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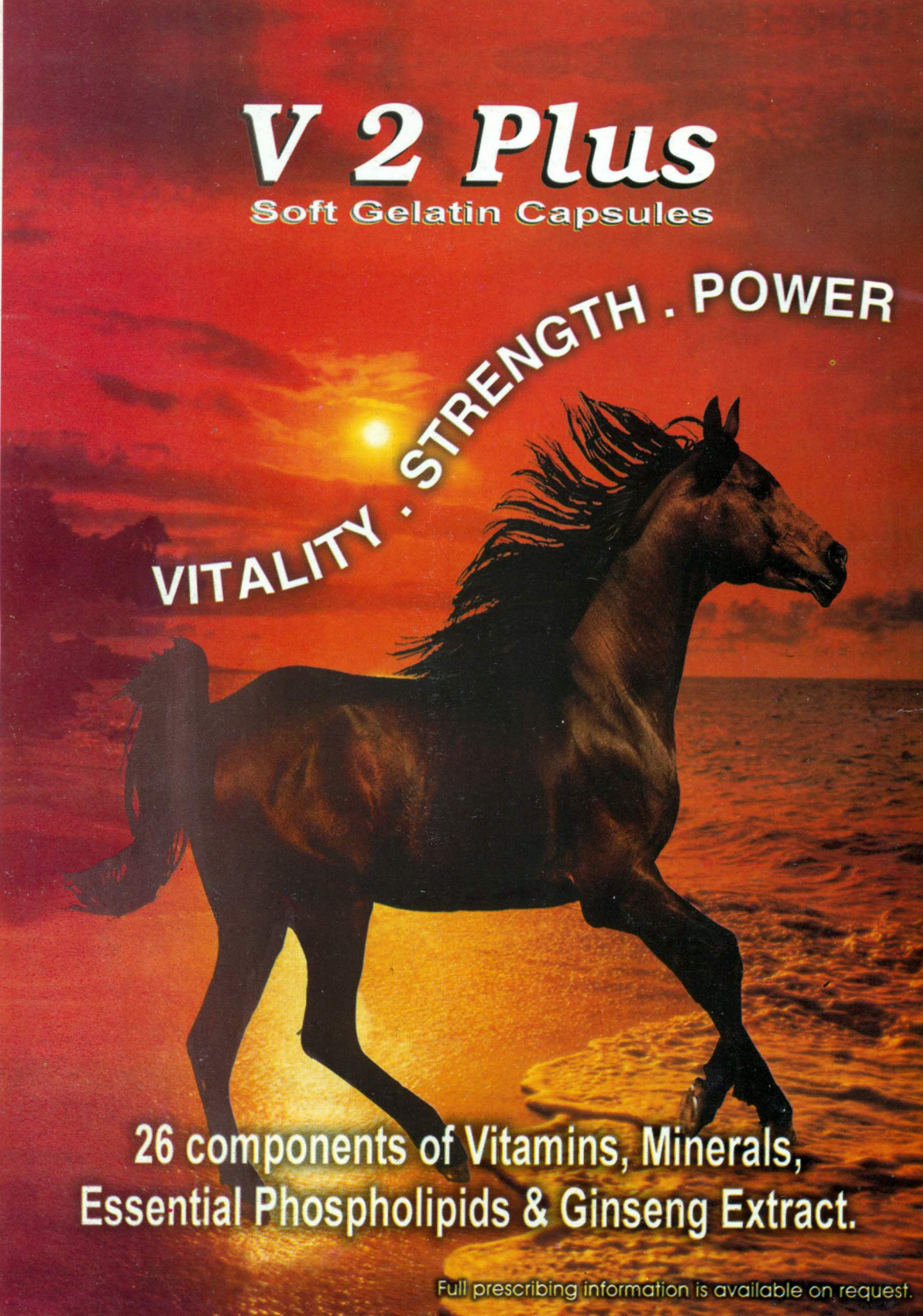
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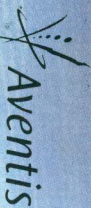
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THE RISK FACTORS AFFECTING THE OUTCOME OF CORONARY ARTERY BYPASS GRAFTING AND CONCLUSION OF PROGNOSTIC SCORING TO BE USED IN SUCH CASES

ABSTRACT

The prevalence of coronary artery atherosclerosis has progressively much increased the number of patients presenting for coronary artery bypass grafting over the years. Between Nov. 1995 and June 1999, coronary artery bypass grafting was done for 234 patients at the Department of Cardiac Surgery at Nasr City Insurance Hospital. 22(9.4%) patients were females while 212(90.6%) were males. Their ages ranged from 36 to 72 years. The grafts done for the studied patients varied from one to four in number using Internal mammary artery and saphenous vein grafts. Early mortality (first month after operation) occurred in 17 patients (7.26%). This number increased during the one year period of follow up reaching 23 patients (9.6%). The results of surgical intervention were correlated to the different parameters of the studied patients trying to detect the risk factors in such patients and concluding a scoring system to be used to predict prognosis when dealing with such cases.

Mohamed Attia, Magdy Mostafa and Farag Ibrahim

J. of Egypt. Society of Cardiothorac. Surg. 1998, VI April No 2.

INTRODUCTION

Coronary artery bypass grafting (CABG) has been used with increased frequency since its introduction into clinical practice more than 25 years ago (1). Recent advances in preoperative and postoperative management have resulted in a dramatic reduction in the perioperative mortality rate for direct myocardial revascularization (2,5).

The search for risk factors affecting short-and long-term survival after coronary artery bypass graft surgery (CABG) dates back to the inception of the procedure over 20 years ago. A detailed understanding of the determinants of morbidity and mortality after CABG would allow surgeons to identify risk factors that could be changed to improve patient outcome, to adjust for baseline differences in outcome studies, and to predict the expected survival curve for an

individual patient. Therefore, in this work we have reviewed the results of CABG in the studied patients and compared these results with the important parameters of the patients to detect the risk factors trying to conclude a scoring system to be used in predicting the prognosis in such cases.

Patient and Methods

Patient population:

The study population consisted of patients undergoing a first CABG at the department of cardiac surgery at Nasr City Insurance Hospital Between November 1995 and June 1999.

The study consisted of patients with significant coronary disease treated for stable angina, progressive angina, unstable angina, post infarction angina, and acute myocardial infarction and patients requiring

CABG for refractory cardiogenic shock and intractable ventricular arrhythmias. Patients with significant ischemic mitral regurgitation (3+ or 4+), prior CABG or prior thrombolytic therapy were not included. Patients with congenital heart disease, post infarction ventricular septal defect or cardiomyopathy were also excluded.

Surgical technique

All operations were done using median sternotomy approach, extracorporeal circulation was instituted by standard techniques (7), and perfusion was maintained at 2.0-2.4 L/min/m². Systemic hypothermia (25-30°C), topical hypothermia and cold blood potassium cardioplegia were used for myocardial protection.

Cardioplegic solution was reinfused at 20-30 minute intervals to maintain an intramyocardial temperature of less than 20°C. Distal anastomoses were done on arrested heart while the proximal ones were done after aortic decamping using partial occluding clamp. Grafts were created from either internal mammary arteries or vein grafts. The patients were then transferred to the surgical intensive care unit.

Data

(Table 1) Pertinent history, physical examination, chest X-ray, Doppler's echocardiography electrocardiographic characteristics, full laboratory investigations and angiographic and surgical data have been collected prospectively for all the studied patients. Follow-up information has been prospectively collected at 6 months and 1 year after surgery.

Results

Sex: The total number of the studied patients was 234. 212 patients (90.6%) were

males while the remaining 22 patients (9.4%) were females.

Age: Their ages ranged from 36 to 72 years with a mean age of 56 years. 13 patients (5.5%) had age between 36 and 45 years, 97 patients (41.4%) had age between 46 and 55 years, 112 patients (47.8%) had age between 55 and 65 years and 12 patients (5.3%) had age between 65 and 72 years.

Previous myocardial infarction: 95 patients (40.6%) gave a past history of myocardial infarction while 139 patients (59.4%) were free from such insult.

Laboratory investigations: Only 2 patients (0.85%) had chronic renal failure. 159 patients (67.9%) were diabetic while the other 75 patients (32.1%) were non-diabetic.

Apart from diabetes, other laboratory investigations were within normal except for the positivity for hepatitis-C virus infection in 31 patients (13.2%) but the liver enzymes were within normal in all of them preoperatively.

Echocardiography: Revealed the presence of diastolic dysfunction in all the studied patients. Akinetic, hypokinetic and dyskinetic areas of variable extent were also present in all of them ejection fraction was between 25 and 35% in 33 patients (14.1%), between 36 and 45% in 20 patients (8.5%) and between 46 and 55% in 181 patients (77.4%).

Angiographic assessment: Showed narrowing and occlusion of variable extent in the different coronary arteries in the studied patients. The lesions were extensive with severe narrowing of the distal part of the vessels making them unsuitable for grafting in 28 patients (11.97%) while the vessels were suitable for grafting in 206 patients (88.03%). Lesions involving the left

(Table 1): Patients data

Data		Number of the patients
Age	36-45yrs	13 pts (5.5%)
	46-55yrs	97 pts (41.4%)
	56-65yrs	112 pts (47.8%)
	65-72 yrs	12 pts (5.3%)
Sex	Male	212 pts (90.6%)
	Female	22 pts (9.4%)
Ejection fraction	25-35%	33 pts (14.1%)
	36-45%	20 pts (8.5%)
	46-55%	181 pts (77.4%)
State of the operation	Elective	227 pts (97.0%)
	Emergency	7 pts (3.0%)
Diabetes	Diabetic	159 pts (67.9%)
	Non-Diabetic	75 pts (32.1%)
Lt main lesion	Present	92 pts (39.3%)
	Absent	142 pts (60.7%)
Use of Internal Mammary artery	Used	183 pts (78.2%)
	Not	51 pts (21.8%)
Pervious Myocardial infarction	Occurred	95 pts (40.6%)
	Not	139 pts (59.4%)
Endarterectomy of the LAD	Done	39 pts (16.7%)
	Not	195 pts (83.3%)
Total revascularization	Done	206 pts (88.03%)
	Not	28 pts (11.97%)

(Table 2): Results in relation to sex

Sex	Total No. of patients	No of early mortalities	No. of late mortalities	Total number of mortalities
Male	212	16(7.5%)	2(0.9%)	18(8.4%)
Female	22	1(4.5%)	4(18.1%)	5(22.6%)

(Table 3): Results in relation to age

Age	Total No. of patients	No of early mortalities	No. of late mortalities	Total number of mortalities
36-45 yrs	13	0(0%)	0(0%)	0(%)
46-55yrs	97	4(4.1%)	3(3.09%)	7(7.19%)
56-65 yrs	112	9(8.03%)	2(1.8%)	11(9.83%)
66-72 yrs	12	4(33.3%)	1(8.3%)	5(41.6%)

(Table 4): Results in relation to diabetes

Diabetes	Total No. of patients	No of early mortalities	No. of late mortalities	Total number of mortalities
Diabetic	159	14(8.8%)	6(3.7%)	20(12.5%)
Non-diabetic	75	3(4.0%)	0(0%)	3(4.0%)

(Table 5): Results in relation to ejection fraction

Ejection fraction	Total No. of patients	No of early mortalities	No. of late mortalities	Total number of mortalities
25-35%	33	6(18.1%)	1(3.03%)	7(21.13%)
36-45%	20	1(5.0%)	1(5.0%)	2(10.0%)
46-55%	181	10(5.5%)	4(2.2%)	14(7.7%)

(Table 6): Results in relation state of the operation

State of the operation	Total No. of patients	No of early mortalities	No. of late mortalities	Total number of mortalities
Elective	227	14(6.16%)	6(2.6%)	20(8.76%)
Emergency	7	3(42.8%)	0(0%)	3(42.8%)

(Table 7): Results in relation to the occurrence of previous myocardial infarction

Previous myocardial infarction	Total No. of patients	No of early mortalities	No. of late mortalities	Total number of mortalities
Used	95	15(15.7%)	0(0%)	15(15.7%)
Not	139	2(1.4%)	6(4.3%)	8(5.7%)

(Table 8): Results in relation to the left main lesions

Left main lesion	Total No. of patients	No of early mortalities	No. of late mortalities	Total number of mortalities
Present	92	13(14.1%)	1(1.08%)	14(15.18%)
Absent	142	4(2.8%)	5(3.5%)	9(6.3%)

(Table 9): Results in relation to the use of internal mammary artery

Internal mammary artery	Total No. of patients	No of early mortalities	No. of late mortalities	Total number of mortalities
Used	183	8(4.37%)	2(1.09%)	10(5.46%)
Not	51	9(17.6%)	4(7.8%)	13(25.4%)

(Table 10): The results in relation to the performance of endarterectomy of the LAD

Endarterectomy of the LAD	Total No. of patients	No of early mortalities	No. of late mortalities	Total number of mortalities
Done	39	9(23.0%)	0(0%)	9(23.0%)
Not	195	8(4.1%)	6(3.07%)	14(7.17%)

(Table 11): The results in relation to suitability of the vessels to grafting

Total revascularization	Total No. of patients	No of early mortalities	No. of late mortalities	Total number of mortalities
Done	206	11(5.3%)	1(0.48%)	12(5.78%)
Not	28	6(21.4%)	5(17.8%)	11(39.2%)

main coronary artery were present in 92 patients (39.3%). While the remaining 142 patients (60.7%) were free from left main lesions.

Operative results: Operation of CABG was done on an emergency basis in 7 patients (3.0%) while it was elective in 227 patients (97.0%). The number of grafts done varied in number from one to four CABG were done using saphenous vein grafts only in 51 patients (21.8%) and using saphenous vein and internal mammary artery grafts in 183 patients (78.2%). Endarterectomy of the left anterior descending (LAD) artery was done in 39 patients (16.7%) while it was not required in 195 patients (83.3%). The extension of the disease and the quality of the vessels allowed total revascularization to be done in 206 patients (88.03%) while it could not be done in 28 patients (11.97%).

Clinically surviving: Patients have shown improvement. There is a high graft patency rate that is correlated with equally good incidence of relief of angina. All patients have returned to a fully active life postoperatively.

Morbidity: Mediastinitis occurred in 3 patients (1.3%) who required mediastinal wash and rewiring. Superficial wound infection occurred in 6 patients (2.6%) which resolved by frequent dressing,

appropriate antibiotic administration according to culture and sensitivity of the discharge and secondary stitching of the wound. Exploration for postoperative bleeding was done in 4 patients (1.7%) where it was controlled by cauterization of the bleeding points in 3 patients and suturing of the site branch of the saphenous vein graft from which the ligature is slipped.

Mortality: Early mortality (first month after operation) occurred in 17 patients (7.26%). This number increased during the one year period of follow up reaching 23 patients (9.6%). Correlating the mortality to sex (Table 2) showed that the number of male deaths in early mortality was 16 (7.5%) which increased in late mortality to 18 (8.4%) while the number of female deaths in early mortality was 1 (4.5%) and increased in late mortality to 5 (22.6%). As regard age (Table 3) non of the early or late mortalities was between 36 and 45 years old.

The number of deaths between 46 and 55 years old was 4 (4.15) in early mortality and increased to 7 (7.19%) in late mortality, the number of deaths between 56 and 65 years old was 9 (8.03%) in early mortality and increased to 11 (9.83%) in late mortality and lastly, the number of deaths between 66 and 72 years old was 4 (33.3%) in early

mortality and increased to 5 (41.6%) in late mortality.

The number of diabetics (Table 4) in early mortality was 14 (8.8%) which increased in late mortality to 20 (12.57%). While the non-diabetics in early mortality were 3 (4.0%) and non of the late mortalities was non-diabetic.

(Table 5) patients with ejection fraction between 25 and 35% constituted 6(18.1%) of the early mortalities which increased to 7 (21.13%) in late mortalities, those with ejection between 36 and 45% constituted 1 (5.0%) of the early mortalities which increased to 2 (10%) in the late mortalities and those with ejection fraction between 46 and 55% constituted 10 (5.5%) of the early mortalities which increased to 14 (7.7%) in the late mortalities.

Patients operated upon electively (Table 6) represented 14 (6.16%) of the early deaths which increased to 20 (8.76%) in late mortality on the other hand, 3 (42.8%) of the patients operated upon urgently died early while none of these patients died during follow up.

15 patients (15.7%) with previous myocardial infarction (Table 7) died early, while none of them died lately. On the contrary, the number of deaths from patients without previous myocardial infarction was 2 (1.4%) in early mortality which increased to 8 (5.7%) in late mortality.

Patients with left main lesions (Table 8) constituted 13 (14.1%) of the early mortalities which increased to 14 (15.18%) in late mortalities.

8 (4.37%) of the patients in whom the internal mammary artery was used (Table 9) died early, this number increased reaching 10 (5.46%) during follow up, while those in whom the internal mammary artery was not used constituted 9 (17.6%) of the early

mortalities which increased to 13 (25.4%) in late mortality.

Patients in whom endarterectomy of the LAD was done (Table 10) represented 9 (23%) of the early mortalities while non of them died during follow up. on the other hand, those in whom endarterectomy of the LAD was not done constituted 8 (4.1%) of the early mortalities which increased reaching 14 (7.17%) in the late mortality. (Table 11) From the patients in whom total revascularization was done 11 (5.3%) died early while during follow up this number reached 12 (5.78%). On the other hand, those in whom total revascularization could not be done constituted 6 (21.4%) of the early mortalities which increased to 11 (39.2%) in the late mortality.

The cause of death was chronic renal failure in 2 patients (0.85%), severe low cardiac output in 7 patients (3.0%), preoperative myocardial infarction in 5 patients (2.1%), secondary haemorrhage complicating mediastinitis in 1 patient (0.42%) and multisystem failure complicating delayed recovery in 2 patients (0.85%).

Myocardial infarction complicated by severe low cardiac output was the cause of death in 5 patients who died during follow up while the six patient died of severe attack of haematemesis from esophageal varices.

Discussion

The number of ischemic patients requiring CABG has markedly increased during the last decade and this requires every effort to be done to improve the prognosis in such operations. Therefore in this work. we have studied the results of CABG done in a group of patients and these results have correlated with different parameters of the patients to detect the risk factors which can be used as predicting

factors for survival when dealing with such operations.

The early mortality rate was 7.26% which increased during the one year follow up period to 9.6%. These results are compatible with those reported by Smith (5) 7.0% early and 10.2% late. Raza (6) and Jones (10) reported late mortality rates of 13.2% and 12.3% respectively, However, these results are obtained over 10 years period of follow up.

The early mortality rate was higher in men (7.5%) than women (4.5%). This may be attributed to the small number of females (9.4%) represented in this work. However, during the period of follow up, the mortality rate in women (22.6%) highly exceeded that in men (8.4%) indicating that the female sex is a risk factor in CABG. This has been proposed in several studies (5,8). The significantly higher operative mortality rate found in women in our experience is similar to that reported by the coronary Artery surgery studies (9,10), Douglas and associates (11) and Hall and associates (12). Possible causes of this higher operative mortality rate in women include age differences between the groups, more severe preoperative angina, adult-onset diabetes mellitus and preoperative heart failure as reported by others (10, 11, 13). This study demonstrated that the long term over all survival and long term event free survival is inferior in women. Fisher (10) Gardner (14), Cosgrove (15) and Richardson (16) and their associates suggest that female gender factor alone is not a significant predictor of operative mortality, but that it is merely a marker for small body stature and small coronary arteries. Although this observation may be quite true from a scientific standpoint, the determination of female gender as a factor and its associated increased mortality is a very practical

indicator of increased mortality in practice.

There was no single mortality below 45 years old while the mortality rate increased progressively over the next decades of age reaching its highest level (41.6%) in patients over 66 years old. indicating that age is a risk factor for the performance of CABG. This is similar to Weintraub (17) findings who stated that mortality rose with each decade after the age of 40 years particularly at 70-79 years. Also, Kaul (18) and associates reported perioperative mortality 14% in old patients confirming advanced age as a risk factor for death early after operation. This has also been recognized for many years and has previously been reported using data from the 1970 s in many studies (9, 10, 19-21). Older patients were sicker by many criteria.

Hypertension was more common with advanced age, as with severe angina, a history of congestive heart failure, diabetes, more frequent three-vessel and left main coronary artery disease, failure of other organs and the need for emergent surgery. Thus, the various disabilities associated with aging account for more risk than any other single clinical correlate (17). Another factor responsible for poor results with aging is the age-related vulnerability of endothelial function after prolonged cardioplegic arrest (22).

Revascularization of ischemic myocardium in patients with severely impaired global left ventricular function remains a surgical challenge. In the past, perioperative mortality after CABG in patients with poor left ventricular function has been reported to be between 10% and 37% (23-21). But more recent reports indicate a much lower mortality (2.3% to 5%) attributed to advances in myocardial

management and surgical technique (18,26-28) . These findings are compatible with the results of this work where the mortality rate was 5% in patients with ejection fraction above 35% which markedly increased to 18.1% in patients with ejection fraction below 35%. Actually, there is a difference in the mortality rate between this work and other reported results regarding patients with poor function which may be due to the difference in the number of patients included in these studies. However, they agree in the fact that the poor ejection fraction is a risk factor in the outcome of CABG.

There was a great difference in early mortality rate between diabetic (8.8%) and non diabetic (4.0) indicating that it is a risk factor for mortality after CABG. This is similar to results obtained in many studies (29-34), who reported that diabetes has an adverse effect on survival after bypass surgery. Also, all the patients who died during the follow up period were diabetic indicating that diabetes is also a risk factor for late mortality after CABG. Similarly, many reports (1,31,16) had reported that diabetes affects the late mortality perhaps because the diabetic patient is more at risk for late complications of diabetes such as more rapid progression of vascular disease. The observed effects of diabetes on survival could be due to an unrecognized higher incidence of diffuse distal disease in diabetic patients. Progression of disease distal to grafts would jeopardize bypass grafting and may accelerate graft failure due to decreased run-off and reduced graft flow (35) .

