clinical application was reported in 1968, primarily for use in cardiogenic shock [6]. Since that time, the IABP has gained widespread acceptance, and it is estimated that 70,000 IABPs are inserted annually in the United States [7].

IABP therapy requires patients to have a critical minimal level of ventricular function. Therefore the IABP has limited use in patients with severe ventricular failure, severe ventricular dysrhythmias or asystole and right ventricular failure [2].

Patients and methods

Between February 1999 and February 2004, a total of 556 patients underwent standard coronary artery bypass surgery (CABG) at our center (Dubai Hospital, Dubai, UAE), of them 57 patients (10.2%) received IABP support, all of them were males. Twenty eight patients (51%) had preoperative IABP (group 1), while 29 patients (49%) had the IABP postoperatively (group 2). The preoperative indications for IABP insertion is 2 or more of the following criteria: preoperative Left ventricular ejection fraction (LVEF) $\leq$ 40%, left main coronary artery stenosis $\geq$ 70%, reoperation and/or unstable angina despite maximum medical treatment). IABP was required postoperatively when the heart could not be weaned off cardiopulmonary bypass in spite of adequate filling and after trial of weaning on maximum pharmacological support of Adrenaline, Dobutamine and Amrinone.

All patients who received IABP had pulmonary artery Swan-Ganz catheter (Baxter – Baxter Health Care Corporation, Irvin, CA, USA) inserted either preoperatively (group 1) or postoperatively (group 2). The Swan-Ganz catheter was used for evaluation of cardiac performance using cardiac index measurement (l/min/m2), calculated from cardiac output data measured repeatedly 4, 12 and 24 hours post bypass. The amount of pharmacological inotropic support pre and post operatively was recorded. Postoperative mortality and morbidity (including all balloon-related complications) as well as required stay in the surgical intensive care unit (SICU) and the total hospital stay, were registered for all patients

All the patients were submitted to thorough history taking with emphasis on risk factors, number of diseased vessels, and preoperative LVEF %. All the patients had history of chest pain and they were classified according to the Canadian Cardiovascular Society Classification of Angina (CCSC) [9]. All preoperative clinical data, catheterization data and operative data were recorded. All the patients were diagnosed to have coronary artery disease based on selective coronary angiography. The Left Ventricular ejection fraction (LVEF%) was calculated using LV angiography according to Simpson's method [10] as well as from intra operative trans-esophageal echocardiography (TEE), and from trans thoracic echocardiography (TTE) during the follow up period.

Patients' profile

The mean age of all patients was 52 ± 1 years (ranging from 40 to 73 years) and both groups were males. In group (1), the mean age was 52.3 ± 1 year, while in group (2) the mean age was 52.2 ± 1.3 years. Ten patients (17.5 %) underwent urgent surgery (within 24 h of admission), mainly due to unstable angina, despite optimal medical treatment. A total of 36 patients (63 %) had a preoperative LV EF $\leq$ 40%, and 10 patients (17.5%) had left main disease. Eleven patients (19%) had recent MI less than 6 weeks. Twenty-one patients (37%) had difficulty in weaning off CPB and 7 patients (12%) developed new ECG changes on the monitor. No Re-do CABG was performed in this series. The preoperative patients' profile in each group is presented in Table (I).

Surgical technique:

Standardized techniques of anesthesia and operative procedures were used in all patients [11]. Intraoperative Trans Esophageal Echocardiography (TEE) was used in all patients. The chest was entered through a median sternotomy incision. The left internal mammary artery (LIMA) was harvested in most cases, simultaneously with the saphenous vein of the right leg. All operations were performed using standard cardiopulmonary bypass,

mild systemic hypothermia down to 33 - 35 C°, topical cold saline slush with combined antegrade/retrograde blood cardioplegia and hot shot. Half of the initial induction dose was given antegrade, the rest was given retrograde via coronary sinus cardioplegia cannula and cardioplegia was repeated retrogradely every 15 minutes or whenever electrical activity resumed. Hot shot was given over 5 minutes prior to de-clamping. All the distal anastomoses were performed first during a single period of aortic cross clamping, and the proximal anastomoses were performed after de-clamping, with a partial occluding clamp.

The aortic cross-clamping time (CC), the cardiopulmonary bypass time (CPB), and, the use of inotropic support were recorded.

All patients in our center routinely receive Dopamine in small dose < 5 µ gm/kg/min during weaning off CPB and the first 24 h postoperatively. If more inotropic support is needed the dose of Dopamine is increased up to 15 µ gm/kg/min or another inotrop is added like Dobutamine, Adrenaline, Noradrinaline or Amrinon. Intra operative parameters are expressed in Table (2).

In the Surgical Intensive Care Unit (SICU), cardiac index (CI) was recorded repeatedly at 4, 12 and 24 hours post bypass calculated from cardiac output data measured via Swan-Ganz catheter inserted preoperatively for evaluation of cardiac performance. Also the need for inotropic support, the IABP support duration, the ventilation time and the SICU stay time were recorded. The postoperative parameters are presented in Table (3).

The intra-aortic balloon pump

The intra-aortic balloon used was a Datascope 8 F 40 cc balloon catheter (Datascope Corp., Fairfield, New Jersey, USA) connected to a Datascope pump 96 System (Datascope, Corp., Fairfield, New Jersey, USA). All IABPs were inserted using a percutaneous route (femoral artery). Preoperatively, the IABP was inserted using local analgesia prior to induction of anesthesia in the operating room on average 1.5 h prior to start of the CPB. There was no failure of percutaneous placement of the IABP. The IABP support was terminated when hemodynamic stability was restored (maintaining a cardiac index > 2.2 L/min/m2 with minimal pharmacologic support). All patients received low molecular weight heparin (LMWH) Enoxaparin 0.5 mg/Kg B D postoperatively once mediastinal drainage subsided (usually after 12 h) regardless of IABP insertion till patient was ambulated. All patients received 100 mg coated Aspirin the night of surgery via naso gastric tube (NGT). All patients received prophylactic antibiotics.

Statistical analysis

Quantitative data were analyzed using paired Student t test and qualitative data were analyzed using the standard error of difference between percentages (U test) and Chi-square test when appropriate. A P value £≤ 0.05 is significant. Data was expressed as mean values ± standard error of mean (mean ± SEM). The statistical analysis was done using the software StatView by SAS Institute Inc., USA.

Results

The two groups were similar with respect to age, sex and angina class. There was no significant difference between both groups as regards: risk factors and number of diseased vessels. Eight patients (28%) had left main disease in group (1), in comparison to 2 patients only (7%) in group (2) and the difference was statistically significant (P< 0.05). The preoperative LVEF% was lower in group (1) with mean of 33 ± 1.7 % compared to patients in group (2) with mean of 45 ± 1.5 % and the difference was significant (P > 0.001). (Table 1).

Variable	Group (1) (No 28)	Group (2) (No 29)	P value
Age (years)	52.3 ± 1	52.2 ±1	NS
CCSC			
II	2/28 (7%)	2/29 (7%)	NS
III	21/28 (75%)	25/29 (86%)	NS
IV (UA)	5/28 (18%)	2/29 (7%)	NS
Risk factors			
Smoking	16/28 (57%)	19/29 (65%)	NS
DM	16/28 (57%)/	19/29 (65%)	NS
Hypertension	17/28 (61%)	18/29 (62%)	NS
Hyperlipidemia	24/28 (86%)	24/29 (83%)	NS
MI < 6 weeks	3/28 (11%)	8/29 (28%)	NS
CA Findings			
2VD	1/28 (4%)	2/29 (7%)	NS
3VD	27/28 (96%)	27/29 (93%)	NS
LM disease	8/28 (29%)	2/29 (7%)	<0.05*
LVEF %	33 ± 1	45 ± 1	< 0.001*

Table (1): Preoperative patients' profile. Data was expressed as mean values ± standard error of mean (mean ± SEM). CCSC: Canadian Cardiovascular Society Classification. UA: Unstable Angina. DM: Diabetes Mellitus. MI: Myocardial Infarction. CA: Coronary Angiogram. VD: Vessel Disease. LM: Left Main. LVEF%: Left Ventricular Ejection Fraction. NS: Not Significant. *: Significant.

The average number of distal anastomosis was 3.5/ patient in both groups. In group (1) the average number of distal anastomosis was 3.6 ± 1/patient while in group (2) it was 3.4 ± 0.8/patient with no statistical difference between both groups.

Thirty five patients (61%) only received left internal mammary artery (LIMA) graft in contrast to our normal

utilization rate of more than 98% of the patients receiving LIMA. Twenty three patients in group (1) and 12 patients in group (2), with high statistically significant difference (P < 0.001).

The mean cross clamp (CC) time in group (1) was 64.9 ± 3.8 minutes and in group (2) was 59.7 ± 6 minutes with no significant difference between both groups, but the mean cardiopulmonary bypass time (CPB) was significantly shorter in group (I) 102.8 ± 7 minutes compared to group (2) 128.8 ± 7 minutes with (P < 0.02). (Table 2)

Variable	Group (1) (No 28)	Group (2) (No 29)	P value
CC (min)	64.9 ± 3	63.7 ± 4	NS
CPB (min)	102.8 ± 7	127.9 ± 7	< 0.02*
Distal grafts	3.6 ± 1	3.4 ± 0.8	NS
LIMA	23/28 (82%)	12/29 (41%)	<0.001*

*Table (2). Operative data. The data was expressed as mean values ± standard error of mean (mean ± SEM). CC: Cross Clamp. CPB: Cardiopulmonary Bypass. LIMA: Left Internal Mammary Artery. NS: Not Significant. *: Significant.*

The preoperative Cardiac index measurement in group (1) was low 1.9 ± 0.06 l/min/m2. It started to rise 5 minutes post termination of CPB, to 2.3 ± 0.06 l/min/m2. The CI continued to rise in the SICU at 4, 12 and 24 hours post bypass in both groups but the rise was more in group (1) patients and it was statistically significant with (P < 0.008), (P < 0.002), and (P < 0.0001) respectively. Group (1) patients showed better improvement of their cardiac performance than the patients in group (2) considering the CI measurement (Table 3).

In group (1) patients, the duration of IABP support time was 21.6 ± 0.9 hours, while in group (2) the duration of IABP support time was 34.7 ± 0.8 hours. The difference was statistically highly significant (P < 0.0001). The IABP could be successfully removed percutaneously with no IABP related mortality or morbidity

The ventilation time was significantly shorter in group (I) 28.7 ± 0.6 minutes compared to group (2) 50.2 ± 5.7 hours with (P < 0005).

The required stay time in the surgical intensive care unit (SICU) was significantly shorter in group (1), 2.0 ± 0.05 days, compared to group (2), 4.7 ± 0.4 days with (P < 0.001).

Hospital stay time was significantly shorter in group (I) 11.8 ± 1.2 days compared to group (2) 14.8 ± 0.6 days with (P < 0.03).

The immediate post-bypass LVEF% was 37.5 ± 1.6 in group (1) and 42.6 ± 1.2 in group (2) and the difference was still significant (P < 0.01). At 3-month follow up of LVEF% revealed no group differences 44.1 ± 1.2 in group (1) and 47.1 ± 0.9 in group (2) patients (Table 3).

Variable	Group (1) (No 28)	Group (2) (No 29)	P value
CI (l/min/m²)			
CI (4 h)	2.7 ± 0.07	2.5 ± 0.02	< 0.008*
CI (12h)	3.1 ± 0.08	2.7 ± 0.02	< 0.0002*
CI (24h)	3.4 ± 0.07	3 ± 0.033	<0.0001*
LVEF %			
Immediate	37.5 ± 1.6	42.6 ± 1.2	< 0.01*
3 months	44.1 ± 1.2	47.1 ± 0.9	NS
IABP support (h)	21.6 ± 0.9	34.7 ± 0.8	< 0.0001*
Ventilation (h)	28.7 ± 0.6	50.2 ± 5.7	<0.0005*
SICU stay (days)	2.0 ± 0.005	4.7 ± 0.4	< 0.001*
Hospital stay (days)	11.8 ± 1.2	14.8 ± 0.6	< 0.03*

*Table 3. Postoperative data. The data was expressed as mean values ± standard error of mean (mean ± SEM). CI: Cardiac Index. LVEF%: Left Ventricular Ejection Fraction. IABP: Intra Aortic Balloon Pump. SICU: Surgical Intensive Care Unit. NS: Not Significant. *: Significant.*

No mortality was found in group (1), but group (2) patients showed mortality of 3.4% (1 patient). This patient was operated on an urgent basis due to unstable angina, had preoperative LVEF of 25 %, had small coronary vessels, and had developed postoperative low cardiac output and ischemic changes on ECG 6 hours postoperatively. He was re-explored and found to have occluded vein graft to obtuse marginal artery, which was re-grafted. The patient developed postoperative non-surgical bleeding and had succumbed on the second postoperative day due to uncontrollable coagulopathy.

Discussion

Since its introduction in the 1960s, the Intra Aortic Balloon Pump (IABP) has become the most widely ap-

plied method in circulatory support because of its availability, price and ease of application [12]. The percutaneous approach has extended the use of IABP to include non operated cardiac patients too. This accounts for the large increase in the preoperative use of IABP reported recently [8].

Many desirable hemodynamic effects of the IABP have been demonstrated: augmentation of myocardial perfusion during diastole, which increases oxygen delivery to the myocardium, reduction of myocardial oxygen consumption through reduction of left-ventricular afterload and left-ventricular wall tension, as well as a modest increase in cardiac output about 10 to 15% [13].

Previous studies in patients with acute coronary occlusion have shown that the augmented diastolic pressure by the IABP results in a redistribution of coronary blood flow towards ischemic areas of the myocardium [5]. Since many of these high-risk patients have an energy depletion of the myocardial cells even a short treatment with IABP would theoretically be beneficial by reversion of ischemic myocardial dysfunction before it leads to cell necrosis [14].

In the present series, the indication of preoperative insertion of IABP include patients presenting with two or more of these criteria: Left ventricular ejection fraction (LV EF $\leq$ 40%), left main stem stenosis $\geq$ 70%, recent myocardial infarction $\leq$ 6 weeks, left ventricular hypertrophy, unstable angina or Redo CABG, while the indications of postoperative insertion of IABP include difficulty in weaning off CPB, patients who develop ST segment changes in the monitor, or patients who developed uncontrollable arrhythmia with hemodynamic deterioration.

In our study preoperative IABP support accounts for 49% of total number of patients receiving IABP. This is in contrast with our previous study 2 where no patients received preoperative IABP. This result could be probably attributed to the fact of increased number of risky cases with poor left ventricular function, unstable angina, higher incidence of left main disease, and lower threshold of IABP insertion.

It is well known that the cardiac performance immediately after myocardial revascularization is improved. This was also demonstrated in the present study. In our study, patients who received preoperative IABP support showed marked improvement in their cardiac performance after the cardio pulmonary bypass demonstrated by the rise in cardiac index values Table (2). The efficacy of the preoperative IABP support was clearly demonstrated in this study coinciding with the results demonstrated by Christenson et al [15].

The IABP is a technique associated with complications. The complications related to the IABP ranges from minor local wound infection or hemorrhage from the access site, which rarely resulted in long-term morbidity, to major vascular complications, including limb ischemia which may lead to long-term morbidity and even death in some patients. The complication rate in the literature ranged from 4 to 30% [13,16,17]. The most common complication is mainly ischemia to the lower limb, most of the time fortunately reversible after removal of the lABP catheter. In our study we experienced no catheter related complications, in contrast to our previous study where the complication rate was 25%, mainly vascular and local wound infection at site of insertion. This could be attributed to the use of more refined small sized catheters (8 F), and more precise techniques of insertion of the IABP. Arafa et al [18] had the same finding where he stated that the significant decrease in major vascular complications that has occurred over the last 5 years can be explained by the increased use of catheters with smaller diameters.

Christenson et al [14] had demonstrated that patients with preoperative IABP had significantly lower mortality rate and a shorter stay in the intensive care unit. In a recent report, Dietl and associates have, in a retrospective study, demonstrated that preoperative IABP significantly improve survival, reduce hospital stay and was more cost-effective than no preoperative IABP treatment [16]. In our study, the total hospital mortality rate in both groups was low 1.7%. In group (1) patients were treated with preoperative IABP for less than 24 hours, and all had survived. This is in agreement with other reports which show that if cardiac recovery is not obtained within the first 24 hours after the initiation of IABP, the chances of survival is low [8]. The mortality rate in group (2) was 3.4% which is low as well compared to other studies [1]. This could be attributed to our lower threshold of postoperative IABP support in any patient showing manifestations of low cardiac output or new ECG changes before any hemodynamic deterioration.

Conclusion

In conclusion, this study has demonstrated the efficacy of preoperative IABP treatment in high risk patients with preoperative Left ventricular ejection fraction (LVEF) $\leq$ 40%, left main coronary artery stenosis $\geq$ 70%, recent myocardial infarction, and/or unstable angina not responding to maximum medical treatment undergoing CABG. The preoperative IABP therapy has improved cardiac performance pre- and postoperatively and was associated with a lower incidence of postoperative low cardiac output, a lower hospital mortality rate and less postoperative morbidity, as well as a shorter

need for SICU and hospital stay. Early postoperative application of IABP before the deterioration of hemodynamic status of the patient had helped to lower mortality rate in our patients compared to other studies. These findings suggest that early and low threshold of use of the IABP is advisable in high-risk patients.

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Coronary revascularization using bilateral internal mammary artery grafting in insulin-treated diabetics Early results

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Background: The use of the left internal mammary artery (LIMA) as the first conduit of choice for coronary artery bypass grafting (CABG) has recently been expanded with its bilateral use, and there is increasing evidence that the bilateral use of internal mammary artery (IMA) confers better long-term results on patients than does single use . However, the results of the use of bilateral internal mammary artery (BIMA) as regard its effect on long term survival and the risk of wound infection in insulin-dependent diabetes mellitus patients has to be determined.

Material& Methods: We retrospectively analyzed 297 consecutive patients after coronary artery bypass grafting. Between April 2000 and December 2005, 297 consecutive insulin-treated diabetic patients underwent elective isolated CABG for coronary artery disease in Kasr El-Aini hospital. Hundred twelve patients who underwent BIMA grafting (BIMA group) were compared to 185 patients in whom single LIMA was used (LIMA group). The complementary grafts in both groups consisted of saphenous vein grafts (SVG).

Results: The two groups had comparable preoperative characteristics .The 30-day mortality was comparable in both groups. No difference (of statistical significance) was found between patients of both groups as regards the preoperative demographic data. The mean harvesting time was significantly higher in the BIMA group. The rates of deep sternal wound infection was similar in the two groups (3.5% in BIMA group vs. 2.1% in LIMA group).Survival at 6 months was 96.4% in BIMA group and 96,2 % in LIMA group (p = NS). At 6 months follow up, Freedom from MI (97.7 ± 0.5 VS. 94.2 ± 1.2%, p =0.0034), and MI in a grafted area (97.9 ± 0.5 VS. 94.7 ± 1.3%, p = 0.0017).

Conclusions: In insulin- treated diabetic patients with multi-vessel coronary artery disease who undergo first myocardial revascularization, BIMA ± SVG provides higher freedom from myocardial infarction, myocardial infarction in grafted areas, and cardiac events, if compared with LIMA + SVG. It plays a protective role in reducing the incidence of late AMI with non significant increase in the risk of sternal wound infection.

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Recent interest has focused on the use of arterial conduits in diabetic patients. The use of bilateral internal mammary artery (BIMA) in diabetics has been a matter of debate due of the risk of sternal infection. Patients receiving bypass grafts with BIMA also had significantly fewer complications of ischemic heart disease during follow-up compared with those having only one internal mammary artery (IMA) graft because arterial revascularization is believed to be the key to this benefit and the improved survival of diabetics is thought to be related

to the use of at least one internal mammary artery.(1-2) And as diffuse coronary artery disease involving distal vessels is more common in diabetic patients, therefore, in diabetic patients, bypass grafting using arterial grafts is desirable. This finding together with a reduction in late ischemic events give further support to the observation that use of BIMA may decrease late cardiac deaths compared with revascularization with left internal mammary artery (LIMA) in this patient category .(3-4)

The use of two internal mammary arteries in CABG has been associated with decreased risk of death, repeated revascularization, and return of angina. However, despite these advantages, use of bilateral IMA grafts in insulin- treated diabetics remains unresolved.(5)

The aim of this study is to compare the results of use of BIMA versus LIMA with saphenous vein grafts in insulin- treated diabetic patients as regard the incidence of postoperative wound infection, and six months follow up for the incidence of myocardial infarction, and cardiac events and early survival.

Patients& Methods :

We retrospectively analyzed 297 consecutive patients after coronary artery bypass grafting. Between April 2000 and December 2005, 297 consecutive insulin-treated diabetic patients underwent elective isolated coronary artery bypass grafting (CABG) for coronary artery disease in Kasr El-Aini hospitals. Hundred twelve patients who underwent BIMA grafting (BIMA group) were compared to 185 patients in whom single LIMA was mobilized (LIMA group). The complementary grafts in both groups consisted of saphenous vein grafts (SVG). The preoperative demographic data and risk factors are demonstrated in table (1)

Table 1. Preoperative patient characteristics in the two groups

Characteristic	BIMA Group no. 112	LIMA Group no. 185	*p* Value
Age (yrs)			
Range	36–79	49–68	
Mean ± SD	65.6 ± 8.6	65.1 ± 6.2	NS
Gender			
Male	75 (67%)	125 (67.5%)	NS
Female	37 (33%)	60 (32.5%)	NS
LMD	25 (22.5%)	40 (21%)	NS
3VD	62 (55%)	100 (54%)	NS
2VD	25 (22.5%)	45 (25%)	NS
LVEF (%)			
Range	25–63	20–67	
Mean ± SD	44.7 ± 11.1	43.3 ± 17.2	NS
Past history of MI	73 (65%)	135 (73%)	NS

LVEF = left ventricular ejection fraction; LMD = left main disease; MI = myocardial infarction; NS = not significant; SD = standard deviation; 1VD = one-vessel disease; 2VD = two-vessel disease; 3VD = three-vessel disease

Operative technique

All operations were performed through a midline sternotomy using cardiopulmonary bypass (CPB). Myocardial protection involved warm intermittent, antegrade blood cardioplegia (30°C to 32°C). Glucose management was aimed at maintaining a level of less than 250 mg/dL by sliding-scale-guided intermittent subcutaneous insulin injections. After performing median sternotomy, a single or bilateral IMA was mobilized from its origin to the distal end close to the bifurcation as a pedicle with surrounding tissue in cases of unilateral IMA or skeletonized in cases of the use of bilateral IMA. The common trunks of sternal branches and intercostal branches arising from the IMA were carefully preserved. Branches were cut less than 1 mm from their origin so as not to obstruct the sternal circulation from the intercostal arteries. Grafting was attempted on all vessels measuring 1.5 mm or more in diameter that showed 70% or greater obstruction. The operative data are shown in table 2.