The saphenous vein continues to be an essential component of surgical myocardial revascularization in human beings. It is the most commonly used conduit alone or in combination with arterial grafts. Saphenous vein has the advantage of being autologous vascular tissue available in the majority of patients in need of this operation. It has been known for decades that the main limitation

of saphenous vein grafts is the propensity for the development of sclerotic changes similar to those seen in the arterial circulation (31, 38) . The reported patency rate of human saphenous vein grafts is variable, but it is generally accepted that the rate is about 80% to 90% at 1 year and 50% to 70% at 7 to 10 years (39). On the contrary, since the unequivocal demonstration in the internal thoracic artery of improved graft patency, patient survival and fewer late postoperative complications, the internal thoracic artery has become the conduit of choice for CABG (35,40-44). It is more suited for this purpose because of its histologic structure and the nature of its endothelial and smooth muscle function (45). These findings agree with the results obtained in this work, where the total mortality rate was 5.4% in patients in whom internal mammary artery was used while it reached 25.4% in those in whom, it could not be used denoting that failure to use internal mammary artery is a risk factor after CABG. It is well known that exposure of the patient to attacks of myocardial infarction cause damage of the myocardium to variable extent. the high mortality rate 15.7% obtained in patients exposed previously to myocardial infarction in relation to 1.4% obtained in those without previous exposure to myocardial infarction denotes that such exposure is a risk factor after CABG. This agrees with findings reported by Smith (5) who reported that the extent of myocardial damage impairs early and late results after CABG. The extent of coronary disease is typically measured by the number of diseased major vessels, presence or absence of left main coronary artery disease and percent narrowing of the major vessels. The extent of the disease determines the suitability of the vessels to grafting and the need for endarterectomy of the vessels. Extensive coronary disease showed a deleterious effect on survival after CABG. These findings are similar to those

obtained in this work where the mortality rate was 23% in patients in whom endarterectomy of the LAD was done in relation to 4.1% in those without endarterectomy. Also, It was 5.3% in patients in whom total revascularization was done while it was 21.3% in those in whom revascularization was incomplete. This means that the performance of endarterectomy of the LAD and incomplete revascularization are risk factors for survival after CABG.

Similarly, the total mortality rate obtained in this work was 15.18% in patients with left main lesion in comparison to 6.3% in those without left main lesions. Also, it was very high 42.8% in patients operated upon urgently while it was only 8.76% in those operated upon electively. This implies that left main lesions and urgency of operation are risk factors for survival after CABG. Such results are similar to those reported in many studies (17,35,45) who stated that in addition to abnormal left ventricular ejection fraction, female gender and advanced age, urgent surgery for unstable angina and the left main coronary disease were the major risk factors for mortality after CABG.

Therefore, we can conclude that female sex, old age above 65 years, ejection fraction below 35%, urgent surgery, diabetes, left main lesions, failure to use internal mammary artery, history of previous myocardial infarction, endarterectomy of the LAD and incomplete revascularization are risk factors for mortality after CABG. However, because these results are obtained while dealing with each factor separately without fixing other factors, we can not consider each factor to be an independent risk factor and the results obtained are shared by all of them. Reviewing the prevalence of these factors in the survivals

and deaths revealed that all early deaths had more than three of them, the late deaths had three of them and all survivals has three or less of them. So, if we suppose to give one degree to each factor, then from a total score of ten, if the patient takes more than three this means poor prognosis, if he takes three this means that he is at potential risk and if he takes less than three this means good prognosis. However, such suspected prognostic scoring needs to be applied over larger series of patients to assess its accuracy when applying it in patients undergoing CABG.

References

- 1- Robert HJ, Karen K, Harry RP, Daniel BM, Peter KS, Charlotte LN, Mark FN, Joseph GR, Robert WA and Robert M. Long-term survival benefits of coronary artery bypass grafting and percutaneous transluminal angioplasty in patients with coronary artery disease. *J Thorac Cardiovasc Surg* 1996, 111:1013-25.
- 2- Favaloro RG, Effler DB and Groves LK. Direct myocardial revascularization by saphenous vein graft. *Ann Thorac Surg* 1970, 19:97
- 3- Hutchinson JH, Green GE and Makhjian HA. Coronary by pass grafting in 376 consecutive patients with 3 operative deaths *J Thorac Cardiovasc Surg* 1974, 67:7.
- 4- Kouchoukos NT, Kirklin JW and Oberman A. An appraisal of coronary bypass grafting. *Circulation*, 1974, 50:11.
- 5- Smith LR, Harrell FE, Rankin S, Califf RM, Pryor DB, Muhlbaier LH, Lee KL, Mark DBI, Jones PH, Oldham HN, Glower DD, Reves JG and Sabiston

- DC. Determinants of early versus late cardiac death in patients undergoing coronary artery bypass graft surgery J. Circulation 1991, 84 (Supple III): III-245 III-253.
- 6- Raza ST, Vidne BA, Farrell EJ, Lajos TZ, Lee AB, Schimert G and Siegel JH. Early and long-term effects of direct myocardial revascularization on cardiac function: A prospective study using multivariable physiological analysis. Ann of Thoracic Surgery 1977, vol 23:99-110.
 - 7- Jones EL., Craver JM, King SB, Douglas JS, Brown CM, Bone DK and Hatcher CR. Clinical, anatomic and functional descriptors influencing morbidity, survival and adequacy of revascularization following coronary bypass. Ann Surg. 1980, 192:390-402.
 - 8- Kennedy JW, Kaiser GC, Fisher LD, Maynard C, Fritz JK, Myers W, Mudd JG, Ryan TJ and Coggin J. Multivariate discriminant analysis of the clinical and angiographic predictors of operative mortality from the collaboration study in coronary artery surgery (CASS). J Thorac Cardiovasc Surg 1980, 80: 876-887.
 - 9- Kennedy JW, Kaiser GC and Fisher LD. Clinical and angiographic predictors of operative mortality from the collaborative study in coronary artery surgery. Circulation 1981, 63:793.
 - 10- Fisher LD, Kennedy JW and Davis KB. Association of sex, physical size and operative mortality after coronary artery bypass in the coronary artery surgery study (CASS) J. Thoracic Cardiovasc Surg 1982, 84: 334.
 - 11- Douglas JS, King SB and Jones EL. Reduced efficacy of coronary bypass surgery in women. Circulation 1981, 64:11.
 - 12- Hall RJ, Elayda MA and Gray A. Coronary artery bypass: Long term follow up of 22, 284 consecutive patients. Circulation 1983, 68:20.
 - 13- Tyras DH, Barner HB, Kaiser GC. Myocardial revascularization in women. Ann Thorac surg 1978, 25:449.
 - 14- Gardner TJ, Horneffer PJ and Gott VL. Coronary artery bypass grafting in women. Ann Surg 1985, 201:780.
 - 15- Cosgrove DM, Loop FD and Lytle BW. Primary myocardial revascularization J. Thorac cardiovasc surg 1984, 88:673.
 - 16- Richardson J and Cyrus R. Reduced efficacy of coronary artery bypass grafting in women. Ann Thorac Surg 1986, 42:516-521.
 - 17- Weintraub W, Graver J, Cohen C Jones E and Guyton R. Influence of age on results of coronary artery surgery. Circulation 1991, 84 (suppl III) : III 226-III-235.
 - 18- Kaul T, Angihottri A, Fields B, Riggins L, Wyatt D and Jones C. Coronary artery bypass grafting in patients with an ejection fraction of twenty percent or less J. Thorac Cardiovasc Surg 1996, 111:1001-12.
 - 19- Faro RS, Golden MD, Javid H, Serry C, Delaria GA, Monson D, Wienberg M, Hunter JA and Hajafi H. Coronary revascularization in septuagenarians J Thorac Cardiovasc Surg. 1983, 86: 616-620.
 - 20- Montague NT, Kouchoukos NT, Wilson TAS, Bennet AL, Knott HW, Lochridge SK, Erath HG and Clayton OW. Morbidity and mortality of coronary bypass grafting in patients 70 years of age and older. Ann Thorac Surg 1985, 39:552-557.

- 21- Gersh BJ, Kronmal RA, Schaff HV, Frye RL, Ryan TJ, Myers WO, Athearn MW, Gosselin AJ, Kaiser GC and Killip T. Longterm (5 years) results of coronary bypass surgery in patients 65 years old or older A report from the coronary artery surgery study. *Circulation* 1983, 68 (suppl II): II 190-II 199.
- 22- Amrani M, Chester A, Jayakumar J and Yacoub M. Aging reduces postschemic recovery of coronary endothelial function. *J Thorac Cardiovasc Surg* 1996, 111: 238-45
- 23- Christakis GT, Weisel RD and Fremes SE. Coronary artery bypass grafting in patients with poor ventricular function. *J Thorac Cardiovasc Surg* 1992, 103: 1083-92.
- 24- Zubiate P, Kay JH and Mendez AM. Myocardial revascularization for the patients with drastic impairment of function of the left ventricle. *J Thorac Cardiovasc Surg* 1977, 73:84-6.
- 25- Hochberg MS, Parsonnet V, Gielchinsky I and Hussain SM. Coronary artery bypass grafting in patients with ejection fraction below forty percent. *J Thorac Cardiovasc Surg* 1983, 86: 519-27.
- 26- Kron IL, Lerman BB, Haines DE, Flanagan TL and Di Mmarco JP. Coronary artery bypass grafting in patients with ventricular fibrillation. *Ann Thorac Surg* 1989, 48: 85-9.
- 27- Milano CA, White WD and Smith R. Coronary artery bypass in patients with severely depressed ventricular function. *Ann Thorac Surg* 1993, 56:487-93.
- 28- Cimoehowski G, Harostock MD and Foldes PJ. Minimal operative mortality in patients undergoing coronary artery bypass with significant left ventricular Dysfunction by maximumization of metabolic and mechanical support. *J. Thorac Cardiovasc Surg* 1997, 113: 655-66.
- 29- Chychota NN, Gau GT, Pluth JR, Wallace RB and Danielson GK. Myocardial revascularization: comparison of operability and surgical results in diabetic and non diabetic patients *J. Thorac Cardiovasc Surg* 1973, 65:856-62.
- 30- Verska JJ and Walker WJ. Aortocoronary bypass in the diabetic patient. *Am J Cardiol* 1975, 35: 774-77.
- 31- Engelman RM, Bhat JG, Glassman E, Spencer FC, Boyd AD, Reed GE, Isom OW and pasternack BS. The influence of diabetes and hypertension on the results of coronary revascularization. *Ann. J Cardiol* 1976, 271:4-12.
- 32- Johnson WD, Pedraza PM and Kayser KL. Coronary artery surgery in diabetics: 261 consecutive patients followed four to seven years *Am Heart J* 1982, 104: 823-827.
- 33- Salomon NW, Page US, Okies JE, Stephens J, Krause AH and Bigelow JC. Diabetes mellitus and coronary artery bypass. *J Thorac Cardiovasc Surg* 1983, 85: 264-71.
- 34- Lytle BW, Kramer JR, Golding LR, Cosgrove DM and Borsh JA, Goormastic M and Loop FD. Young adults with coronary atherosclerosis 10 years results of surgical myocardial revascularization. *J Am Coll Cardiol* 1984, 4:445-53.
- 35- Moris JJ, Smith LR, Jones RH, Glower DD, Morris PB, Muhlbaier LH, Reves

- JG and Rankin JS. Influence of diabetes and mammary artery Grafting on survival after coronary bypass. *Circulation* 1991, 84 (Suppl III). III 275-111 284.
- 36- Lawrie GM, Morris GCJR, Baron A, Norton J and Glaeser DH. Determinants of survival 10 to 14 years after coronary bypass: Analysis of preoperative variables in 1,448 patients. *Ann Thorac. Surg* 1987, 44:180-85.
- 37- O'Brien JE, Yishi, Ali F, Bauer T, Zalewski A and Mannion J. Wound healing around and within saphenous vein bypass grafts. *J Thorac Cardiovasc Surg* 1997, 114: 3 8-45.
- 38- Bourassa MG. Fate of venous grafts: the past, the present and the future. *J Am Coll Cardiol* 1991, 17: 1081-3.
- 39- Chax A, Ruan X, Fishbein M, Sandhu M and Matloff J. Influence of vein valves in the development of arteriosclerosis in venoarterial grafts in the rabbit. 1995, 110:1381-90.
- 40- Lytle BW, Loop FD, Cosgrove DM, Ratliff NB, Eastley K and Taylor PC. Long term (5-12 years) serial studies of internal mammary artery and saphenous vein coronary bypass grafts. M. Attia, M. Mostafa and F. Ibrahim *J Thorac Cardiovasc Surg* 1985, 89: 248-58.
- 41- Barner HB, Standeven JW, Reese J. Twelve-year experience with internal mammary artery for coronary artery bypass. *J Thorac Cardiovasc Surg* 1985, 90: 668-75.
- 42- Spence P, Montgomery Wand Santamore W. High flow demand on small arterial coronary bypass conduits promotes graft spasm *J Thorac Cardiovasc Surg* 1995, 110: 952-62.
- 43- Yoshida H, Hong-De M, Kouchi X, Onakix, Shi Q and Sauvage Comparison of the effect of monopolar and Bipolar cauterization on skeletonized, Dissected internal thoracic artery. *J Thorac Cardiovasc Surg* 1995, 110:504-10.
- 44- Atecor A. Fifteen years experience with internal mammary artery graft. *Ann Thorac Surg* 1986, 42:S22-S27.
- 45- Kushwaha S, Bustami M, Tad J Karimi S, Ilsley CD, Mitchell A and Yacoub M. Late endothelial Function of free and pedicled internal mammary artery grafts. *J. Thorac Cardiovasc Surg* 1995, 110: 453-62.

INDEPENDENT PREDICTORS OF OUTCOME AFTER TRIPLE VALVE SURGERY

ABSTRACT

Background: Valve repair or replacement for rheumatic heart disease still represents the major workload cardiac surgery in Egypt. The aim of this study is to evaluate the independent predictors of early and late outcome after triple valve surgery.

Methods: From January 1994 to December 1998, 108 patients benefited from both: aortic and mitral valve replacement with mechanical bilealett valves, combined with tricuspid valve repair (93%) or replacement with a bioprosthesis (7%). The mean patients' age was 31.9 ± 8.1 years, mean NYHA class was 3.55 ± 0.61 and 88.9% were females.

Results: Twenty patients (18.5%) had a bad postoperative outcome: 8 patients remained in NYHA class III or IV (7.4%) and 12 patients died in hospital (11.1%). While low left ventricular ejection fraction% and the presence of atrial fibrillation were found to be independent predictors of bad outcome ($P=0.002$ and 0.006 ; respectively), the former was the only independent predictor of hospital mortality ($P=0.019$). Patients were followed up for 211.1 patient-years and the linearized incidences of prosthetic valve endocarditis, anticoagulant related hemorrhage, prosthetic valve thrombosis and late mortality were 0.9%, 0.9%, 1.8% and 5.2%; respectively. The 5-years-actuarial survival rate ($67.04 \pm 13.64\%$) was significantly higher for patients in NYHA class I or II ($79.5 \pm 9.3\%$); compared class III or IV patients ($24.4 \pm 28.7\%$; $P=0.05$). Independent predictors of late mortality were advanced NYHA class III or IV and the occurrence of prosthetic valve related complications ($P= 0.018$ and 0.0001 ; respectively).

Conclusion: Early outcome after triple valve surgery is dependent upon advancement of rheumatic heart disease as indicated by low preoperative ejection fraction % and occurrence of atrial fibrillation. Advanced postoperative NYHA class III or IV and the occurrence of prosthetic valve malfunction were independent predictors of late outcome.

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INTRODUCTION

Valve replacement continues to be the most important advance in the treatment of patients with severely symptomatic valvular heart diseases, however, the major problems have always been the complications (1).

In our country, rheumatic valvular heart disease form 80% of patients seen in cardiac or cardiothoracic clinics at the private or

governmental hospitals. They posed special problems: first patients usually present late with bad ventricular functions, severe Pulmonary hypertension, liver failure or bad nutritional and general conditions. Second, 50% of them are either below the age of 20 or women in the childbearing period (2). When first seen, many of these patients have significant polyvalvular lesions. The aim of this report is to evaluate the results of triple

valve surgery and to determine the predictors of early and late postoperative outcome.

Patients and Methods

From January 1994 to December 1998, 3017 rheumatic patients were referred to our institution for valve repair or replacement. Among them 108 patients (3.5%) benefited from both: aortic and mitral valve replacement, combined with tricuspid valve repair or replacement.

They were 96 females (88.9%) and 12 males (11.1%) with a mean age of 31.9 ± 8.1 years (range: 14-46 years). Preoperatively, patients benefited from full clinical examination, determination of the NYHA functional class, chest X-Ray, electrocardiography and echocardiographic examination to measure the left ventricular end systolic diameter, end diastolic diameter and ejection fraction percentage. Coronary angiography was performed for patients older than 40 years routinely (30 patients; 28%) and all were free. The indication for operation in patients with NYHA class II was either history of heart failure or annoying arrhythmias. Patients' demographic data are shown in table 1.

All patients were operated upon classically through median sternotomy and routine aorto-bicaval cannulation. Cardiopulmonary bypass was instituted with moderate hypothermia (28°C). Myocardial protection was achieved with intermittent antegrade cold blood cardioplegia and topical myocardial cooling using iced saline slush. All the patients had their aortic and mitral valves replaced using bileaflet mechanical valves: St Jude valve in 129 positions (60%) and Carbomedics valve in 97 positions (40%). The average aortic valve size was 20.1 ± 1.2 mm, (range 19 to 23 mm)

mitral valve mean size was 27 ± 1.3 mm (range 25 to 31 mm). Implanted valves were secured into position using interrupted 2/0 ethibond sutures buttressed with Teflon pledgets. Surgery of the tricuspid valve included 85 Devega's repairs (76%), commissurotomy and Devega's repair in 18 patients (17%) and tricuspid valve replacement using Carpentier Edwards porcine valves in 5 patients (7%). Tricuspid valve surgery was always performed on a beating heart. The recorded intraoperative and postoperative variables included: aortic cross clamping time, cardiopulmonary bypass time, high inotropic support (if more than 100ng/kg/min adrenaline was needed), ICU stay, duration of mechanical ventilation, postoperative complications and total hospital stay.

According to surgeon's preference, patients were anticoagulated with either oral anticoagulants alone or combined to a daily dose of 225 mg dipyridamole, given in three divided portions. The target INR was 2.5-3.5 in the former and 2-2.5 in the latter mode of anticoagulation therapy. All patients were followed up at our outpatient clinic on a monthly basis. They benefited from a full clinical examination and prothrombin time evaluation. A control echocardiographic study was done every six months, or whenever indicated. Mortality and morbidity data were recorded along the guidelines of Edmunds and colleagues (3).

Statistical analysis:

Data were expressed as mean \pm SD or numbers (%) and were analyzed by the SPSS software package of windows. Distribution of categorical variables was analyzed by the Chi-Square contingency tables. Continuous (or ordinal) data were analyzed by the unpaired Student's test. Variables with a P value < 0.1 on univariate

Table (1): Patients demographic data

Variable	Value
Age (years)	31.96 ± 8.17
NYHA class	3.55 ± 0.61
CTR %	55.14 ± 10.10
LVEDD (mm)	38.66 ± 11.70
LVEDD (mm)	55.70 ± 14.03
LVEF (%)	62.77 ± 5.38
Valve pathology:	
a) pure regurgitant lesions -AR, MR, TR	20 (18.5%)
b) pure stenotic lesions -AS, MS, TS	8 (7.4%)
c) combined lesions -(AR, AS) + (MR, MS) + (TR ± TS)	80 (74.1%)

Data are presented as mean (± SD) or numbers (%). AR aortic valve regurgitation, AS = aortic valve stenosis, CTR = cardiothoracic ratio, LVEDD = left ventricular end diastolic diameter, LVEF = left ventricular ejection fraction, LVEDD = left ventricular end systolic diameter, MR = mitral valve regurgitation, MS = mitral valve stenosis, NYHA = New York Heart Association, TR = tricuspid valve regurgitation, TS tricuspid valve stenosis.

analysis were introduced in a stepwise regression analysis model for evaluation of independent predictors of outcome. A Cox regression model-that takes into consideration the duration of follow up of each patients- was used to evaluate independent predictors of late mortality. Survival was estimated by the actuarial method and the calculated cumulative percentages of different patients groups were compared by the Logrank test.

Results

Among the operated 108 patients, 88

(81.5%) had a good outcome. Postoperatively, these patients were in NYHA class I or II and returned to their normal activities within 2 months of surgery. The remaining 20 patients (18.5%) had a bad postoperative outcome. These included 12 hospital mortalities and 8 patients who remained in NYHA class III or IV and failed to return to their normal activities. A comparison between both patients' groups is shown in table 2. Variables with a P value >0.1 on univariate analysis were introduced in a stepwise logistic regression analysis model, which

Table 2: Factors associated with early good outcome after surgery.

Variable	Good outcome group (n=88)	Bad outcome group (n=20)	P* value
Age	31.4 ± 8.3	34.4 ± 6.9	Ns.
Preoperative NYHA class	1.5 ± 0.66	3.8 ± 0.41	0.05
CTR	52.5 ± 8.1	66.6 ± 10	0.000
LVEF (%)	63.3 ± 4.5	50.1 ± 7.8	0.017**
PAP (mm Hg)	56.22 ± 7.5	70.22 ± 3.12	0.04
LVESD (mm)	37.2 ± 10.4	44.8 ± 15	0.009
LVEDD (mm)	53.7 ± 13.1	64.2 ± 14.7	0.002
Presence of atrial fibrillation	16(18%)	12(60%)	0.000**
Presence of tricuspid stenosis	10(11.4)	8(40%)	0.000
CPBT (min.)	136.8 ± 8.2	139 ± 12.7	Ns.
ACCT (min.)	87.5 ± 11.4	92.2 ± 9.3	Ns.
ICU (h)	14.8 ± 5	150.4 ± 46.5	0.000
Ventilation (h)	7.16 ± 3.5	96 ± 8	0.03
Hospital stay (d)	12.1 ± 1.9	12.9 ± 3.2	Ns.
High inotropic support #	24(30%)	20(100%)	0.000

Data are presented as mean (±SD) or number (%). Good outcome group = patients in NYHA class I or II postoperatively, Bad outcome group = hospital mortalities and patients in NYHA class III or IV postoperatively, * = Chi -Square test or unpaired Student's test, as indicated, ** = significant variables on multivariate analysis, # = adrenaline ≥ 100 ng/Kg/minute. ACCT= Aortic cross clamping time, CPBT = cardiopulmonary bypass time, CTR= cardiothoracic ratio, ICU = Intensive care unit, LVEDD = left ventricular end diastolic diameter, LVEF = left ventricular ejection fraction, LVESD = left ventricular end systolic diameter, n = number of patients, Ns. = non-significant, NYHA = New York Heart Association, PAP= pulmonary artery pressure.

showed that independent predictors of bad outcome were low preoperative left ventricular ejection fraction percentage (P=0.002) and the presence of atrial fibrillation (P=0.006).

The main cause of hospital mortality was

persistent myocardial failure (9 patients, 75%). Other causes included: cerebrovascular stroke in 2 patients (17%) and multiorgan failure following early prosthetic valve endocarditis in another patient (8%). Table 3 shows variables that

Table 3: Comparison between hospital survivors and mortalities.

Variable	Hospital survivors (n= 96)	Hospital mortalities (n=12)	P* value
Age	31.2 ± 8	38.0 ± 6.8	0.006
NYHA class	3.5±0.6	4.0±0.0	Ns.
CTR	54.6±10.4	59.3±5.1	Ns.
LVEF (%)	62.4±5.3	48.8±6.1	0.048**
PAP (mm Hg)	58.6±0.24	88.7±2.61	0.03
LVESD (mm)	36.9±10.11	52.7±14.9	0.001
LVEDD (mm)	53.5±12.6	73.3±12.1	0.001
Presence of tricuspid stenosis	14(14.6%)	4(33.3%)	Ns.
Presence of atrial fibrillation	20(21%)	8(66%)	0.002
CPBT (min)	136.5±8	143.3±14.9	0.015
ACCT (min)	87.5±10.4	95.0±11.2	0.029
ICU stay (h)	39.3±12.2	165.3±55.5	0.000
Artificial ventilation (h)	68.6±35.3	136.0±82.7	0.00
High inotropic support #	32(33.3%)	12 (100%)	0.000

Data are presented as mean (±SD) or number (%). * Chi-Square test or unpaired Student's test, as indicated, ** = significant variables on multivariate analysis, # = adrenaline \geq 100 ng/Kg/minute. ACCT = aortic cross clamping time, CPBT = cardiopulmonary bypass time, CTR = cardiothoracic ratio, ICU = Intensive care unit, LVEDD = left ventricular end diastolic diameter, LVEF = left ventricular ejection fraction, LVESD = left ventricular end systolic diameter, n = number of patients, Ns. = non-significant, NYHA = New York Heart Association, PAP= pulmonary artery pressure.

were significantly associated with hospital mortality on univariate analysis. Stepwise logistic regression analysis showed that low preoperative left ventricular ejection fraction % is the only independent predictor of hospital mortality after triple valve surgery (P=0.019).

Patients were followed up for 1 - 60 months with a mean period of 26.4 ± 19.9 months, which is equivalent to 211.1 patient / years.

A total of 11 late mortalities were encountered (11.4%; 5.2 per 100 patients year), with an actuarial survival rate of 67.04 ± 13.64% at 5 years. Late mortality was mainly prosthetic related (72.7%) due to prosthetic valve thrombosis in 4 patients (4.2%; 1.8 per 100 patients year), prosthetic valve endocarditis in 2 patients (2.1%; 0.9 per 100 patients year) and oral anticoagulant-related hemorrhage in another

Table 4: Factors affecting late mortalities.

Variable	Late mortalities (n=11)	Late survivors. (n=85)	P* value
Age (years)	30 ± 9.7	31.4 ± 7.9	Ns.
Female sex	10 (90.9%)	78 (91.8%)	Ns.
Atrial fibrillation #	3 (27.3%)	17 (20%)	Ns.
NYHA class #			
-I and II	8 (72.7%)	80 (94.1%)	0.016**
-III and IV	3 (27.3%)	5 (5.9%)	
LVESD (mm) #	36.2 ± 11.3	36.6 ± 7.7	Ns.
LVEDD (mm) #	49.2 ± 10.4	49.1 ± 7.1	Ns.
LVEF (%) #	55.5 ± 9.7	54.6 ± 9.4	Ns.
Prosthetic valve related complications	5 (45.5%)	3 (3.5%)	0.001**

Data are presented as mean (± SD) or number (%). * = Chi-Square test or unpaired Student's test, as indicated. # = significant variables on multivariate analysis, # = data collected during the last visit at the outpatient clinic. LVEDD= left ventricular end diastolic diameter, LVEF= left ventricular ejection fraction, LVESD= left ventricular end systolic diameter, Ns. = non-significant.

2 patients (2.1% ; 0.9 per 100 patients year). The other 3 patients died from progressive cardiac failure (27.3%). All 6 events of anticoagulant-related complications were recorded among the 70 patients who were on oral anticoagulants alone (7.5%); compared to none in the 26 patients on oral anticoagulants combined to dipyridamole. Table 4 summarizes the factors affecting late mortality. Cox regression analysis showed that independent predictors of late mortality were postoperative NYHA class III or IV (P= 0.018) and the occurrence of prosthetic valve related complications (P = 0.0001). Figure 1 shows the actuarial survival rates by the early postoperative NYHA class. Patients in NYHA class I and II had significantly higher actuarial survival rates

compared to patients in NYHA class III and IV (P=0.05).

Discussion

Following multiple valve replacement, the majority of patients usually improve by one NYHA functional class (4) however, on the expense of considerable risks of high mortality and increased hospital morbidity and expenses (4-6). In our study, the majority of patients have benefited from triple valve surgery, for being in NYHA class I or II postoperatively. On the other hand, the bad outcome group comprised 18.5% of surgical candidates who have either remained in NYHA class III or IV or died during the early postoperative course.

As previously reported, bad outcome was significantly associated with parameters suggesting a long standing or advanced valvular heart disease (6). These included: advanced NYHA functional class (6), low preoperative left ventricular ejection fraction percentage (5,6), increased left ventricular dimensions, high pulmonary artery pressure, the presence of atrial fibrillation (7) or tricuspid valve stenosis. Stepwise regression analysis has shown that a low preoperative ejection fraction percentage and the presence of atrial fibrillation were independent predictors of bad outcome after triple valve surgery.

The reported incidence of hospital mortality after multiple valve surgery shows a considerable variability between 8.3 and 23 % (8-11). In addition to the previously reported older age at operation (5,6,8,9), high pulmonary artery systolic pressure > 60 mmHg (9) and prolonged ischemic and bypass times (10); our hospital mortality was significantly associated with echocardiographic data of advanced rheumatic heart disease as indicated by increased left ventricular dimension and impaired function. On the other hand, the significantly associated higher need for inotropic support and prolonged duration of both: mechanical ventilation and ICU stay should be considered as consequences of the patients' critical condition, rather than being causes of mortality. In concordance with Christakis and colleagues (8), logistic regression analysis has shown that low preoperative left ventricular ejection fraction percentage was the only independent predictor of hospital mortality after elective triple valve surgery. Unsurprisingly, and as being previously observed (12,13), persistent cardiac failure is the commonest mode of hospital death. Our 10.1% mortality rate could be explained by the absence of redo and emergency cases, the

comparatively younger age of our patients and the absence of a concomitant myocardial revascularization procedure; compared to series reporting higher hospital mortality figures (9, 11).

Hospital survivors were followed up to five years and, as previously observed (6,13), the majority of patients remained in NYHA class I or II. On the other hand, 11 mortalities (11.5%) were encountered during this period; which is comparable to the 26.4% late mortality rate reported during a 10-years follow-up period after double valve replacement with St Jude medical prosthesis (14). The overall 5-years actuarial survival rate of our group of patients was $67.04 \pm 13.04\%$. Survival was significantly related to the patients' NYHA functional class after surgery; being $79.5 + 9.3\%$ for patients in class I or II; compared to only $24.4 + 28.7\%$ for patients in NYHA class III or IV ($P=0.05$). The 5-years actuarial survival rate of the former group of patients appeared to be comparable to the 76-89% rate reported after double valve replacement (6,13). In our study, advanced NYHA class III or IV was found to be an independent predictor of late mortality after triple valve surgery.

As previously noted (15), late mortality was mainly due to prosthetic valve malfunctions and the commonest encountered complication was prosthetic valve thrombosis. Although our incidence of valve thrombosis was double the 0.84% linearized rate reported by Jamieson and Coworkers (16), no thromboembolic events were recorded among the group of patients benefiting from combined oral anticoagulant and dipyridamole therapy. Since 1990, and according to the surgeons' preference, patients were anticoagulated with oral anticoagulants either alone or in combination with antiplatelet therapy. In the former regimen, and as recommended by both the American Heart Association and the American Society of Cardiology (17),

the targeted INR range was between 2.5-3.5. In the latter, patients targeted a lower INR range between 2 and 2.5; which has been reported to be safe in patients with mechanical bileaflet valves (18) and was shown to be significantly more protective from thromboembolism than the former (19). However, in the absence of any recommendation from the major European and American Societies (17,20), the use of combined therapy is still largely limited.

On the other hand, prosthetic valve endocarditis is a serious postoperative complication that is associated with a high risk (40%) of hospital mortality (10). In our 2 cases, the infection involved both valves and adjoining interventricular fibrous body. Although reconstruction of the latter has been reported with an encouraging hospital mortality rate of only 16% (21), one of our cases did not survive surgery and the other showed 2 instances of recurrence 4 and 9 weeks after surgery; the last being a fatal superimposed fungal infection.

In Conclusion

This study showed that the majority of patients have improved to NYHA class I or II after surgery, however, on the expense of high hospital mortality and morbidity, that were mainly in the form of persistent heart failure. Early outcome is dependent upon advancement of rheumatic heart disease as indicated by low preoperative ejection fraction % and occurrence of atrial fibrillation. Advanced postoperative NYHA class III or IV and the occurrence of prosthetic valve malfunction were independent predictors of late outcome.

References

1- Rahimtoola SH: Lessons learned about the determinant of the results of valve surgery. *Circulation* 1988; 78 (6): 1503.

- 2- Gaafar H: Problems of cardiac surgery in Egypt. *Egyptian heart Journal*. 1990 June, 34: 7.
- 3- Edmunds HL, Clack RE, Cohn LH, Grundemeir GL, Miller DC, and Weisel RD. Guidelines for reporting morbidity and mortality after cardiac valvular operations. *J Thorac Cardiovasc Surg* 1990; 112: 708.
- 4- Armenti F, Stephenson LW, Edmunds LH Jr. Simultaneous implantation of the St. Jude Medical aortic and mitral prostheses. *J Thorac Cardiovasc Surg* 1987; 94: 733.
- 5- Ferraris VA, Fierraris SP, Singh A. Operative outcome and hospital cost. *J Thorac Cardiovasc Surg* 1998; 115 (3): 593.
- 6- Kirklin JW and Barratt-Boyes BG. Combined aortic and mitral valve disease. In *Cardiac Surgery*, second edition, Vol. 2, ed. JW Kirklin and BG Barratt-Boyes. Churchill Livingstone, New York, 1993, pp. 573-586.
- 7- Melvin DB and Tecklenberg PL. Computer based analysis of preoperative and postoperative prognostic factors in 100 patients with combined aortic and mitral valve replacement. *Circulation* 1973; 47: 48.
- 8- Christakis GT, Weisel RD and David TE. Salemo TA, and Ivanor JRN. Predictors of operative survival after valve replacement. *Circulation* 1988; 78 (3): 1.
- 9- Galloway AC, Gross EA, Baumann G, Lamendola CL, Grooke GA, Harris LJ, Colvin SB and spencer FC. Multiple valve operations for advanced valvular heart disease: Results and Risk factors in 513 patients. *JACC* 1992; 9 (4): 725.

- 10- Fernandez J, Laub GW, Adkins MS, Anderson WA, Chen C, Baley BM, Nealon LM and Me Grath LB. Early and late-phase events after valve replacement with the St. Jude Medical prosthesis in 1200 patients. *J Thorac Cardiovasc Surg* 1994; 107: 394.
- 11- Fiore AC, Swartz MT, Sharp TG, Kesler KA, Barner HB, Naundeim KS, Grunkemeir GL, Moroney DA and Kaiser GC. Double -valve replacement with Medtronic - Hall or St. Jude valve. *Ann Thorac Surg* 1995; 59: 1113.
- 12- Blackstone EH and Kirklin JW. Death and other time - related events after valve replacement. *Circulation* 1985; 72 (4): 753.
- 13- Muller XM, Tevaearai HT, Stumpe F, Fischer AP, Hunri M, Ruchat P and Von Segesser LK. Long term results of mitral-aortic valve operations. *J Thorac Cardiovasc Surg* 1998; 115: 1248.
- 14- Arom KV, Nicoloff DM, Kersten TE, Northrup WF, Lindsay WG and Emery RW. Ten - year follow up study of patients who had double valve replacement with St. Jude Medical prosthesis. *J Thorac Cardiovasc Surg* 1989; 98: 1008.
- 15- Ibrahim .M, O'kane H, Cleland J, Gladstone D, Sarsam M and Patterson C. The St. Jude Medical prosthesis. A thirteen-year experience. *J Thorac Cardiovasc Surg* 1997;108:221.
- 16- Jamieson VW, Miyagishima RT, Tyers GF, Lichenstein SV, Munro AI and Burr LG. Bileaflet mechanical prostheses in mitral and multiple valve replacement surgery. Influence of anticoagulant management on performance. *Circulation* 1997; 96 (suppl II): II-134.
- 17- Committee on management of Patients with Valvular Heart Disease. ACC/AHA Guidelines for the management of patients with valvular heart disease. Executive Summary. A report of the American College of Cardiology American Heart Association Task Force on Practice Guidelines. *J heart Valve Dis* 1998; 7: 672.
- 18- Kontozis L, Skudicky D, Hopley MJ, Sareli P. Long-term follow-up of St. Jude Medical prosthesis in a young rheumatic population using low-level warfarin anticoagulation: an analysis of the temporal distribution of causes of death. *Am J Cardiol* 1998, 81(6), 736.
- 19- Pouleur H, Buyse M. Effects of dipyridamole in combination with anticoagulant therapy on survival and thromboembolic events in patients with prosthetic heart valves. A meta-analysis of the randomized trials. *J Thorac Cardiovasc Surg* 1995; 110: 463.
- 20- Ad Hoc Committee of the Working Group on Valvular Heart Disease, - European Society of Cardiology. Guidelines for prevention of thromboembolic events in valvular heart disease. *J Heart Valve Dis* 1993; 2: 398.
- 21- David TE, Kuo J and Armstrong S. Aortic and mitral valve replacement with reconstruction of the interventricular fibrous body. *J Thorac Cardiovasc Surg*; 114: 766.

CURRENT CONCEPTS OF MITRAL VALVE RECONSTRUCTIVE SURGERY

ABSTRACT

During the last decade, there has been a renewed interest in surgical reconstruction of the insufficient mitral valve because of the reconfirmation of the limitations of existing prosthetic valves. To evaluate the early and mid-term results of mitral valve reconstruction for mitral insufficiency, data from 43 consecutive patients underwent mitral valve repair, were analysed. Twenty four (55.8%) of the patients were males, and the mean age was 36 ± 13.2 years (range 13 to 52 years). 35 patients (81.4%) of the patients were in NYHA functional class III or IV. The cause of mitral disease was rheumatic in 36 patients (83.7%), degenerative in 5 patients (11.6%), and suspected to be congenital in 2 patients (4.6%). Combined stenotic and insufficient lesions of the mitral valve were present in 29 patients (67.4%), while the remainder were isolated mitral insufficiency. Isolated mitral valve repair was performed in 35 patients (81.4%), while it was associated with other surgical procedures in the others. We used 11 different techniques for reconstruction, with a total of 118 techniques employed in 43 patients to obtain valve competence, with average of 2.7 procedures per patient. The average aortic cross clamptime was 62.3 minutes in patients with isolated mitral repair, while it was 99.4 minutes in the overall experience, including the other patients with combined procedures. There were one intraoperative death and one early post operative (third day) deaths (4.6%). Among the survivors, with follow up, there were 97.6% freedom from cardiac death, and 95% freedom from need for reoperation with valve replacement for significant residual regurge and 100% free from anticoagulant related complications.

The results indicate that mitral reconstruction with different techniques (using basically Carpentier reconstructive techniques) is widely applicable and durable, and encouraging to be the procedure of choice for most patients with mitral insufficiency. Freedom from late thromboembolic and anticoagulant complication is particularly notable.

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INTRODUCTION

Open heart surgery became a clinical reality in 1955, but a reliable prosthetic heart valve was not available until 1961. The first prosthetic mitral valve implanted on September 21, 1960 by Albert Starr (1) During this time, Lillehei et al. (2), and Merendino and Bruce (3), separately

reported mitral annuloplasty techniques that were successfully used in selected patients. In 1957, the first successful repair of a regurgitant mitral valve was reported by Lillehei and associates. Once prosthetic valves became available however, interest in mitral reconstruction sharply decreased for more than 20 years. At least three groups maintained some interest, however, in

reconstruction. McGoon, (4) in 1960 reported his technique of leaflet plication for isolated ruptured chordae tendinae. Kay and Egerton (5) in 1963 reported a technique of annuloplasty combined with repair of ruptured chordae tendinae. Reed et al., (6) in 1965, reported a technique of asymmetric mitral annuloplasty, particularly valuable in children.

Renewed interest in mitral reconstruction began in Europe in the late 1970s, primarily with the work of Carpentier et al (7) in Paris, Duran et al., (8) in Spain, and Shore et al., (9) in England. However the pioneering work of Carpentier in 1983 (10), reported his experience in 1421 cases of mitral valve repair and covering nearly all techniques mitral valve reconstruction in cases with mitral insufficiency as techniques become widely applied in most centres all over the world.

After many years of application of Carpentier techniques, they proved to be efficient for solution of all problems in mitral valve reconstruction. However controversies remain in some points like; left ventricular performance (11,12), systolic anterior motion with left ventricular outflow tract obstruction (13), also regarding the comparison between the flexible rigid rings for annuloplasty (12). There is also some new techniques for chordal replacement such as glutaraldehyde-tanned xenograft pericardial chordae (14) and polytetrafluoroethylene stents (14,15,16) (neither types elongates or shrinks).

This study was undertaken to observe the early and mid-term results for mitral valve reconstruction using mainly Carpentier techniques-with some modification-in trial to formulate efficacy of these techniques as applied in our patients, considering that the

majority of them are rheumatic patients, and to what extent these techniques are applicable and durable.

Patients and Methods

Patient Population

Patients selected for mitral valve repair were those who, at the time of surgery, were found to have anatomic defects suitable for the reconstructive procedure, mainly no (or minute) calcification, no or minimal leaflet and annulus fibrosis, good pliability and exertion of the leaflet, no or minimal subvalvular apparatus fibrosis. The atrial fibrillation, huge or aneurysmal left atrium, or left atrial thrombi were not prohibiting factors against mitral valve repair. There were no other exclusion criteria for reconstruction whenever the valve was repairable, so the patients were not excluded because of age, poor ventricular function, or concomitant valve disease.

43 Consecutive patients underwent mitral valve reconstruction in Zahraa University Hospital from January 1997 through July 1999 were studied. The patient characteristics are shown in table 1. The mean age of the patients was 36 ± 13.2 years (range 13 to 52 years). The distribution of patients with age was; 10 patients (23.2%) under the age of 18, 29 patients (67.4%) between 18 and 45 years, and only 4 patients (9.3%) over 45 years. The grouping of the age distribution in this manner because of the different concepts and indications for valve reconstruction, preservation of the native valve, and avoidance of anticoagulant therapy complications in each of those age groups. Preservation of the native valve, avoidance of anticoagulant therapy complications, and avoidance of outgrowing problems of the applied mechanical prosthetic valves were the main motive

factors for mitral valve reconstruction preference in the age group under 18 years. The avoidance of anticoagulant therapy complications was the main factor to think about valve repair rather than replacement in the productive period of life between 18 and 45 years. While there are usually no pushing forces to prefer the valve reconstruction in the age above 45 years except in cases with isolated mitral insufficiency with good pliable valve apparatus (most often in degenerative diseases), so the incidence is low. There were 24 male (55.8%) and 19 female (44.1%) patients with no sex predominance. There were 35 patients (81.4%) in NYHA functional class III or IV, because it is not common to operate on patients in class II except in some special situation like significant mitral valve pathology with accompanied other valve lesion and not correlated well to the patient symptomatology. The mitral valve disease was rheumatic in origin in 36 patients (83.7%) and degenerative in only 5 patients (11.6%). There were 2 patients (4.6%) with undetectable etiology even after pathological examination of the specimen. One of them with marked annular dilatation and significant mitral insufficiency but no other detected pathology, and the other patient with significant anterior mitral leaflet (AML) prolapse with primary chordal elongation and significant regurgitation. The etiology in each of these 2 patient was suggested to be congenital in origin. No other causes (ischemic - traumatic-etc) were detected in our series. The etiology was proved or highly suggested preoperatively from the history and laboratory investigations in only 28 patients (65.1%) and from the gross appearance of the valve at surgery and pathological examination of the excised valve in the remainder.