Table (2): Operative Data

Characteristics	BIMA Group	LIMA Group	*p* value
Mean time of harvesting (min.)	35	15	0.001
No. of grafts done (mean)	3.5 ± 1.2	3.7 ± 1.3	NS
Cross- clamp time (mean in min.)	44 ± 11	38 ± 14	NS
CPB time (mean in min.)	91.2 ± 9.5	92.4 ± 8.5	NS

CPB : cardiopulmonary bypass ; min. : minute

Results

The two groups had comparable risk profiles and there were no difference (of statistical significance) was found between patients of both groups as regards the preoperative demographic data.The mean harvesting time was significantly higher in the BIMA group (p = 0.001). Complementary grafts were in the form of saphenous veins in both groups.The Operative data are demonstrated in table number (2). The rates of deep sternal wound infection was similar in the two groups (3.5% in BIMA group vs. 2.1% in LIMA group. In-hospital mortality (BIMA group: one patient (0,9 %,) LIMA group: another patient (0,5%) , p = NS),and all the mortality in both groups were due to heart failure in patients already with low preoperative ejection fraction. Perioperative myocardial infarction was 4%, BIMA group and 4.7% in LIMA group (p = NS).The early postoperative complications are shown in table 3.

Table (3) : Early postoperative complications

	BIMA Group	LIMA Group	*p* value
superficial wound infection	5(4.4%)	8 (4.3%)	NS
deep wound infection	4 (3.5%)	4 (2.1%)	NS
myocardial infarction	4 (3,5%)	8 (4.3%)	NS
reexploration for bleeding	1 (0.9%)	0	NS
respiratory failure	0	1 (0,5%)	NS
Early cardiac death	1 (0.9%)	1 (0,5%)	NS

Grafts were distributed equally to the coronary territories in both groups . One mammary artery was directed to the LAD in 294 patients in the whole study group and only three patients received SV grafts to the LAD due to insufficient flow of LIMA . In the BIMA group, a second arterial conduit, either LIMA or right internal mammary artery (RIMA) was used to revascularize the left coronary system in 148 patients either in situ, free separate ,or inverted Y-shaped or sequential arterial grafts.The RCA was grafted using either RIMA or SVG in 160 patients. The rest of the graft distribution is demonstrated in table (4).

Table 4. Coronary arteries revascularized with internal mammary artery and saphenous Vein.

	Revascularized Coronary Arteries			
	LAD	D	LCX	RCA
LEFT IMA	275	72	19	0
RIGHT IMA	19	25	32	36
SVG	3	56	117	124

D = diagonal branch; IMA = internal mammary artery; LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery; SVG = saphenous vein graft.

Follow up:

All patients were followed up after surgery 3 and 6 months in the outpatient clinic for a period ranged from 6- 60 months and the dead line of follow up was June 2006. After this period of follow up, two patients died in the BIMA group and five in the LIMA group due to cardiac -related causes and one in each group due to non-cardiac causes.The final number of patients who completed the follow up (survivers) was 108 (96,4%) patients in the BIMA group compared to 178 (96,2%) patients in the LIMA group (p = NS). At 6 months follow up, Freedom from MI (97.7 ± 0.5 vs. 94.2 ± 1.2%, p =0.0034), and MI in a grafted area (97.9 ± 0.5 vs. 94.7 ± 1.3%, p = 0.0017).Only one patient (0.9%) in the BIMA group suffered from delayed sternal union who required operative fixation and rewiring and discharged after one week with no complications.The Late follow up data are shown in table 5.

Table (5): The Late follow up (6-month)

	BIMA Group	LIMA Group	P value
Death due to non-cardiac reason	1 (0,9%)	1 (0,6%)	NS
Late cardiac death	2 (1,8%)	5 (2,7%)	NS
Freedom from death	108 (96,4 %)	178 (96,2%)	NS
Acute MI	1 (0.9%)	3 (1,6%)	NS
Acute MI in grafted area	2,1± 0.5%	5,31±1,3%	P=0,0017
Redo PTCA	2 (1.8%)	1 (0,6%)	NS
Cerebrovascular stroke	4 (3,6%)	1 (0.6%)	NS
Delayed sternal wound complications	1 (0.9%)	0	NS

MI : myocardial infarction ,PTCA : percutaneous transluminal coronary angioplasty

Discussion:

The second graft of choice in diabetics remains in question. For various reasons, there has been some reluctance to use bilateral IMA: inadequate length of the right IMA (RIMA) to be bypassed to a distal branch of the left circumflex (LCX) or right coronary artery (RCA); increased likelihood of sternal infections; technical difficulty; the prolonged time for harvesting conduits; and the possibility of the RIMA being injured during reentry when it is placed anterior to the heart for revascularization of the left anterior descending (LAD) artery. In diabetic patients particularly insulin –dependent type, the majority of surgeons have avoided using bilateral IMA for fear of deep sternal infections . (5-6)

Despite increasing popularity of the radial artery, this conduit is less resistant to arteriosclerosis, intimal hyperplasia, and medial calcification in comparison to IMA.(1) Equally important is the fact that competitive flow may preclude its use in non critical target coronary stenoses. Moreover, the natural history of the radial artery grafting in insulin-treated diabetics is currently undetermined and the IMA has been the only conduit

so far that has improving effect on survival in diabetics. The long-term impact of non-IMA arterial grafts awaits confirmation.(7)

It has been demonstrated that left IMA bypass to the anterior descending artery has a better long-term survival because of the favorable properties of arterial conduits as compared to venous conduits .(8) Therefore, a good question has arisen, if single IMA is good, bilateral IMA could be even better.(9)

Diabetics are more prone to infection and poorer healing, thus most surgeons believe it is an unnecessary risk to harvest BIMA in this group . (10) Insulin-dependent diabetes makes most surgeons even more reluctant to harvest BIMA, despite the evidence that it is this group who will benefit most from BIMA grafting in the long term.(1-2) An additional benefit concerning long-term morbidity and mortality was described after a surgical technique revascularizing preferentially left-sided coronary arteries (LAD and circumflex artery) with BIMA .(4-11-12-13-14)

BIMA grafting is thought to be associated with an increased perioperative risk of morbidity and mortality as well as an extended incidence of sternal complications . In a study by Gansera et al, consisting of 1487 patients with BIMA grafting, the incidence of sternal instability revealed 2.0% for the LIMA group versus 4.2% for the BIMA group. Meanwhile this complication is reduced to 0.6% versus 1.4%,in the authors opinion, a remarkable improvement depending on advantages in surgical techniques (lower traumatic and faster, 'small-pedicled' harvesting of IMA grafts/the use of seven or eight wires for sternal closure and avoiding the use of bone wax). (15) These results compares favorably with those of Momin et al, who showed that the perception that BIMA grafting increases the risk of sternal complications in insulin-dependent diabetic patients.(7)

In fact, however, many surgeons do not recommend the routine use of BIMA grafts for CABG.(16-17) It appears that the increasing risk of sternal infection probably due to sternal ischemia is the main reason for avoiding BIMA grafting. In the present study, BIMA grafting was performed without any increase in mortality or morbidity. We carefully preserved the common trunks of sternal branches and intercostal branches arising from the IMA during harvesting of the IMA, and the sternum was fixed firmly with stainless steel wires and chest binder was applied in the early postoperative days.

Concerning freedom from cardiac events and necessity of interventions (PTCA/STENT) as well as reoperation, the results of our study were similar to those of Pick et al. (18) and Lytle et al.(19). Nevertheless, there are no randomized data comparing BIMA and LIMA surgical strategies in large numbers, different target vessels and different surgical techniques (in situ / free grafts / pedicled / unpedicled); many confounding variables make statistical analyses difficult. The largest patient population (2001 BIMA grafts) with the longest postoperative interval was issue of a nonrandomized study from the Cleveland Clinic (19), and documented clearly the superior benefit concerning decreased risk of death by 6.3% and decreased risk of reoperation by at least 8.3%, by 12 postoperative years if patients received BIMA grafts rather than LIMA grafts.

In addition, the blood glucose level was managed by employing regular insulin injection every 6 hours according to a sliding scale during both the preoperative and postoperative periods. It appears that these techniques contributed to the relatively low incidence of chest wound infection in our series.

Quality of the harvested vessel is a further important variable by which the technique of skeletonization should be judged. The performance of skeletonized conduits has been assessed in a number of retrospective trials and accumulating data, however, suggest that skeletonized BIMA can be performed safely in certain diabetic subgroups. Reduced damage of arterial branches supplying the sternum is one of the theoretical advantages of skeletonization. Careful dissection with scissors or bipolar diathermy is the recommended method of skeletonizing the IMA. With regard to sternal blood supply, studies demonstrated significantly lower sternal vascularity in patients undergoing harvesting of pedicled as compared to skeletonized conduits.(20-21)

Long-term survival and freedom from cardiac-related events after coronary artery bypass grafting are related to the completeness of revascularization, subsequent progression of native vessel disease, and late attrition of bypass conduits [22-23]. The relative resistance of the IMA to arteriosclerosis is well known (24), and 10-year patency of 80% to 90% is almost twice that expected with saphenous vein grafts .(25) Internal mammary arteries have other advantages including ideal coronary-to-conduit size match, functioning endothelium (26) and the capacity for flow regulation in response to varying myocardial demand .(27)

To compare survival of patients receiving single and bilateral internal mammary artery grafts more than 20 postoperative years, assess magnitude of benefit, and identify predictors of benefit, Lytle,et al,(9) demonstrated that bilateral internal mammary artery grafting produces improved survival compared with single internal mammary artery grafting during the second postoperative decade, and the magnitude of that benefit increases through 20 postoperative years.These results were also

reported by many other authors. (28-29-30-31)

Our study demonstrates clear advantages for the use of BIMA grafts in coronary revascularization of insulin –dependent diabetics by virtue of reduction in the late risk of MI and recurrent angina (acute MI in grafted area was 2,1± 0.5% in BIMA group vs. 5,31±1,3% in LIMA group P=0,0017 - statistically significant) . There was also an improvement in survival free of cardiac death. It seems reasonable, therefore, to expand use of BIMA grafting, especially when the right IMA can be used to bypass a major branch of the left coronary system. Final clarification of the long-term survival benefits for this category of patients receiving more than one arterial graft will need to await the results of larger patient series, after possibly longer follow-up. Meanwhile, diabetic patients can be offered BIMA grafts with the expectation of improved freedom from recurrence of angina, late MI, and other late cardiac events.

Several limitations of this study need to be addressed. This is a retrospective study and the comparison involved BIMA with single IMA and saphenous veins. A prospective, randomized, long-term comparison between the use of BIMA versus the use of LIMA and saphenous veins would be further required to determine the strategy of choice in this diabetic subsets.

Conclusions:

BIMA grafting can be performed safely in insulin-treated diabetics. This approach confers superior long-term cardiac outcome and is, therefore, recommended in this diabetic subset.This study demonstrates that BIMA grafting is feasible in the majority of patients undergoing multiple CABG and can be achieved without any increase in risk of sternal wound infection, moreover the use of BIMA give the patient better long term results as regard survival, freedom from myocardial infarction, myocardial infarction in grafted areas, and cardiac events.

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Implications of valve prosthesis-patient mismatch after aortic valve replacement with small sized mechanical prosthesis

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Background: The functional and hemodynamic implications of Valve Prosthesis-Patient Mismatch (VP-PM) after aortic valve replacement (AVR) with various small sized mechanical prosthesis in patients with a small aortic annulus still represent a dilemma to the surgeon.

Patients and Methods: This prospective study included 68 patients who underwent elective isolated AVR with various mechanical bileaflet prostheses labeled size 19, 21 and 23 during a 2 year period. The medical and the surgical records of all patients were collected, reviewed and analyzed. Survival status, functional status and hemodynamic performance were assessed in all patients after surgery.

Results: According to the Guidelines used for defining VP-PM in this study, after AVR, 58 patients (85.3%) showed mild VP-PM, 9 patients (13.2%) showed moderate VP-PM, and only one patient (1.5%) showed severe VP-PM. At follow up, patients with size 21 and 23 valves prosthesis were asymptomatic. Amongst the 30 patients who received size 19 valve prosthesis, one patient (3.3%) had New York Heart Association (NYHA) class III symptoms, 5 patients(16.7%) had NYHA class II symptoms and the remaining were asymptomatic. The mean postoperative peak systolic gradient (PSG) in the patients receiving size 19 valves was significantly higher than those receiving size 21 and size 23 valves ($p<0.05$ and $p<0.01$ respectively). Also the mean Postoperative left ventricular mass index (LVMI) in patients with size 19 valves was significantly higher compared to size 23 and 21 valves ($p<0.05$).

Conclusion: In spite of having VP-PM the functional outcome and hemodynamic performance of size 21 and 23 valves was found satisfactory. As against this the VP-PM seen in patients in the group receiving size 19 valve was poorly tolerated.

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Patients with small aortic roots undergoing AVR) are not an uncommon finding, and they still represent a special challenge to the surgeon regarding the operative technique and selection of prosthesis (1). In the late seventies Rahimtoola (2) noticed that patients receiving small sized mechanical prosthesis faced problems including improvement in functional status less than expected, progressive deterioration of cardiac function, acute valve thrombosis and sudden death. He identified this as VP-PM. The problem of VP-PM and small aortic annulus is very closely related.

VP-PM is technically present, when the implanted valve has an Effective Orifice Area (EOA) less than that of the normal valve for that Body Surface Area (BSA) (2). The normal area of the aortic valve ranges from 2.6 - 3.6cm2

(2.0cm2/ m2 BSA). Mechanical prosthesis of size less than 25, have an EOA of less than 2.5cm2 and by definition these valves are inherently stenotic. Thus theoretically the concept of VP-PM should be considered whenever AVR is performed with various small sized prosthesis (3-6).

The aim of our study was to evaluate the functional and hemodynamic implications of VP-PM after AVR with various small sized mechanical prosthesis in patients with a small aortic annulus.

Patients and Methods

This prospective study included 68 patients who underwent elective isolated AVR with various mechanical bileaflet prostheses labeled size 19, 21 and 23 during a 2 year period between October 2004 and September 2006 at Zagazig University Hospital and Ain Shams University Hospital.

These patients included in the study also fulfilled the following criteria: 1) Isolated aortic valve disease with no significant involvement of other valves, 2) Had no previous history of valve replacement or repair, 3) Sinus rhythm, and 4) Had no associated coronary artery disease as presence of Ischemic Heart Disease has been reported as an independent prognostic factor in the improvement in functional class after aortic valve surgery (7, 8).

All patients underwent isolated AVR by standard anaesthesia and surgical techniques. Through a median sternotomy, cardiopulmonary bypass was performed with a membrane oxygenator and by ascending aorta and two stages venous cannulation with standard moderate hypothermic (28°C). Cardiac arrest was induced and maintained using antegrade intermittent hyperkalaemic cold (4oC) crystalloid cardioplegia through the coronary ostia with topical hypothermia. Reinfusion of cardioplegia was done every 20 minutes. AVR with mechanical bileaflets valves was performed with the standard routine technique in all patients. The largest suitable valve was always selected for a given patient. Aortic prosthesis was implanted in anatomic position using non pledgetted everting horizontal mattress polyester sutures (Ethibond 2-0, Ethicon Inc). No aortic ring enlargement procedure was undertaken. De-airing, weaning from cardiopulmonary, decannulation and chest closure were conducted in the usual manner.

The medical records of these 68 consecutive patients who fulfilled the entry criteria for the study were collected, reviewed and analyzed, including preoperative clinical data, 2D and Doppler transthoracic echocardiographic results, cardiac catheterization hemodynamics if done. Also, all the surgical records were reviewed in order to determine the size and type of the aortic prosthetic valve used and the aortic cross clamp and cardiopulmonary bypass durations.

All patients were followed up for a minimum of six months. Survival status, New York Heart Association (NYHA) functional class and echocardiography with Color Doppler study were assessed in all patients after surgery. Adverse clinical events were recorded.

Comprehensive Two dimensional with Colour Doppler echocardiographic assessment at rest, in supine position was performed in all patients (< 30 days) before AVR and from minimum 6 months after surgery by a Hewlett Packard 5500 ultrasound system with a 2.5 MHz transducer (HP, Andover, MA).

The left ventricular end systolic and end diastolic dimensions, posterior and septal wall thickness, and left ventricular volumes were determined by planimetry of the two dimensional recordings of the apical 4 chamber and short axis views. The thickness of the interventricular septum and left ventricular posterior wall was measured at the level of the chordae tendinae according to the criteria of the American Society of Echocardiography (9). Left Ventricular Mass (LVM) was calculated using the Devereux formula. Left Ventricular Mass Index (LVMI) was calculated by indexing the LV mass to the body surface area. The Effective Orifice Area (EOA) was calculated using the continuity equation as described by Skjaerpe et al (10). To make the values comparable between the patient groups the prosthetic EOA was indexed with the body surface area of the patient to give the Effective valve orifice area index (EOAI). The velocities across aortic valve and prosthesis were recorded with a continuous wave Doppler technique from the apical, supra-sternal and right parasternal positions. From the highest velocities obtained the transprosthetic pressure drop was calculated using the Modified Bernoulli equation. The Trans Prosthetic Gradients were then calculated by applying the formula.

The Guidelines used for defining VP-PM in this study were the same as that recommended by Rahimtoola (2). The EOAI was used to divide the patients into three groups. Those with EOAI more than or equal to 0.9 cm2/m2BSA were included as Mild VP-PM, between 0.6 and 0.9 as Moderate VP-PM and less than or equal to 0.6 as Severe VP-PM.

Statistical analysis

Continuous variables are presented as mean ± standard deviation and categorical variables were expressed as percentages. The data was subjected to independent and paired Students t-test and chi-square test to determine the p-value and statistical significance of the variables

being compared. Differences were considered statistically significant if the p value was less than 0.05.

Results

The preoperative demographic and clinical data of all operated patients are shown in Table 1 and the operative data is shown in table 2.

TABLE 1*:* Preoperative Clinical Data (n= 68)

Variables	
Age (y, range)	31.9 ± 11.2 (18 to 52)
Sex (n):	
Male	49 (72.06%)
Female	19 (27.94%)
Body surface area (m^2, range)	1.5 ± 0.1 (1.2 to 1.8)
NYHA Functional Class (n):	
II	18 (26.5%)
III	41 (60.3%)
IV	9 (13.2%)
Heart rate (beats/min)	78 ± 12
Aortic valve pathology(n)**:**	
Stenosis	29 (42.7%)
Insufficiency	16 (23.5%)
Mixed lesion	23 (33.8%)
Etiology(n)**:**	
Calcific	9 (13.3%)
Bicuspid	2 (2.9%)
Rheumatic	57 (83.8%)

TABLE 2*:* Operative Data (n= 68)

Variables	
Labeled valve size(n)	
19	31(45.6%)
21	26 (38.2%)
23	11 (16.2%)
Valve type(n)	
SJM- stander	28 (41.2%)
CarboMedics	22 (32.4%)
Sorin	18 (26.4%)
Aortic cross-clamp time (min)	75.6 ± 16.7
Cardiopulmonary bypass time (min)	112.4 ± 19.8

According to the Guidelines used for defining VP-PM in this study, after AVR 58 patients (85.3%) showed mild VP-PM and 9 patients (13.2%) showed moderate VP-PM. Only one patient (1.5%) in this study showed severe VP-PM. Of the 58 patients with mild VP-PM, 23 patients (39.7%) received size 19 valve prothesis, 24 patients (41.4%) received size 21 valve prothesis and all the 11 patients who received size 23 valve prothesis (18.9%). Seven patients (77.8%) of the 9 patients with moderate VP-PM received size 19 valve prothesis and the remaining two (22.2%) received size 21 valve prothesis. The only patient in this study showed severe VP-PM received size 19 valve prothesis (table 3).

TABLE 3*. Criterion for VP-PM Rahimtoola et al1)*

Degree Of VP-PM	**EOAI Criteria**	**Patients (n)(%)**	**Valve size used**(n) 19	21	23
Mild VP-PM	EOAI > 0.9 cm^2/m^2 BSA	58(85.3%)	23	24	11
Moderate VP-PM	EOAI-0.6 - 0.9 cm^2/m^2BSA	9(13.2%)	7	2	0
Severe VP-PM	EOAI <0.6 cm^2/m^2 BSA	1(1.5%)	1	0	0

VP-PM, valve prosthesis-patient mismatch; EOAI, effective orifice area index; BSA, body surface area

Nonfatal complications occurred in two cases (3%) in the postoperative period. One patient was reexplored for bleeding and one had a sternal infection. One patient died (1.5%) in the immediate postoperative period from low cardiac out put syndrome. This patient had moderate VP-PM and received size 19 valve prothesis.

Follow up was available for all the survivors (67 patients). Follow up period was 10.2±4.1 months (range from 6 months to 18 months). There were no late deaths over the follow-up period. Those patients with size 21 and 23 valves prosthesis were asymptomatic. Amongst the 30 patients who received size 19 valve prosthesis, one patient (3.3%) had NYHA class III symptoms (this patient with severe VP-PM), 5 patients(16.7%) had NYHA class II symptoms (these patients with moderate VP-PM) and the remaining were asymptomatic.

There was a significant fall in PSG in all patients after AVR irrespective of the size of the valve used ($p<0.05$) (Table 4). The mean regression in PSG was 44.04±22.01 mm Hg in patients receiving size 19 valves, 22.7±23.04 mm Hg in size 21 and 11.6±25.7 mm Hg in size 23 valves. There was no statistically significant regression in PSG between size 19 and 21(NS) and size 21 and 23 (NS), however there was a statistically significant regression in PSG of size 23 compared to size 19 valves ($p<0.01$). The mean postoperative PSG in the patients receiving size 19 valves was significantly higher than those receiving size 21 and size 23 valves ($p<0.05$ and $p<0.01$ respectively) (Table 4).