The echocardiographic (echo) findings for those patients including many varieties such as; left ventricular (LV) function with

ejection fraction (EF) was >60% in 10 patients (23.2%), between 50 and 60% in 19 patients (44.1%), between 40 and 50% in 11 patients (25.5%), and below 40% in 4 patients (9.3%). Left atrial (LA) thrombi were detected in 4 patients (9.3%), and almost always (100% in patients with atrial fibrillation (AF), and with left atrial diameter > 5 cm. LA thrombi were usually detected with transoesophageal echocardiography (TOE). TOE was performed for 20 patients (46.5%).

There was only one (2.3%) redo surgery for a female patient who underwent closed mitral commissurotomy 6 months before. She presented at this time with mitral insufficiency grade III/IV and restenosis (mitral valve area 1.2 Cm²).

Operative Techniques

A median sternotomy incision with standard cardiopulmonary bypass (CPB) was used. Excellent myocardial protection was essential because periods of ischemic arrest for 1,2 hours or rarely more may be required for complex repairs, especially when additional cardiac procedures were performed. The mean aortic crossclamp time was 99.4 minutes in the overall experience with valve reconstruction, but it was 62.3 minutes in patients undergoing isolated mitral valve reconstruction. The standard myocardial protection routine includes cold potassium crystalloid cardioplegia in conjunction with topical hypothermia, keeping myocardial (septal) temperatures well below 15°C.

Exposure was obtained with a long left atrial incision, posterior to the interatrial septum. The selfretaining mitral retractor was usually essential to provide optimal exposure of the valve. Good exposure with a still dry operative field is critical to precise mitral valve reconstruction.

Valve Analysis:

The final decision in all patients regarding the feasibility of valve reconstruction was made at operation. So, the key stone of mitral reconstruction is to visually examine all components of the mitral valve apparatus and to decide which abnormalities are causing the insufficiency, then which techniques should be chosen to correct these problems. We have to think that lesions affecting the mitral apparatus are manifold and complex. Initially the atrial endocardium was inspected for a "Jet Lesion" which may provide a clue to the site of the dominant insufficiency. Dilatation of the annulus is principally an increase in the anteroposterior diameter of the valve due to dilatation of the mural leaflet annulus. The aortic leaflet annulus is not dilated, and this is a fundamental anatomic fact that provides a valuable guideline for annuloplasty. Evaluation of valve leaflets are usually passes in 2 directions; first is, leaflet-itself - pathology, in the form of fibrosis, thickening, calcifications, and second is, leaflet pliability and motions in the forms of either excessive or restricted motion and this is usually (not always related to chordal pathology; elongation or shortening). Exerting traction with a nerve hook on different points of the free edges of the leaflets makes it possible to assess leaflet pliability and to check leaflet prolapse or restricted motion. This is usually helped by finding out a nonprolapsed area as a "reference point" (usually on the posterior leaflet near the anterior commissure) and if the leaflet tissues can be elevated above this reference point or normal plane of the annulus, the degree of prolapse could be assessed. According to Carpentier (7) it is significant when it is more than 1 cm prolapse. Lastly evaluation of the subaortic apparatus; chordae tendinae

regarding shortening, elongation, fibrosis, amalgamation or other deformity, and papillary muscles regarding also the shortening, elongation or other deformities.

We used 11 different techniques in mitral valve reconstruction in our patients, encountered in table (2). Multiple surgical techniques were used to obtain mitral valve competence. A total of 118 reconstruction techniques were employed in 43 patients, with average of 2.74 procedures per patient. If we exclude the 29 commissurotomy procedures for the associated stenosis (commissural fusion) so we have 89 reconstruction techniques employed, with average of 2.06 procedures per patient as an average to obtain mitral competence with isolated mitral insufficiency.

The annular dilatation is usually looked for firstly. It is principally an increase in the anteroposterior diameter of the valve. It involves exclusively the posterior leaflet annulus (never the aortic leaflet). In rheumatic disease, the dilatation is often greatest toward the posteromedial commissure; with degenerative or ischemic diseases, the posterior annulus is symmetrically dilated. The Carpentier annuloplasty (rigid) ring has been used in the majority of patients (90.6%). Late in this study - the last 18 patients - we were dividing most of the flat anterior part of the ring, not to be fixed with the aortic leaflet annulus for 2 reasons; firstly there is no true fibrous annulus anteriorly (it is a part of the fibrous skeleton of the heart) and so never dilate, second may lead to systolic anterior motion (17), may offer some degree of LV out flow tract obstruction, and might affect LV systolic performance (11).

The ring annuloplasty was performed as the major step of valve reconstruction in the majority of patients (39 patients), however

in only 11 patients (25.5%) it was the only reconstructive technique.

We did not use the other flexible annuloplasty rings (e.g Duran ring), only because of the availability of the Carpentier rigid ring at the time of this study and not due to any objection for the flexible rings. We used suture annuloplasty in 8 patients (18.6%) in the form of commissural stitches. This was the only annuloplasty technique in 3 patients but was in conjunction with ring annuloplasty in the other 5 patients. These commissural stitches were done as a posteromedial annuloplasty (Asymmetric annuloplasty of Reed (18)) in 4 patients, and in both commissures (Kay sutures (19)) in the other 4 patients. In the 8 patients, the stitches were done by the use of 2/0 Ethibond sutures with Teflon pledget on both sides. The principle of these stitches was mainly posterior annulus advancement which was rather important than simple shortening or plication of the posterior annulus. Chordal shortening plasty was performed in 13 patients (30.2%) with leaflet prolapse due to chordal elongation. In 11 patients, it was the anterior leaflet, and only in 2 patients was the posterior leaflet prolapsed. We used the papillary muscle trench of Carpentier (10) to invaginate the excess length of the chordae. Quadrangular (Segmental) resection of a central segment of the mural leaflet with variable amount of resection varied from 30-50% of the leaflet was done in 6 patients (13.9%), the resulting defect (varied from 1.5-3 cm in width) was corrected by either annular plication (2 patients) or sliding plasty (4 patients) of Carpentier. This quadrangular resection was done for either excessive redundant posterior leaflet tissues with or without prolapse, or for restricted posterior leaflet motion. Chordal replacement was done in 3 patients (6.9%) with either polytetrafluoroethylene (PTFE) strands (15,16) or 2/0 Ethibond sutures for chordal rupture, either

already presented pathology or intended iatrogenic division. Chordal transposition in 2 patients (4.6%) one from the posterior to the anterior leaflet and the other was secondary chorda from the anterior leaflet to the site of the main primary chorda of the anterior leaflet. Chordal separation (fenestration) of fused, amalgamated shortened chordae tendinae (mainly or exclusively in rheumatic patients) was done in 6 patients (13.9%). Resection of secondary chordae for restricted leaflet motion was done in 4 patients (9.3%). Papillary muscle shortening for elongated muscle was done in 3 patients (6.9%) with cuneiform resection of triangular horizontal part of the muscle, and then closed again with interrupted sutures. Debridement and variable degrees of decalcification were done in 5 patients (11.6%).

At the end of the reconstruction procedures, the repaired valve was assessed by injection of about 300 C.C of saline in to the left ventricle through the mitral valve, with the help of 50 C.C Syringe. The repair was judged to be satisfactory with 2 findings (features); first, and most important, if the line of leaflet closure is parallel to the mural part of the ring (smiling valve), since this indicates good opposition of the leaflets and a good surface of coaptation, second, is the degree of competence of valve holding of the injected saline with "ballooning" anterior leaflet tissues. Minimal degree of regurge with the presence of the previous 2 features is accepted well.

There were 9 patients (20.9%) with other concomitant valve procedures; patients with associated aortic valve replacement, 1 patient with associated tricuspid valve repair, and 2 patients with triple valve surgery.

Post operatively; The patients with isolated mitral repair using ring annuloplasty are routinely put on the following program

Table (1): Preoperative clinical and echocardiographic data

	Number	%
Total number of patients	43	100
Age	36 + 13.2 year	
Mean		
<18 years	10	23.2
18-45 „	29	67.4
>45 „	4	9.3
Gender		
Male	24	55.8
Female	19	44.1
ECG		
Sinus	31	72
AF	12	27.9
NYHA functional class		
II	8	18.6
III	25	58.1
IV	10	23.2
LVEF		
> 60 %	10	23.2
50-60 %	19	44.1
40-50%	11	25.5
<40%	4	9.3
Left atrial thrombi	4	9.3
Tricuspid valve disease	17	39.5
Aortic valve disease	12 (including 8 significant lesions)	27.9

AF, atrial fibrillation. ECG, Electrocardiogram. NYHA, New York Heart Association. LVEF, left ventricular ejection fraction

to prevent thrombus formation on the rings; warfarin for the first 3 months with a variable readjustable dose to maintain the INR test (of prothrombin activity) about 2.2. Then dipyridamol (antiplatelet) 75 mg/ day for another 3 months, and finally to complete one year on aspirin (i.e. 6 months) with a low dose 330 mg/day.

The patients followed up with a nearly

monthly visit for a mean period of follow up 14.5 months (range 1 to 32 months) with at least 1 echocardiographic examination done during the period of follow up.

Results

There were 2 operative mortalities (4.6%) one intraoperative and one early postoperative (third day) deaths. The

Table (2): Different mitral valve reconstruction techniques.

Technique	Number /total number of patients	%
1) Ring annuloplasty	39 / 43	90.6
2) Chordal shortening plasty	13 / 43	30.2
3) Commissural stitches	8 / 43	18.6
4) Chordal separation (fenestration)	6 / 43	13.9
5) Quadrangular resection of mural leaflet.	6/ 43	13.9
6) Leaflet and annular debridement and decalcification	5/43	11.6
7) Resection of secondary chordae	4/43	9.3
8) Chordal replacement	3/43	6.9
9) Papillary muscle shortening (Cuneiform resection)	3.43	6.9
10) Chordal transposition	2/43	4.6
11) Commissurotomy	29/43	67.4
Total number of techniques	118	

intraoperative death was the patient underwent redo surgery with previous unsuccessful closed mitral commissurotomy 6 months before, and the mortality was because of excessive uncontrolled bleeding from the injured right ventricle. The second early postoperative death was because of postoperative low cardiac output syndrome and biventricular pump failure, was ventilated for 2 days with hemodynamic compromise. This case of mortality was in a patient who underwent associated aortic valve replacement. So, there was only one death in the group with isolated mitral repair (1/35; 2.8%). However, this was a case of redo-surgery, and so no deaths in the group of patients who underwent isolated mitral repair without previous cardiac operations (0/34; 0%). There were no deaths in the group of patients who were in NYHA functional class II, one death in the group of patients who were in functional class III, and one death in those in functional class IV.

Early postoperative cardiac morbidity; out of the survivors (41

patients), 4 patients (9.7%) were deviated from the straight forward simple postoperative course of the others. 3 patients had low cardiac output syndrome, and responding well to the inotropic support and other manipulation after an average period of 39 hours (range of 21 to 59 hours). Only one patient required mechanical ventilation for > 24 hours. All the 4 patients were preoperatively in functional class III/IV.

Mid-term and late study outcome:

The postoperative survivors (41 patients) were followed up for a median of 14.5 months (1 to 32 months). There were 18 patients followed up for > 2 years.

The two years actuarial survival rate was 97.5 % with only one late cardiac death 18 months postoperatively (2.4%) of intractable heart failure. This patient was 30 years old man, in NYHA functional class IV preoperatively with ejection fraction 43%. He underwent double valve surgery with complex mitral reconstructive procedure using ring annuloplasty, chordal shortening,

Table (3) Pre and postoperative Doppler echocardiographic results in patients with degenerative or congenital diseases of the mitral valve (n = 7 patients).

	Preoperative (n=7)	Postoperative 6 months (n=7)	Postoperative 15 months (range 12-18 (n=7))
Regurgitation			
None or grade I	0	6	6
Grade II	1	1	1
Grade III	2	0	0
Grade IV	4	0	0
Mitral valve area (cm ²)	2.32 ± 0.91	3.2 ± 0.4	3.1 ± 0.6
LVEDD (mm)	61.5 ± 8.2	51.7 ± 6.3*	48.7 ± 7.3*
LVESD (mm)	42.3 ± 5.9	36.4 ± 8.2*	33.0 ± 6.1*
Left atrial diameter (mm)	55.6 ± 8.71	45.8 ± 8.4*	44.8 ± 7.9

LVEDD, left ventricular end diastolic diameter. LVESD, left ventricular endsystolic diameter. Values are expressed as mean ± 1 standard deviation *Denotes a statistically significant reduction in valves when compared with previous ones (P<0.05).

and chordal fenestration techniques. This patient was treated for the last 2 months of his life during his terminal illness in other city hospital, so we did not know much about his progress, but he had mitral insufficiency grade III.

Excluding the patient who died, there were 2 patients (2/40; 5%) in need for reoperation for valve replacement as they have significant-moderate to severe mitral insufficiency (Grades III and IV). One patient is already reoperated with mitral and aortic valve replacement after 29 months of the original surgery. This patient was 18 years old man at the time of the first operation which was repair with only suture annuloplasty. The other patient is waiting for reoperation with mitral valve replacement.

Both 2.4% late cardiac death, and the 5% in need for valve replacement were patients with rheumatic valvulitis. The 7 patients with degenerative or congenital valvular lesion who underwent mitral repair have

100% freedom from cardiac death and reoperation for valve replacement.

Clinical examination and evaluation of patients at follow up reveals; 32 are in NYHA functional class 1, 8 are in class II and 1 in class III. No or very faint systolic murmurs were found in 27 patients, soft systolic murmurs not considered to be hemodynamically significant were found in 5 patients, and typical soft pansystolic murmurs were found 9 patients. The majority of patients (38/41;%) mentioned that they have got much improvement after operation, while only 3 patient returning to the preoperative complaints. No patient was getting worse than before operation.

Regarding the degree of mitral regurgitation in the 40 survivors (with echocardiographic examination), 31 have non or grade I mitral regurgitation, 7 have grade II mitral regurgitation, and 2 patients have significant (grade III or IV) regurgitation; one of them already reoperated and the other is followed up and

Table (4): Pre and postoperative Doppler echocardiographic results in patients with rheumatic diseases the mural valve (n = 36 patients).

	Preoperative (n=36)	Postoperative 6 months (n=34)	Postoperative 15 months (range 12-18 (n=34)
Regurgitation			
None or grade I	0	26	25
Grade II	1	5	6
Grade III	15	2	1
Grade IV	20	1	2
Mitral valve area (cm ²)	2.2 ± 0.6	2.8 ± 0.5	2.7 ± 0.8
LVEDD (mm)	59.5 ± 9.8	49.4 ± 5.9*	47.2 ± 8.1
LVESD (mm)	35.4 ± 6.8	30.3 ± 4.2*	29.6 ± 6.1
Left atrial diameters (mm)	58.2 ± 6.3	46.2 ± 5.6	45.9 ± 6.2

For abbreviation see table 3

Denotes a statically significant reduction in values compared to the previous ones (P<0.05)

Table (5): Operative mortality for mitral repair

Reference	n	% mortality
Oury et al.	34	0
Duran et al.	255	1.8
Yacoub et al.	86	5.0
Oliveira et al.	82	4.9
Adebo and Ross	85	1.2
Antunes et al.	100	4.0
Bonchek et al.	18	5.5
Lessana et al.	130	2.3
Carpentier	1421	3.6
Nunley and Starr	48	6.3
Speneer et al.	103	2.0

After Cosgrove, et al. (21).

planned for surgery.

So, among the total 41 post operative survivors (including the late postoperative

death), there were 3 patients (7.3%) who have had significant mitral regurgitation > grade II. All were rheumatic patients.

The results of preoperative and postoperative Doppler echocardiographic studies are shown in Tables 3 & 4.

Variable degrees of left ventricular outflow tract obstruction (LVOTO) is often present in patients with ring annuloplasty (39 patients). This degree of LVOTO was insignificant - less than 10 mmHg pressure gradient - in the majority of patients (36 patient (92.3%)), while in the remaining 3 patients it varied between 10-30 mmHg pressure gradient with no hemodynamic alteration or symptoms.

During the period of follow up, None of the patients developed any of the thromboembolic complications (0%). Also there was no incidence of bacterial endocarditis (0%).

Discussion

Patients selected for mitral valve

reconstruction (repair) were those patients who, at the time of surgery, were found to have anatomic defects suitable for the procedure (repairable valve). This selection was usually somewhat difficult to be definitely judged preoperatively because the pathologic changes in the vast majority of our patient's valves were rheumatic in origin and couldn't be accurately described with echocardiography.

Among the 43 patients in this series, there were only 15 patients (34.8%) who recorded in the operative list as the planned procedure is "Mitral valve repair", while the remaining were listed as "Mitral valve surgery" or "Mitral valve repair versus replacement" except only one patient who was planned for replacement and then underwent repair during operation. There were another 18 patients preoperatively planned for "Mitral valve repair versus replacement" and then at the time of surgery, about 5-10 minutes were spent in trial to make a plan for valve repair, or the trial for reconstruction actually started then finally the decision was to replace the valve. So, the decision for mitral reconstruction usually was passing in 2 stages; the first one is preoperatively, depending on both echocardiographic findings and patient characteristics (like age, female in child bearing period, ..etc), at this stage we discuss the chance for valve repair with the patient and inform him / her that the final decision will be at the time of surgery, which is the second stage at which the final decision for repair was made.

Regarding the techniques of mitral valvuloplasty; we used 11 different techniques (table 2). The prosthetic annuloplasty ring is one of the major steps of valve reconstruction and is mandatory in most cases (90.6%). The basic principle of the ring annuloplasty is not only to reduce

the size of the dilated annulus, but also to restore the shape of the orifice. As a matter of fact, the annular dilatation is exclusively in the mural leaflet annulus, to which we give the great interest with the annuloplasty technique, so late in this series we intend to divide the anterior flat part of the Carpentier ring anterior to the site of commissures to decrease the deleterious effect of ring in inducing minimal degree of LVOTO. Also we used the sutures for fixation of the ring in a special manner to help advancement of the mural leaflet annulus by applying a relatively wider distance between the 2 points of every suture in the native mural annulus than the opposite 2 points for the same suture in the prosthetic ring. This is done in a progressive manner from the central point of the mural annulus toward both commissures, which helps greatly in remodeling of the shape of the orifice by relative stretching of the mural leaflet and good coaptation at leaflets closure.

Regarding all other valvuloplasty techniques, the Carpentier techniques seem to us clearly superior to all other forms of mitral reconstruction. This view is somewhat controversial because each surgeon's experience is limited to the technique used at his institution. However, the detailed review of all published reports that was used in the preparation of this report, considering both the size of the data base and the length of follow up, is supportive of the above conclusion. Obviously, different techniques sometimes used for specific problems such as; a symmetric annuloplasty of Reed et al., (18), commissural suture plication of Kay et al., (19), Chordal replacement with PTFE stents of Revuelta et al (16) and David et al., (15) and mural leaflet segmental resection of Yacoub et al., (20), but the Carpentier methods are the most versatile and the the

most applicable for all types of problems.

The surgical results reported in this series are remarkably similar to those reported by others. Of note is the low operative mortality (OM) rate of 4.6% for the entire series and the particularly low OM rate of 2.8 % in the subset of patients who had isolated mitral valve repair. This is nearly similar to the accumulated experience reported in the literature of 11 series including 2362 mitral valve repairs with an average OM of 3.3% (21) (Table 5). Mitral valve reconstruction is associated with an OM lower than that reported for mitral valve replacement. Many series (20,22-24) have compared similar groups of patients undergoing mitral valve replacement and mitral valve repair. The combined OM rate for 480 patients undergoing mitral valve repair was 1.9% as opposed to 10.3 % for 544 patients undergoing mitral valve replacement ($P < 0.0001$).

The incidence of reoperation observed in this series (5%) is somewhat similar to that reported in other series (20-24) and can be expected to decrease since this represents the learning phase of our experience with mitral valve reconstruction. Because of the added complexity of mitral reconstructive techniques, there has been concern about the distinct "learning curve" which is gradually ascending with mitral reconstructive surgery, and that with time late results, considering reoperation for valve replacement, improved. The learning curve in mitral valve repair includes, beside the experience and large amount of knowledges, a big degree of imagination of "which procedure will correct which problem or pathology".

With the use of our 1 year postoperative regimen of anticoagulant and antiplatelet therapy. We have no thromboembolic problem (0%) for a maximum of about 3 years follow up. This denotes that the

clearest advantage of mitral valve reconstruction (beside preservation of the patient's native valve) is the striking freedom from late thromboembolic complication and also anticoagulant-related hemorrhage.

These results demonstrate that mitral reconstructive surgery is applicable and durable for patients with mitral valve disease. It is expected that, with increasing experience, an increasing number of patients will be perceived as candidates for mitral valve repair and that long-term results of mitral valve surgery will reflect this trend with lower operative mortality rates and improved long-term results regarding freedom from cardiac death and freedom from reoperation with valve replacement for residual significant mitral insufficiency.

References

- 1- Starr A, Edwards ML; Mitral replacement: Clinical experience with a ball-valve prosthesis. *Ann. Surg.* 1961; 54: 726.
- 2- Lillehei CW, Gott VL, DeWall RA, Varco RL: Surgical correction of pure mitral insufficiency by annuloplasty under direct vision. *J. Lancet* 1957; 77: 446-449.
- 3- Merendino KA, Bruce RA: One hundred seventeen surgically treated cases of valvular rheumatic heart diseases with preliminary report of two cases of mitral regurgitation treated under direct vision with aid of a pump-oxygenator. *JAMA* 1957; 64-755.
- 4- McGoon DC Repair of mitral insufficiency due to ruptured chordae tendineae. *J. Thorac Cardiovasc. Surg.* 1960; 39:357 - 362.
- 5- Kay JH, Egerton WS: The repair of mitral insufficiency associated with ruptured chordae tendineae. *Ann Surg.*

- 1963; 157: 351-360.
- 6- Reed GE, Tice DA, Clauss RH; Asymmetric exaggerated mitral annuloplasty: Repair of mitral insufficiency with hemodynamic predictability. *J Thorac Cardiovasc Surg.* 1965; 49: 752-761.
 - 7- Carpentier A, Chauvaud S, Fabiani J-N, Deloche A, Relland J, Lessana Am, d'Allainès C, Blondeau P, Piwnica A, Dubost C: Reconstructive, surgery of mitral valve incompetence: Ten-year appraisal. *J Thorac Cardiovasc Surg.* 1980; 79: 338-348.
 - 8- Duran CMG, Pomar JL, Cucchiara G: A flexible ring for atrioventricular heart valve reconstruction. *J. Cardiovasc Surg.* 1978; 19: 417-420.
 - 9- Shore DF, Wong P, Paneth M: Results of mitral valvuloplasty with a suture plication technique. *J Thorac Cardiovasc Surg.* 1980; 79:349-357.
 - 10- Carpentier A. Cardiac valve surgery - the "French Correction." *J. Thorac Cardiovasc Surg.* 1983; 86 323-337.
 - 11- David TE, Komeda M, Pollick C, and Burns RJ. Mitral valve Annuloplasty: The effect of the type on left ventricular function. *Ann. Thorac Surg,* 1989; 47: 524-8.
 - 12- Castrol LJ, Moon MR, Rayhill seg et al., Annuloplasty with flexible or rigid ring does not alter left ventricular systolic performance. *J Thorac Cardiovasc Surg.* 1993; 105 (4) 643 - 59.
 - 13- Grossi EA, Galloway AC, Parish MA, et al., Experience with twenty-eight cases of systolic anterior motion after mitral valve reconstruction by the Carpentier technique. *J Thorac Cardiovasc Surg,* 1992; 103 (3) : 466 - 70.
 - 14- Frater RW, Vetter HO, Zussa C, and Dahm M. Chordal replacement in mitral valve repair. *Circulation,* 1990; 82 (5) suppl. IV: 125 - 30.
 - 15- David TE, Bos J, Rakowski H. Mitral valve repair by replacement of chordae tendinae with PTFE sutures. *J. Thorac Cardiovasc. Surg.* 1991; 101: 495-501.
 - 16- Revuelta JM, Rinaldi RG, Gaite L, et al., Generation of Chordae tendinae with PTFE stents. *J Thorac cardiovasc Rug,* 1989; 97: 98-103.
 - 17- Cosgrove DM, Chavez AM; Lytle BW, Gill CC, Stewart RW, Taylor PC, Goormastic M, Borsh JA, Loop FD Results of mitral valve reconstruction. *Circulation* 1986; 74 (suppl I) :1-82-87.
 - 18- Reed GE, Pooley RW, Moggio RA: Durability of measured vasc Surg. 1980; 79:321 - 325.
 - 19- Kay GL, Kay JH, Zubiata P, Yokoyama T, Mendez M Mitral valve repair for mitral regurgitation secondary to coronary artery disease. *Circulation* 1986; 74 (suppl I): 1-88-1-98.
 - 20- Yacoub M, Halim M, RadleySmith R, McKay R, Nijuelde A, Towers M: Surgical treatment of mitral regurgitation caused by floppy valves: repair versus replacement. *Circulation* 64 (suppl II): II-210, 1981.
 - 21- Cosgrove DM, Chavesz AM, Lytle BW, et al., Results of mitral valve reconstruction. *Circulation,* 1986; 74 (suppl I) 82 - 7.
 - 22- Oury JH, Peterson KL, Folkerth TL, Daily PO: Mitral valve replacement

versus reconstruction: an analysis of indications and results of mitral valve procedures in a consecutive series of 80 patients. *J Thorac Cardiovasc Surg.* 73: 825, 1977.

23- Duran CG, Pomar JL, Gallo I, Poveda J, Ochoteco A, Ubago JL Conservative operation for mitral insufficiency critical analysis supported by

postoperative hemodynamic studies in 72 patients. *J. Thorac Cardiovasc Surg.* 79 :326, 1980.

24- Adebo OA, Ross JK: Surgical treatment of ruptured mitral valve chordae: a comparison between valve replacement and valve repair. *Thorac Cardiovasc Surgeon* 32: 139, 1984.

EVALUATION OF FACTORS AFFECTING THE POSTOPERATIVE RENAL FUNCTIONS IN PEDIATRIC OPEN HEART SURGERY

ABSTRACT

In a prospective study, 190 random (consecutive) pediatric patients undergoing open heart surgery by several surgeons in the Cardiothoracic Departement, Kasr AlEini University Hospitals, were evaluated for factors affecting their postoperative renal functions. The patients consisted of 84 mates and 106 females - with a mean age of 5.52 years, ranging from " 1-12 years.

Acute renal failure (APF) requiring dialysis occurred in 24 patients. 12.6 Only 45% of the patients operated upon showed preoperatively completely normal renal function. Preoperative creatinine and urea levels were significantly higher in the patient group with ARF than the patient group without ARF.

Preoperative heart failure was a feature in 22 of the patients (11.6%). The incidence of postoperative ARF was 45.5% (10/22) in the patients who had preoperative heart failure, whilst only 8.3% (14/168) of the patients who had no preoperative heart failure suffered from postoperative ARF ($p < 0.0004$).

Among the 190 patients, 19 (10%) were cyanotic. The incidence of postoperative ARF in cyanotic patients was 68.42% (13/19), while in noncyanotic patients it was 6.43% (11/171), a difference which was statistically significant ($p = 0.0122$).

The mean ischemic time for all patients operated upon was 58.66 ± 28.4 minutes, whilst the mean time for patients who had ARF postoperatively was 88.66 ± 26.48 minutes and for those who had a postoperative course without this complication the mean aortic occlusion time was 51.07 ± 23.52 minutes ($p = 0.0046$).

The patient group with ARF had a mean ventilation time of 75.66 ± 58.04 hours, while the group without APF had a mean ventilation time of 18.18 ± 23.94 hours ($p < 0.0005$). The mortality rate of patients who suffered postoperative renal failure was 91,7% (22/24). In conclusion, it was noticed that the complexity of the cardiac pathology, also the presence of preoperative renal impairment,, and the relatively long duration of aortic cross-clamping increase the incidence of acute renal failure significantly. Prolonged postoperative mechanical ventilation, which is a general indicator of major perioperative problems, can be interpreted as a result of ARF, or resulting in ARF.

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INTRODUCTION

With the increasing performance of heart operations in the pediatric age group, specially the neonatal cardiac surgery with an increasing complexity of the surgical

procedures, the problem of postoperative renal failure has become more important during recent years.

Acute renal insufficiency after cardiopulmonary bypass in the pediatric age group leads to significant morbidity and mortality from fluid overload and electrolyte disturbances, impede pulmonary gas exchange, and postpone weaning from mechanical ventilation. The limitations placed on free water intake result in severe restriction of nutrition while diuretic therapy causes electrolyte imbalance.

Artificial renal support either in the form of peritoneal dialysis, or hemodialysis, or continuous arteriovenous hemofiltration has been reported in acute renal failure after cardiac operations in infants and children (Paret et al, 1992) (1). Continuous venovenous hemofiltration is also a valid and simple method for controlling fluid overload in neonates and infants with renal insufficiency resulting from low cardiac output syndrome after cardiac surgery (Leyh et al, 1996) (2).

Several studies dealing with acute renal failure after cardiac surgery in the pediatric age group have been published (table 1). The incidence of severe renal failure ranged from 3.4 to 9%. The majority reported a fairly high mortality rate of 58-65% in the pediatric age group (Chesney et al, 1975 (3); Gomez-Campdera et al (4), 1989; Frost et al, 1991(5); Paret et al, 1992 (1), Llopart et al, 1997) (6).

A critical circulation caused by different factors is reported to play an important role in the pathogenesis of acute postoperative renal dysfunction (Kron et al, 1985) (7).

In order to define and evaluate different factors that affect the postoperative renal functions in infants and children undergoing

open heart surgery, the present work aims at analysis of preoperative, intraoperative, and postoperative variables in 190 pediatric patients with and without serious acute renal failure following open heart surgery. Defining the factors that put the patient at increased risk of postoperative ARF, allows for better preparation of the patient to avoid the occurrence of ARF, which is associated with a high mortality rate.

Patients and Methods

A prospective study was performed including 190 random (consecutive) pediatric patients (age less than, or equal 12 years) operated upon by different surgeons in the Cardiothoracic Surgery Department, Faculty of Medicine, Cairo University. There were no exclusion criteria, and all patients were included in the study, regardless of their preoperative renal function status.

Preoperative characteristics of the patients as the type of cardiac affection, age, urea and creatinine levels, cyanosis, and heart failure were recorded for analysis. Intraoperative and postoperative data which comprise ischemic time, amount of blood transfusion, hemodynamic instability, and duration of artificial ventilation were also recorded for analysis to determine the perioperative risk factors which might be responsible for the occurrence of ARF postoperatively.

The patients consisted of 84 males and 106 females - with a mean age of 5.53 years, ranging from 1 - 12 years.

Table 2 describes the types of cardiac affections, ventricular septal defect (VSD) being the most commonly encountered pathology (42.1%). Among the 190 patients, 19 (10%) were cyanotic.

Table 1. Reported incidence and mortality rate of acute renal failure following pediatric cardiac surgery

	Incidence, % (n)	Mortality,%
Chesney et al, 1975	8.4 (7/83)	65
Gomez et al, 1989	9.0 (14/156)	58
Frost et al, 1991	3.4 (68/1988)	63
Average	6.9 (89/2227)	62

All patients were operated upon using standard cardiopulmonary bypass with non-pulsatile perfusion. Cold crystalloid potassium cardioplegia with local cooling with ice slush was used as myocardial protection. Systemic hypothermia was routinely used with a degree of 28°C.

A patient was classified as having acute renal failure (ARF) postoperatively, when urine production was less than 0.5 ml/kg/hour for more than 3 successive hours (Chesney et al, 1975) (3) or when serum creatinine was > 2.6 mg% (Koning et al, 1985) (8) or blood urea was > 70 mg% (filberman et al, 1979) (9).

Differences between means of variables were tested for statistical significance using Chi-square and Fisher's exact test. The t-test for equality of means with 2-Tail significance was also used. All values are presented as mean + standard deviation (SD), and the standard error of mean was calculated, and p values were used.

Results

Twenty four patients (12.6%) suffered postoperative acute renal failure with a postoperative mean serum creatinine of 2.61 + 0.32 mg%, and a mean blood urea level of 103.54 + 19.12 mg%.

Among those 24 patients, 22 patients died (91.7%).

Preoperative factors in relation to acute renal failure were found to be as follows.

- The ages of the children operated upon ranged from 1 to 12 years with a mean age of 5.5 + 2.7 years. The mean age of children who had postoperative renal failure was 3.58 + 2.6, and the mean age of children who had no postoperative renal failure was 5.8 + 2.6 (p = 0.001) (table 3).

- Preoperative impairment of renal function was a frequent finding. Although it was mild in most patients, there were 11 patients with creatinine levels exceeding 1.5mg%. Only 45% of the patients operated upon exhibited completely normal renal function. Preoperative creatinine and urea levels were significantly different between the patient groups with APF and without ARF - for creatinine p = 0.017, and for urea p = 0.012 (table 3). - The incidence of preoperative heart failure was 11.6% of all patients (22/190). Among the patients with congestive heart failure preoperatively, there were 45.5% (10/22) of the patients who had postoperative ARF, whilst among the patients without congestive heart failure preoperatively, 8.3% (14/168) of the patients had postoperative ARF. The difference was

Table 2. Types of cardiac affection associated with acute renal failure following pediatric cardiac surgery

Cardiac Affection	Number of Patients	Percent of Patients (%)
NONCYANOTIC HEART DISEASE:	171	
Atrial Septal Defect	32	16.84
Atrial Septal Defect - Aortic Stenosis	1	0.5
Atrial Septal Defect - Patent Ductus Arteriosus	6	3.2
Atrial Septal Defect - Pulmonary Stenosis	28	14.74
Ventricular Septal Defect	81	42.63
Ventricular Septal Defect - Atrial Septal Defect	8	4.21
Ventricular Septal Defect - Pulmonary Stenosis	5	2.63
Subaortic membrane	7	3.7
Mitral Valve Disease - Aortic Regurge	1	0.5
Mitral Regurge - Aortic Regurge	1	0.5
Mitral Regurge - Tricuspid Regurge	1	0.5
CYANOTIC HEART DISEASE:	19	
Atrial Septal Defect - Pulmonary Stenosis	3	1.6
Ventricular Septal Defect - Pulmonary Stenosis	4	2.11
Fallot Tetralogy	9	4.74
Transposition of Great Arteries	3	1.6
Total	190	100

statistically significant with a p value < 0.0004.

- The incidence of postoperative ARF in cyanotic patients was 68.42% (13/19), while in noncyanotic patients it was 6.43% (11/171), a difference which was statistically significant (p 0.0122).

- As regards the cardiac pathology, table 4 shows the number of patients and the incidence of ARF for each disease group.

An intraoperative factor in relation to acute renal failure was found to be as follows.

The mean ischemic time for all patients operated upon was 58.66 + 28.4 minutes, whilst the mean time for patients who had ARF postoperatively was 88.66 + 26.48 minutes, and for those who had a postoperative course without this complication the mean aortic occlusion time was 51.07 + 23.52 minutes (p = 0.0046).

Table 3: Preoperative patient data

	All patients	No ARF patients	ARF patients	p value
Age years (mean \pm SD)	1 - 12 (5.5 \pm 2.7)	1.5 - 12 (5.8 \pm 2.5)	1 - 12 (3.5 \pm 2.6)	p = 0.001
Preoperative Creatinine mg% (mean \pm SD)	0.4 - 1.7 (0.8 \pm 0.3)	0.4 - 1.7 (0.8 \pm 0.3)	0.7 - 1.7 (1.1 \pm 0.3)	p = 0.017
Preoperative Urea mg% (mean \pm SD)	8 - 71 (25.4 \pm 13.1)	8 - 55 (22.3 \pm 8.2)	18 - 71 (44.1 \pm 20.1)	p = 0.012

ARF = acute renal failure

Table 4: Number of pediatric patients and incidence of acute renal failure following cardiac surgery for each -disease group

Cardiac Affection	Number of patients	Incidence of ARF
Fallot Tetralogy	7	29.2 %
Ventricular Septal Defect - Atrial Septal Defect	4	16.7 %
Ventricular Septal Defect - Pulmonary Stenosis	3	12.5 %
Atrial Septal Defect - Pulmonary Stenosis	3	12.5 %
Transposition of Great Arteries	3	12.5 %
Ventricular Septal Defect	1	4.15 %
Atrial Septal Defect - Aortic Stenosis	1	4.15 %
Mitral Regurge - Aortic Regurge	1	4.15 %
Mitral Regurge - Tricuspid Regurge	1	4.15 %
<i>All cases</i>	24	100.00 %

A postoperative factor in relation to acute renal failure was found to be as follows.

A protracted postoperative course was noticed to be associated with this grave complication of ARF as evidenced by the artificial ventilation time of the patients. The patient group with ARF had a mean ventilation time of 75.66 + 58.04 hours,

while the group without ARF had a mean ventilation time of 18.18 + 23.94 hours (p < 0.0005).

Preoperative factors in relation to acute renal failure were found to be as follows.

Perioperative hemodynamic instability could be reflected by the lowest systolic blood pressure recorded, and by the need for

Table 5: Perioperative data reflecting the degree of hemodynamic instability in pediatric patients undergoing cardiac surgery who suffered postoperative acute renal failure

	Number of patients	Percentage of patients
Lowest systolic blood pressure		
more than 90 mm Hg	1	4.16 %
71 - 90 mm Hg	5	20.84 %
51 - 70 mm Hg	11	45.84 %
less than 50 mm Hg	7	29.16 %
Administration of Catecholamines		
No catecholamines	1	4.16 %
Epinephrine	2	8.35 %
Epinephrine + Dopamine	21	87.49 %

catecholamines during and after surgery (table 5). # The amount of blood which was transfused to all patients ranged from 0 to 7 units with a mean of 3.6 ± 1.4 . Patients with ARF needed a minimum of 4 and a maximum of 7 units with a mean of 5.6 ± 0.8 , while those without ARF used from 0 to 6 units with a mean of 3.3 ± 1.2 units. The mean difference is 2.2 and was found to be significant with a p value < 0.001 .

Discussion

Patients with preexisting chronic renal dysfunction are at high risk for developing acute renal failure postoperatively. For these patients it has been recommended that they are appropriately hydrated preoperatively, and prepared with the use of calcium blockade, free oxygen radical scavengers, osmotic diuretics, and renal dose dopamine infusions. This combination tends to block the entry of calcium into the cell, thought to be one of the primary reasons for initial cellular dysfunction, as well as promote a forced diuresis, maintain renal plasma flow, and reduce metabolic demand of the tubular cells. Thus, if the kidney is subjected to

periods of hypoxia, the cells might be more tolerant (Paganini & Bosworth, 1991) (10). In this study, only 45% of the patients operated upon exhibited preoperatively completely normal renal function. Preoperative creatinine and urea levels were significantly higher in the patient groups with ARF than in the patient group without ARF - for creatinine $p = 0.048$, and for urea $p = 0.021$. Similar results were reported by Mangos and associates (1995) (11), as acute renal failure developed in only 1.1% of their patients with normal pre-operative renal function (creatinine less than or equal 0.13 mmol/L) and none required dialysis. ARF developed however in 16% of the patients with impaired pre-operative renal function.

Preoperative impairment of renal function may occur either as a result of preexisting renal disease or because of an absolute decrease in cardiac index which would result in a prerenal etiology of a decrease in glomerular filtration rate (Byrick and Rose, 1990) (12). In the present study, none of the patients had a preexisting renal disease. Thus the preoperative renal impairment and its significant contribution

to the postoperative ARF can only be explained by the severity of the cardiac lesion, as preoperative heart failure and cyanotic heart disease were significantly more frequent in children who developed postoperative renal failure.

There is a marked reduction in renal function during aortic cross-clamping which occurs despite the use of various methods of renal protection (Roberts et al, 1983) (13). The longer the ischemic time, the higher the incidence of renal dysfunction (Abet et al, 1976) (14). Aortic cross clamping for more than 30 minutes always results in renal injury, but the injury is self limited in most instances (Meyers et al, 1984) (15). This effect could be explained by the marked elevation of plasma renin which is associated with aortic clamping (Joob et al, 1984) (16). In our study there was a statistically significant relation between ischemic time and renal dysfunction postoperatively.

A clear statistically significant relationship was demonstrated in this work between the development of ARF and the duration of postoperative positive pressure ventilation, a finding similar to the work of Koning and associates in 1988 (17). Although this relationship might be explained by a greater need for artificial ventilation in patients with postoperative low cardiac output, but Marquez and coworkers in 1979 (18) implicated inferior vena cava hemodynamics during artificial ventilation as a factor in kidney dysfunction in addition to changes in the cardiac output. Intermittent Positive Pressure Ventilation impedes the venous return to the thorax due to raised intrathoracic pressure. This leads to pooling of blood in the inferior vena cava and to an increase in renal venous pressure (Koning et al, 1988 (17); Byrick and Rose, 1990 (12)).

Data in the present study showed that

mortality differences in patients when classified by renal dysfunction postoperatively were significant and the mortality rate of ARF was extremely high (91.7%). Table 1 shows the mortality rate for ARF in the different studies reviewed.

Conclusion

In conclusion, it was noticed that the age of the child, the complexity of the cardiac pathology, specially if associated with a right to left shunt or if associated with heart failure preoperatively, also the presence of preoperative renal impairment, all these factors predispose the surgical candidate to ARF postoperatively. The relatively long duration of the aortic crossclamping, the increased need for blood transfusion, hemodynamic instability, and also prolonged postoperative mechanical ventilation can be interpreted as a general indicator of major perioperative problems which result in APF.

With regard to the poor prognosis of acute renal failure Following cardiac surgery, Abet et al (1976)(14) pointed out: "Therapy of this postoperative complication, therefore, appears to be better directed toward its prevention rather than treatment once established".

Prevention should be accomplished by operative intervention before development of advanced disease with left ventricular dilatation and secondary kidney failure. In addition preoperative preparation of the patients at risk should be optimized, to reduce the incidence of ARF following open heart surgery in pediatries. For these patients it has been recommended that they are appropriately hydrated preoperatively, and prepared with the use of calcium blockade, free oxygen radical scavengers, osmotic diuretics, and renal dose dopamine infusions.