Also there was a significant fall in LVMI following surgery in all patients ($p<0.05$) (table 4). The mean Postoperative LVMI in patients with size 19 valves was significantly higher compared to size 23 and 21 valves ($p<0.05$). There was a statistically significant regression in the LVMI in size 19 group compared to size 21

(p<0.05) but no difference in regression in LVMI between size 19 and 23 (NS). In spite of having a preoperative LVMI more than that in size 21 group, the patients in size 23 group had a more significant regression in the LVMI (p<0.05) and the residual LVMI was even less than size 21 valves (Table 4).

TABLE 4. *Echcardiography data(n=67)*

Parameters	Size 19 (n= 30)	Size 21 (n= 26)	Size 23 (n= 11)	P value 19 vs. 21	19 vs. 23	21 vs. 23
1] PSG						
Mean preoperative	92.6±17.6 mm Hg	58.7±22.4 mm Hg	42.3±25.2 mm Hg	<0.05	<0.05	NS
Mean postoperative	46.6±29.3 mm Hg	34.8±12.7 mm Hg	28.6±9.8 mm Hg	<0.05	<0.01	NS
Mean regression	44.04±22.01 mm Hg	22.7±23.04 mm Hg	11.6±25.7 mm Hg	NS	<0.01	NS
2] LVMI						
Mean preoperative	247.87±97.5 gm/m^2	154.3±57.9 gm/m^2	189.7±67.11 gm/m^2	<0.01	<0.05	NS
Mean postoperative	156.3±64.63 gm/m^2	127.9±26.8 gm/m^2	122.23±31.34 gm/m^2	<0.05	<0.05	NS
Mean regression	97.8±103.07 gm/m^2	26.8±68.2 gm/m^2	63.3±53.21 gm/m^2	<0.05	NS	<0.05

PSG, peak systolic gradients; LVMI, left ventricular mass index.

Discussion

The concept of VP-PM had been introduced by Rahimtoola (2) in the 1970s. This concept of VP-PM was introduced to describe the condition of when the effective orifice of aortic valve prosthesis is less than that of a normal human valve. VP-PM leading to clinical symptoms and requiring reoperation is a reality. Its mechanism is high Transprosthetic energy loss that increases left ventricular work reduces left ventricular mass regression and this can lead to an increased operative mortality, decreased long-term survival and reduced symptomatic benefit. It has been accepted that patients receiving prothesis ≤ 21 mm show higher gradients than patients receiving a larger valve (11, 12)

Nonetheless, VP-PM has frequently been observed, mostly for two reasons. First, patients with aortic valve disease frequently exhibit annulus calcification and fibrosis as well as left ventricular (LV) hypertrophy, and these pathologic processes can reduce the size of the aortic annulus. Second, because the prosthesis is inserted within the same aorta and has its own structural support; the EOA of the prosthesis is necessarily less than that which a normal native valve would have within the same aorta. Obviously, the support apparatus of mechanical valves or stented bioprostheses creates a relative obstruction to the flow and it has been shown that the EOA available for blood flow represents only 40% to 70% of the total area occupied by the valve (1). In addition, the EOA of the implanted valve is further reduced, by tissue in-growth and endothelialisation (3).

Concern has been raised about significant residual gradients when small aortic prostheses are used, particularly in patients with a large BSA, in whom VP-PM may often occur (2). There were publications by groups in favor of the hypothesis that VP-PM is an independent predictor of mortality (13, 14). In contradiction there are others that found that survival after AVR appears not to be adversely affected by VP-PM (15). Recently, the low gradients demonstrated across newer mechanical prosthesis (7) has lead many investigators to question the relevance of VP-PM in the era of tilting disc and bileaflet prosthesis and prompted many to relegate this phenomenon, as reminiscent of the era of ball and cage prostheses. This raises issues regarding whether patients should be subjected to technically demanding and certainly more risky procedures like aortic root widening when a simple aortic valve replacement would be functionally adequate. Although for patients with small aortic ring, there are appropriate annulus-enlarging techniques to implant a larger valve, they often result in increasing morbidity and mortality risks of the operation, thus limiting their applicability (16). Another alternative might be the use of valvular homografts, which have good hemodynamics but are not readily available to most centers (1).

In this study we tested the hypothesis that VP-PM had significant implications on clinical and hemodynamic outcomes after AVR with small aortic prostheses. We observed that some degree of VP-PM was present in all our patients (Table 3). One patient died (1.5%) in the immediate postoperative period from low cardiac out put syndrome. This patient had moderate VP-PM and received size 19 valve prothesis. Even though many previous studies reported high mortality in small-size valves (13, 14) it is still uncertain if VP-PM may affect the postoperative mortality (15). Rao et al. (14) reported the in vitro calculated EOA/BSA < 0.75 cm2/m2 to have a strong impact on survival. In our study, follow

up period was 10.2±4.1 months (range from 6 months to 18 months) and there were no late deaths over the follow-up period.

The functional outcome of the size 21 and 23 prostheses were found to be satisfactory despite the VP-PM and all those patients with size 21 and 23 valves prosthesis were asymptomatic. As against this the VP-PM seen in patients in the group receiving size 19 valve was poorly tolerated and one patient (3.3%) had NYHA class III symptoms (this patient with severe VP-PM), 5 patients(16.7%) had NYHA class II symptoms (these patients with moderate VP-PM), even though the drop in PSG and LVMI regression were maximum in this group. Fernandez and coworkers (17) failed to demonstrate any correlation between P-PM and postoperative clinical status.

The hemodynamic performance of the size 21 and 23 prostheses were found to be also satisfactory. In this study the patients with size 19, 21 and 23 valves showed significant drop in the TPG with size 19 valves recording the maximum drop. These observations compared favorably with those reported by Sharma et al (18) and Butchart and associates (19). However the residual gradient across size 19 valves following surgery remained significantly high (mean PSG = 46.6±29.3 mmHg). The PSG across size 21 and 23 were comparable to those reported by other investigators. Similarly significant regression was seen in the LVMI in the three groups. The regression was maximal in patients with size 19 valves. Yet the mean postoperative LVMI of this group (156.3±64.63gm/m2 BSA) was significantly higher than that of the patients with size 21 (127.9±26.8gm/m2 BSA) and 23 valves (122.23±31.34gm/m2 BSA) at the end of the follow up period. The explanation for this is evident in the observations made in table 4. Though the drop in PSG and LVMI is maximal in size 19 valves, the mean Postoperative PSG and LVMI are comparable to the mean preoperative PSG and LVMI in patients with size 21 and 23 prostheses as the high Preoperative LV Mass in size 19 group could explain the high residual LVMI inspite of the significant fall in the gradients in the group also can be explained by the presence of an element of residual obstruction in the valve rather than the high preoperative LVMI.

Del Rizzo et al. (7) showed a strong correlation between EOAI and the extent of LV mass regression. The improvement in the gradients and the LVMI in spite of implanting stenotic valves can be explained by the fact that studies on the animal heart have shown the relationship between transvalvular gradients and EOA to be curvilinear with no gradients demonstrated across the valve until the EOA falls below 40-60% of normal valve area (2). By a similar argument it can be said that even minor changes in the EOA of the valve after surgery can result in significant improvements in the gradients across the valves in spite of the valve being stenotic. However this trend shown by the TPG and LVMI is finite as proven earlier by Natsuaki (6) and Sharma (18). They showed that the drop in TPG and regression in the LVMI reaches a stable value by 6 months following surgery. The lower PSG and LVMI in the patients with size 21 and 23 valves contribute towards the better functional outcome in these patients (20).

In conclusion, our study indicates that VP-PM of varying severity occur in all our patients after AVR , but its clinical significance may be less then previously hypothesised. In spite of having VP-PM the functional outcome and hemodynamic performance of size 21 and 23 valves was found satisfactory. As against this the VP-PM seen in patients in the group receiving size 19 valve was poorly tolerated.

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ASSESSMENT OF DIFFERENT TECHNIQUES OF AORTIC VALVE REPLACEMENT IN PATIENTS WITH SMALL AORTIC ANNULUS

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***Background*: patient-prosthesis mismatch is considered to be present when the in vivo prosthetic valve effective orifice area is less than that of a native human valve. Accordingly patient-prosthesis mismatch exists with all valves even those of contemporary design because these continue to represent a compromise to some degree compared to normal human aortic valves.**

***Patient and methods*: Patients in this study were classified into two groups. Group I: Patients who underwent aortic valve replacement without aortic root dilatation. Group II: Patients who underwent aortic valve replacement concomitant with one of aortic root dilatation techniques. The main pathology in both groups was rheumatic fever. In this study, the majority of patients (52) had aortic stenosis (89%) and seven (11%) patients had aortic regurgitation. We used mechanical bi-leaflet prosthetic valves in all patients in both groups.**

***Results*: As regards the morbidity, in Group I, two cases developed infective endocarditis while in Group II, in patients who underwent Konno technique two patients developed bleeding and two patients developed complete heart block and were paced using permanent pacemaker. As regards the mortality, in Group I, two patients died from infective endocarditis while in Group II, one patient died from bleeding in patients who underwent Konno technique. The postoperative morbidity was higher in Group II than in Group I while there was insignificant difference as regarding the postoperative mortality.**

***Conclusion*: Annulus enlargement is an obvious solution for patients having small aortic annulus especially when faced with an unexpected intraoperative finding. In this study Konno technique had the advantage of larger size prosthesis in relation to the Manouguian technique in spite of its complications.**

Replacement of the aortic valve has become a relatively simple procedure with low mortality in most patients (Foster et al., 1986). Annular enlarging procedures can be logically divided into two groups, anterior radical enlargement and posterior limited enlargement (Rossiter et al., 1980). Small aortic prostheses providing acceptable palliation especially with patient with small body surface area (Kawachi et al., 199). Mechanical aortic valves are frequently implanted in small aortic roots. Small sized bioprosthetic valves have unacceptably high gradient and the implantation of a homograft needs special setup and training (Barner et al., 1994). Whatever the aortic prosthesis surgeon chooses to use it will always cause some degree of obstruction to the flow since its effective orifice area is smaller than the aortic annulus. In patients with small aortic annulus, the decision to use a small prosthesis "less than 21 mm in diameter" or to enlarge the aortic annulus remains controversial (Otaki et al., 1997). Patients who underwent enlargement of a small aortic an-

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nulus had long-term survival and freedom from cardiac and valve-related death comparable to these of patients "who received larger aortic prostheses" (Sommers and David, 1997).

Patient and methods

This study was done at Ain Shams University hospital in the Cardio-thoracic surgery department in the period between January 2004 and December 2005. This study included 59 patients. The patients were divided into two groups:

Group I:	**Included 16 patients who received aortic valve prosthesis 19 mm or 21 mm without aortic root dilatation.**
Group II :	Included 32 patients who underwent aortic root dilatation with: I-Konno technique : 16 patients. II-Manouguian technique: 16 patients. In both techniques the patient received bileaflet mechanical valve prosthesis.

The patient's age group ranged from 8 to 75 years old, the rheumatic valvular lesion was the main pathology. In group I there were 10 (37%) females and 17 (63%) males. On the other hand, in group (II) there were 24 (75%) females while males were 8 (25%). In group I, the body surface area ranged from 0.85-2.1 m2 with the mean of 1.4 + 0.3 m2 ;while in group II, the range was from 0.74 -1.9 m2 with the mean of 1.6+0.2 m2. We used mechanical bileaflet prosthetic valves in all patients in both groups. In group I, 14 (52%) patients received size 19 mm, 13 (48%) patients received size 21 mm, while in G II, 2 (6%) received size 17 mm, 9 (28%) patients received size 19mm, 20 (63%) received size 21mm, and 1 (3%) received size 23mm. The number of patients who received size 21 mm was higher in group II than group I due to enlarging the aortic annulus. Two cases received 17 mm aortic valve size in the patients who underwent Manouguian technique. In this study, in group I patients whose mean body surface area was 1.4 m2, aortic valve replacement with a 19 mm and 21mm mechanical valve prosthesis was found to be adequate with acceptable gradients and good functional benefits. In group I the aortic annulus ranged from 18-28 mm with the mean of 21.1+2.4 while in group II, the aortic annulus ranged from 14-21 mm with the mean of 18.5+1.4 mm, preoperatively. There was significant difference between GI and GII as regarding the preoperative ejection Fraction (EF). The EF ranged from 48-72% with the mean of 58.5+4.4%.

All patients in this study were evaluated preoperatively by detailed medical history, clinical examination, and echocardiography.

Operative procedure

Through a standard median sternotomy incision, the heart was approached, routine cannulation myocardial protection was achieved by Mild or moderate systemic hypothermia, intermittent cold blood cardioplegia (4ºC) and Surface cooling with iced saline.

Surgical technique

A transverse aortotomy was made 1.5 cm above the level of the right coronary artery. Excision was usually started with heavy scissors; meticulous debridement of the calcium was then performed by Rongeurs. The annulus was sized accurately. The valve prosthesis was implanted either intra-annular or supra-annular. Aortotomy was closed using two rows of 3/0 or 4/0 Proline continuous transverse mattress suture line which was reinforced by continuous over and over suture line.

Concomitant procedures

Annular enlargement procedures: In patients with a small aortic annulus in which it was impossible to seat a satisfactory size, consideration was given to the aortic annulus enlargement procedures .Two techniques were used:

I Manouguian technique

This was accomplished by extension of the aortotomy incision across the aortic valve into the annulus at the commissure between the non-coronary and left coronary cusps. This allowed placement of a Dacron or pericardial patch extending from below the annulus to the aortotomy. At the level of the annulus, the patch was used to hold the prosthesis sutures. The upper triangular end of the patch was incorporated into the aortotomy closure to increase the diameter of the aortic root above the prosthesis.

II Konno technique

The aortic incision was carried through the aortic annulus to the left of the right coronary orifice. The pulmonary outflow tract was opened in transverse fashion

approximately 1 cm below the pulmonary valve and the incision was extended medially to the aortic annulus. At this point, the ventricular septum was well visualized and was opened obliquely just beneath the pulmonary valve in the right ventricular outflow tract to avoid the conduction system and prevent infarction of the ventricular septum. A double-layer elliptical Dacron patch was then sewn into this opened ventricular septum up to the level of the aortic annulus. The valve was then sewn into position. It was anchored to the native aortic annulus first and then the sutures that anchored the valve to the double-layer patch were completed. It was preferred to use interrupted, non-pledget-supported, non-absorbable sutures placed in a horizontal fashion to seat the valve into the native annulus. Interrupted, pledget-supported non-absorbable sutures were used to anchor the valve to the patch. These latter sutures were placed through the patch from outside to inside, which prevent bleeding through the synthetic patch material at the suture holes by sandwiching the patch between the Teflon pledget and the valve ring.

Follow up of the patients

early follow up was done within two weeks after the operation while late postoperative follow up was done within three to six months and for all patients, NYHA functional class, and resting echocardiography were assessed.

Statistical analyses

Data were entered in the SPSS software version 10 for windows for statistical analyses. Comparison between the continuous variables of the patients in group I and group II were compared using the Student's t test for unpaired data. Comparisons between preoperative, early postoperative and late postoperative continuous variables of each group were compared analysis of variation (ANOVA test) and when significant a Scheffe F test was used for pairwise comparison. Improvement in NYHA classification, early and late postoperative was compared using chi-square test (Friedman test). Correlation between echocardiographic findings and other parameters was done using Pearson correlation. Univariate analysis of variance was done to detect parameters that predict or determine the size of the prosthesis using general linear model. Factors that found significant in the univariate analysis of variance were entered in regression analysis to detect the best predictors of the size of prosthesis that could be used. For outcomes a level of significance < 0.05 was considered statistically significant. All statistical tests were two sided.

Results

Patient population and preoperative profile

Body surface area: In group 1 the body surface area ranged from 0.85-2.1 m² with the mean of 1.4±0.3 m² while in group II, the range was from 0.74-1.9 m² with the mean of 1.6±0.2 m². There was statistically significant difference between both groups as regarding the body surface area, P value <0.05.

Aortic annulus (mm)	GI	GII
Range	18-28	14-21
Mean	21.1	18.5
SD	2.4	1.4
T. Test	5.1	
P value	<0.001	

Table (1): Comparison between GI and GII as regarding the Aortic Annulus (AA) in mm

This table shows that there was highly significant difference between G1 and GII as regarding the aortic annulus, P value <0.001.

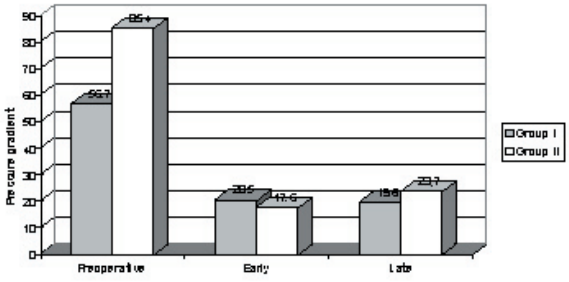

Figure (1): Mean pressure gradient across the aortic valve in group I and group II preoperative, early and late postoperative

Morbidity

There were no complications in group I. In group II, two patients had early postoperative bleeding and two patients had complete heart block in patients underwent Konno technique.

Mortality

In group I, two patients died from infective endocarditis. In group II, one patient died from early postoperative bleeding in Konno technique.

Post-operative complications	GI	GII	Chi-square	P value
Morbidity				
Bleeding	93%	88%		
Infective endocarditis	% 0	6%		
Arrhythmia	7%	% 0	8.06	0.05
	% 0	6%		
Mortality				
number	2	1	0.5	0.5
Positive	7%	3%		

Table (2): Post-operative complications as regarding morbidity and mortality in both group.

This table shows that the postoperative morbidity was significantly higher among group II than in group I (likelihood chi-square 8.06 and P value 0.04). Also it shows that there was insignificant difference between both groups as regarding postoperative mortality (chi-square 0.5and P value 0.5).

Follow up methods

All patients in this study were contacted early post-operative within two weeks after the operation, then after a period of three to six months postoperative. Patient contact was made in the out patient clinic and complete medical examination was done to all surviving patients. Echo-Doppler was done to every patient two weeks after the operation and then three to six months after the operation Comparing early postoperative echocardiographic data of the left ventricle in group I and group II:

Discussion:

This study was conducted as a prospective randomized study on 59 patients who underwent isolated aortic valve replacement in Ain Shams Cardiothoracic surgery department during the period from 2004-2005. In group I there were 10 (37%) females and 17 (63%) males. On the other hand, in group (II) there were 24 (75%) females while males were 8 (25%) This was higher than what was reported by De Paulis, et al., (1997) where a higher number of female series consistent with the fact that women have smaller body surface area and smaller aortic root. Medalion, et al., (1998), reported in their series that there were a clear association of 19-mm valve size with female sex and a small body surface area. Bech-Hanseen, et al., (1999) found in their series that most patients receiving small prosthetic valves were elderly women. in group I, the body surface area ranged from 0.85-2.1 m2 with the mean of 1.4+0.3 m2 while in group II, the range was from 0.74 -1.9 m2 with the mean of 1.6+0.2 m2. Madhu Sankar et al., (1999) reported a body surface area ranging from 0.64 - 1.69 m2 (mean 1.33: 0.3 m2). Bech-Hanssen et al., (1999) reported body surface area with the mean of 1.74±0.2.. In this study, in group I patients whose mean body surface area was 1.4± 0.3 m2, aortic valve replacement with a 19 mm and 21mm mechanical valve prosthesis was found to be adequate with acceptable gradients and good functional benefits. Madhu-Sankar et al., (1999) reported body surface area with the mean of 1.33 m2 in their series in group I the aortic annulus ranged from 18-28 mm with the mean of 21.1+2.4 while in group II, the aortic annulus ranged from 14-21 mm with the mean of 18.5+1.4 mm, preoperatively. In group II the aortic annulus post-operatively ranged from 17-23 mm with the mean of 20.25+2.75 mm. In series, reported by Aydo et al., (1999) the aortic annular sizes were ranging from 15-19 mm with the mean of (17.4 mm) before aortic root dilatation and 20-24 mm with the (mean of 22.1 mm) after the procedure. There was significant difference between GI and GII as regarding the preoperative ejection Fraction (EF). In GI, the EF ranged from 55-72% with the mean of 62.5+6.3% while in GII, the EF ranged from 48-72% with the mean of 58.5+4.4%. In study reported by Vijayanagar et al., (1998) the mean ejection fraction prior to valvular surgery was 63.9±17.3 %. In group I among the surviving 25 patients, there was gradual improvement in the function status of nearly all patients. Early postoperative, there was 19 patients (77 %) in functional NYHA class I and 6 patients (23 %) in functional class II. Late, postoperative there was 23 (92 %) patients in NYHA class I and 2 (8 %) patients in NYHA class II. This was due to improvement of left ventricular function and performance. This result confirms the work done by De Paluis et al., (1997). In Group II, among the surviving 31 patients, in this group, there were gradual improvement in the functional state , early, there was, 22 (72 %) patients in group I and 11 (28 %) patients in group II where late, post-operative there were 28 (90 %) patients in NYHA class I and 3 (10 %) patients in NYHA class I. The previous result confirms what was reported by Medalion et al, (1998). The mean pressure gradient in group I was 20.5±9.6 mm Hg while in group II the mean was 17.6±4.4 mm Hg. Hanayama et al., (2002) defined abnormal postoperative pressure gradient as those patients whose mean gradient across the aortic valve was more than 21 mm Hg. In group I there was a significant difference as regarding the pressure gradient across the aortic valve by time (P value < 0.001). The highly difference was found between preoperative versus early and late gradients while, the difference between early and