References

- 1- Pare G, Cohen AJ, Bohn DJ, Edwards H, Taylor R, Geary D, Williams WG (1992): Continuous arteriovenous hemofiltration after cardiac operations in infants and children. *J Thorac Cardiovasc Surg*; 104: 1225.
- 2- Leyh RG, Nitzold A, Kraatz EG, Sievers HH, Bernhard A (1996): Continuous venovenous; hemofiltration in neonates with renal insufficiency resulting from low cardiac output syndrome after cardiac surgery. *Cardiovasc Surg*; 4: 520.
- 3- Chesncy RW, Kaplan BS, Freedom RM, Haller JA, Drummond KN (1975): Acute renal failure: An important complication of cardiac surgery in infants. *J Pediatr*; 87: 381.
- 4- Gomez-Campdera FJ, Maroto-Alvarez E, Galinanes M, Garcia E, Duarte J, Rengel-Aranda M (1989): Acute renal failure associated with cardiac surgery. *Child Nephrol Urol*; 9: 138.
- 5- Frost L, Pedersen RS, Lurid O, Hansen OK, Hansen TIE (1991): Prognosis and risk factors in acute., dialysis requiring renal failure after open heart surgery. *Scand J Thorac Cardiovasc Surg*. 25: 161.
- 6- Llopart T, Lombardi R, Forselledo M, Andrade R (1997): Acute renal failure in open heart surgery. *Ren Fail*; 19: 319.
- 7- Kron IL, Joob AW, van Meter C (1985); Acute renal failure in the cardiovascular surgical patient. *Ann Thorac Surg*; 39: 590.
- 8- Koning HM, Koning AJ, Leusink JA (1985): Serious acute renal failure following open heart surgery. *Thorac Cardiovasc Surg*; 33: 283.
- 9- Hilbertitan M, Myers BD, Carric BJ, Derby G, Jamison RL, Stinson EB (1979): Acute renal failure following cardiac surgery. *J Thorac Cardiovasc Surg*; 77: 880.
- 10- Paganini EP, Bosworth CR (1991): Acute renal failure after open heart surgery: newer concepts and current therapy. *Seminars in Thoracic and Cardiovascular Surgery*; 3: 63.
- 11- Mangos GJ, Brown MA, Chan WY, Horton D, Trew P, Whitworth JA (1995): Acute renal failure following cardiac surgery: incidence, outcomes and risk factors. *Aust N Z J Mod*; 25: 284.
- 12- Byrick RJ, Rose DK (1990): Pathophysiology and prevention of acute renal failure: the role of the anesthetist. *Can J Anaesth*; 4: 457.
- 13- Roberts AJ, Nora JD, Hughes WA (1983): Cardiac and renal responses to cross clamping of the descending thoracic aorta. *J Thorac Cardiovasc Surg*; 86: 732.
- 14- Abel RM, Buckley MJ, Austen WG, Barnett GO, Beck CH, Fischer JE (1976); Etiology, incidence, and prognosis of renal failure following cardiac operations. Results of a prospective analysis of 500 consecutive patients. *J Thorac Cardiovasc Surg*; 71: 323.
- 15- Meyers BM, Miller C, Michigan JT (1984): Nature of the renal injury following total renal ischemia in man. *J Clin Invest*; 73: 329.
- 16- Joob AW, Harman PK, Fredlender AE

- (1984): Effect of renin-angiotensin system blockade on renal blood flow and function during and after thoracic aorta cross clamping. *Surg Forum*, 35: 318.
- 17- Koning HM, Ieuskink JA, Nas AA, Van Scheyen EJ, Van Urk P, Haas FJ, Koning AJ (1988): Renal function following open heart surgery: the influence of postoperative artificial ventilation. *J Thorac Cardiovasc Surg*; 36:1.
- 18- Marquez JM, Douglas ME, Downs JB, Wu WH, Mantini E, Kuck EJ, Calderwood HW (1979): Renal function and cardiovascular responses during positive airway pressure. *Anaesthesiology*; 50: 393.

MINIMALLY INVASIVE CLOSURE OF ISOLATED ATRIAL SEPTAL DEFECTS VIA LIMITED RIGHT ANTEROLATERAL THORACOTOMY VERSUS MEDIAN STERNOTOMY

ABSTRACT

Objectives: The purpose of this prospective study is to assess the ease, accuracy, safety, and cosmetic outcome of closure of isolated atrial septal defects (ASD) through a limited right anterolateral thoracotomy in comparison with the standard approach through a median sternotomy.

Background: Operative closure of atrial septal defect is considered a high-benefit and low risk operation. The approach through a median sternotomy carries the possible complications of median sternotomy, disfigurement of the shape of the chest wall in children, in addition to the fact that the midline scar may be unsightly. The alternative approach through a right anterolateral thoracotomy is proposed, with better and safer healing of the wound and still without increasing operative risks.

Material and Methods: Forty consecutive patients of both sexes, in the different age groups underwent surgical repair of an isolated atrial septal defect at the department of Cardiothoracic Surgery, Faculty of Medicine, Cairo University. They were evaluated preoperatively and postoperatively by history, physical examination, electrocardiography, and echocardiography. Intraoperative data were also collected including intraoperative findings, operation time, bypass time, aortic cross-clamping time, intraoperative hemodynamic or electrical instability, and intraoperative complications. The patients were divided randomly into two groups: group A using standard median sternotomy, and group B using anterolateral thoracotomy for closure of the atrial septal defects. Patients returned for evaluation 3 months after operation and were examined clinically and by electrocardiography, and echocardiography, and for the cosmetic result of the wound in the different surgical approaches.

Results: There were 11 males and 29 females who had an age range from 1 - 40 years (mean 17.5 ± 10.7 years). There were no significant differences between the 2 groups in the preoperative data of age, sex, NYHA class, or Qp/Qs.

Intraoperatively the only significant difference was in the mean perfusion time (58.7 minutes for the thoracotomy group, 51.5 minutes for the sternotomy group with $p=0.02$). Postoperative complications in the form of wound infection, pneumonic changes, supraventricular arrhythmias were present in both groups. As regards cosmetic results, 5 patients had chest deformities and 5 patients had obvious keloid formation in their scars in the sternotomy group, whilst in the thoracotomy group, there was one incidence of breast asymmetry and 6 patients who complained of different sorts of pain, hyperesthesia, paresthesia, and anesthesia related to the wound and breast.

Conclusions: The results indicate that surgical closure of isolated ASD through a limited right anterolateral thoracotomy is of significant importance in preserving the chest wall integrity and improving cosmetic result whilst being a safe and effective approach, and should therefore be recommended for all patients with atrial septal defects of any sex and at whatever age they present.

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INTRODUCTION

Operative closure of atrial septal defects has been performed since the beginning of the cardiac surgery era. In patients who underwent operation early, long-term survival has proved to be similar to that of age- and sex-matched control populations (Murphy et al, 1990) (1).

Because the operation for atrial septal defects is considered a low risk and high benefit procedure, complications and aesthetic result has become an important issue (Laks and Hammond, 1980) (2). Median Sternotomy is the most commonly used approach for cardiac operations, despite its association with complications such as mediastinitis, sternal dehiscence, osteomyelitis of the sternum (Rutledge et al, 1985) (3). Right anterolateral thoracotomy has been recommended as an alternative to sternotomy for mitral valvular surgery and for the correction of some congenital heart defects (Dobell and Jain, 1984; Szarnicki et al, 1978) (4; 5).

With the right anterior thoracotomy, the exposure of the right heart is adequate for bicaval as well as aortic cannulation. In women, the unilateral submammary incision used in this approach remains cosmetically hidden. However, the breast tissue must be partially mobilized and this is associated with physical size defects in the ipsilateral breast in 7.4% and periareolar numbness or hyperesthesia in 38.8% of patients (Dietl et al, 1992) (6). Mobilization of the pectoral muscles and breast tissue en bloc with a muscle sparing thoracotomy can reduce the incidence of nipple hyperesthesia to 12.5%, but does not eliminate this complaint altogether. Pain and post-thoracotomy skeletal muscle dysfunction is also common. In addition, post-thoracotomy pain and other

complications (atelectasis, right phrenic palsy, rib fractures) are destined to occur (Dietl et al, 1992) (6). Grinda reported his results with ASD closure via thoracotomy in 80 female patients. Mean hospital stay was 9 days (Grinda et al, 1996) (7). Rosengart reported a mean hospital stay of 6 days (Rosengart and Stark, 1993) (8). Sequelae of thoracotomy pain (splinting, respiratory compromise, inactivity, extremity dysfunction) certainly affected the timing of discharge in these otherwise healthy patients.

Comparative studies evaluating the safety and effectiveness and cosmetic results of surgical closure of isolated atrial septal defects using right anterolateral thoracotomy versus median sternotomy do not exist. This work was undertaken to compare the results of right anterolateral thoracotomy of those with median sternotomy in patients needing correction of isolated atrial septal defects to determine the right approach for the right patient.

Material and Methods

Included in this prospective study are all patients who were undergoing surgery for isolated atrial septal defect at any age, of both sexes, in the Cardiothoracic Surgery Department, Faculty of Medicine-Cairo University during a 2-year period.

Excluded from the study were the patients with an associated lesion such as a patent ductus arteriosus and pulmonary stenosis. Also excluded were patients with no left to right shunt, or reversal of shunt. Another cause for exclusion was loss of the patient for follow up 3 months postoperatively.

The patients were divided randomly into 2 groups:

Group A with 20 patients were operated upon using the standard sternotomy approach, and the other 20 in group B were operated upon using the right anterolateral thoracotomy approach.

All patients were operated upon with the use of cardiopulmonary bypass and moderate hypothermia of 31°C, and ischemic arrest.

Operative Technique of the right anterolateral thoracotomy approach:

The patient is placed in a 45-degree anterior oblique position. The position was maintained with the right scapula supported by 1 sandbag, and the right buttock supported by another. The right hip was extended and supported by a pillow. The right groin is usually prepared and draped so that the iliac artery can be cannulated should the necessity arise.

A small anterolateral thoracotomy incision is made, using the inframammary groove in female patients. In younger children the incision starts about 4 cm below the nipple. It runs from the line about 2 cm anterior to the nipple (parasternal line) in the fourth intercostal space and extends straight posteriorly to the anterior axillary line. The breast and pectoralis major muscle were dissected en bloc from the chest wall. The serratus anterior and latissimus dorsi muscles must not be divided, and care was taken to preserve both the long thoracic nerve of Bell (nerve to serratus anterior) and the thoracodorsal nerve (nerve to latissimus dorsi). The chest was entered through the fourth intercostal space. It is usually not necessary to divide the latissimus dorsi muscle. The right internal mammary vessels were always respected.

The right lobe of the thymus is resected. The lung is retracted posteriorly using wet

sponges. The pericardium is then opened longitudinally, anterior to the phrenic nerve, and suspended posteriorly. The pericardial incision is extended superiorly over the ascending aorta up to its reflection, and inferiorly giving adequate exposure to the inferior vena cava. Pericardial stay sutures are put on traction at the inferior and middle aspect of the incision. The two top pericardial stay stitches are sutured to the ribs to elevate the aorta into the operative field.

A tape is passed around the aorta. Standard purse-strings are placed on the lateral aspect of the ascending aorta for aortic cannulation, and another purse-string was placed proximally on the ascending aorta for administration of cardioplegia and to help in deairing maneuvers, on the right atrial appendage, and at the right atrial-inferior caval junction for bicaval cannulation. Tapes are passed around the cava in standard fashion.

After heparin administration, standard cannulation is done, and the operative procedure is performed in the same way as in sternotomy with mild hypothermia and cardioplegia arrest. A particular point of interest of this operation is the deairing of the cardiac cavities. First of all, emptying of the left atrium is avoided; second, suturing of the patch is started at the inferior aspect of the defect and is finished superiorly, with bleeding of the left atrial blood into the right atrium. The atriotomy is then closed, the caval snares released, ventilation resumed, and the aortic root needle vent is connected to suction.

The ventricular pacing wire is placed during cardiopulmonary bypass, because of poor exposure of the ventricle. The following steps are identical to those in the sternal approach. Pericardial and pleural drains are inserted and the pericardium adapted, the thoracotomy is then closed in

Table (1): Age distribution in 40 patients with septal defects for surgical closure.

Age group	less than 10 years	11-20 years	21-30 years	31-40 years	all age groups
Number of patients	12	11	10	7	40
Thoracotomy group	4	7	5	4	20
Sternotomy group	8	4	5	3	20
P value	n.s	n.s.	n.s.	n.s.	n.s

layers in routine fashion.

The two groups were compared for the following: gender, age, symptoms, echocardiography, length of operation, length of cardiopulmonary bypass time, perioperative blood replacement, duration of mechanical ventilation, length of intensive care unit stay, length of postoperative hospitalization, operative and postoperative complications, and survival were recorded.

Each patient returned for evaluation 3 months after operation and was subjected to clinical examination, radiological examination, electrocardiography, and echocardiography.

Statistical Analysis:

Associations between qualitative variables were tested using Chi-square and Fisher's exact test. The t-test for equality of means with 2 - Tail significance was also used. All values are presented as mean + standard deviation (SD), and the standard error of mean was calculated, and p values were used, where the level of significance was set at $p < 0.05$.

Results

Forty patients (11 males and 29 females) with uncomplicated atrial septal defects, aged 1 to 40 years (mean 17.5 ± 10.7 years), body weight 7.5 to 65 kg (35.11 ± 19.5) were operated upon for closure of an isolated

atrial septal defect,

Age and Sex Distributions:

Table 1 and table 11 show the age and sex distributions of the patients in this study by dividing them into four age groups.

Symptoms:

The distribution of preoperative functional classes in the 40 patients with a septal defect for surgical closure is shown in table 11.

Echocardiography:

Echocardiography performed preoperatively for all patients showed the following characteristics for the patients (Table IV):

Types of Septal Defects:

According to the preoperative findings there were 4 types of defects:

1. Sinus venosus type ASD in 5 patients (12.5%)
2. Ostium Secundum ASD in 29 patients (72.5%)
3. Ostium Primum ASD in 6 patients (15%)

The left to right shunt (Qp)/Qs in these patients ranged from 2:1 to 5:1 with a mean of $2.8:1 \pm 0.9$.

Table (II): Sex distribution in 40 patients with septal defects for surgical closure.

Sex	Male	Female	Both
Number of patients (%)	11 (27.5%)	29 (72.5%)	40 (100)
Thoracotomy group (%)	5 (25%)	15 (75%)	20 (100)
Sternotomy group (%)	6 (30%)	14 (70%)	20 (100)
p value	n.s	n.s.	n.s

Table (III): Incidence of functional classes in 40 patients with septal defects for surgical closure.

NYHA	I	II	III	all patients
Number of patients (%)	25 (62.5)	10 (25)	5 (12.5)	40 (100)
Thoracotomy group (%)	12 (60)	5 (25)	3 (15)	20 (100)
Sternotomy group (%)	13 (65)	5 (25)	2 (10)	20 (100)
P value	n.s	n.s.	n.s.	n.s

NYHA = New York heart association (class I, II, III).

Table (IV): Preoperative echocardiographic data in 40 patients with septal defects for surgical closure.

	All Patients	Thoracotomy	Sternotomy	p value
Sinus venosus type ASD	5	3	2	n.s.
Ostium Secundum ASD	29	15	14	n.s.
Ostium Primum ASD	6	2	4	n.s.
Qp/Qs	2 - 5 (2.8 ± 0.9)	2 - 4 (2.7 ± 0.7)	2 - 5 (2.9 ± 1.0)	n.s.

Qp/Qs = pulmonary to systemic flow

Table (V): Comparison of preoperative data in 40 patients with septal defects for surgical closure.

	Thoracotomy	Sternotomy	p value
Operating time (min)	182.9 ± 18.8	175.1 ± 15.1	n.s.
Perfusion time (min)	58.7 ± 14.8	51.5 ± 19.9	0.028
Ischemic time (min)	33.1 ± 7.5	34.3 ± 12.1	n.s.
Ventilation time (hours)	8.4 ± 1.7	8.9 ± 2.1	n.s.
ICU time (days)	1.42 ± 0.8	1.4 ± 0.6	n.s.
Hospital stay (days)	11.5 ± 1.7	11.5 ± 2.8	n.s.

ICU = Intensive care unit

Table (VI): Postoperative complications in 40 patients with septal defects for surgical closure.

Complications	Sternotomy group	Thoracotomy group	All Patients
Not related to the approach:			
Wound dehiscence	1		1
Secondary wound healing	1	1	2
Pneumonia of the left lung		1	1
Supraventricular tachycardias	2	1	3
Related to the approach:			
Right pleural effusion		1	1
Right pneumothorax	1	1	2
Atelectasis of the right lung		1	1

Table (VII): Postoperative cosmetic results in 40 patients with septal defects during follow up.

	Sternotomy group			Thoracotomy group	P - value
	< 10 years		>10 years		
	CT ratio <55%	CT ratio >55%			
Chest deformity	1	4	0	0	P = 0.024
Keloid	2		3	1	n.s.

Table (VIII): Postoperative problems related to the thoracotomy approach in 20 patients with septal defects during follow up.

Problems	Patients Number (%) (n=20)
Breast asymmetry	1 (5%)
Chest pain	2 (10%)
Parasthesia & Anesthesia around wound	4 (20%)
Restricted shoulder movement	1 (5%)

Coexisting anomalies were:

Partial anomalous pulmonary venous drainage in 4 patients.

Left persistent superior vena cava draining into the coronary sinus in 2 patients. Patent ductus arteriosus in 1 patient.

Perioperative Data:

For both groups together the mean cardiopulmonary bypass time was 58.15 ± 17.4 min (range: 30 - 110 min); the mean aortic cross-clamp time was 37.7 ± 9.9 min (range 15 - 55 min). After a mean time of 8.6 ± 1.9 hours (range: 6 - 13 hours) the patients were extubated. The patients were transferred to the regular ward after a mean time of 1.4 ± 0.7 days (range: 1-4 days). They were discharged on day 8 - 16 (mean: 11.5 ± 2.3 days).

Looking at each of the two groups individually, we find that in **group A (sternotomy group)**, the, mean cardiopulmonary bypass time was 51.5 ± 19.9 min (range: 30 - 103 min); the mean aortic cross-clamp time was 34.3 ± 12.1 min (range: 15-55 min). After a mean time of 8.9 ± 2.1 hours (range: 7 - 13 hours) the patients were extubated, The patients were transferred to the regular ward after a mean time of 1.4 ± 0.6 days (range: 1 - 3 days). They were discharged on day 8 - 16 (mean: 11.5 ± 2.8 days).

In **group B (thoracotomy group)**, the mean cardiopulmonary bypass time was 58.7 ± 14.8 min (range: 44 - 110 min); the mean aortic cross-clamp time was 33.1 ± 7.5 min (range: 20-47 in). After a mean time of 8.4 ± 1.7 hours (range: 6 - 12 hours) the patients were extubated. The patients were transferred to the regular ward after a mean time of 1.4 ± 0.8 days (range: 1 - 4 days). They were discharged on day 9 - 16 (mean:

11.5 ± 1.7 days).

A statistically significant increase in perfusion time and in hospital stay was noticed in the thoracotomy group (Table V).

Postoperative Morbidity and Mortality:

Table VI shows the early complications of surgery for each group of patients individually, and for all patients together. There are complications not related to the approach of sternotomy or thoracotomy, but there are also complications related to the approach of thoracotomy, but do occur in sternotomy patients as well.

In neither of the two groups phrenic nerve injury occurred.

Overall mean postoperative blood loss was $330 \text{ ml} \pm 95 \text{ ml}$ (range. 70 - 700 ml). In 8 patients blood units were needed for priming, 6 of those had no blood after cardiopulmonary bypass. Only one patient received blood units postoperatively due to our restricted transfusion policy.

There were no postoperative mortalities and all patients of this study showed up after 3 months or more for evaluation.

Follow-up:

Follow up was possible in the 30 patients included in this study, with a mean follow up time of 4.3 ± 1.1 months (3 - 7 months).

As regards symptomatology, clinical examination, electrocardiography, radiologically, and echocardiographically, there were no differences noted between the two groups during follow up of the patients.

There were however differences as regards the effects of the different approaches

In the **Sternotomy group**, there were two major problems related to this approach

(Table VII) .

From 9 young patients less than 10 years, a deformity of the chest wall was evident in 5 patients, which was very similar to a pigeon chest. This deformity was more evident in the children with enlarged hearts.

In all age groups ketoid formation was evident in 5 patients (25%) out of the 20 patients, which was more evident in the dark skinned persons.

Postoperative pain related to the sternotomy approach was present in the form of shoulder pain in 2 patients (10%), paresthesia and hyperesthesia around the wound in 5 (25%) patients. In the **Thoracotomy group**, there were other problems related to that approach which were evident (Table VIII)

1 female patient (5%) complained of breast asymmetry. She was operated upon at the age of 16 years. Two patients (10%) complained of disturbing chest pain in addition to hyperesthesia in areas of the breast. Paresthesia and anesthetic areas were noticed by 4 patients (20%). Restriction of shoulder movements was observed in 1 patient (5%) and was related to pain.

Discussion

Operative closure of ASD has been performed successfully since 1952. Studies (Murphy et al, 1990; Hanlon et al, 1969) (1,9) show that many years after operation, most patients consider themselves healthy and are free from any medical or operative interventions since the operation. Many of them are not followed up any longer by a cardiologist. Because the operation for ASD is now considered a safe and high-benefit procedure, more attention is dedicated to the aesthetic results of the operation (Rosengart and Stark., 1993; Lancaster et al, 1990)

(8,10) .

Median sternotomy remains the standard approach used by most surgeons, but the residual scar may be cosmetically unsatisfactory and a source of psychological displeasure modifying the patient's body image, particularly in young female patients (Rosengart and Stark, 1993; Dietl et al, 1992; Bedard et al, 1986) (8,6,11) .

Alternative approaches to median sternotomy have been developed over time to conceal the scar. Brom was the first to describe a bilateral transsternal submammary incision in 1956 (Massetti et al; 1996)(12). A modified approach consisting of a bilateral submammary incision combined with a vertical sternotomy, after development of a superior flap to expose the suprasternal notch and an inferior flap extending beyond the xyphoid process. Certain complications may occur after the modified bilateral submammary incision; these include problems with wound healing in 3% to 23% of patients, hematoma in 3% to 11% and breast maldevelopment in 1% (Bedard et al, 1986) (11) .

Another cosmetically acceptable approach is the right submammary anterolateral thoracotomy (Grinda et al, 1996; Rosengart and Stark., 1993) (7,8) . Surgical exposure is satisfactory, including the potential to repair sinus venosus defects. Central cannulation can be performed, although sometimes aortic cannulation is uncomfortable. Many successful ASD closures have been accomplished through this approach. However, post-thoracotomy pain and breast maldevelopment are notable complications.

Transcatheter closure devices have been tried as a non-surgical method of ASD closure. However, these devices are still

imperfect with Rosenfeld reporting a 41% failure rate when used to close ASDs larger than 13 millimeters (Rosenfeld et al, 1995) (13). Late failure from unbuttoning and wire fracture (Lloyd and Beckman, 1994) (14), device related thromboembolism (Prewitt et al, 1992) (15) and device infections have also been reported.

Right anterolateral thoracotomy can be considered a preferable alternative approach in selected cases, and is already used successfully in some reoperative mitral and other congenital heart operations (Praeger et al, 1989; Kirklin and Barratt-Boyes, 1988a; b; Tribble et al, 1987) (16,17,18,19).

Nevertheless, many studies have reported breast and pectoral muscle maldevelopment associated with paresthesia after the anterolateral and posterolateral chest approaches (Kirklin and Barratt-Boyes, 1989a; Cherup et al, 1986) (17,20). The reason is that the breast tissue in a male or female infant lies in the areolar border by as much as 1.5 cm. Although the areola and breast mass lie in the fourth interspace in the infant, the complex migrates down to the seventh interspace by the completion of female development. The pectoral muscle also spans the second through sixth interspaces and inserts medially on the sternum and on the sixth costal cartilage. The innervation of the pectoralis major comes from the medial and lateral pectoral nerves, and nutrient vessels run longitudinally above the muscle layer. Therefore, any transverse incision of the breast and pectoral muscle evolves gradually toward atrophy of the inferior segment. In the right anterolateral thoracotomy approach, it is mandatory to respect the breast tissue and the muscle layer.

In this study, we found among the thoracotomy group 1 female patient operated upon at the age of 16 years who complained of breast asymmetry. To avoid

soft tissue problems related to breast maldevelopment and paresthesia, hyperesthesia, or anesthesia of the chest wall and breast we used a submammary incision without division of the breast tissue and pectoral muscle, as Cherup and colleagues in 1986 (20) recommended. Complete development of the breasts is necessary to identify its anatomic limits; therefore in younger children we and other investigators start the incision about 4 cm below the nipple. It runs from the line about 2 cm anterior to the nipple (parasternal line) in the fourth intercostal space and extends straight posteriorly to the anterior axillary line (Dabritz et al, 1999) (21). In spite of all precautions 6 patients out of 20 patients subjected to thoracotomy complained of different degrees of anesthesia and paresthesia.

As regards aortic cannulation, Grinda and associates in 1996 (7), preferred not to cannulate the aorta directly with the thoracotomy approach. They have always performed external iliac cannulation without any complications in these young female patients unaffected by atherosclerotic pathology. Direct aortic cannulation appeared to them as a delicate procedure. They believe that peripheral arterial cannulation allows for better intercostal exposure depending on the patients anatomic lesions and morphology. With peripheral cannulation, the surgeon would not be inclined to compensate for potential technical difficulties encountered with direct aortic cannulation by enlarging the incision, which should not exceed 12 cm. They have found many advantages of performing iliac cannulation rather than the classic femoral approach. First, the incision above the crural arch is short and parallel to the natural skin fold, and is perfectly hidden by an undergarment. Second, the external iliac approach does not cross the lymph nodes, thus avoiding local complications. Third,

the external iliac artery has a larger diameter, which is important in low-weight adolescents.

We think however, that direct aortic cannulation can be performed in the thoracotomy approach safely as stated also by other authors like Rosengart and Stark in 1993, Dietl and co-workers in 1992, Lancaster and associates in 1990, and Gross and associates in 1953 (8,6,10,22). In our group of patients subjected to the thoracotomy approach, aortic cannulation presented no hazard to the patient, although special techniques may be sometimes required to introduce the aortic cannula into the deeply seated ascending aorta.

Technical problems: related to the anterolateral thoracotomy approach did not occur. The exposure of the intracardiac anatomy is excellent. In the 20 patients who had a closure of any kind of ASD via anterolateral thoracotomy no technical problems were encountered from this approach. Surgical correction of complex lesions, as Ostium Primum lesions with mitral repair, did not turn out to be more difficult than via the sternotomy approach. On the contrary the exposure of the AV-valve area is better from a more lateral approach. This opinion was shared with Grinda and associates in 1996 (7), who stated that the different types of ASD, including those with associated partial anomalous pulmonary venous connections, are accessible by anterolateral thoracotomy, and that the partial atrioventricular canal defect should not be excluded as a type of repair suitable through an anterolateral thoracotomy, provided the mitral valve repair is not too complex.

Poor exposure of the ventricles required a modification of our strategies regarding de-airing, pacing-wire insertion, and

defibrillation. We always allowed the left heart to fill with blood before the ASD is closed completely. Only the aortic root is de-aired before the aortic crossclamp is opened. The ventricular pacing wire is inserted on the empty beating heart during cardiopulmonary bypass. Defibrillation can be performed with small internal paddles. Other authors used modifications of standard techniques used with sternotomy also, to ensure safety and accuracy in performing the different necessary steps (Dabritz et al, 1999, Yi-Cheng et al, 1998, Grinda et al, 1996) (21,23,7).

Modes to **arrest the heart** varied with different authors. Experience has proved that ventricular fibrillation, especially in nonhypertrophied hearts, under certain conditions (mild hypothermia during a half hour and maintained with acceptable perfusion pressure) results in no demonstrable decline in myocardial function or myocardial damage (Dietl et al, 1992; Murphy et al, 1990; Kirklin and Barrat-Boyes, 1988b) (6,1,18).

In this study however, we advocated cardioplegic arrest with aortic clamping in both approaches. We did not find that it was necessary to modify our technique used with the sternotomy approach, as did Dabritz and associates in 1999, and as recommended by Grinda and co-workers in 1996 (21,7). In our experience there was no difficulty at all in inserting cardioplegia through the aortic root or in applying the aortic cross-clamp.

Associated abnormalities on the right or left outflow tracts and left superior vena cava draining in the left atrium contraindicate this approach according to Grinda and associates in 1996, and Kumar and associates in 1993 (7,24). Dabritz and co-workers however stated in contrast, that they do not consider the pulmonary valve

stenosis, persistent left caval vein, prior anterolateral thoracotomy, or prior insertion of an ASD closure-device as a contraindication for anterolateral thoracotomy approach. Especially in children and young patients they stated it is easy to expose the pulmonary artery by traction sutures on the empty heart and to perform commissurotomy (21).

In this study 2 patients had a persistent left superior vena cava, which was dealt with through transatrial cannulation without problems. Apart from that in one patient a patent ductus arteriosus was not diagnosed preoperatively and was dealt with through the right thoracotomy approach, which proved to be a tedious task, but possible without hazards or complications.

The mean perfusion time was significantly higher in this study in the thoracotomy group as compared with the sternotomy group. This was most probably due to the increased time needed for applying the aortic clamp securely, the deairing of the heart, and putting the pacemaker wires, before cardiopulmonary bypass could be discontinued. Our mean perfusion time with 58 minutes is comparable to that reported by Dabritz and associates in 1999 (21), which was 55 minutes. Yi-Cheng and coworkers in 1998 (23) reported a mean cardiopulmonary bypass time of 46 minutes.

In this study, there was no statistically significant difference in hospital stay between the sternotomy and the thoracotomy group. With a mean hospital stay duration of 11.5 days however, the hospital stay is longer than in other studies with means of 6 days (Rosengart and Stark, 1993) (8); 6.9 days (Yi-Cheng et al, 1998) (23); 9.4 days (Grinda et al, 1996) (7), and 10.7 days (Masseti et al, 1996) (12). This can be attributed to the fact that we are a reference center, and many patients come

from other cities which delays discharge.

Short-term cardiologic results for both approaches in our series seem to be comparable to those of other literature reports (Murphy et al, 1990; Hanlon et al, 1969) (1,9): No early deaths were observed, morbidity was minimal, and in the form of supraventricular tachycardia in 3 cases in both groups.

The major indications for the thoracotomy approach rather than median sternotomy was the preservation of the chest wall integrity and shape in addition to cosmetic reasons.

Masseti and associates in 1996 (12) reported about 41 patients operated through a thoracotomy, in which there was no difference between the two sides of the chest, and where the breast volume and symmetry were unchanged. Rosengart and Stark in 1993 (8) concluded that the cosmetic result of a thoracotomy is superior to that of median sternotomy.

In the present study, the patient group submitted to sternotomy demonstrated an ugly scar with keloid formation in 5 patients (25%) out of the 20 patients of that group. This keloid was more evident in patients with a darker skin color, but occurred nevertheless in all skin complexions. In the thoracotomy group however, only one patient had a keloid, although 2 others had broad scars due to healing by secondary intention following wound infection.

In addition to the keloid, a far more distressing finding was evident in children less than 10 years of age in the sternotomy group. Five patients (25%) showed a chest wall deformity in the form of a bulge of the sternum giving a pigeon chest like appearance. This chest wall deformity was especially evident in patients with a cardiothoracic ratio greater than 55%. None of the patients operated upon through a

thoracotomy approach showed chest wall deformities.

An unsightly scar in the middle of the thorax may cause psychological disturbance, especially in young female patients (Losken, 1990; O'Hara et al, 1989)(25,26). The traditional operation heals the cardiac pathology, but it detracts from the body image. The experience of an operation for a patient who is doing well, as are the majority of ASD patients, has been widely regarded as a stressful life event that requires coping and adaptation. The emotional and psychological drawbacks of this experience lead the patient to evaluate more the symbolic value of the scar. The right anterolateral thoracotomy approach for ASD is a better alternative because of the limited extension of the scar.

References

- 1- Murphy JG, Gersh BJ, McGoon MD, Mair DD, Porter CJ, Ilstrup SM, McGoon DC, Puga FJ, Kirklin JW, Danielson GK. Long term outcome after surgical repair of isolated atrial septal defect. Follow-up at 27 to 32 years. *N Engl J Med* 323: 1645, 1990.
- 2- Laks H, Hammond GL. A cosmetically acceptable incision for the median sternotomy. *J Thorac Cardiovasc Surg* 79:146, 1980.
- 3- Rutledge R, Applebaum RE, Kim BJ. Mediastinal infection after open heart surgery. *Surgery* 97:88, 1985.
- 4- Dobell ARC, Jain AK. Catastrophic hemorrhage during redo sternotomy. *Ann Thorac Surg* 37:273, 1984.
- 5- Szarnicki RJ, Stark J, de Leval M: Reoperation for complications after inflow correction of transposition of the great arteries: technical considerations. *Ann Thorac Surg* 25: 150, 1978.
- 6- Dietl CA, Torres AR, Favalaro RG. Right submammary thoracotomy in female patients with atrial septal defect and anomalous pulmonary venous connections. *J Thorac Cardiovasc Surg* 104:723, 1992.
- 7- Grinda JM, Folliguet TA, Dervanian P, Mace L, Legault B, Neveaux JY. Right anterolateral thoracotomy for repair of atrial septal defect. *Ann Thorac Surg* 62 (1): 175, 1996.
- 8- Rosengart TK, Stark JF. Repair of atrial septal defect through a right thoracotomy. *Ann Thorac Surg* 55:1138, 1993.
- 9- Hanlon CR, Barner IIB, Willman VL. Atrial septal defect results of repair in adults. *Arch Surg* 49:275, 1969.
- 10- Lancaster LL, Mayroutis C, Rees AH, Slater AD, Ganzel BL, Gray LA. Surgical approach to atrial septal defect in the female: right thoracotomy versus sternotomy. *Am Surg* 56:218, 1990.
- 11- Bedard P, Keon WJ, Brais MP, Goldstein W. Submammary skin incision as a cosmetic approach to median sternotomy. *Ann Thorac Surg* 41:339, 1986.
- 12- Massetti M, Babatasi G, Rossi A, Neri E, Bhoyroo S, Zitouni S, Maragnes P, Khayat A. Operation for Atrial Septal Defect Through a Right Anterolateral Thoracotomy: Current Outcome. *Ann Thorac Surg* 62:1100, 1996.
- 13- Rosenfeld VIM, van der Velde ME, Sanders SP, Colan SD, Parness IA, Lock JE, Spevak PJ. Echocardiographic predictors of candidacy for successful transcatheter

- atrial septal defect closure. *Cathet Cardiovasc Diagn* 34 (1): 29, 1995.
- 14- Lloyd TR, Beekman RH. Transcatheter closure of atrial septal defect and patent ductus arteriosus. In: Topol EJ, editor. *Textbook of interventional cardiology*. 2nd ed. Philadelphia: WB Saunders. pp 1298-1311, 1994.
 - 15- Prewitt KC, Gaither NS, Farb A, Wortham DC. Transient ischemic attacks after long term clamshell occluder implantation for closure of atrial septal defect. *Am Heart J* 124:1394, 1992.
 - 16- Praeger PI, Pooley RW, Moggio RA, Somberg ED, Sarabu MR, Reed GE. Simplified method for reoperation on the mitral valve. *Ann Thorac Surg* 48: 835, 1989.
 - 17- Kirklin JW, Barratt-Boyes BG. Atrial septal defect and partial anomalous pulmonary venous connection. In: Kirklin JW, Barratt-Boyes BG, eds. *Cardiac surgery*. 1st ed. New York: Churchill Livingstone, pp 463-497, 1988 b.
 - 18- Kirklin JW, Barratt-Boyes BG. Right anterolateral thoracotomy for cardiopulmonary bypass. In: Kirklin JW, Barratt-Boyes BG, eds. *Cardiac surgery*. 1st ed. New York: Churchill Livingstone, pp, 29-82, 1988 a.
 - 19- Tribble CG, Killinger WA, Harman PK, Crosby IK, Nolan SP, Kron IL. Anterolateral thoracotomy as an alternative to repeat median sternotomy for replacement of the mitral valve. *Ann Thorac Surg* 43: 380, 1987.
 - 20- Cherup LL, Siewers RD, Futrell JW. Breast and pectoral muscle maldevelopment after anterolateral and posterolateral thoracotomies in children. *Ann Thorac Surg* 41: 492, 1986.
 - 21- Dabritz S, Sachweh J, Walter M, Messmer BJ. Closure of atrial septal defects via limited right anterolateral thoracotomy as a minimal invasive approach in female patients. *European Journal of Cardio-thoracic Surgery* 15: 18, 1999.
 - 22- Gross RE, Watkins E Jr, Pomeranz M, Godsmith E. Method for surgical closure of interauricular septal defects. *Surg Gyn Obstet* 96: 1, 1953.
 - 23- Yi-Cheng Wit, Chau-Hsiung Chang, Pyng Jing Lin, Jaw-Ji Chu, Hui-Ping Liu, Min-Wen Yang, Hung-Chang Hsieh, Feng-chun Tsai. Minimally invasive cardiac surgery for intracardiac congenital lesions. *European Journal of Cardio-thoracic Surgery* 14 (Suppl. I): S 154, 1998
 - 24- Kumar AS, Prasad S, Rai S, Saxena DK. Right thoracotomy revisited. *Texas Heart Inst J* 20: 40, 1993.
 - 25- Losken MW. Psychological aspects of breast surgery. *Aesthetic Plast Surg* 14: 107, 1990.
 - 26- O'Hara MW, Ghoneim MM, Hinrichs JV, Mehta MP, Wright EJ. Psychological consequences of surgery. *Psychosom Med* 51: 356, 1989.

TEPID BLOOD CARDIOPLEGIA IN CORONARY REVASCULARIZATION

ABSTRACT

This study was carried out on 87 patients who were candidates for coronary artery bypass grafting in Prince Sultan Cardiac Center (Saudi Arabia) together with Cardiothoracic Surgery Department Ain Shams University. According to the temperature of cardioplegia used, they were divided into two groups: Group A (Tepid blood cardioplegia) which included 47 patients with the cardioplegia temperature 28-30°C and without topical cooling, and Group B (Conventional cold blood cardioplegia) which included 40 patients with their cardioplegia temperature 8-10°C and with topical cooling. All the patients were subjected to pre-operative, intra-operative and post-operative hemodynamic studies together with measuring the cardiac enzymes (LDH CK, and CK-MB) and coronary sinus samples were taken and calculated for oxygen extraction acid release and lactate release. Forty five patients in group A (95.7%) showed spontaneous defibrillation and resumption of sinus rhythm after aortic declamping while only one patient in group B resumed sinus rhythm (2.5%) with a highly significant p value ($P < 0.001$). Cardiac enzymes especially the myocardial band (CK-MB) were significantly lower in group A than group B ($P < 0.001$) in most of the post-operative samples. This study showed that tepid blood cardioplegia had superiority over the conventional cold blood cardioplegia in both metabolic and functional recovery, based on the higher incidence of spontaneous defibrillation and lower incidence of ventricular arrhythmia. For these reasons it can be recommended for high-risk cases.

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INTRODUCTION

Since the introduction of normothermic blood cardioplegia in 1991 (1) many studies (2) have shown its superiority on myocardial protection compared with those of conventional cold blood cardioplegia. During coronary artery bypass procedures interruptions or inadequate distribution of normothermic cardioplegia may induce anaerobic metabolism and warm ischemic injury (3). To avoid this problem, tepid (29°C) blood cardioplegia was recently introduced. The technique has been reported

to reduce anaerobic myocardial lactate and acid release without inhibiting myocardial metabolic activity. Decreasing the heart temperature from 37° to 29°C may provide a buffer to ischemic injury when cardioplegia delivery is interrupted or nonhomogenous (4).

Aim of the work

The aim of this work is to compare between two methods of blood cardioplegia, tepid and cold blood cardioplegia concerning the functional and metabolic recovery during coronary artery bypass surgery.

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2- Prince Cardiac Center (Saudi Arabia) Department of Cardiothoracic Surgery.

Patients and Methods

This study was carried out on 87 patients who were candidates for coronary artery bypass grafting in Prince Sultan Cardiac Center (Saudi Arabia) together with the Cardiothoracic surgery department Ain Shams University (Egypt). According to the temperature of blood cardioplegia used the patients were divided into two groups:

Group A: (Tepid blood cardioplegia) which included 47 patients with the cardioplegia temperature 28-30°C and without topical cooling.

Group B: (Conventional cold blood cardioplegia) which included 40 patients with their cardioplegia temperature 8-10°C and with topical cooling.

Exclusion criteria included combined procedures (e.g. CABG + AVR, CABG +MVR ,... etc) and redo CABG.

All the patients were subjected to the following

(1)-Preoperative Study

a-Complete clinical examination and history taking especially for risk factors including hypertension , diabetes mellitus , and previous infarctions , medications , and NYHA functional class.

b-Complete laboratory investigations including complete blood count, coagulation profile, liver and kidney function tests and basic cardiac enzymes (LDH,CK,CK-MB) .

c-Chest X- ray and basic twelve leads electrocardiogram (ECG) .

d-Echocardiography to determine the ejection fraction and regional wall motion.

e-Cardiac catheterization and coronary angiography

f-certain investigations if necessary such as stress ECG and Dobutamine stress test.

(2)- Intra-operative study

A Swan Ganz catheter was inserted in all patients and all the hemodynamic data were recorded including pulmonary artery pressure (PAP), pulmonary capillary wedge pressure (PCWP) systemic vascular resistance (SVR), pulmonary vascular resistance (PVR), cardiac output (CO), cardiac index (CI and right and left ventricular systolic work index (RVSWI), (LVSWI).

Other data were recorded as total cardiopulmonary bypass time (CPBT) aortic cross clamping time (ACT), use of hemofilters, number of vessels grafted, type of graft used, mode of heart rebeating and arrhythmia, use of intra-aortic balloon or left ventricular assisted device.

Use of blood cardioplegia

In all patients a retrograde coronary sinus cannula was inserted through the right atrium and blood cardioplegia was prepared so as to confirm a delivery ratio of 4:1, which entails mixing four volumes of oxygenated blood to one volume of crystalloid cardioplegia, and was used according to the following protocol:

a) A liter of warm blood cardioplegia (37°C) of high potassium (1.6 meq/L) was given through the aortic root (antegrade) immediately after aortic cross clamping for induction of electromechanical arrest (warm induction high K+).

b) Moderate systemic hypothermia (25°C) started once the ECG is flat. The cardioplegia was shifted to the retrograde route through the coronary sinus when fashioning the distal ends, cooled down to

28-30°C (Tepid cardioplegia) in group A and given as low K⁺ (K⁺ concentration 8 meq/L) in a semicontinuous manner (interrupted only if the surgical exposure was difficult).

c) This process was repeated until the completion of all distal ends anastomoses then a hot shot (37°C) was given retrogradely before aortic declamping .

d) Coronary sinus samples were taken and calculated for oxygen extraction, acid release and lactate release before applying the cross clamp, before giving the hot shot immediately after cross clamp is off, 10 minutes after declamping and 10 minutes after finishing all the top ends.

e) Cold blood cardioplegia (group B)

Cold blood cardioplegia (temperature 8°C) was given intermittently antegrade starting with one liter high K⁺ (no warm induction) after cross clamping followed by semicontinuous retrograde (low K⁺) cold blood cardioplegia which was interrupted during each distal end anastomosis.

f) Hot shot was given upon completing the last distal end anastomoses and before aortic declamping.

g) Cold iced saline was applied almost constantly around the heart (topical cooling in group B only).

(3) - Post-operative study

The patients were transferred to the surgical ICU for close monitoring of all vital data, and blood samples for cardiac enzymes (CK,CK-MB) were drawn from all patients in the first hour after arrival to the ICU, after 6 hours 12 hours 24 hours, and 48 hours. Inotropic support was accurately recorded, and the incidence of low cardiac output

necessitating intensive inotropic supports and with all its clinical manifestations were recorded.

The incidence of post-operative significant arrhythmias was recorded together with the incidence of postoperative myocardial infarction (defined as appearance of new Q waves in at least two precordial leads or ischemic ST segment changes associated with concomitant increase of CK-NW levels). The ventilation time ICU and hospital stays were recorded. A postoperative echocardiogram was done to compare between the pre and post-operative data The post-operative complications were recorded and an outpatient complete follow up was done routinely 4 and 8 weeks post-operatively .