late gradients was insignificant. This correlates with that reported by Gonzalez –Juanatey, et al., (1996) who noted that the pressure gradient across the aortic valve dropped significantly after aortic valve replacement .. The data obtained in our study goes with that obtained by De Paulis, et-al., (1997) who reported regression of the left ventricular hypertrophy after aortic valve replacement in patients with small aortic roots. This regression of the myocardial hypertrophy and improvement in the left ventricular function after aortic valve replacement was also documented by Arom, et al., (1994), Hayashi, et al., (1994) and Sawant, et al., (1997), Bech-Hanseen, et.al., (1999). In this study in group II , the effective orifice area index with the mean of 0.9±o.1 cm2/m2 and this was in agreement with that reported by Dumesnil, et al., (1990) who demonstrated effective orifice area index from 0.8 to 0.9 cm2/m2 ,a transition point below which the transvalvular aortic gradient become high. Kirkilin and Barratt – boyes, (1993) assumed an effective orifice area of 1.27 cm2 for the 19-mm St. Jude valve, the valve area index for high – risk patients body surface area greater than 1.7 m2 is 0.75 cm2/m2 and the value for very high risk patients (body surface area greater than 1.9 m2) is 0.67cm2/m2. These values were well below the 0.8- to 0.9 cm2/m2 transition point demonstrated by Dumesnil, et al., (1990), to be the point at which gradients become high. As regarding the postoperative morbidity there was two cases with infective endocarditis in group I (7 %) , while in group II , two patents had early post-operative bleeding and were explored, and two patients (6 %) had complete heart block in patients underwent Konno technique. Erez, et al., (2002) reported that a problem seen with Konno aortic root enlargement was the development of complete heart block. The incidence of pacemaker insertion after the Konno procedure was six of 72 (8.3%). This is nearer to that reported by Sommers and David (1997) in their series where the operative morbidity was similar in both groups where the GI involved patients with aortic valve replacement alone and group II involved patients with aortic valve replacement with patch enlargement Also as regarding mortality, in group I, two (7 %) patients died from infective endocarditis while in group II, one patient died from post operative bleeding from Konno procedure. There was no significant difference between both groups as regarding post-operative mortality, either early post-operative or within 6 months postoperative. Sommers and David, (1999) reported in their series that the enlargement of the aortic annulus during aortic valve replacement increased the operative mortality from 3.5% to 7% but this difference did not reach statistical significance. When we regarded the post-operative complications in relation, to the technique used in group II, either Konno or Manougion, there was significant difference between both techniques as regarding the postoperative complications (likelihood chi-square 6.1 and P value 0.05). It also showed that there was insignificant difference between both techniques as regarding the postoperative mortality (likelihood chi-square 0.49 and P value > 0.05). Castro, et al., (2000) reported that their results showed that aortic root enlargement could be performed readily with minimal added risk to the standard aortic valve replacement where they used the Manougiuan technique to enlarge the small aortic annulus. There were no complications encountered in patients who had been undergone, enlargement of the aortic annulus by the Manougian technique. This denoted that the extension of the incision in the Monougian technique was safer than the extension of the incision in the Konno technique (Otaki, et al. 1997). The anterior mitral leaflet (AML) is the ideal site for extension of the aortic root incision because there is continuity between the posterior lateral part of the aortic root and the AML. The AML is functionally passive and no impairment of mitral valve functions results from the patch enlargement technique. The AML consists of collagenous fibers and is quite strong and resistant .This confirms what was reported by Manouguian, et al., (1979), Nicks, et al., (1970) and Blank, et al., (1976) and also reported by Ranganathan, et al., (1970). In this study there were no cases with mitral regurgitation. The reason, for the absence of mitral regurgitation after extension of the aortic root incision into the AML are, the origin of the AML from the left fibrous annulus between the left and right trigone so it is not folded or stretched during the cardiac cycle (Ranganathan, et.al., 1970). While in patients with Konno technique, there was no complication in 75% of patients while 12.5% developed early post-operative bleeding and two patients (12.5 %) developed complete heat block. Erez, et al., (2002) reported that Konno aortoventriculoplasty might be performed safely, excellent results may be achieved despite previous aortic root enlargement and it was a good surgical option for complex left ventricular outflow tract obstruction and might even reduce reoperation in children by allowing placement of a larger prosthesis. In this study Konno technique had the advantage of larger size prosthesis in relation to the Manougion technique in spite of its complications. This confirms what was reported by Rastan, et al., (1978) who demonstrated that by Konno technique, the diameter of the aortic annulus and the subaortic area can be doubled if necessary. The effectiveness of Konno technique was better demonstrated in patients in whom stenotic aortic valvular prosthesis also has to be changed

(Rastan, et al., 1978). The aortogram of patients must be studied carefully prior to Konno procedure to prevent such a complication as reported by Rastan, el al., (1978). In this study, there was significant difference between Manougian and Konno techniques as regarding the size of the prosthesis inserted during the technique (Chi-square 8.9 and P value <0.05), where large-size prosthesis (23 mm) was replaced using Konno technique. The correlation between the mean aortic annulus and size of the prosthesis in group II revealed that there was significant difference between the mean aortic annulus in relation to the size of the prosthesis. This was due to enlarging the small aortic native annulus and implantation of larger prosthesis sizes than that measured intra-operatively before enlarging the annulus. This was reported by Otaki, et al., (1997) who performed two-directional aortic annular enlargement for aortic valve replacement in the small aortic annulus. Also, reported by Raston, et al.,(1978) who performed Konno technique to enlarge the small aortic annulus.. To obtain a larger orifice, Otaki, et al., (1997) made an additional anterior aortotomy incision and extended it to the ventricular septum but it didn't reach the ventricular septum as in the Konno procedure. The combination of posterior and anterior enlargements increased the diameter of the aortic annulus to 23 mm in case number 1 and 24 mm in case number 2 and to 26 mm in case number 3. (Otaki, et al., 1997) This study denoted that the gradient across the aortic valve decreased significantly with the increase in the effective orifice area index (EOAI). This confirms what reported by Gonzalez- Juanatey, et al., (1996) who reported that there were significant negative correlations between valve size and peak and mean transvalvular pressure drops. In this study, the aortic annulus was a highly significant predictor for determining the size of the prosthesis inserted and the aortic root was considered as second predictors. Annulus enlargement is an obvious solution especially when faced with an unexpected intra-operative finding. Another alternation is to use stentless biologic valves because they have excellent hemodynamic features. There are also prosthetic valves reported to have improved hemodynamic performance including the "top hat", CarboMedics model and the HP series of the St. Jude medical valves (Sommers and David, 1997). Aortic homografts are appropriate for the small aortic root, as their hemodynamic behavior is excellent but their durability as well as their availability is limited. Another newer option is to modify the sewing cuff so as to create a supra-annular prosthesis. This allows the use of a larger size than would be possible for a prosthesis implanted in the intra-annular position (Bernal, et al., 1999). The limitation of this study was that the limited number of the patients included in this study. Also, the follow up period was within six months after the operation and long-term follow up was not available. Stentless valves were not used in this study which was another limitation factor. Dumesnil, et al., (1990), Pibarot, et al., (1998), Pibarot and Dumesnil (2000) pointed out that in the smaller prosthetic sizes, an increase of one valve size chronically reduced cardiac work by approximately 20% . However, other investigators have reported no deleterious effect on long-term survival among patients who received mismatched valves. This belief was strengthened by the recent review by Medalion, et al., (2000) of data from Cleveland Clinic, which demonstrated no association between apparent mismatch and postoperative mortality In a more recent study, it has been demonstrated that indexed geometric orifice area grossly overestimates and correlates poorly with the indexed effective orifice area and there fore should not be used to identify patients who have a high transvalvular gradients on the basis of Patient-patient mismatch.(Pibarot, et al., 2001) .In this study , we also specifically examined valve size in relation to the body surface area. It has been suggested by Kratz, et al., (1994) that patients with body surface area greater than 1.9 m² or even patients with body surface area greater than 1.7 m² who receive small size St. Jude valves are more likely to experience late sudden death. He, et al., (1995) have suggested that body surface area greater than 1.7 m² is a predictor of late death for patients who require concomitant coronary artery bypass grafting in addition to receiving small valves. On the other hand, Sawant, et al., (1997) did not find body surface area greater than 1.7 m² to be a risk factor for long-term survival in patients who received 19-mm St. Jude valves. There was no in-hospital mortality among these patients and the long term survival and event-free survival were similar to those who had larger valves and a body surface area greater than 1.7 m². In our study, 9 patients with body surface area more than 1.7 m² received 19-mm valves but with a single mortality in these patients. In our study, we performed standard Manouguian technique with accepted results, which can be achieved, also with limited Manouguian technique as reported by Mayumi, et al., (1995) who used a limited Manouguian incision to enlarge the aortic annulus, restricting the incision to within the intervalvular trigone and preserving the mitral anterior leaflet thereby allowing a prosthesis two sizes larger to be inserted without occurrence of mitral regurgitation .New designs of prosthesis such as the St. Jude HP valve or Medtronic-Hall and Carpentier-Edwards pericardial valves may improve the hemodynamic results in patients with small aortic roots (Car-

rel, et al., 1996). Carrel, et al., (1996) reported that the hemodynamic performance of the 21mm St. Jude HP valve corresponded closely to that of the standard 23 mm St. Jude valve and could be recommended in a normal-sized adult patient with a narrow aortic annulus. Zingg, et al., (1997) compared the hemodynamic characteristic and early clinic results of the 21 mm St. Jude Masters or HP valves with standard 21-mm and 23-mm St. Jude valves. They reported that the hemodynamic performance of the 21mm Masters or HP valves corresponded closely to that of the standard 23mm, so reducing the need for annulus enlargement.

Conclusion

Annulus enlargement is an obvious solution for patients having small aortic annulus especially when faced with an unexpected intra-operative finding. Surgeon should dilate the small aortic annulus if the expected effective orifice area index is less than 0.8 cm^2 / m^2 in adult patients or if the aortic annulus is too small so that a 19 mm 0r 21 mm cannot be introduced in teenagers.

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Manouguian S., Abu-Aishah N. and Neitzel J. (1979): Patch enlargement of the aortic and mitral valve rings with aortic and mitral valve

Minimal-Access for thymectomy is preferable for the treatment of Myasthenia Gravis

Cardiovascular

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Myasthenia Gravis (MG) is an autoimmune disease characterized by varying degrees of weakness of the skeletal (voluntary) muscles of the body and resulting from the production of antibodies against postsynaptic nicotinic acetylcholine receptors at the neuromuscular junction. (1) Ocular weakness is the first manifestation in half of the patients, who usually complain of ptosis or diplopia. Muscular deficit is symmetrical and generalized weakness is observed in up to 85% of the patients. However, the clinical course may be extremely different, and the onset of symptoms may be gradual or abrupt. In addition, there may be spontaneous remissions or aggravations. (2, 3)

Myasthenia Gravis may be associated with various abnormalities of the thymus gland. The thymus gland lies behind the breastbone and is an important part of the immune system in infancy and early childhood. (4)

The hallmark of myasthenia gravis is muscle weakness that increases during periods of activity and improves after periods of rest. Certain muscles such as those that control eye and eyelid movement, facial expression, chewing, talking, and swallowing are often, but not always, involved in the disorder. The muscles that control breathing and neck and limb movements may also be affected. (5)

The degree of improvement after surgery is not predictable, but can be significant. Myasthenia Gravis patients who experience more than minimal symptoms should consider thymectomy for treatment. University of Maryland thoracic surgeons offer four different surgical approaches for thymectomy, including some which are minimally invasive, to best meet our patient's needs. (6, 7)

The treatment of MG may be surgical or clinical. Clinical treatment includes the use of anticholinesterase agents, immunotherapy (corticosteroids, azathioprime, immunoglobulins), and plasmapheresis. The surgical removal of the thymus gland is controversial. The degree of improvement after surgery is not predictable, but can be significant. (8, 9) The optimal approach and the extent of the resection to be performed are still under discussion. The sternotomy does have the advantage of providing excellent visualization and allowing an extended resection when necessary. The optimal surgical approach varies with the surgeon's experience and preference and most of the approaches are currently acceptable. (10)

Our surgical approach by partial sternotomy, aiming at removing all thymic and perithymic tissue, was consistently applied to each patient of the series. Such an approach allows excellent visualization of the thymus, perithymic tissues and its vascular attachments. This study aims at evaluating thymectomy by partial median sternotomy in the treatment of patients with MG, as well as the complications and the clinical outcome of the treatment.

Over a time range of 5 years, 42 consecutive patients with Myasthenia Gravis had an en-bloc thymectomy. They were evaluated in the Cardiothracic surgery, neurology departments in the Zagazig university hospital and special hospitals.

To establish the diagnosis of myasthenia, all patients had undergone a careful neurological work-up prior to surgery that included physical examination, chest CT scan of mediastinum with IV contrast and positive electromyography test.

According to clinical manifestations and appearance of signs and symptoms of the disease, patients were selected to make thymectomy indicated. Before surgery, anticholinesterase and glucocorticoid medications were administered till the morning of surgery, as prescribed by the patient's neurologist with the goal of maximizing muscle strength.

patients were treated with mestinon (cholinesterase inhibitor) and corticosteroids. Plasmapharesis was used in patients who had severe symptoms. Exclusion criteria were the presence of a thymoma, and the presence of a myasthenic crisis.

The patients' disease was categorized by a modified Osserman classification (8) (table1). Because this is the classification that was used in most patients throughout their preoperative care and evaluations, we believe that it was most appropriate to use this classification rather than attempt to retrospectively reclassify patients according to the more detailed Myasthenia Gravis Foundation of America Clinical Classification.

Patient records were examined for the following parameters: age at onset of disease and at operation, duration of disease until surgery, patient sex, preoperative medication, medically optimized preoperative level of symptoms, operating time, duration of respiratory ventilation, length of stay in the intensive care unit and overall length of hospitalization, and postoperative complications.

Anesthetic Management

No patient was premedicated. Before induction of anesthesia 10% Xylocaine spray was used for topical anesthesia of the pharynx and larynx. After 3 minutes of pre-oxygenation with 100% oxygen by facemask, anesthesia was induced with fentanyl 1ug/Kg and propofol 2mg/Kg. During laryngoscopy topical anesthesia of the vocal cords and trachea was obtained with the application of 4% Xylocaine following which the trachea was intubated with an adequate sized single lumen endo-tracheal tube. All patients received Ringer's Lactate solution 6-8 ml. Kg/hr during the procedure. Mechanical ventilation was adjusted to maintain the End tidal CO2 (EtCO2) between 30-35 mmHg with an inspiration/ expiration ratio of 1:2. Anesthesia was maintained with nitrous oxide and oxygen (60:40) and a continuous infusion of propofol 3-10 mg/Kg/ hr and supplemented by fentanyl boluses 0.25 µg/Kg as required.

Intraoperative monitoring included electrocardiogram, invasive radial artery blood pressure monitoring, pulse oxymetry, EtCO2 and expiratory gas analysis. Neuromuscular transmission was monitored with Train of Four (TOF). The forearm was immobilized in order to prevent interfering movements. The ulnar nerve was stimulated supramaximally at the wrist with train of four stimuli (60mA for 200 µsec) at 30 second intervals and the acceleration of the thumb was assessed. Nasopharyngeal and skin temperature was monitored and maintained above 34°C.At the end of surgery all patients were extubated in the operating room and transferred to the intensive care unit (ICU) for monitoring.

Surgical Access

An incision was made from 1 to 2cm below the sternal notch extending to the third or fourth intercostal spaces. The incision was carried down through the subcutaneous tissue to expose the upper sternal border, presternal fascia, and the musculature, which were incised down to and through the sternal periosteum. The superior mediastinum, above the manubrium, was dissected. The bone of the manubrium was divided with a compressed air or an electric-powered saw in a downward dissection. The entire manubrium and the upper part of the sternal body down to the fourth intercostal space were divided.

With the sternum retracted, adequate visualization of the thymus and its cervical extensions was obtained for performance of a total thymectomy including its surrounding fat, starting superiorly from the base of the thyroid gland and proceeding inferiorly until the pericardium. Initially the phrenic nerves were identified and avoid excessive manipulation and lesion, to avoid postoperative diaphragmatic palsy, which could seriously impair the clinical outcome of the patient. With sharp and blunt dissection the overlying mediastinal

pleurae were pushed to the sides to bring the thymus and innominate vein into view. The dissection of the right inferior horn off the pericardium with its associated pericardial fat pad was done, following by the right superior horn which was then freed circumferentially up to the thyrothymic ligament. By using a right-angled clamp and blunt dissection technique, the middle portion of the right lobe and associated fatty tissue are pulled back from the area above the phrenic nerve up to the junction of the innominate vein and superior vena cava and the lateral arterial blood supply was ligated and divided. The mediastinal pleurae were not intentionally opened during the course of the dissection. This completes one-half of the resection. The same steps were carried out on the left side. After resection, the thymic bed was carefully assessed to assure a radical thymectomy, adequate hemostasis, and that the pleural spaces were intact. The sternum was then sutured with stainless steel threads no. 4 or 5, muscular layers were sutured with a 2-0 Vicryl thread, the subcutaneous and skin layers were sutured to conclude the procedure. A full sternotomy to complete the operation was not needed in our series.

Successful management of these patients required close cooperation among the neurologist who was responsible for the late follow-up, thoracic surgeon, anesthetist, nurses, and physiotherapists.

The results of surgery and the patient's state were assessed after three months, as regards complete remission of neurological symptoms and if there was need for further medication or not.

Table (1): Modified Osserman Classification.

Osserman Score	Description
0	Asymptomatic
1	Ocular signs and symptoms
2	Mild generalized weakness
3	Moderate generalized weakness with bulbar manifestations
4	Severe generalized weakness, respiratory dysfunction, or both

The response to thymectomy during the postoperative follow-up was graded in accordance with the classification system proposed by Keynes (9) (table 2).

Table (2): keynes classification system.

Degree of response	Definition
A	Complete remission for more than 90 days
B	Absence of symptoms after medication dose is decreased
C	Clinical improvement with no alteration in drug regimen
D	No clinical improvement with the same medication dose
E	Clinical worsening

Results

There was no intraoperative or postoperative mortality. None of the patients required reoperation. In this study, 28 female and 16 male patients underwent surgery and were evaluated. The mean age was 26 years (range, 16 to 42). The mean length of disease evolution was 22.3 months, (range, 3 to 90 months).

By the modified Osserman classification, 9 patients had a maximum preoperative severity of illness placing them in class 1, 15 in class 2, 12 in class 3, and 6 patients in class 4, with a mean preoperative Osserman classification of 2.5 (table 3).

Two patients required ventilatory support after the operation and they were treated with plasmapheresis.

Among the intraoperative complications, there was only one patient developed phrenic nerve injury causing diaphragmatic palsy which was detected by roentgenogram. Pleura was opened in 7 patients, 4 on left side, 3 on right one and 2 patients both pleurae were opened. There was no residual pneumothorax or hemothorax in this series of patients. Mean length of ICU stay was 1.5 days (range, 0.5 to 4.0 days).

There was any serious complications related to partial sternotomy. Patients rarely complained of pain

within the first 72 postoperative hours even if there was pain, it was easily controlled with common non steroidal analgesics, good cosmetic results, no re-operation in our series, no postoperative bleeding, and no injury of the internal thoracic arteries. In 12 patients we had to use a chest tube after inadvertent rupture of the pleural space.

Of the 42 patients who underwent thymectomy by partial median sternotomy, 7 (16.6%) had complete remission of the symptoms, 25 (59.5 %) had a significant improvement, and 8 patients (19.04%) had a mild improvement of the symptoms. Only 2 patients (4.76%) did not show improvement of the baseline symptoms.

Table (3): demographic data, onset of symptoms and osserman classification.

Patients	42	
Gender		
Male	16	38.09%
Female	28	66.6%
Age		
Mean	26 years	
Range	16-42 years	
Evolution		
Mean	22.3 months	
Range	3-90 months	
Osserman score		
Class 1	9	21.42%
Class 2	15	35.71%
Class 3	12	28.57%
Class 4	6	14.28%

able (4): complications and outcome.

Variables	No. of patients and %	
Phrenic nerve injury	1	2.38%
Pleural injury	7	16.6%
Left	4	9.52%
Right	3	7.14%
Ventilatory support	2	4.76%
Complete remission	7	16.6 %
Significant improvement	25	59.5%
Mild improvement	8	19.04%
No improvement	2	4.76%

Discussion

Myasthenia Gravis is a neuromuscular disease, with an autoimmune pathogenesis, which manifests itself with weakness of voluntary muscles. Dysfunction of postsynaptic acetylcholine neuromuscular junction is the causative mechanism leading to the clinical symptoms. (11, 12) Most investigators prefer thymectomy as the standard method in treatment of myasthenia gravis, especially in the generalized form. Thymectomy leads to improvement in the symptoms and lowering of the dose of the medication. (13, 14) Only Werneck and associates (13) reported that there was no difference, especially with respect to survival, between groups treated with and without thymectomy. (15)

The surgical technique to be used, remains controversial and a matter of discussion. Many surgeons advocate minimal procedures to reduce morbidity and others are in favor of a more radical approach that provides better exposure, permitting total removal of the gland, but with greater morbidity and mortality. However, variations in anatomic configuration make it difficult or impossible to remove the total thymus tissue with most of these procedures. (16)

Thymectomy may be carried out by median sternot-

omy. Scott and Detterbeck (17) reported on the total median sternotomy approach, opening both pleurae, in 100 consecutive patients, they reported good results, there was no mortality, and there was improvement or remission of MG in 78% of the patients. They believe that the advantage of the bilateral opening of the pleurae is to provide good visualization of the phrenic nerves, avoid damaging them and allowing the full resection of the fat adjacent to the thymus. We believe that systematic opening of the pleurae is not required as it may increase the incidence of postoperative pleural complications and certainly increases the pain resulting from the drainage of the pleural spaces.

Other authors prefer trans-cervical approach. Ferguson (18) reported the trans-cervical approach to perform thymectomy. The initial motivation for using this approach was its less invasiveness, that it requires a shorter hospital stay, and has lower perioperative morbidity compared with the trans-sternal approach. These advantages reported by Shrager and colleagues in (16) who reported a good long-term remission rate (44.2%).

The use of video-assisted thoracoscopic surgery (VATS) has become an additional option for thymectomy in some patients. Yim and colleagues (19) have reported on the use of video-assisted thoracoscopy by approaching the right hemi thorax and Mineo and associates (20) used left-sided approach for thoracoscopic thymectomy. When compared to total sternotomy, they reported shorter hospitalization time, less pain and lower morbidity rate. However, they also concluded that: "the true role of this approach in thoracic surgery awaits long-term results, and even among the surgeons performing VATS thymectomy, there is controversy over the exact technique and, in particular, whether the thymus should be approached from the left or right."

We believe that video-assisted thoracoscopy is a good approach; however, when compared to partial sternotomy, it is more technically difficult and causes more pain.

Partial sternotomy technique permits excellent visualization of thymus gland, its vascular attachment and all peripheral thymic tissues. In partial sternotomy, positive outcomes are achieved in up to 85% of cases as reported in series of Pêgo-Fernandes and associates. (21)

Whatever these techniques, the surgeon must be extremely careful in resectioning the thymic tissue. If it is a cervical approach, total sternotomy, mini partial sternotomy, video thoracoscopy, or any other approach, the incision should be enlarged or the technique should be changed whenever there is the slightest chance of unsatisfactory resection. At present, persistence of symptoms in patients with MG who have undergone previous thymectomy has been attributed to thymus remnants. (22)

In this study, all patients were operated by partial sternotomy for thymectomy was performed. This technique allowed good visualization and access for the dissection of tissues that might contain embryonic extraglandular thymic tissue. In our patients, the diagnosis was made by clinical examination and CT of the mediastinum to determine the changes in the size of the thymus. CT can be helpful in detecting thymomas, but is not helpful in the detection of other pathological findings of the thymus. (23)

In this study as well as in recent other studies, no mortality were encountered irrespective of surgical approach. (24)

Morbidity rates have differed, depending on the approach chosen for thymectomy. Several investigators reported on the intraoperative and postoperative complications after trans-sternal thymectomy in detail. They had a phrenic nerve palsy rate of 5%, and a recurrent nerve palsy rate of 3%. Impaired wound healing occurred at a rate of 9.3–16% in the form of wound infection, seroma, and keloid formation and defective wound healing. Atelectasis and pneumonia occurred at a rate of 8–14 %.(25) Jaretzki and associates (15) rated the risk of postoperative empyema, deep sternal wound infection, sternal wound dehiscence, chylothorax, and pulmonary embolism at 1% each.

Pego-Fernandes and associates in (21) reported their complications with a partial sternotomy in 478 myasthenia patients. There were four patients who needed postoperative ventilation, one patient developed osteomyelitis of the sternal bone, and five patients had subcutaneous fluid collection. In this study mediastinitis, wound infection and pneumonitis were not encountered, and phrenic nerve palsy occurred in one case (2.3%). Two patients required ventilatory support after the operation and they were treated with plasmapheresis. Pleura was opened in 7 patients(16.6%), 4 on left side, 3 on right one and 2 patients both pleurae were opened, the incidence was similar to the reviewed literature data in study of Granetzny and associates (26) who reported in manubriotomy group (24cases) left pleura was opened in 4 patients(16.7%).

In our study, 42 patients who underwent thymectomy by partial median sternotomy, 7 (16.6%) had complete remission of the symptoms, 25 (59.5 %) had a signifi-

cant improvement and 8 patients (19.04%) had a mild improvement of the symptoms. Only 2 patients (4.76%) did not show improvement of the baseline symptoms. this results were similar to study of Pêgo-Fernandes and associates (21)in which there were no operative mortality, significant improvement (complete or significant remission of symptoms) in 75.2% of the patients, and a partial improvement in 17.4% of the cases, according to Osserman's(8) classification.

Conclusion

The surgical approach by partial median sternotomy is preferable approach, which allows extensive removal of ectopic thymic tissue in addition to the thymus through a less invasive approach and it is associated with a significantly smoother postoperative course and less pulmonary complications, when compared with thymectomy through a full sternotomy. This is important, as anatomic studies have evidenced the presence of thymic tissue in the mediastinal fat, which is usually not completely resected when the trans-cervical or video-assisted thoracoscopy approach are used.

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The benefit of surgical lung biopsy in diagnosis and prognosis of diffuse infiltrative lung disease

Cardiovascular

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Background: Surgical lung biopsy is considered the gold standard in diagnosing patients with diffuse infiltrative lung disease. In this study we investigated if the histopathological results have changed the management and outcome of these patients.

Methods: Forty consecutive patients with diffuse infiltrative lung disease were prospectively subjected to surgical lung biopsy performed at Cairo University Hospitals, between 2001 and 2005. Data gathered included patients characteristics, radiographic appearance, histopathological diagnosis, change in therapy, and survival.

Results: There were 16/40 male (40 %), 24/40 females (60 %). The mean age was 31.8 ± 19.2. The main complaint was dyspnea and dry cough. Diagnosis was reached in 100 % of patients after surgical lung biopsy. The histopathological diagnosis included idiopathic interstitial pneumonias and fibrosis (60 %), neoplasia (20 %), sarcoidosis (12.5 %), others (7.5 %). Change in therapy occurs in 52.5 % of patients. Mortality related to procedure was zero, 30 days mortality was (15 %) and mortality at 6 months was (35 %). Predictor of early mortality was found to be arterial oxygen saturation below 70 % and neoplasia.

Conclusion: Surgical lung biopsy is a safe and accurate diagnostic tool for diffuse infiltrative lung disease. Change of therapy and improvement can be achieved after surgical biopsy. We recommend that early referral for surgical biopsy should be considered for patients with undiagnosed diffuse pulmonary disease, especially before respiratory condition deteriorates.

Many acute and chronic lung disorders with variable degrees of pulmonary inflammation and fibrosis is collectively referred to as interstitial lung diseases (ILD's) or diffuse parenchymal lung diseases. Idiopathic pulmonary fibrosis (IPF) is one of several idiopathic interstitial pneumonias. IPF is now recognized as a distinct clinical disorder. Usual interstitial pneumonia (UIP) is the histopathological pattern that identifies patients with IPF. The histological patterns of desquamative interstitial pneumonia (DIP), respiratory bronchiolitis – associated interstitial lung disease (RBILD), nonspecific interstitial pneumonia (NSIP), Lymphoid interstitial pneumonia (LIP), acute interstitial pneumonia (AIP) are considered separate entities and are to be excluded from the group of patients with IPF [1].

Interstitial lung diseases usually present with dry cough, progressive dyspnea and is accompanied by a greater or lesser degree of respiratory failure [2, 3]. Initial diagnosis is assumed on the basis of advances in images and / or minimal invasive diagnostic procedures, such as computed tomography-guided biopsy, bronchoalveolar lavage (BAL) and transbronchial lung biopsy (TBLB). However, in many instance diagnosis is difficult to reach due to inaccessibility of the lesion or small size of the presented tissue sample [4,

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5]. In such circumstances surgical lung biopsy (SLB) is considered the gold standard and the final diagnostic modality used in patients with undiagnosed diffuse infiltrative lung disease [6]. In this study we prospectively investigate the benefit of SLB in changing therapy, outcome, and survival after the procedure.

Patient and Methods

Between February 2001 and December 2005, forty consecutive patients with diffuse infiltrative lung disease were admitted at Cairo University Hospitals. Their medical data were prospectively gathered including demographic data, clinical presentation, high resolution computerized tomographic study, arterial blood gases (ABG) measurements.

Before referral of patients to surgical lung biopsy all patients underwent bronchoalveolar lavage (BAL) and transbronchial lung biopsy (TBLB) that were inconclusive and a diagnosis could not be reached. Pathological diagnosis following SLB, change of therapy achieved if any, outcome whether improvement or deterioration were also recorded.

All patients were followed up at the out patient clinic, follow up extended for 6 months.

Video-assisted thoracoscopic (VATs) lung biopsy was intended in all patients, however when patients could not tolerate single lung anesthesia or adhesions were extensive open lung biopsy was done through a 5 – 10 cm anterior sub-mammary mini-thoracotomy. VATs lung biopsy entails the use of 1 – 3 Endo GIA staples (Ethicon, Inc, Somerville, NJ) to secure pulmonary edges. When open technique was used, tissue sample were excised distal to a curved vascular clamp. The raw pulmonary edge was secured by 2 rows of running sutures with 3 / 0 prolene.

Ten patients had VATS, while the rest had open lung biopsy. The specimens were sent for microbiological and pathologic studies. The site of biopsy was based on computer tomography findings, areas with dense opacifications are usually end stage fibrosis and were avoided. In heterogeneous distribution of opacifications multiple lobar biopsies were taken.

At the completion of the procedure, the lung was reinflated and all suture lines were checked for hemostasis and aerostasis. Two chest tubes (24F) were inserted through the anterior and inferior incisions and placed under direct vision. All chest tubes were removed when the drainage was minimal, the lung was fully re-expanded, and any air leak had resolved.

Change in therapy was defined as either a change or stoppage of the initial therapy, improvement was defined as amelioration of clinical and radiological findings. Mortality was recorded on 30 days, 3 and 6 months post-procedure.

Statistical analysis

Statistical analysis was performed on IBM/PC using SPSS version 14 for windows. Both statistical analysis and tabulation were done according to Altman [7]. The Chi-square 'X^2' test was used for the analysis of categorical data. The level of significance was set at $p < 0.05$.

Results

Forty consecutive patients with diffuse infiltrative lung disease were subjected to surgical lung biopsy. There were 16/40 males (40 %) and 24/40 females (60 %). The average age was 31.8years (range 8 – 66 years). The main presenting complaints are shown in (Table 1.)

Table 1. Patients presenting complaints

Complaints	Group I	Group II	p-value
Dyspnoea			
No. of patients and %	16/24 (66.7 %)	9/16 (56.3 %)	0.5
Dry cough			
No. of patients and %	13/24 (54.2 %)	5/16 (31.3 %)	0.1
Cyanosis			
No. of patients and %	6/24 (25 %)	2/16 (12.5 %)	0.33
Clubbing			
No. of patients and %	5/24 (20.8 %)	1/16 (6.3 %)	0.2
Crepitations			
No. of patients and %	5/24 (20.8 %)	6/16	0.24

High resolution computed tomography showed bilateral reticulonodular shadows ± cystic opacities or bilateral alveolar filling and ground glass appearance (Table 2). The average arterial oxygen tension was 70.5 mmHg (range 45 – 97), while the average arterial carbon dioxide tension was 41.6 mmHg (range 28 – 50) (Table 3).

In this study16/40 patients (40 %) had a preoperative arterial oxygen tension < 55 mmHg and were admitted on the respiratory intensive care unit for oxygen supplements and/or mechanical ventilation.

Ten patients had VATs (25 %) while the rest had open lung biopsy (75 %). The pathologic diagnosis following SLB were idiopathic pneumonias (in 60 % of patients), neoplasia (20 %), sarcoidosis (12.5 %), others (7.5 %). Accordingly, patients were divided into 2 groups. Group I (24 patients) had idiopathic pneumonias (Table 4), and Group II (16 patients) who had other specific diagnosis (Table 5).

The rate of change in therapy in this group was 6/24 patients (25 %), Including one patient with chronic haemosiderosis, two patients with non specific interstitial pneumonia (NISP), two patients with lymphocytic interstitial pneumonia (LIP), and one patient with acute interstitial pneumonia AIP. The response rate was favorable in 4 out of these 6 patients. The mortality in this group was 8 patients (33.3 %) and16 patients (66.6 %) survived at 6 months. In group II in which specific diagnosis was reached in 16 patients (40 %). The change of therapy was observed in 15/16 patients (93.8 %). Survival in group II was 10/16 patients (62.5 %) at 6 months with a mortality of 37.5 %.

In this study there was no surgical mortality directly related to the procedure. One patient had prolonged air leak for 5 days that stopped when 150 cc of autologous blood was infused through the chest tube. Air leak stopped within 24 hours.

Discussion

Accurate diagnosis for patients with diffuse infiltrative lung disease remains a clinical challenge. This is not surprising since over 200 causes have been reported in the literature. When the diagnosis remains unknown despite of careful clinical, radiological and serological evaluation, lung biopsy may be indicated. The less invasive bronchoscopic BAL and TBLB is the next step in diagnosis. However, when bronchoscopy is contraindicated or inconclusive, patients are referred for surgical lung biopsy [8, 9].

Open lung biopsy has long been regarded as the gold standard, achieving an accurate diagnosis in more than 90% of patients with diffuse infiltrative lung disease [6]. Establishing a precise diagnosis is clinically important, as it will provide an appropriate therapeutic strategy. In 54% to 73% of patients surgical lung biopsy results changed the therapeutic treatment of patients with diffuse infiltrative lung disease [3, 9]. Finally, lung biopsy results also have prognostic value [11, 12].

Most surgeons performed open lung biopsy through a small (usually anterior) thoracotomy. Compared to the standard posterolateral thoracotomy, the mini-incision is more aesthetic and has lower postoperative morbidity [13]. However, its main disadvantage is reduced exposure, thus limiting the choice of biopsy site. With the recent evolution of video technology, videothoracoscopic surgery has proved to be a useful tool for diagnosis. Pain and lung dysfunction are also reduced in the postoperative period [14]. This point is particularly important because most patients with diffuse infiltrative lung disease have significantly impaired preoperative pulmonary function tests. In addition, videothoracoscopy offers excellent visualization of the pleural cavity with greater intrathoracic accessibility to the surgeon compared with the minithoracotomy.

In this study, diagnosis following surgical lung biopsy was 100 %. This compares favorably with other reported series that varies from 71 – 100 % [4, 15]. The diagnosis of idiopathic pneumonias was made in 24 patients (60 %) (table 4) in this series. These include entities like UIP, NISP, LIP, AIP, DIP and chronic haemosiderosis. However, we could reach a specific diagnosis in 40 % of patients (table 5) including congenital cystic lung, sarcoidosis, LAM and malignancy. This data is compatible with other reported series where diagnosis of idiopathic pneumonias ranged from 39 – 52 % and other specific diagnosis from 40 – 60 % [3, 11]. In our group of patients there was no patient with diffuse infiltrative lung disease due to infection. Other series reported infectious causes to ranged from 0 – 4 % [2, 3, 16].

In our study, the most important clinical symptoms and signs were recorded for both groups of patients. Dyspnoea and crepitations as an auscultatory finding were found to be of similar incidence in both groups. Dry cough and cyanosis were common in group I in patients than in group II. Clubbing of fingers was an infrequent finding in group II (table 1).

Usual interstitial pneumonitis (UIP) is the pathological pattern of disease known as idiopathic pulmonary fibrosis (IPF). In our study, it was diagnosed in 10 of the 24 patients with idiopathic pneumonias in group I (42 %). In this subgroup of patients dyspnoea was the main symptom occurring in all patients. Crepitations were found in 5 out of 10 patients (50 %) and this was less than other studies [17] where crepitations were heard in 80 % of patients. In our study, clubbing of finger was

noted in 50 % of patients with UIP and this was similar to other series ranging from 25 – 50 % [17, 18]. As in other series [19] cyanosis was found in late stages of the disease (3 out of 10 patients with UIP in this series).

In our study, abnormal ABG measurements was in 12 out of 24 patients (50 %) in group I. Of these approximately 21 % had hypoxia only, 12.5 % had hypoxia and hypocarbia. These results agree with studies showing that resting ABG may be normal initially or may reveal mild hypoxia and respiratory alkalosis [20]. In 16.7 % (4/24 patients) there was hypoxia and hypercarbia (type II respiratory failure). Two of these had a pathological diagnosis of AIP (Hamman-Riche syndrome) which is a rare fulminant form of lung injury lung injury that presents acutely [21, 22]. In this series, these patients died within 3 months. The ABG measurements in group II revealed normal value in 9/16 patients (56.3 %). However, hypoxia and hypercarbia was present in two patients with metastatic adenocarcinoma whom died later.

In this series, 6 patients in group I changed therapy after SLB. Two of these were diagnosed as having LIP which is an uncommon form of idiopathic pneumonia with a propensity to progress into low-grade lymphoma with patients developing pleural effusion or mediastinal lymphadenopathy [23, 24]. Thus, chemotherapy was initiated and both patients survived at 6 months. Another two patients were diagnosed as NSIP and later appeared to have rheumatoid arthritis. NISP is the interstitial lung disease common with connective tissue disorders [25, 26].

Unlike patients with UIP, the majority of patients with NSIP have a good prognosis with most showing improvement after treatment with corticosteroids. This was the case of these 2 patients who were also treated for rheumatoid disease concomitantly and survived at 6 months. Change of therapy also occurred in one patient who had AIP after SLB who initially was presumed to have IPF. The dose of steroid was increased and other measures of treatment of the resulting diffuse alveolar damage (DAD) but the patient died within weeks. The last patient in group I who had change in therapy was a patient discovered to have chronic haemosiderosis secondary to prolonged lung congestion due to congestive heart failure. Initial steroids treatment was stopped and anti-failure measures were initiated with improvement and survival at 6 months.

In group II SLB revealed specific etiologies including neoplasms, sarcoidosis, congenital cystic lung and lymphangioleiomatosis (LAM) in patients whom were treated as other pathologies mainly IPF. All of these patients received specific treatment according to etiology revealed and thus, the rate of change in therapy was 15/16 patients in this group (93.8 %). The only patient left without changing therapy was a patient diagnosed as having congenital cystic lung.

The overall change in therapy in both groups was 52.5 % comparing to other studies showing 46 – 80 % change [3, 11].

Mortality rate in group I was 33.3 % with 16 patients surviving at 6 months. In the 8 that dies in this group, 2 had DIP and developed pulmonary embolism after initial response to pulsed therapy. Two patients had AIP and died within weeks to 3 months. Four patients had UIP and died in less than 6 months. Mortality rate in group II was 37.5 % with 10 patients surviving at 6 months. The 6 patients that died were diagnosed as metastatic adenocarcinoma and died 2 – 8 weeks after diagnosis

The overall survival in both groups was 85 % at 30 days post-procedure, 75 % at 3 months and 65 % at 6 months. Mortality has significantly been related to preoperative arterial oxygen tension below 55 mmHg and disease progression particularly when malignancy was the diagnosis.

Surgical lung biopsy is a safe procedure, our group of patient showed no procedure related mortality. Morbidity was also acceptable with one patient who had prolonged air leak that could be controlled with autologous blood.In conclusion, surgical lung biopsy is a safe and accurate procedure with acceptable morbidity. A significant change in therapy and response should be expected. However, outcome greatly depends on the pathology. It should be done early for patients with undiagnosed diffuse infiltrative lung disease, particularly before respiratory deterioration develops.

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A prospective randomized trial for thoracoscopic talc poudrage versus povidone-iodine for pleurodesis of effusion due to metastatic breast cancer

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Objectives: The purpose of this study is to compare the efficacy, safety, and complications
Of thoracoscopic talc poudrage versus povidone-iodine for pleurodesis of effusion due to metastatic breast cancer.
Methods: Between January 2002 and December 2005 a total number of 42 patients with malignant pleural effusion due to metastatic breast cancer were enrolled in this prospective randomized study. Patients were divided into 2 groups. Group I (22 patients) received pleurodesis through a thoracoscopic talc poudrage, while group II (20 patients) received pleurodesis through a thoracostomy tube utilizing povidone-iodine.
Results: In group I, 3/22 (13.6%) had reaccumulation of fluid after talc poudrage, 4/22 (18.1 %) patients complain of fever in the 1st 48 hours, another 4/22 (18.1 %) patient had severe chest pain that responded to narcotics. In group II 3/20 (15 %) had reaccumulation of fluid after povidone-iodine,
1/20 (5 %) had intense burning chest pain. No fever was encountered in any patient in group II. Follow up extended to 4 years.
Conclusion: Povidone-iodine could be considered as alternative to the common used talc poudrage in pleurodesis of patients with malignant pleural effusion due to metastatic breast cancer. Moreover, the drug is available, cheap, and safe, can be given through a thoracostomy tube and can be repeated if needed.

Malignant pleural effusions are a common clinical problem in patients with neoplastic disease. Metastatic breast cancer is the second common cause after bronchogenic carcinoma and account for 25 % of all malignant pleural effusions [1]. About 7 – 11% of breast cancer patients develop malignant pleural effusion during the course of the disease [2]. There is severe reduction in the quality of life in these patients with the development of malignant pleural effusion due to progressive dyspnoea, dry cough, chest pain and reduced physical activity [3]. The appearance of malignant pleural effusion denotes the presence of pleural metastasis. However, patients with breast cancer with pleural metastasis are not considered to be in the terminal stage of the disease, and with the systemic chemotherapy and / or hormonal management the median survival may extend from several months to years [4,5].

Drainage of the pleural cavity and subsequent obliteration of the pleural space offers the palliative treatment of choice for these patients [6,7]. In practice, talc pleurodesis is most often used as palliative treatment for recurrent malignant pleural effusion, its success rate being approximately 90% without relapse [8,9]. Povidone-iodine in 10 % solution primarily used as an antiseptic has been shown to be effective alternative sclerosing agent in some series [10].

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In our study, we compared the efficacy, safety and complication of both agents to palliate patients with malignant pleural effusion due to metastatic breast cancer.

1.Patients and Methods.

This prospective randomized study enrolled 42 patients with malignant pleural effusion as a result of cancer breast. Patients were admitted to Cairo university hospitals between 2002 and 2005.

We excluded from our study patients who had poor performance status, known allergy to iodine, trapped lung, unimproved dyspnoea after thoracentesis, pleural fluid pH < 7.2or glucose < 60 mg/dl and metastasis outside the chest. The patients were either metastatic at presentation or previously received adjuvant chemotherapy then relapsed after a period of follow up. All the patients had visceral metastasis and were treated by chemotherapy.

All patients had informed consent and randomization was done using sealed envelope method. Patients who developed pleural effusion were admitted to hospital and review of their medical records include age, stage, estrogen and progesterone receptors, HER2 gene expression, date when first seen, date of relapse, adjuvant chemotherapy, first line metastatic chemotherapy, and date of progression. Both groups received the same protocol for adjuvant chemotherapy as either FAC or FEC (5-flurouracil, Adriamycin and Cyclophosphamide or 5-flurouracil, 4-epidoxorubicin and Cyclophosphamide). Metastatic patients at presentation were treated by FAC protocol, where as those with disease relapse and who had previously received adjuvant chemotherapy were given Docetaxel single agent or in combination with cisplatin protocol or Vinorelbene/ 5 Flurouracil

Demography of the patients is summarized in Table (1)

On admission therapeutic thoracentesis was done for every patient and pleural fluid amount was estimated and sent for biochemical (pH, protein, LDH and glucose), bacteriological and cytological evaluation. Patients were then randomized into two groups according to the sclerosing agent used. Group I received talc poudrage (Steritalc® F2 manufactured by Novatech, France),

And group II received 10 % povidone—iodine (Betadine® manufactured by Nile Co. for pharmaceuticals and chemical industries. Cairo, A.R.E; licensed by Mundi pharma AG - Basel - Switzerland).

Surgical technique.

Under general anesthesia and a double lumen endotracheal tube, video assisted thoracoscopic evaluation of the affected hemithorax was done using 2 ports. Pleural fluid was completely removed, any adhesions were freed using blunt and sharp dissection. At this stage manual bagging of the lung by the anesthesiologist to exclude trapped lung and a thoracoscopic multiple pleural biopsies were taken for pathological study. Installation of local anesthetic as well as 10 mg morphia IV was given before agents used. For group I insufflation with 4 grams talc under thoracoscopic guidance, while group II received 20 ml 10 % povidone—iodine in 40 ml normal saline solution infused into the chest tube that was then clamped for 4 hours before opening. Chest tube was removed when chest radiograph confirms full lung expansion and 24 hour drainage was less than 100 ml.

Follow up.

All patients were followed up for duration of chest drainage, complications (fever and pain), and hospital stay. Follow up after discharge was done at out patient clinic at 2 weeks for the first month, 4 weeks for the next 2 months and then every 3 months. At follow up progression of the disease, reaccumulation of fluid (radiological and clinical) as well as perioperative mortality (30-days) and late mortality were looked for. In this study we considered radiological reaccumulation of pleural fluid without evidence of recurrence of dyspnoea and the need for thoracentesis as a success. Patients continued their chemotherapy regimens according to their protocol. They received 6 - 8 cycles according to the response of the tumor. The patients were then followed up monthly till disease progression which was documented

Results.

Forty two patients with malignant pleural effusion due to breast cancer were randomized into two groups. Group I (22 patients) received talc poudrage while group II (20 patients) received povidone-iodine for pleurodesis. Patients characteristic were similar between study arms (table 2).

Thoracoscopic findings were those of malignant pleural effusion and pulmonary atelectasis in all patients. The surgical procedure took on average 31 min to perform (ranged from 21 to 54 min) and was followed by immediate extubation of all patients. The mean amount of pleural effusion drained from group I was 2977 ± 789.6 ml and from group II was 3086.5 ± 777.6 ml. There were no serious complications in the early postoperative period. Side effects of the agents used were considered to be acceptable. The main patients complaint in group I was development of severe pain in 4/22 (18.1%) of patients that responded to repeated doses of morphine analgesia for 48 hours. Fever was a complaint of another 4/22 (18.1 %) of patients for the first 48 hours. Fever did not exceed 38 ºC and responded to paracetamol tablets. In group II there was one patient who developed

intense burning sensation 3 hours after Table 2: Patients

Table (1) Demographic data of patients included in the study at presentation

Age	T	N	M	ER	PR	HER	1st line met ttt	PFS(ms)
43	2	2	0	MILD	MOD	NEG	NAV/5FU	10
52	3	2	1	NEG	NEG	MILD	FAC	6
33	2	1	0	NEG	NEG	MOD	TAXOTERE /CIS	15
48	3	1	1	MILD	MILD	MOD	FAC	8
56	2	2	1	HIGH	HIGH	NEG	FAC	6
29	4	2	0	NEG	NEG	HIGH	TAXOTERE /CIS	4
64	2	3	1	MOD	MOD	HIGH	FAC	7
35	3	2	1	NEG	NEG	HIGH	FAC	6
42	2	1	0	MILD	MILD	MILD	NAV/5FU	7
55	2	2	0	MILD	MILD	n/a	TAXOTERE /CIS	7
62	2	1	1	MOD	MOD	MILD	FAC	5
48	2	1	1	MOD	MILD	MILD	FAC	8
54	3	2	0	MILD	MILD	n/a	NAV/5FU	6
39	2	1	1	MOD	MOD	MOD	FAC	3
56	3	1	1	NEG	MILD	NEG	FAC	5
52	2	2	0	NEG	NEG	HIGH	TAXOTERE	7
61	2	1	0	MOD	MOD	n/a	TAXOTERE/CIS	6
34	2	2	1	NEG	NEG	n/a	FAC	5
55	2	1	0	NEG	NEG	NEG	TAXOTERE	6
49	3	2	1	MILD	NEG	MILD	FAC	4
41	2	1	0	MILD	NEG	HIGH	NAV/5FU	4
53	2	2	1	MOD	MILD	NEG	FAC	5
46	3	1	1	MOD	MOD	n/a	FAC	8
57	3	2	0	MILD	MOD	NEG	NAV/5FU	7
62	4	2	1	NEG	MOD	n/a	FAC	7
51	2	1	0	NEG	NEG	MOD	TAXOTERE	8
49	3	2	1	NEG	MILD	NEG	FAC	5
54	2	1	0	MOD	MILD	HIGH	NAV/5FU	5
32	4	2	1	NEG	NEG	HIGH	TAXOTERE/XEL	6
43	2	2	0	NEG	NEG	NEG	TAXOTERE/CIS	8
56	3	1	1	HIGH	MILD	MILD	FAC	4
48	2	1	1	NEG	NEG	MOD	FAC	5
57	3	2	0	HIGH	HIGH	NEG	TAXOTERE/CIS	7
60	2	2	1	MOD	MOD	HIGH	FAC	10
44	2	1	1	MILD	MILD	n/a	FAC	7
53	3	1	0	MILD	MILD	n/a	TAXOTERE	10
44	3	1	1	MOD	MILD	MILD	FAC	9
55	2	2	0	MILD	MILD	NEG	TAXOTERE	7
45	2	2	1	NEG	NEG	MOD	FAC	4
38	3	2	1	NEG	NEG	MILD	FAC	6
62	4	2	0	MOD	MOD	n/a	TAXOTERE	8
54	3	1	1	NEG	NEG	NEG	FAC	7

ER; Eostrogen receptors , PR ; Progesteron receptors HER; HER 2 neu gene overexpression, Met; metastatic Ttt; Treatment , PFS ; Progression free survival, MOD ; moderate ,NEG; negative , n/a : non applicable

characteristics in both groups

	Group I (talc poudrage) n = 22	Group II (Povidone-iodine) n = 20	P value
Age			
Range	29 – 64	32 - 62	0.2
Mean ± STD	48.22 ± 9.9	50.2 ± 7	
Stage			
II	8 (36.3 %)	6 (30 %)	
III	2 (9 %)	3 (15 %)	
VI	12 (54.5 %)	11 (55 %)	
Pleural effusion as the 1st presentation (No. of patients)	12 (54.4 %)	10 (50 %)	0.2

STD= standard deviation.

the procedure that was controlled by a single dose of non steroidal anti-inflammatory analgesia. No patient developed fever in this group. In all patients dyspnoea and cough were greatly improved after drainage. They were discharged on both radiological and clinical evidence of complete resolution of their pleural effusion, the mean hospital stay was 5.7 ± 2 days for group I and 4.45 ± 1.1 for group II all patients. At subsequent follow up 32 patient (76.1 %) were alive at 8 months, 22 patient (52.3 %) were alive at 2 years and 11 patient (26.1 %) were alive at 4 years.

There were 3/22 (13.6 %) patients with reaccumulation of pleural fluid in group I. One had only radiological reaccumulation at 2 months post-procedure, she never developed any clinical dyspnoea during 14 months follow up and was then considered as success. 2 patients developed clinical recurrence with dyspnoea appearing 39 and 51 days post-procedure and were considered as failure. Repeated sonar guided thoracentesis was done for each of them. In group II 3/20 (15 %) developed reaccumulation of fluid with recurrence of dyspnoea at 33, 41and 49 days post-procedure. In all patients a thoracotomy tube could be placed and repeated pleurodesis using povidone-iodine was done. During follow up no recurrence could be detected at more than 6 months. There was no statistical difference between the success rate for group I in this study (91 %) and group II (85 %) (Table 3).

3. Discussion

The current finding of this randomized trial revealed no difference between thoracoscopic insufflated talc and povidone-iodine to prevent recurrence of malignant pleural effusion at 30 days post-procedure and was statistically insignificant 2/22 in group I (91 %) and 3/20 (85 %) in group II success at long term follow up extended for 4 years. An equivalent design was used between the study arms in patients with malignant pleural effusion due to breast cancer. Patients with malignant pleural effusion due to breast cancer had a longer survival than any other cause of malignancy [11]. This allowed us to have the opportunity to follow the patient at longer period.

Table 3: Pleural effusion management and results

	Group I (talc poudrage) n = 22	Group II (Povidone-iodine) n = 20	P-value
Success rate of the agent used (%)	2/22 (91%)	3/20 (85%)	0.2
Complications			
1. Pain	4/22 (18.1%)	0/22	0.02
2. Fever	4/22 (18.1%)	1/22 (5%)	0.1
Amount of pleural effusion drained (ml)	2977 ± 789.6	3086.5 ± 777.6	0.3
Hospital stay (days)	5.7 ± 2	4.45 ± 1.1	0.009
Mean survival (months)	27.7	33.8	0.2

The success rate of talc poudrage for pleurodesis in the published literature range from 68 – 97 %. Varying definitions of recurrence (radiological, symptomatic) and choice of denominator may account for some discrepancies among studies [12]. In this study talc poudrage had a success rate of 91 %. Paucity of data regarding success of povidone-iodine exists in the literature. Povidone-iodine is a famous anti-septic and less commonly used as a sclerosing agent. The success rate range from 64.2 – 96.1 % (10, 13,14]. In our study success rate was 85 %.

In this study our exclusion criteria which include poor performance status, pleural fluid pH < 7.2 or glucose < 60 mg/dl and metastasis outside the chest were

not meant to improve results but rather improve survival and allow better judgment over a longer period between the two agents used. Approximately one-third of malignant effusions have a pleural fluid pH of less than 7.30 at presentation (15); this low pH is associated with glucose values of less than 60 mg /dl (16). The cause of these low-glucose, low-pH malignant effusions appears to be an increased tumor mass within the pleural space compared with those with a higher pH effusion, resulting in decreased glucose transfer into the pleural space and decreased efflux of the acidic by-products of glucose metabolism, CO2, and lactic acid, due to an abnormal pleural membrane (17). Malignant effusions with a low pH and glucose concentration have been shown to have a higher initial diagnostic yield on cytological examination, a worse survival, and a poor response to pleurodesis than those with normal pH and glucose (18).

Chest pain and fever are the most common adverse effects of all pleurodesis agents (19). The intensity of chest pain reported with talc has ranged from nonexistent to severe but, generally, has been minimal with an incidence of 7%. Talc causes fever (usually 38 °C) in 16–69% of cases (20), characteristically occurring 4 to 12 h after instillation and lasting no longer than

72 h.

Pain and fever were the major morbidity in our study. Pain was more significant in group I following talc poudrage, it was controlled by narcotics given via intravenous drip for 48 hours in most cases. Fever was another troublesome complication that lasts 48 hours, it didn't exceed 38 °C and patients were given paracetamol as an antipyretic. In group II, no fever was encountered and only one patient developed pain that was controlled by non steroidal anti-inflammatory drug. Other complications related to talc use as ARDS did not develop in our study. It has been postulated that this follows systemic absorption of talc and is related to dose and particle size [21]. In our study we didn't exceed a dose of 4 gms of talc in any case and we used Seritalc® with less than 50 % of particles less than 20 μm. This type of talc has been extensively used in Europe without any report of respiratory failure [22].

Malignant pleural effusions continue to be a common problem in patients with metastatic disease. There have been numerous studies addressing the etiology, diagnosis, and treatment, although there still remains no standardized approach to this disorder. Local treatment of malignant pleural effusions is palliative and should be directed at minimizing discomfort, cost, and complications. This study showed no statistical difference between the use of talc poudrage which is considered as the standard and povidone-iodine as a sclerosing agents.

We conclude that povidone-iodine could be considered as an alternative agent for talc poudrage. The agent was found to be safe, available, and cheap, could be repeated and can be given through thoracostomy tube. As we continue our effort to optimize the sclerotherapy protocol, we should recognize that this is a palliative procedure aiming at improving the quality of life of patients who suffer end stage cancer.

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Multimodality Treatments in Locally Advanced Stage Thymomas

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***Background*:A complete surgical resection is the main target in the treatment of thymomas; unfortunately, it is not always achievable in stage III and IVA thymomas because of the local invasion of the neighboring organs or the presence of diffuse pleural or pericardial implants. Chemotherapy or radiotherapy or both can be used either as the first line of therapy to increase the ability to perform a radical resection or after operation to reduce the incidence of recurrence. These observations have led to the development of multimodality therapy.**

***Objective*:The aim of this study was to evaluate the effectiveness of the multimodality treatment in terms of the tumor resectability after induction chemotherapy and to determine disease-free and overall survival rates of patients with locally advanced unresectable thymoma that received a multimodality treatment regimen.**

***Patients&Methods*:Nine patients with newly diagnosed, histological proven, unresectable malignant thymoma, consecutively enrolled from December 2000 to June 2004 , underwent a multimodality treatment regimen consisted of neoadjuvant chemotherapy (three courses of cisplatin and etoposide), followed by surgical resection, postoperative radiation therapy, and consolidation chemotherapy (three courses of cisplatin, and etoposide).**

***Results*:All the patients were valuable for assessment. Disease responded to neoadjuvant chemotherapy completely in 1 patients (11%) and partially in 6 patients (66%); with an overall response of 77% .Two patient had a minor response (22%). 8 patients had surgical resection; 1 refused surgery. Tumors were removed completely in 5 patients (62.5%%) and incompletely in 3 (37.5%%) . All the patients had received radiation therapy and consolidation chemotherapy. Seven patients are alive (77% at 4 years), with a median follow-up of 31 months, and six patients are disease free (66.6% disease-free survival at 4 years).The major side effect from neoadjuvant and consolidation chemotherapy was myelosuppression. Two patients (22%) experienced grade III/IV neutropenia, which included neutropenic fever in one patient(11%), grade III anemia in two patients (22%) and grade III thrombocytopenia in one patients (11%).The most common nonhematologic side effects were fatigue, nausea and vomiting, and decreased appetite. One patient(11%) experienced acute respiratory distress syndrome after surgical resection.**

***Conclusion*:Optimal therapy for stages III and IVA has still to be defined. The multimodality treatment of stage III and IVA thymic tumors which may be reached by integration of surgery, radiotherapy, and chemotherapy, contributed to improve a good long-term outcome and the neoadjuvant chemotherapy improves the respectability rate and the survival of locally advanced stages of the disease. However, a longer follow-up, a larger series of patients, and possibly a randomized trial are required to draw definitive conclusions.**

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Thymoma is the most common tumor of the anterior mediastinum. This tumor is associated with unique paraneoplastic syndromes, such as myasthenia gravis, hypogammaglobulinemia, and pure red cell aplasia. (1,2,3) The rarity of this tumor, however, has somewhat obscured the optimal treatment for this disease. For the majority of patients who present with localized tumor, surgical extirpation remains the standard of choice. (2) However, radical resection is not always feasible for invasive and metastasizing lesions (stages III and IVA in the staging of Masaoka and associates) and these tumors should be approached in a multidisciplinary fashion . (4,5)

Chemotherapy or radiotherapy or both can be used either as the first line of therapy to increase the ability to perform a radical resection or after operation to reduce the incidence of recurrence. Adjuvant radiotherapy seems to improve local control and survival. (6) In more advanced disease, systemic therapy has been demonstrated to produce a 50% to 80% objective response rate.(7) These observations have led to the development of multimodality therapy for the treatment of patients with advanced thymoma. (8,9)

The aim of the study was to evaluate the role of multimodality therapy in terms of the tumor resectability after induction chemotherapy and to determine disease-free and overall survival rates of patients with locally advanced unresectable stage III and IVA thymoma that received a multimodality treatment regimen.

Patients and methods;

Nine patients with Masaoka stage III or IVA tumors were enrolled in this study. The resectability of disease was determined by the thoracic surgeons before patients entered the protocol. Patients had WHO performance status of less than 2, bidimensional measurable disease, adequate bone marrow (absolute granulocyte counts > 1500 cells/mm3 and platelet counts > 100 000 cells/mm3), adequate hepatic function (serum total bilirubin level < 1.5 mg/dL , and adequate renal function (serum creatinine level < 1.5 mg/dL and creatinine clearance >80). Left ventricular ejection fraction in all participants was examined by using two-dimensional echocardiography before treatment. Signed informed consent was obtained, complete medical history and physical examination were taken, labarotory work up including (heamatological profile, kidney and liver functions before and between chemotherapy ,computed tomography were obtained at the begging , before and after surgery and the end of treatment, six months and then once a year during follow up. Computed tomography scan was repeated after induction chemotherapy to evaluate the response: complete remission was described as the complete disappearance of the tumor mass; partial remission was defined as a decrease of 50% or more in the size of the lesion; and stable disease was defined as a regression of less than 50% of the mass with no new lesions appearing and no deterioration of patient performance. The Profiles of patients before operation are shown in table (1).

Table (1) Profiles of patients before operation

Patients NO	SEX	AGE (Y)	WHO performance	MASOAKA Stage	HISTOLOGY	Paraneoplastic syndrome
1	F	33	0	111	EPITHELIAL	MYATHENIA GRAVIS
2	M	51	1	111	EPITHELIAL	-
3	M	45	1	1VA	LYMMPHO-CYTIC	-
4	F	50	1	111	MIXED	SYSTEMIC LUPUS
5	M	65	2	111	MIXED	MYATHENIA GRAVIS
6	F	32	1	1VA	LYMPHO-CYTIC	-
7	M	37	0	111	MIXED	-
8	M	46	1	1VA	MIXED	MYATHENIA GRAVIS
9	M	54	1	111	EPITHELIAL	-

Multimodlity Treatment Protocol

This study was designed for patients with pathologically confirmed malignant thymoma. The Multimodality treatment protocol consisted of three courses of neoadjuvant chemotherapy, surgical resection, radiation therapy, and three courses of consolidation chemotherapy. The neoadjuvant chemotherapy consisted of cisplatin, 75mg/m2 , on days 1 and etoposide 100 mg/m2 on day 1 to day 3. This cycle was repeated three times at 3- to 4-week intervals. Within 3 to 4 weeks after the last neoadjuvant chemotherapy cycle, computed tomography was then performed to assess the tumor respectability which was then followed by surgery.

The operations were performed through a full median sternotomy incision in all patients. A complete excision of the tumor was always attempted; whenever this proved impossible, the residual tumor was clipped to better define the radiation therapy portals. All patients underwent an extended thymectomy . After median sternotomy, both pleural envelopes were opened widely

by elevating each hemisternum and incising the parietal pleura lateral to the mediastinal reflection to facilitate complete removal of all possibly involved mediastinal pleura. An accurate assessment of the gross extent of the tumor and its invasiveness and an inspection of the total pleural (parietal and visceral) surface for droplet metastases was then performed. If the tumor was found to be small, apparently noninvasive, and readily movable, a total thymectomy (including the cervical tongues) with removal of all mediastinal fat around the tumor. If an invasive tumor was found, only debulking was performed.

Radiotherapy to the mediastinal or residual tumor areas was performed using opposite anterior and posterior parallel fields at doses of 45 Gy for complete resections or 55 Gy for incomplete resections delivered for a period of 5 or 6 weeks, respectively. Then, three cycles of the same chemotherapy were taken . Survival was calculated from the date of the diagnosis until the date of the last follow-up in September 2006.

Results:

From December 2000 to June 2004, a total of 9 patients were consecutively enrolled in the study. Six patients were males Three patients were diagnosed by CT guided biopsy and the rest of the patients by anterior mediastinotomy. The mean age was 52 years (range 34-63), three patients had myathenia gravis. Six patients were Masoaka stage III and the other three patients were stage IVA .

Neoadjuvant chemotherapy produced complete response in one patient (11%), partial responses in five (55%), with an overall major response rate of 77% and two patients (22%) had minor response. Eight patients had surgical resection; 1 refused surgery. Tumors were removed completely in five (62.5%) patients and incompletely in three (37.5%).

Those three patients (37.5%) had incomplete resection after induction chemotherapy and radiologic evidence of invasion of the great vessels (ascending aorta, main pulmonary artery and superior vena cava) was confirmed at anterior mediastinotomy before induction chemotherapy; extended full-thickness tumor invasion of the vessels was still present at operation and was the reason for incomplete resection. Only debulking was done for the latest three patients with no trial of vascular or pericardial reconstruction.

Sites of Infiltration of Surrounding Structures

At the time of surgical exploration, three patients (33.3%) were found to be already invading the pericardium; 3 (33.3%) into the lung parenchyma; 2 (22,2%) into the great vessels, including the innominate veins, the superior vena cava, the aorta, or the pulmonary arteries; and 1 (11.1%) into the heart. There were also 1 tumor (11,1%) with concomitant pleural dissemination that were detected at surgery. The site of infiltration of the surrounding structures in all patients is reported in table (2).

Table (2). Site of Infiltration of Surrounding Structures

(%) .No	Structure
3(33,3%)	Lung
3 (33,3%)	Pericardium
2 (22,2%)	Superior vena cava
2 (22,2%)	Left brachiocephalic vein
1 (11,1%)	Heart
2 (22,2%)	Ascending aorta
1 (11,1%)	Pleural metastasis
2 (22,2%)	Pulmonary artery

All the patients had been received radiation therapy .There were five patients whose tumors had complete resection received 45 Gy; the three patients who had incomplete resection and the patient who refuse surgery received 55 Gy. All patients had consolidation chemotherapy and only one patient refused the last two cycles.

No patient was lost to follow-up. Seven patients are alive 4 years, with a median follow-up period of 31 months,(77%) and 6 patients are disease-free survival at 4 years (66%)

Toxicity

A total of 52 cycles of chemotherapy were taken .Myelosuppression was the most common hematological side effect with grade 3 neutropenia occurred in two patients. One of them developed febrile neutropenia , Grade 3 anemia in two patients, and thrombocytopenia grade3 in one patient. Fatigue ,alopecia ,and vomiting were the most common nonhematological toxicities.The remaining toxicities are listed in table (3).

TABLE (3): TOXCITIES OF CHEMOTHERAPY

TOXICITY	Grade(1-2)	%	Grade(3-4)	%
Neutropenia	3	33	2	22
Thrombocytopenia	2	22	1	11
Anemia	4	44	2	22
Alopecia	5	55	2	22
Fatigue	4	44	1	11
Nusea&vomiting	3	33	1	11
Neurology	1	11	0	0
Mucosities	1	11	1	11

There were no operative mortality or sternal reopening for bleeding in our study. The postoperative surgical complications were observed and included one case of sternal dehiscence which was managed successfully by sternal rewiring, one with pulmonary embolism which was managed with conservative medical treatment, and one with recurrent bilateral pleural effusions previously had systemic lupus erythrematosus and pleural effusions before the operation that responded markedly to repeated thoracocentesis. One patient experienced acute respiratory distress syndrome after surgical resection due to myasthenic crisis and mechanically ventilated then weaned off successively after two days. The rest of the postoperative complications are shown in table (4).

Table (4) Postoperative complications

Complication	**Number**
Sternal dehiscence	*1*
Pulmonary embolism	*1*
Mechanical Ventilation >24h	*1*
Pleural effusion	*1*
Reoperation for bleeding	*0*
Pneumonia	*1*
Myesthenic symptoms	*1*
Mortality	*0*

Discussion

Surgical intervention is the most effective treatment modality for thymoma. Although surgery remains the mainstay in the treatment of thymoma, the best strategy and which multimodality treatment should be adopted in the more advanced and invasive tumors have yet to be determined. The main goal to achieve in the treatment of thymic cancers is the complete removal of the neoplasm, and, on the basis of the experience with other neoplasms, it may be reached by integration of surgery, radiotherapy, and chemotherapy.(10,11,12)

Malignant thymoma (stage III and IVA) deserves special consideration. Radical resection, postoperative control of residual tumor, and prevention of local and distant recurrence should be pursued if cure rather than prolonged survival is to be achieved. (13) En bloc resection of the primary tumor and the involved structures is certainly one of the keys to success. (14)

The issue of whether subtotal excision is superior to biopsy only in unresectable tumors is controversial and unresolved. Previous reports have suggested no difference in survival, whereas others suggest that subtotal excision is superior. (15) In general, a complete resection should be always tried with care taken to avoid maneuvers that could lead to excessive perioperative morbidity with consideration for preoperative therapy. For those with invasive or residual disease, postoperative therapy is warranted.

Long-term survival has been reported despite the necessity of resecting and replacing the SVC; hence, SVC involvement should not deter complete resection. Pleural implants should be removed by extrapleural dissection, which can lead to long-term survival, although if multiple pleural implants are found preoperatively, systemic therapy before surgery is preferred. (16) In our study , there were two patients with gross invasion of the SVC with pleural deposits for whom only debulking was performed as there was also involvement of the heart in one patient and the ascending aorta in the second patient and clips were implanted to mark areas of close margins or residual disease to assist the radiation oncologist in treatment planning .

Theoretically, the primary chemotherapy should reduce the bulky disease, downstage it, and increase the resectability rate. However, 30% to 40% of the lesions are invasive , and radical resection is often limited by either extended local infiltration or dissemination outside the mediastinum. (13) The ability to perform a radical resection is the key factor for cure , and must be regarded as the goal of treatment even in advanced-stage lesions. To increase the number of radically resected cases and ultimately increase the cure rate, the clinicopathologic grouping based on the combination of the classification of Müller-Hermelink and colleagues, (17) and the staging of Masaoka and co-workers, (2) may help identify patients who require a multimodality approach.

However, the reported survival for patients with advanced disease is unsatisfactory, even after radical resection (10-year survival rates ranging between 35% and

53%). Furthermore, up to 50% of patients undergoing operation, whether radical or not, will have local recurrence within 5 years. For this reason, adjuvant therapy has been recommended for all invasive lesions. On the contrary, surgical risk is significantly increased when the tumor has invaded into the surrounding structures, especially the heart or great vessels. In patients having partial resection or biopsy alone, surgery proved to be difficult and risky.(17)

Macchiarini et al, were among the first to evaluate preoperative chemoradiotherapy in patients with potentially resectable disease. They demonstrated that seven patients with clinical stage III thymoma received three cycles of cisplatin, epirubicin, and etoposide before surgery. Four patients experienced complete remission, whereas the remaining three patients developed either microscopic disease (n = 2) or gross residual disease (n = 1). (18)

In our study, due to the rarity of this neoplasm , only nine patients with locally advanced disease were enrolled . Cisplatin and etoposide chemotherapy were chosen due to the previous European and Research study using this regimen in 16 patients with advanced and metastatic disease also in recurrent disease which was a highly effective regimen with overall response of 60% .(19) In our study the overall response is 77% this may be explained by the fact that our patients are newly diagnosed and didn't include metastatic or recurrent disease.

A similar trial was also developed by Rea et al, sixteen patients with stage III and stage IVA disease were treated with a doxorubicin, cisplatin, vincristine, and cyclophosphamide regimen every 3 weeks for three to four cycles. After chemotherapy, surgery was performed, and if residual was present, postoperative radiation therapy was given. Patients with a complete remission received three additional cycles of chemotherapy. (20) Results of this trial demonstrated seven complete and five partial responses and a projected 2-year survival rate of 80% which was comparable to our study in which the overall survival is 77%in 4 years .

In anther study by Kim et al, using the multimodality treatment, the intergroup trial studying PAC (cisplatin, adriamycin and cyclophosphamide) chemotherapy surgery and radiation in 23 patients demonstrated a high response rate of around 70% which also comparable to our study. (21)

Cisplatin and etoposide is common regimen in non small and small cell bronchogenic tumors which is save and has predictable toxicity. (22,23) In our study, all the toxicities were predictable and comparable to other studies using this regimen .

It had been also suggested by previous report that even though the radicality of the operation is a prognostic factor whenever an invasive thymic tumor was resected after neoadjuvant chemotherapy, it may be so crucial, and the goal of a complete tumoral clearance may be achieved through a multimodality treatment. Moreover, radiotherapy may prove to be more effective after neoadjuvant chemotherapy and surgery, both because of an effect of radiosensibility induced by the chemotherapy and because of a smaller disease mass, and determine a better clearance of the tumoral bed. (24)

The optimal coordination of chemotherapy, radiation therapy, and surgery has yet to be defined. Consequently, there is a need for prospective, rapid-accruing intergroup-driven trials to help identify the optimal therapy of this disease. (25)

In patients with Masaoka stage III and IVa thymoma, operative approaches range from biopsy alone to nearly complete tumor removal. Comparison between different series is challenging because of the varying amount of postoperative residual disease. The definition of what constitutes a subtotal resection has ranged from 10% to less than 100% of the initial disease volume.(26,27)

Death after thymoma resection in the perioperative period is now rare and should be less than 1%. Historically, the majority of deaths occurred in patients with myathenia gravis from respiratory complications with poorly controlled myasthenia. (28) In the current study , there were no operative or in-hospital mortalities due to the modern preoperative preparation, intensive care, and, in two cases, plasmapheresis had been essentially performed .

Conclusions:

The standardization of the multimodality protocol led to an evident improvement in terms of the rates of radical resection and survival. The incidence of recurrence is decreased at the time of follow-up. However, a longer follow-up, a larger series of patients, and possibly a randomized trial are required to draw definitive conclusions. The multimodality treatment of stage III and IVA thymic tumors allows a good long-term outcome; the neoadjuvant chemotherapy improves the respectability rate and the survival of locally advanced stages of thymoma.

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Surgical Treatment of Bronchiectasis in Children

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Background: **Bronchiectasis defined as permanent dilatation of bronchi with destruction of the bronchial wall and still a serious problem in developing countries like our country.**
Surgical treatment of childhood bronchiectasis has not been discussed because of decline in prevalence and experience with this disease.
It remain controversial as to which children would benefit from surgery and surgical points that may affect the outcome. Therefore a retrospective study was done to evaluate the results of surgical treatment of bronchiectasis in children.
Patients & Methods:The record of 19 cases who under went surgery for bronchiectasis between 2000-2003 were analyzed retrospectively for age, sex, clinical picture, radiological examinations ,details of surgery including type of resection, operative morbidity and mortality, follow up & outcome.
Result:19 patients under went pulmonary resection
Mortality rate 0, morbidity (26.4%) ,mean age (9.5), male: female(1:2) ,lobectomy(10 cases,52.6%), bi-lobectomy(5 cases,26.3%), pneumonectomy(4cases,21.1%), complete resection(16 cases), Incomplete resection(3 cases), course after surgery was well on(78.9%) , Improved on(5.3%), unchanged on(10.5%)
Conclusion:* Decision for surgery should be made in cooperation with chest disease unit (pediatric)
*** Anatomic localization should be mapped clearly by high resolution CT chest scan.**
*** Morbidity & Mortality rates of bronchiectasis surgery are within acceptable ranges.**
*** Complete resection should be performed when possible**
Pneumonectomy is well tolerated in children without increase in morbidity & mortality.

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Bronchiectasis which is defined as irreversible dilatation of bronchial tree was first described by Laennec in 1819, today with improvement of health care and the availability of suitable antibiotics, the prevalence of bronchiectasis has declined and patient with early disease can be treated conservatively in developed countries.

Bronchiectasis still constitutes an important problem in developing countries because of tuberculosis, pneumonia and other infection; few recent reports of surgical management of bronchiectasis are available in English literature.

The purpose of this study was to evaluate the indication, postoperative complication, and survival with lung resection in children with bronchiectasis.

Patients & Methods:

We review the records of all children who underwent surgery for bronchiectasis between January 2000-December 2003 at Shifa medical centre, department of chest surgery, Gaza-Palestine

The records of 19 patients were analyzed for age, sex, clinical presentation ,radiological finding, detail of surgery including type of resection, mortality, morbidity, follow up and out come.

Surgical treatment was considered if the symptoms persist in spite of courses of medical treatment (Broad-spectrum antibiotic, mucolytic & intensive chest physiotherapy, bronco dilators.)

All patients have done preoperative high resolution CT scan to evaluate the type, severity and distribution of bronchiectasis; also bronchoscopy was done to rule out bronchial obstruction, stenosis or endobronchial tumor, pulmonary function test was done in some cases.

All patients were hospitalized before surgery for intensive chest physiotherapy, antibiotics, bronchodilators and bronchoscopy to aspirate bronchial secretion to prevent spillage during operation.

Posteriolateral thoracotomy was performed in all patients, lobectomy, bilobectomy, formal pneumonectomy was used in all patients, Intercostals nerve blockage, chest tube drainage which is connected to underwater seal. Post operatively, patients admitted to I.C.U for 24 hours, then in department to continue treatment with broad-spectrum antibiotics, bronchodilator , mucolytics and chest physiotherapy.

The complication was analyzed , follow up was done for a period ranging from 36-72 months and high resolution chest CT scan after one year of surgery. The out -come of surgery was evaluated at last follow up visit and rated according to the following criteria:

- Well: patient free of symptoms .
- Improved: Patient symptoms reduced in degree.
- Unchanged: Patient symptoms persist.
-Worse: patient symptoms more severe than at the time of resection.

Data were analyzed by using (x2) test and P value less than 0.05 was accepted to be significant.

Results:

19 patients under went 19 pulmonary resection with diagnosis of bronchiectasis during study period.

The etiology was post lung infection(15 cases,79%) , congenital(2 cases,10.5%), post aspiration of foreign body aspiration(2 cases,10.5%) .

Initial evaluation was made through X-ray chest confirmed by high resolution CT scan.

Operative resection consisted of:

Formal pneumonectomy (4 cases,21%)

, loboctomy (10 cases.52.6%) , biloboctomy (5 cases,26.3%) , and all patient had complete resection.

Intraoperatively complication occur in two patients. The first had cardiac arrest respond to resuscitation and operation completed. The second patient developed severe hypoxia during induction of anesthesia and operation referred to later date.

Post Operative Complications were:

Atalectasis (2 cases, 10.5%), persistent air leak (1 case, 5.3%), wound infection (1 case, 5.3%), Empyema (1 case, 5.3%), Mean hospitalization period 8 days, Mean follow up (36-72 months)

The patient who had underwent surgery were rated, well (16 cases, 84.2%), Improved (2 cases, 10.5%), unchanged (1 case, 5.3%), and all patients who were well or improved had complete resection.

Discussion:

Bronchiectasis is pathologically defined as a condition in which there are abnormal and permanent dilatations of proximal bronchi in association with a variable degree of destruction of bronchial wall, and pneumonitis, It was described by Laennie in 1819 ,the common cause of bronchiectasis is bacterial infection , foreign body aspiration,bronchopulmonary sequestration ,cystic fibrosis and kartagner syndrome.

The morphologic classes are cylindrical, varicose and saccular (Cystic), two thirds of the patients in our series had cystic bronchiectasis, in this study we observed that the lower lobes affected more than the upper lobes and left side more than right, because the retaining of secretion can be thought to more easily occur in left side because of its smaller diameter and greater angle and its spatial relationship to the left pulmonary artery.

The most common isolated organism is Staphylococcus aureus and, Pseudomonas aeruginosa.

The incidence of the disease declined significantly over recent decades since the advent of antibiotics therapy, immunizations, better health care in developed countries but still a serious problem in developing countries like our country due to increase incidence of tuberculosis, malnutrition, inadequate health care system.

Initial treatment is conservative by broad spectrum antibiotics for elimination of micro organism from lower respiratory tract ,intensive chest physiotherapy , mucolytics and bronchodilators, the main indication for surgery is failure of medical treatment ,increase the quality of children lives and protect them from complication such as empyema, lung abscess and haemoptysis ,excellent result can be achieved by careful & proper selection of candidate and each child should be evaluated

separately for surgery.

The indication for surgery in adult have been reported to be resistance to conservative treatment for reasonable period of at least two years, In children in addition to the above criteria , growth retardation , inability to follow educational study because of frequent attacks of respiratory infection & hospitalization ,socioeconomic status of the family should be also considered when decision of surgery was made.

When complication was present , it help the surgeon in their decision for surgery, however when bronchiectasis affect multiple lobes or bilateral the decision is quit difficult because complete resection of all affected lobes usually impossible. all children should be free of active pulmonary infection at the time of operation be giving :Antibiotic with chest physiotherapy , bronchodilators, bronchoscopy should be performed in all patient preoperatively to exclude bronchial obstruction and to clear airways, localization should be mapped well by high resolution chest CT scan,pulmonary function test is not required in children with localized disease and needed in cases of extensive involvement of lungs.The aim at operation is to excise all diseased lung area when ever possible and to preserve as much healthy lung parenchyma as possible and the resection should be performed within anatomic limits, loboctomy was the most frequent operation in our series (10 cases52.6%)

, followed by biloboctomy(5 cases26.3%),pneumon ectomy(4 case.21%))

Pneumonectomy has been well tolerated without increase in complication in current series.

The success of surgery is directly related to extension of disease , underlying cause and completeness of surgery.

The aims of surgical therapy is to improve the quality of life of patients who have debilitating pulmonary symptoms despite medical treatment and to prevent complication such as empyema ,recurrent haemoptysis , lung abscess. patients with clearly symptomatic localized childhood bronchiectasis is ideal surgical candidates.

Conclusion:

Decision for surgical intervention should be made in cooperation with the chest disease unit & should be limited to patients with localized disease and it can be performed with a definite strategy and strict criteria. Complete resection should be performed whenever possible ,preservation of as much lung parenchyma as possible. The basic guideline for operative therapy of bronchiectasis are infection control, preoperative bronchoscopy precise anatomic localization and anatomic resection.

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Risks and complications of resternotomy in adult's cardiac operations

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Background: Resternotomy is associated with increased morbidity and mortality. The increased risk of redo procedure is related to the complications of resternotomy which include severe haemorrhage, damage of underlying vital structures which may be requiring cardiopulmonary bypass. Our aim was to determine the incidence of complications directly attributable to redo-sternotomy and to ascertain whether the use of femoro-femoral CPB (FF) prior to redo-sternotomy alters operative morbidity and mortality.

Patients and methods: 46 patients undergoing cardiac surgery necessitating redo-sternotomy between 2000 and 2006 were reviewed, 29 males and 17 females, the median age was 50.75 years (range 38 to 62.5 years). Elective FF was performed in 18 (39%) of cases and 28 (61%) were performed without the aid of prior femoro-femoral CPB (WFF).

Results: four (8.6%) patients initially planned for WFF were converted to emergency FF due to serious complications. Complications directly attributable to redo-sternotomy occurred in 13 (28.2%) cases; 9 (19.5%) in the WFF group 1 and 4 (8.7%) in the FF group 2. Overall mortality was 3 patients (6.5%).

Conclusion: In summary, our results suggest that morbidity risk for the operation increases significantly with redo-sternotomy alone. Three deaths in our series from direct complications attributable to redo-sternotomy signify an added risk. Hence the necessity for careful surgical technique and judicious use of elective FF-CPB is emphasized.

Cardiac reoperations are traditionally associated with higher in-hospital mortality and morbidity in comparison with primary procedures. Resternotomy for reoperative cardiac surgery has become increasingly common with an aging patient population.1 The increased risk of redo procedure is partly related to the complications of resternotomy which include severe haemorrhage, damage to previous conduits requiring cardiopulmonary bypass through the femoral vessels and sternal fractures.2,3 Reoperations remain complex and time-consuming for the surgeon; injuries to cardiac structures during isolation are dreadful complications in such settings, mainly in patients who have already undergone more than one procedure Resternotomy is associated with increased morbidity and mortality. The exact incidence of these complications is unknown and underestimated in the literature for two reasons: (a) lack of consistent definition and (b) underreporting as it may imply a technical error.The actual incidence of resternotomy hemorrhage is unknown but reported to range between 2 – 6% per patient reoperation.4

Factors associated with an increased risk of resternotomy i.e. 'high-risk resternotomy' include: multiple previous surgeries, enlarged heart chamber

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or vessel, history of mediastinitis or sternal wound infection, or patent grafts from previous bypass surgery which are particularly vulnerable to inadvertent division, with often disastrous consequences and recent previous operation (<5 years).5,6

Our aim in this study was to determine the incidence of complications directly attributable to redo-sternotomy and to ascertain whether the use of femoro-femoral CPB (FF) prior to redo-sternotomy has any affect on perioperative mortality and morbidity.

Patients and methods

Over a time range of 6 years between 2000 and 2006, 46 patients included in this study who underwent repeat sternotomies. Retrospective data were obtained by medical records in our archive. There were 29 males and 17 females. The median age was 50.75 years (range 38 to 62.5 years) and the overall mortality was 6.5 % (3 patients). 28 patients (61%) redo-operations were performed without the aid of prior femoro-femoral CPB (WFF, group 1) and 18 (39%) with femoro-femoral CPB (FF, group 2). Four (8.6%) patients initially planned for WFF were converted to emergency FF due to serious complications encountered during redo-sternotomy. The initial surgical procedures were aortic valve replacements (AVR) in 12 patients, mitral valve repair/replacement (MVR) in 24 patients and coronary artery bypass grafting (CABG) in 10 patients.

Re-operations included AVR in 8 patients, MVR in 12 patients, MVR and TV repair in 11 patients, combined AVR and MVR in 9 patients, CABG in 4 patients, combined MVR and CABG in 2 patients.

Indications for reoperation included hemodynamically significant failure of mitral valve (MV) repair, prosthetic valve dysfunction (PVD), progressive aortic or mitral valve disease and graft occlusion or stenosis and/or progression of native coronary artery disease (CAD). Study end points were bleedin, occurrence of injuries and arrhythmias during surgery, and incidence of minor postoperative morbidity and outcome.

SURGICAL PROCEDURE

Prior to proceeding with a resternotomy, the relationship between anterior structures and the posterior aspect of the sternum (as visualized on chest x-ray, or computed tomography (CT), must be assessed carefully

The usual anesthetic preparation and haemodynamic monitoring lines were used and two external defibrillator pads were placed on the chest wall.

We perform a slightly longer than standard skin and subcutaneous incision. The sternal wires or other material that had been used for previous sternal closure were left in place. Then the linea alba was divided and the xiphoid process was excised.

Preparations for emergency femoral-femoral cardiopulmonary bypass (CPB) should be complete prior to beginning the resternotomy. Sternal wires from the previous operation should be carefully undone, but left in place as a safeguard during sternal division. An oscillating (not reciprocating) bone saw was then usually used to divide the anterior and posterior tables. Following this, the pericardium and other mediastinal structures adhering to the posterior aspect of the sternum was dissected with electrocautery or scissors using rake-retraction before trying to place a small sternal retractor. The pericardial dissection plane was developed at the cardiophrenic angle, and then advanced cephalad and laterally on the surface of the right heart. Cephalad dissection started with inominate vein identification; from there, dissection carried down the superior vena cava - noting location of the right phrenic nerve. The dissection was done carefully to avoid injuries to patent vein or mammary grafts, the right atrium and ventricle, the pulmonary artery, aorta, and the innominate vein. For mitral valve surgery, aortic-bicaval cannulation. For isolated aortic valve surgery, we used ascending aorta-right atrial cannulation. In some patients, dissection of the heart was difficult and required institution of cardiopulmonary bypass.

The handling of patent vein or mammary grafts and the need to relocate sites for aortic perfusion, cross clamping, cardioplegia and aortotomy because of previously placed bypass grafts,all add technical complexity to the procedure and potentially increase perioperative risk. Reentry problems include injuries to grafts, the right atrium and ventricle, the pulmonary artery, aorta, and the innominate vein.

Repairing small ventricular or atrial lacerations was done after releasing the adhesions surrounding the laceration. Repair of great vessel injuries was done under CPB.

Most patients underwent operations with moderate hypothermia and cardioplegic arrest. Elective FF-CPB before repeat sternotomy was used in 40 patients and 6 patients were put on FF-CPB as an emergency. The criteria for FF-CPB were preoperative judgment and surgeon preference.

Statistical analysis

Descriptive statistics of preoperative and intraoperative characteristics as well as intraoperative complica-

tions and mortality are reported for the entire cohort (n = 125). Univariate and multivariate analysis using Fisher's exact test and logistic regression was performed to determine predictors of outcome. A value of $p < 0.05$ was taken as significant.

Results:

Overall hospital mortality was 6.5% (3 of 46) in both groups. The cause of death was low output syndrome secondary to ventricular dysfunction and uncontrollable hemorrhage.

Preoperative clinical features and operative demographics of the two groups are summarized in table 1. No statistically significant differences could be detected. Complication directly attributable to redo-sternotomy as cardiac lacerations, occurred in a total of 11 (23.9%) cases; 8 (17.4%) in group 1 and 3 (6.5%) in group 2. These comprised of minor injuries to the right ventricle 3 (6.5%), right atrium 2 (4.3%), aorta 3 (6.5%),innominate vein 1 (2.2%) previous saphenous vein grafts 1 (2.2%) and previous internal mammary artery grafts 1 (2.2%). 4 patients (8.6%) were requiring emergent femorofemoral bypass due to severe hypotension or arrhythmias (Table 2).

Table (1): Clinical and demographic data of patients.

Variable	Group1 (WFF-CPB, *n* = 28)	Group2 (FF-CPB, *n* = 18)	*p* Value
Mean age(y)	45±1	48±5	NS
Male/female	16/9	13/8	NS
NYHA class 3–4	17(62.3%)	11(60%)	NS
Chronic pulmonary disease	5(18.8%)	4(20%)	NS
Hypertension	12(42.8%)	8(44%)	NS
Diabetes	9(32.1%)	6(33.3%)	NS
Serum creatinine > 200 µmol/L	5(17.8%)	3(16.6%)	NS
LV ejection fraction >0.40	16(57.1%)	11(61.1%)	NS

NS: Non significant
HS: highly significant.

In table 2 perioperative and ICU data are reported, as regards, arrhythmias during cardiac isolation, injuries to the cardiac chambers or great vessels during cardiac isolation, aortic cross-clamp time, CPB time and period of ventilation, which showed difference between both groups in some items. Postoperative mediastinal drainage in the first 24 hours was reduced in the femrofemoral group 2 ($p < 0.05$), so reexploration for bleeding after admission to the ICU had a significantly lower incidence in group 2 in comparison to that in group 1.

Table (2): Perioperative and ICU data.

Variable	Group1(WFF-CPB, n = 28)	Group2 (FF-CPB , n = 18)	p Value
Cardiac injuries:			
Right atrium	2	0	
Right ventricle	2	1	
Aorta	2	1	
Saphenous graft	1	0	
LIMA	1	0	
Innominate vein	1	0	
Arrhythmia	9(32.1%)	4 (10%)	HS
CPB time (min)	89±11.2	77±12.4	NS
cross-clamp time (min)	66±10.3	69±12.2	NS
Postoperative bleeding (mL/m2 per 24 hours)	958±28	552±67	HS
Mechanical ventilation > 24 hours	14	13	NS

The occurrence of postoperative complications (renal failure, respiratory insufficiency, inotropic support greater than 24 hours, low cardiac output, sepsis,) were not statistically different. Finally, the length of ICU and hospital stay were not statistically different in both groups (table 3).

Table (3): postoperative complication and outcome.

Variable	Group1(WFF-CPB, *n* = 28)	Group2 (FF-CPB , *n* = 18)	*p* Value
Low output syndrome (%)	12	11.5	NS
Bleeding (%)	6.6	4.7	HS
Sepsis (%)	9.8	11	NS
Renal Failure (%)	5.4	4.1	NS
ICU stay (days)	2.8±0.6	3.2±3	NS
Hospital stay (days)	23 ± 3.2	21± 2.3	NS
30-day mortality	3(6.5%)	0	HS

Discussion

The presence of dense adhesions between the cardiac chambers and the surrounding tissues and the loss of normal planes of dissection can make cardiac reoperations extremely hazardous and time consuming, independently from the functional status of the patients and the indication for surgery.7

The number of cardiac re-operations is steadily increasing. The increased risk of redo procedure is partly related to the complications of resternotomy which include severe haemorrhage requiring cardiopulmonary bypass and sternal fractures.8 In accordance with others, 9,10 our experience suggests that enlarged cardiac chambers behind the sternum and lack of retrosternal space were the main risk factors for sternal re-entry.

The overall mortality in the redo operation group reported in the literature6, 10 is 13.8%, our series has demonstrated a 30-day mortality of 6.5% following re-entry sternotomy. There were 3 deaths out of 46 cases; one catastrophic tear in aorta with concomitant right ventricular tear and simultaneous ventricular fibrillation; one hemorrhage from a tear in an innominate vein with low cardiac output. All these occurred in the WFF group although in this two cases, FF institution was undertaken on an emergency basis. Lytle and colleagues11 reported 3 deaths among 1500 coronary re-operations due to complications of repeat median sternotomy whereas Macmanus and colleagues12 reported 8 cases of severe hemorrhage in 122 repeat sternotomies.

The incidence of direct complications may have been higher in our series but the judicious employment of FF had influenced our results as preparations for FF were made electively due to the possibility of inadvertent entry into the heart or great vessels when the sternum was divided.

Our series demonstrated that cardiac structures were injured 11 times at repeat sternotomy. The risk of injury to a patent internal thoracic artery graft has been reported in 2 series: one by Lytle et al., 13 reporting damage in 3.5% of 489 patients, and other by Baillot et al14 reporting a rate of 8% among 100 cases. Culliford and Spencer15 in a review of their experience, stated that the most common reasons for complications were lack of precise technique and insufficient attention to hemostasis.

Several surgical approaches are available to patients undergoing repeat operations. Macmanus and associates 12reported institution of CPB through the femoral vessels prior to repeat sternotomy in certain instances. Byrne JG.,and associates16 reported in their study that partial upper hemisternotomy for reoperative aortic valve replacement avoided unnecessary lower mediastinal dissection, thereby reducing blood loss, transfusion needs, and total operative duration. These beneficial effects made the partial upper hemisternotomy an excellent alternative to conventional full resternotomy for reoperative aortic valve replacement.

Some autherss maintain that repeat median sternotomy may be facilitated by certain maneuvres at the time of the initial cardiac procedure. Cliff and associates17 showed that both serosal injury and blood are necessary to produce cardiac adhesions. Careful handling of the heart and complete evacuation of pericardial blood may reduce postoperative adhesions. Where appropriate, approximation of the pericardium or placement of synthetic biomaterials may also facilitate re-operation.

A significant limitation of our study related to the fact that repeat sternotomy was only one parameter of outcome in redo cardiac surgery. Clinical results were more likely to depend on the complexity of the primary diagnosis and the procedure as well as the quality of the surgical repair. Moreover, likelihood of local morbidities relating to trauma to the femoral vessels due to FF bypass has not been quantified due to the retrospective, observational nature of this study.

The main question surgeons confront is whether re-operations have an incremental effect on operative mortality compared with primary procedures. in summary our series has demonstrated that repeat sternotomy carries added risks to the operation, which could be improved with an organized surgical approach and judicious use of elective femoro-femoral bypass. In addition, as suggested in previous studies,17,18 a lateral chest X-Ray or CT scan may be useful in determining the likelihood and extent of adhesions between the heart, great vessels and the sternum.

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New management technique for deep sternal surgical site infection.

Cardiovascular

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***Background*:surgical site infection is the third most frequently hospital –acquired – infection among all hospitalised patients. This is remaining a substantial cause of morbidity and mortality among surgical patients. This work is introducing a new technique in management of deep sternal surgical site infection (DSSSI) after cardiac surgery.**

***Patients and methods*: four males and one female of age ranged between 32 and 63 years old underwent a new management technique for DSSSI. The method's steps included debridment of the soft tissues and the bones, retro-sternal insertion of fenestrated plastic tube to drain the coming down blood, approximation of the sternum using Dixon's sutures, advancement of the pectoralis muscles to the chest midline after undermining then, closure in mass using thick proline taking all layers from the skin down to the bone then from the same level to the skin of the opposite side. An enforcement second interrupted suture layer is taken to approximate the muscles and the skin. The wound is exposed after 24 hours. The plastic tube is removed when the blood stoops coming down and a colostomy bag replaces it. This bag is fixed at the removed tube site by its appliances. The bag is removed when the discharge becomes serous and criteria of infection have been gone.**

***Results*: there was no early mortality however it was reported late mortality out of five (20%) after 4 months. Hospital stay ranged from 25 days to 46 days. In follow up ranged of 6 months to 3.5 years there was no recurrence of deep infection, stitch sinuses, mechanical skin dehiscence or sternal gap. There was residual chest wall pain related to the site of the harvested internal thoracic artery in 2 patients (40%). This was controlled by given anti-inflammatory medications on demand.**

***Conclusion*: the current method of using less surgical materials in infected field is an alternative to the other methods with less postoperative complications.**

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Surgical site infection is the third most frequently hospital –acquired – infection among all hospitalised patients (1). This is remaining a substantial cause of morbidity and mortality among surgical patients (2). Many methods have been tailored to fit the circumstances of those patients suffering from deep sternal surgical site infection (DSSSI), or mediastinitis. Early treatment protocol used open packing of the debrided wound (3). This method treated the situation like an abscess. Sternal and mediastinal debridment followed by continuous or intermittent closed system irrigation has gained popularity for many years (4). Using omental, muscle or myocutaneous flap in one or two sitting reconstruction after debridment recording advantages in some patients (5).

The current work is introducing a new technique in management of DSSSI after cardiac surgery.

Patients

Five out of 567 patients (0.9 %), four males and one female of age ranged between 32 and 63 years old (mean 53.2 +/-12.36) had DSSSI and underwent the current management technique. This was done in Al-Azhar University Hospitals from January 2002 and July 2005 (3.5 years). The primary diagnosis for all patients was ischaemic heart diseases (IHD). All had coronary artery bypass grafting (CABG) and mitral valve replacement in patient number 3. The operation was performed electively in 4 and emergency in the last patient (table1).

Pt. No.	Sex	Age	Diagnosis	Time of surgery	Operation
1	M	32	IHD	Elective	CABG X 1+3
2	M	58	IHD	Elective	CABG X 1+1+1
3	M	62	IHD+IMVI	Elective	CABG X 1+MVR
4	M	53	IHD	Elective	CABG X 1+1
5	F	61	IHD	Emergency	CABG X 2

Table 1: sex, age, diagnosis, time and operation of the studied Patients.

Method

Preparation; once the patient was diagnosed of dehiscence with deep infection. The patient was re-admitted to the hospital and an urgent Echocardiography and plane postero-anterior and deed lateral chest X ray was performed. The site of discharge or collection was lad opened at the most dependant area to drain the collection like an abscess. Removing all suture materials, wires and necrotic looking tissues were followed the drainage. Swap for culture and sensitivity from the wound's discharge was taken as a routine procedures. This was immediately concomitant by administration of three intra-venous (IV) antibiotics regimen until the results of the swap come back. The regimen consists of Augmentine 1.2 grams twice daily, Garamycine 80 milligrams 8 hourly IM for 24 hours and Metronidazole 100 milligrams IV twice daily for 48 hours then replaced by oral 500 milligrams twice daily. The wound dressing had to be changed as many as needed. The wound was regularly cleaned by 0.9% saline. The skin edges were soaked with glycerol during changing the dressing. All measures been taken to improve the general hygiene. Clinical judgement, full blood picture and ESR monitored the patients' progress.

The studied patients were considered in post-operative complications status from the nutritional point of view. In such circumstances they had given 40-45 Kcal/Kg as energy and 0.2gram nitrogen/Kg for protein supplement. Reassurance of the patient and elevation of his mode were taken in consideration as well to alleviate the effect of the psychological trauma of re-operation soon after the first procedures.

The operative steps; consists of, debridment of the skin, subcutaneous tissues, muscles, bones and removing all the necrotic tissues around the heart with wash using warm saline until the purple colour of the viable tissues would be seen. The pectoralis major muscles with the skin was undermined and advanced as a myo-cutaneous flap. The myo-cutaneous flap dissected off the costal cartilages in a length enough to cover the sternum without tension. Laying 3/8 inch's diameter drainage tube with multiple side holes under the sternum for draining blood, serous and pus. Retained viable sternum was approximated by Dixon No.2, two interrupted stitches to adjust the supra-sternal notch and one to approximate the last intercostal spaces. No stainless steel wire was used in this technique. This was followed by approximation of the myo-cutaneous flap in the midline without over ridding by vertical simple stitches taking all layers from the skin down to the bone and the cartilage using proline or nylon no.2. An additional vertical mattress sutures between the previous ones to adjust the skin edges using Proline no. 2/0 were used.

Twenty-four hours after the operation the wound was exposed and chest binder was applied for 2 months. Once the blood stops coming down, the drainage tube is removed and replaced by colostomy bag to drain any discharge after cessation of the blood. The appliances of the bag is fixed around the centre of the exit of the drainage tube to be removed when the criteria of infection is gone (no discharge, signs of granulation tissues have appeared and the ESR, white cell count has come down). The site of the draining tube was covered by sacked glycerol gauze to be changed as required until the granulation tissues fill the pit.

Follow up**:** the studied patients were assessed by clinical examination for mediastinal dehiscence, recurrence of DSSSI, progress of wound

healing, scars, keloid and sinuses. They followed as well by full blood picture, ESR, culture and sensitivity from the wound discharge, ECG, plane CXR and echocardiography.

Statistical analysis:

Statistical analysis was performed using SPSS version 13.0. Values were given as the mean ± with standard deviation (SD).

Results

Pre-operative assessment of risk factors of arteriosclerosis and wound infection showed that diabetes was present in 80%, hypertension in 60%, smoking in 60%, family history of related disease in 20% and hyperlipideamia in 20%. However, last patient was suffering from hypothyroidism and she was on replacement therapy (table 2).

Pt. No	Diabetes	Hypertension	Fam.hist.	Smoking	Hyperlipidemia	Other	Others
1	Y	Y	Y	Y	Y	12	N
2	N	N	N	Y	N	16	N
3	Y	N	N	Y	N		N
4	Y	Y	N	N	N		N
5	Y	Y	N	N	N		Hypothyroid.

Table 2: Pre-operative risk factors for DSSSI.

The per-operative assessment for the risk factors that induced DSSSI revealed that the first patient developed on table ventricular tachycardia after wound closure. This was required urgent reopening and resuscitation for 5 minutes. The second patient was re-opened for missed swap before transfer to the intensive care unit. For the second time, after 24hours from the first operation, routine postoperative plane CXR discovered a missed tip of the two stages venous cannula in the inferior vena cava. He was reopened for the second time to retrieve the tip of the cannula (table 3). Wound infection occurred in range of 12 to 17 days postoperatively mean (14.4+/-2.3). The new technique was performed in range of 3 to 10 days from the time of discovering the infection mean (5.8+/-2.8).

Pt. No	Events
1	VT after wiring needed resuscitation for 5 minutes
2	Opened for missed swap in the first time*
3	Opened for missed fractured tip of the 2 stages cannula*
4	Ok
5	Ok
	Ok

Table.3: Per-operative events of risk factors

The culture and sensitivity revealed that infection with Staff Aureus occurred in 2 patients, Pseudomonas in a patient, Enterococci in an-other patient and Methicillin resistant staphylococcus aureus in the last patient. The 3 IV antibiotic regimens were effective and continued after the culture and sensitivity came back in 4 patients. However, the last patient was converted to Vancomycin (Table 4).

Pt. No	T. infection	T. surgery	Ant. before	Organism	Ant. after Cul
1	12	5	IV 3	Stap.a	IV 3
2	15	7	IV 3	Pseu	IV 3
3	17	10	IV 3	Entero	IV 3
4	12	4	IV 3	Stap.a	IV 3
5	16	3	IV 3	MRSA	Vancomy

Table 4: Timing (T) of infection, surgery, type of organisms and the antibiotics been used.

Retro-sternal chest tube was removed in range of 2 to5 days mean (3.4+/-1.1) and the tension suture in range of 13 to 16 days postoperatively mean (14.2+/-1.1). The colostomy bag that replaced the retrosternal tube was removed in range of 6 to 15 days mean (10.2+/-3.8). The period of stay in the hospital from the time of discovery of the infection to discharge home ranged from 26 to 46 days mean (30.8+/-8.7) (table 5).

Pt. No	T. tube re	T. suture re	T bag re	Stay in hospital
1	3	14	15	25
2	5	16	7	30
3	4	13	13	27
4	2	14	6	26
5	3	14	10	46

Table 5: Time (T) of tube, suture, bag removal (re) and staying in the Hospital.

In follow up ranged of 6 months to 3.5 years there was no mediastinal gap, recurrence of deep infection, stitch sinuses or mechanical skin dehiscence. There was residual chest wall

pain related to the site of the harvested thoracic artery in 2 patients (40%) (Table6). This was controlled by given anti-inflammatory .medications on demand

M dehiscence	St. sinus	Skin disruption	Keloid	Pain
------	-----	------	-----	yes
-----	-----	------	-----	Yes
------	------	------	------	-----
-----	-----	------	-----	-----
------	-----	------	-----	-----

.Table 6: Post-operative complications

The over all results showed that; there was no early mortality however; in the follow up range mentioned; it was reported (20%) late mortality after 4 months (Figure 1). That patient was barber and he lost his career. It was not possible to get him out of his depression and eventually died from anorexia associated .with marked loss of weight

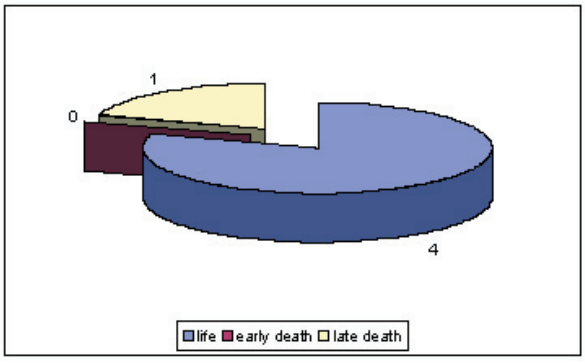

Figure 1: Over all results.

Discussion:

Currently, deep sternal surgical site infection is infrequent (0.15-5%) (2,6). However, This is remaining a substantial cause of morbidity and mortality among surgical patients. The decline of incidence relates to the introduction of the guidelines of prevention of cross infection and using prophylactic antibiotics (1). Others highlighted the importance of measuring the impact on the DSSSI of specific procedures and patient's circumstances rather than all surgery (7). This has paid attention to the risk index to each patient considering the expectation of the incidence of DSSSI. Some of the important patient's risk factors include obesity, insulin dependant diabetes mellitus, peripheral vascular arteriosclerosis, long-term low cardiac output, and immunocompromized patients (8,9,10). Procedures more than 5 hours, reopening of the patient before signs of healing, inadequate haemostasis with insufficient drainage and using bilateral mammary artery in coronary artery bypass grafting are between operative incriminating factors of DSSSI (2,8,9,10,11).

Before restriction of using the antibiotics with preference to culture and sensitivity, coagulase negative staphylococci and group D enterocci were common. However, after restriction, Methicillin resistant staphylococcus aureus and vancomycin resistant enterococci are common (12).

Despite early diagnosis and prompt treatment, the out come of DSSSI is not satisfactory. This relates to the extensive necrosis of the vital mediastinal tissues with consequent spread of infection and loss of tissues cooptation before clinical diagnosis take place. Loss of tissues cooptation induces discomfort and limitation of the respiratory functions. In addition toxins that are released from the microorganisms and the necrotic tissues produce toxaemia, shock and multiple organs failure.

Management of DSSSI is a subject of controversy. Few decades ago it was dependant on surgeon's own experience. However, the treatment has evolved over the past 40 years. At the beginning it was treated like an abscess in the form of open drainage followed by debridment with the wound left open and allowed to granulate for gradual closure by secondary intention. This technique was associated with significant prolonged hospital stay, morbidity and mortality (3,13). Schumaker and associates in 1963 described the technique of closed catheter antibiotics irrigation following debridment and rewiring of the sternum (14). Thirteen years later, Lee and colleagues treated patients who did not respond to catheter irrigation and rewiring with wide debridment, followed by omental flap closure (15). Jurkiewicz and associates expanded on this concept by using muscle flap to fill the dead space remaining after radical debridment (16). Adequate sternal immobilization appears to have an effect on the incidence of postmedian sternotomy mediastinitis (18). Robicsek was the first to describe sternal closure and muscle padding to provide sternal stability (18,19). This was followed by using the pectoralis major muscle as a myocutaneous flap for more support to the sternum (20). However, the out come results of each management depends greatly

on individual circumstances and the response mechanism of his body (19,21,22,23).

In the current technique the pectoralis major muscle was used as an advancement myocutaneous flap. After debridment of the skin and the muscle edges without separation, it had been undermined for a distance enough to get proper approximation of the edges in the midline without tension. The flap is suitable supportive cover with blood supply for the fragile inflamed sternum. This technique is different than the other reported pectoralis major flap of complete dissection to the muscle off its insertion (18,20,24). We tried to minimize using diathermy in dissection to preserve the perforators of the intercostals blood vessels. The technique intended to approximate the flap using the secondary intention sutures technique. The basic rules were no gaps between the flap edges or deed space between the flap and the sternum. Other enforcement layer was taken to adjust the skin edges. Once the wound was dressed at the end of the procedures a chest belt is applied and was kept on and off for two months later. The corner stone of this technique is to keep stability of the sternum by careful handling and mobilization of the patients when they are under anaesthesia. Lifting up the patients from there arms was forbidden by all means. No vigorous movements would be allowed before 2 months of the date of the operation.

The initial stage of this technique was to control the invasive sepsis. This was achieved by draining the collection, removing all suture materials, wires and necrotic looking tissues. This was concomitant with taken culture from debrided components with subsequent organism sensitivity to the available antibiotics. Immediately the triple antibiotic regimen was started, until the results of the cultures come back. We found that the triple antibiotic regimen was effective and we did not need to change it after the results of the sensitivity came back except in one patient.

The nutritional status under circumstances was considered, for given the maximum required calories and proteins to avoid the consequences of the catabolic event. Reassurance of the patient was mandatory. It has been found that these patients were suffering from psychological trauma of re-operation soon after the first procedures. We intended to explain to them that surgical infection do not result from the mere presence of contaminated bacteria, but rather from a complex interaction between the host's defence mechanism and the pathogenic organism (20).

The surgical stage consists of debridment of necrotic tissues and approximation of the healthy tissues. The technique was tried to limit using foreign surgical sutures and avoided stainless steel wires. The first remains for some times and forms nudes of re-infection or stitch sinuses. The stainless steel wires cut through the fragile oedematous retained sternum and it lasts forever. Occasionally it forms small painful lumps under the skin. In considerable number of patients treated using wires, they needed removal of some of them at some stage in their life. We approximate retained viable sternum by Dixon No.2, two interrupted sutures to adjust the suprasternal notch and one to approximate the last intercostals spaces. For the same purpose of limiting foreign surgical materials, the drainage tubes used intra-operatively were removed once the blood stoops coming down. We would believe that removal of the tube at this stage gets rid of port and track of infection. In addition removal would help the granulation tissues to fill the retro-sternal space as early as possible. The technique replaced this drainage tube by a colostomy page when the blood coming down through it disappears completely. The appliances will fit at the exit of the drainage tube. It was found that this was quite useful method for the general patients' hygiene and to send the patients home to be looked after by local medical persons. Discharging patients from the hospital when they become ready to do so without long waiting for granulation tissues to reform is shortening hospital stay and its complications. Once the exit site filled by granulation tissues the colostomy bag and its appliances was replaced by soaked dressing with glycerol.

With this technique there was no early mortality among 5 patients. In their follow up period and up to writing this work there was no reported mediastinal gap, recurrence of deep infection, stitch sinuses or mechanical skin dehiscence. There was residual chest wall pain related to the site of the harvested internal thoracic artery in 2 patients. This was controlled by given anti-inflammatory medications on demand.

We would agree that prophylaxis is better than cure (20). This would be achieved by avoiding the risk as much as possible from the patient's side and environmental surgical procedures of the other side. If infection could happen, on time wise decision of surgical intervention might change a lot fore ward in the patient's life.

Conclusion: the current method is an alternative to

the other methods of managing deep sternal surgical site infection with less postoperative complications.

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