Statistical Analysis

All data were entered on the (SPSS) statistical analysis program (Release 6.1.3-24 August 1995) for windows. All data were expressed as the mean \pm the standard deviation. Multiple comparison tests were applied for comparison between the two groups which included; Modified Benferriani least significant difference tests (LSD), Student-Newman Keuls tests, and Tukey Honestly Significant test (HSD) The P value was considered Non -Significant (NS) if >0.05 Significant (S) if <0.05 and Highly Significant (HS) if <0.001 (5).

Results

All the demographic data are recorded in (table 1) with no significant difference between both groups except for the incidence of left main stem lesion (LMS) $>40\%$ which was significantly higher in group A (18 patients (3 8.3%) Vs 5 (12.5%) in group B.

Some of the intraoperative data are shown in (table 2) with a highly significant

Table (1): Demographic data.

Data	Group A(TBC) N=47	Group B(CBC) N=40	Significance
Age (years) mean±SD	57.4 ±9.2	57.9 ± 9.2	NS
Sex (% of females)	5 (10.6 %)	8 (20 %)	NS
Weight (kg) mean± SD	73.4 ± 1.6	70.6 ± 1.4	NS
History of myocardial inf.	29 (61.7 %)	31 (77.5 %)	NS
Hypertension	20 (42.6 %)	24(53.7 %)	NS
Diabetes	19(40.4 %)	18 (45 %)	NS
Smoking	22 (46.8 %)	15 (37.5%)	NS
Average NYHA	2.1 ± 0.6	1.9 ± 0.54	NS
Poor LVF EF < 30 %	4 (8.5 %)	1(2.5 %)	NS
EF (mean ± SD)	45.85 ± 8.2 %	46.5 ± 7.78 %	NS
LMS (>40 %)	18 (38.3 %)	5 (12.5 %)	HS
Prox. Anastomoses	1.9± 0.6	2.2 ± 0.9	NS
Distal Anastomoses	3.0 ± 0.66	3.02 ±0.86	NS
LIMA	45 (95.7 %)	36 (90 %)	NS
Endartrectomy	2 (4.2%)	0 (0 %)	NS

Table (2): Intra-operative Data.

Variable	Group A	Group B	Significance
Bypass Time(min) Mean \pm SD	112.26 \pm 24.2	114.5 \pm 30.3	NS
Cross Clamp time (min) mean \pm SD	74.9 \pm 17.9	62.9 \pm 17.1	NS
Spont. Defib.(No)	45 (95.7%)	1 (2.5 %)	HS
Use of Significant Inotrops	4(8.4 %)	9 (22.5 %)	NS
Use of IAB	1(2.1 %)	2 (5%)	NS
Low CO	3 (6.3 %)	6 (15 %)	NS
Use of Hemofilters	42 (87.2 %)	11 (27.5 %)	HS

IAB: Intra-aortic balloon.**Low CO: Low cardiac output.****Table (3): The Postoperative events.**

Variable	Group A (TBC) NO = 47	Group B (CBC) NO = 40	Significance
Arrhythmias (Ventricular)	7 (14.7 %) 1 (2.1 %)	5 (12.5 %) 3 (7.5 %)	NS NS
Anti-arrhythmic drugs	7 (14.7 %)	5 (12.5%)	NS
Perioperative MI	1 (2.1%)	0 (0 %)	NS
ICU stay (hours) Mean \pm SD	33.8 \pm 17.9	41.38 \pm 20.9	NS
Ventilation (hours) Mean \pm SD	15.5 \pm 23.2	12.7 \pm 12.0	NS
Ejection fraction EF .mean \pm SD	45 .8 \pm 9.7	48.5 \pm 7.9	NS

Table (4): Hemodynamic recovery:

Variable Mean \pm SD	Time	Group A(TBC) 47 patients	Group B(CBC) 40 patients	Significance
MABP(mmHg)	Preoperative	83 \pm 9	82 \pm 12	NS
	Postoperative	76 \pm 11	77 \pm 2.7	NS
MPAP(mmHg)	Preoperative	13 \pm 2.5	15.5 \pm 2.4	NS
	Postoperative	17 \pm 2.6	17.5 \pm 1.3	NS
PCWP(mmHg)	Preoperative	8.8 \pm 1.5	8 \pm 2.5	NS
	Postoperative	11 \pm 2.0	11 \pm 0.8	NS
CO (Liter/m)	Preoperative	6.0 \pm 1.7	6 \pm 1.1	NS
	Postoperative	5.7 \pm 1.1	6.0 \pm 1.0	NS
CI (Liter /m/m ²)	Preoperative	2.5 \pm 0.5	2.6 \pm 0.3	NS
	Postoperative	3.0 \pm 0.5	3.1 \pm 0.3	NS
SI (ml /m ² /beat)	Preoperative	33 \pm 3.7	34 \pm 8.7	NS
	Postoperative	35 \pm 5.4	33 \pm 3.5	NS
RVSWI (g-m/m ²)	Preoperative	13 \pm 1.9	13.6 \pm 5.3	NS
	Postoperative	16 \pm 4.0	14.7 \pm 1.4	NS
LVSWI (g-m/m ²)	Preoperative	30 \pm 11	24 \pm 12	NS
	Postoperative	28 \pm 7.1	26 \pm 3.5	NS

MABP: Mean arterial blood pressure.

MPAP: Mean pulmonary blood pressure.

PCWP: Pulmonary capillary wedge pressure.

CO: Cardiac output (Liter per minute).

CI: Cardiac index (Liter per minute).

SI: Stoke index.

RVSWI: Right ventricular systolic work index.

LVSWI: Left ventricular systolic work index.

Table (5): Postoperative cardiac enzymes.

Enzymes (mean±SD) IU	Group A (N=47) TBC	Group B (N=40) CBC	P value Significance
CK- 1	860 ± 340	827 ± 582	NS
CK -2	875 ± 453	1081±796	NS
CK -3	831 ± 495	1005± 799	NS
CK -4	639 ± 344	690 ±533	NS
CK -5	485 ± 247	640 ± 236	HS(P < 0.001)
CKMB -1	7.21 ± 3.1	10.8 ± 5.1	HS (P< 0.001)
CKMB -2	6.52 ± 4.0	11.8 ± 10.3	HS (P< 0.001)
CKMB -3	6.53 ± 3.2	7.1 ±2.6	NS
CKMB-4	3.93 ± 1.6	7.05±5.8	HS (P< 0.001)
CKMB -5	4.00 ± 1.4	5.25±2.3	NS

Table (6): Metabolic recovery.

Metabolic elements mean ±SD	Group A :TBC N = 47 Patients	Group B : CBC N= 40 Patients	Significance
Lactate release			
(mmol/ Liter) -1	2.1 ± 2.2	2.3 ± 1.6	NS
-2	-0.47 ± 0.68	-0.03 ± 0.4	NS
-3	-0.06 ± 0.8	-0.5 ± 0.36	NS
-4	-0.22 ± 0.67	-0.23 ± 1.4	NS
-5	-0.13 ± 0.82	0.63 ± 0.6	NS
Average	0.24 ± 1.03	0.18 ± 1.05	NS
Oxygen extraction			
(ml / dl) -1	3.5 ± 2.7	6.5 ± 1.8	NS
-2	-0.47 ± 2.2	-2.8 ± 0.9	NS
-3	1.7 ± 2.2	1.2 ± 2.7	NS
-4	4.9 ± 2.1	5.2 ± 2.7	NS
-5	-4.1 ± 2.8	-4.1 ± 4.08	NS
Average	2.76 ± 2.4	1.2 ± 3.6	NS
Acid release			
(nmol/L) -1	-0.35 ± 0.7	-1.1 ± 0.6	NS
-2	-0.62 ± 0.4	-1.2 ± 0.7	NS
-3	-0.5 ± 0.6	-0.9 ± 0.2	NS
-4	-0.84 ± 1.5	-1.74 ± 0.9	NS
-5	-1.07 ± 0.9	-1.7 ± 0.7	NS
Average	-0.67 ± 0.8	-1.33 ± 0.62	NS

difference between both groups regarding cross clamping time and spontaneous defibrillation ($p < 0.001$) and a significant difference regarding using significant inotropes in group B ($p < 0.05$). Seventy three patients (83.9%) had no complications regarding the retrograde coronary sinus cannula while difficult cannulation was encountered in 4 patients (4.6%) slipped cannula in 9 (10.34%) and ruptured coronary sinus which was successfully repaired during surgery in one patient (1.15%).

Post-operative events are shown in (table 3). The incidence of post-operative arrhythmias in both groups was similar but the ventricular arrhythmias were higher in group B although not statistically significant (7.5% in group B Vs 2.1% in group A). There was only one case of perioperative myocardial infarction in group A (Tepid group) with no significant difference between both groups ($p > 0.05$). This patient had extensive perioperative endarterectomy and diffuse coronary artery disease. He died early post-operatively. Five patients were explored for bleeding from both groups (5.8%) and 4 had wound problems (4.6%) 72 had neurological complications (2.3%) in the form of cerebral stroke, 4 patients had pulmonary complications (4.6%) with 4 of them had pneumonia and one had ARDS and all needed prolonged mechanical ventilation, and one patient (1.2%) had stress gastric ulcer and acute gastrointestinal bleeding and treated.

From the hemodynamic point of view there was no significant difference between both groups regarding the preoperative and the postoperative data (Table 4) But there was a tendency towards better post-operative RVSWI and LVSWI in group A

than in group B although not statistically significant.

The total creatine kinase (CK) and creatine kinase myocardial band (CK-NW) were measured at 1, 6, 12, 24, and 48 hours after arrival to the ICU. These were referred to as CK 1, 2, 3, 4, 5 and CK-MB 1, 2, 3, 4, 5 respectively. (Table 5) shows a highly significant difference between both groups regarding CK5 and CK-MB 1,2, and 4. For detection of metabolic recovery coronary sinus samples were taken five times (1,2,3,4,5) just before aortic cross clamping before giving the hot shot of cardioplegia, just after release of cross clamp, 10 minutes after release of the clamp, and finally after performing all top ends All samples were measured for lactate release, acid release, and oxygen extraction of the myocardium. The average values of all measurements are shown in (table 6) with no significant difference between both groups.

Discussion

The average age, body weight, and percentage of female patients in this study were respectively 57.6 ± 9.2 years, 73.2 ± 1.6 Kg and 14.9% female patients which are comparable to different studies (6-7-8). Past history of myocardial infarction was positive in 66.4% of the patients which is a high incidence in comparison to other studies (40 and 46% in Rahimotoola et al study (6), 41 and 44% in the study made by Sharma and colleagues (7) but similar to the incidence reported by Cutis et al (9) being 69.3%).

The incidence of hypertension and smoking as risk factors were 51 and 42.5% respectively which was similar to the incidence in other studies {(44% in Rahmitoola study (6) and 58% in a study made by Ott and colleagues (10)}. But the

incidence of diabetes mellitus in our study was 42.5% which was higher than reported in the previous studies being 13 and 25% respectively. Poor left ventricular function (EF <35%) was in 5.7% of the patients which was less than reported by Loop and colleagues (11) being 10.9%.

The only mortality in the study was in one patient in group A with poor LVF (EF < 30%) but he had another factor which was affecting the outcome since extensive endarterectomy to the right coronary artery was done. This procedure was reported by some surgeons to have a high incidence of peri-operative myocardial infarction (12). This explains the low incidence of endarterectomy in our study being 2.3% on the contrary to what was reported by others (13) who still continue to employ endarterectomies even in the LAD and reporting good results.

The incidence of left main stem lesion (>40% diameter stenosis) was in 23 patients (27.4%) and it was higher in group A (38.3%) than group B (12.5%), but it did not affect the postoperative outcome in both groups, although careful myocardial protection is recommended in patients with critical left main lesions (80-90%) especially in the presence of unstable angina and poor LVF (14).

The average bypass time in group A and B was similar with no statistically significant difference between both groups, but the average aortic cross clamping time was higher in group A than in B (74,9 ±17.9 Vs 62.9 ±17.1 minutes) and although this was a highly significant difference ($p < 0.001$), the incidence of spontaneous defibrillation and resumption of sinus rhythm in the tepid group (group A) was very much higher than in the cold group (group B) with a P value < 0.001.

Spontaneous resumption of sinus rhythm has been considered by many surgeons as an indicator of myocardial recovery after a period of aortic cross clamping which could reflect to some extent the state of myocardial protection (1-15).

Also the effectiveness of the hot shot (warm blood cardioplegia) which was given routinely before declamping is more prominent when using tepid blood cardioplegia helping to resuscitate the myocardium and washing out the acid metabolites and replenishing ATP stores and enhancing aerobic metabolism. This effect is not useful by using cold blood cardioplegia because the myocardial temperature is much lower than normal so the myocardium is not ready for its resuscitation.

Nine patients (22.5%) in group B (cold group) needed significant inotropic support and 6 (15%) of them had low cardiac output (LCO), while only 4 patients (8.4%) in group A needed significant inotropic support and 3 of them (6.3%) were in LCO. This tendency of the tepid group towards better myocardial protection has been reported by other authors since cold cardioplegia depresses myocardial metabolic activity and delays ventricular functional recovery (2).

Although the incidence of ventricular arrhythmia in the tepid group was only 2.1% compared with 7.5% in the cold group, the incidence of atrial arrhythmias was lower in group B although not statistically significant ($p > 0.05$). These observations go with the results of Kao and colleague (16) which suggested that the temperature of the blood cardioplegia solution was a determinant factor for the supraventricular arrhythmia and explains the lower incidence of atrial arrhythmias when cold blood cardioplegia was used.

The left ventricular ejection fraction EF did not show any significant differences between both groups neither in the pre-operative nor the post-operative assessment although other investigators proved better myocardial performance with tepid antegrade /retrograde blood cardioplegia (4). This observation may be apparent in our the study when we used more sophisticated methods of measuring the ventricular volume or dimension. The right and left ventricular stroke work indices were used as load -indices of the ventricular function (RVSWI, and LVSWI) (17) Although statistically not significant, there was a little tendency of better post-operative (RVSWI LVSWI) in the tepid group than the cold cardioplegia group and all these data can put better myocardial preservation in the account of the tepid group. Other hemodynamic data did not show a significant difference between both groups.

The activity of the MB (myocardial band) isoenzyme of creatine kinase (CK-MB) is the most widely used isoenzyme marker for myocardial infarction and ischemic injury because, of its greater cardio-specificity (15). Group A showed a highly significant lower levels of CK-5 (48 hours from arrival to the ICU) than group B, and the same was observed regarding CK-MB 1-2-, and 4 (one hour 6 hours, and 24 hours from arrival to the ICU). These data can confirm better myocardial protection and better metabolic recovery using the tepid blood cardioplegia rather than the cold blood cardioplegia (4-18).

It was observed from the study that oxygen consumption was much less in tepid than cold cardioplegia on cross clamp before giving the warm shot ($P=0.08$) which was associated with less acid release ($P=0.058$)

and slightly more lactate production. After resuscitating the heart with hot shot the lactate and acid washouts were much less in tepid than cold blood cardioplegia group Myocardial oxygen extraction was less after 10 minutes from declamping the aorta in tepid group than the cold blood group. However, the oxygen debt was similar in both groups after fashioning all top ends and both lactate and acid release were less in tepid than cold group.

These results prove clearly that tepid blood cardioplegia had better metabolic protection and recovery than the intermittent cold blood group. It is also clear that the hot shot given before declamping the aorta in cold group is not as effective as in tepid blood group probably because the myocardium was still cold and not fully resuscitated by the hot shot (4).

Summery and Conclusion

This study showed that tepid blood cardioplegia had superiority over the cold blood cardioplegia in both metabolic and functional recovery, based on the higher incidence of spontaneous defibrillation lower incidence of CK and CK-MB levels, lower incidence of ventricular arrhythmias and better postoperative hemodynamics. For these reasons, it can be recommended for high risk cases.

References

- 1- Lichtenstien SV, Ashe KA, EL Dalati H, et al Warm Heart Surgery J Thorac Cardiovasc Surg 1991;101:269.
- 2- Yau TM Ikonomidis JS, Weisel, RD, et al. Ventricular function after normothermic versus hypothermic cardioplegia J Thorac Cardiovasc Surg 1993; 105:833.

- 3- Landymore RW, Marble AE Engo P, et al. Myocardial oxygen consumption and lactate production during antegrade warm blood cardioplegia Eur J Cardiovasc Surg 1995; 110:800.
- 4- Hyashida N, Ivanov JRN Carson SM et al. Tepid Antegrade and retrograde cardioplegia. Ann Thorac Surg 1995; 59:723 .
- 5- Knapp RG and Miller MC (1992). Clinical Epidemiology and Biostatistics: Harwel, Pennsylvania .
- 6- Rahimtoola SH Fesseler CL, Grunkemeier GL et al. Survival 15 to 20 years after coronary bypass surgery for angina JACC 1993; 21:151.
- 7- Sharma GR, Deupree RH Khuri SF, et al Coronary Bypass Surgery improves Survival in high risk unstable angina. Circ 1991;84 :2610.
- 8- The WOSCOPS Study group. Screening Experience and Baseline Characteristic in the West of Scotland Coronary Prevention Study. Am J Cardiol 1995; 76:485.
- 9- Curtis JJ, Walls JT and Salsm NH Impact of unstable angina on operative mortality with coronary revascularization at varying time intervals after myocardial infarction J Thorac Cardiovasc Surg 1993; 102:867.
- 10- Ott RA, Gutfinger DE, Miller MP, et al Rapid recovery after coronary artery bypass grafting: Is the elderly patient eligible. Ann Thorac Surg 1997; 63:634.
- 11- Loop FD, Higgins TL, Panda R, et al. Myocardial protection during cardiac operations. J Thorac Cardiovasc Surg 1992; 104:608.
- 12- Yeh TJ, Heidary D and Shelton L.Y- grafts and sequential grafts in coronary bypass surgery: A critical evaluation of patency rates. Ann Thorac Surg 1979; 27:163.
- 13- Brenowitz JB, Kyser KL and Johnson MM. Triple vessel coronary artery endarterectomy and reconstruction: Results in 144 patients. J Am Coll Cardiol 1988; 11:706.
- 14- Engelman RM and Levitsky S.A TextBook of Cardioplegia for Difficult Clinical Problems Mount Kisco NY. 1992 pp 18-19.
- 15- Hears DI and Brinbridge MV: Protection of the ischemic myocardium. Raven. New York, 1981.
- 16- Kao HK, Chen YF, and Hsueh TC (Taiwan). The superiority of blood cardioplegia in prevention of supraventricular arrhythmias and conduction disturbances following open-heart surgery. 1989; 5 (10): 548.
- 17- Matswaka R, Matsuda H and Shirakura R. Changes in left ventricular performance after global ischemia Assessing LV pressure - volume relationship. Ann Thorac Surg 1994; 57:151.
- 18- Yau TM, John SI, weisel RD, et al Which Technique of cardioplegia prevents ischemia Ann Thorac Surg 1993, 56: 1020.

MANUBRIOTOMY VERSUS STERNOTOMY IN THYMECTOMY MYASTHENIA GRAVIS EVALUATION PULMONARY STATUS

ABSTRACT

In a prospective study, the effect of thymectomy on the pulmonary status of 50 consecutive patients with myasthenia gravis were evaluated over a time range of 4 years in the chest and chest surgery departments in the Cairo University Clinics.

The patient were divided into two groups:

Group I included 26 patients who underwent thymectomy through sternotomy. The mean age of the patients in this group was 24.8 ± 10.5 (5 - 41) years. They were 19 females and 7 males. Thirteen of the patients were in Osserman classification 2a, and 12 were in class 2b, and 1 was in class 2c.

Group II included 24 patients who underwent thymectomy through manubriotomy. The mean age of the patients in this group was 25.2 ± 9.2 (12 - 41) years. They were 13 females and 11 males. Eight of the patients were in Osserman classification 2a, 14 were in class 2b, and 2 were in class 2c.

When compared to group I in which postoperative ventilation was required in 15.4% of patients, postoperative ventilation was not necessary in patients of group II with a statistically significant difference ($p = 0.04$). The mean duration of stay in the Intensive Care unit was 111.4 hours in group II, and 169.7 hours in group I ($p = 0.03$). The Peak Inspiratory Flow Rate and the Forced Vital Capacity were also statistically significantly better in group II. There was no mortality in both groups, and the morbidity was higher in the sternotomy group.

Thymectomy through manubriotomy is the method of choice for surgical treatment of myasthenia gravis.

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INTRODUCTION

The lives of some of the patients suffering from myasthenia gravis are in almost constant danger on account of respiratory crises developing abruptly (Blaugrund et al, 1964) (1). It has been suggested that such patients may have global respiratory muscle (Black mid Hyatt, 1971) (2), and reduced pulmonary (Gibson et al,

1977) (3), and chest wall (Estenne et al, 1983) (4) compliance. Weakness of respiratory muscles may be the reason for respiratory symptoms in some myasthenic patients and may lead to more or less pronounced disturbances in pulmonary function (Rochester and Arora, 1983) (5). An improvement in respiratory muscle function and lung function indices several months after thymectomy was demonstrated (Radwan et al, 1988) (6), however, in the

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immediate postoperative period pain due to the sternotomy aggravates the ventilatory performance of the already vulnerable patients (Kirsch et al, 1991) (7). The aim of this work was to assess the effects of manubriectomy versus sternotomy as a route for thymectomy, as regards their effects on the postoperative respiratory status, which is already affected due to the myasthenic affection of the patients.

Patients and Methods

Over a time range of 4 years, 50 consecutive patients with myasthenia gravis had an en-bloc thymectomy. They were evaluated in the chest and chest surgery Departments in the Cairo University Clinics.

Inclusion criteria were the presence of myasthenia gravis for surgical excision, which is Osserman class IIa or more, regardless of age or sex.

Exclusion criteria were the presence of chest deformities, associated pulmonary and cardiac pathology, and the presence of a myasthenic crisis, or the need for preoperative plasmapheresis.

To establish the diagnosis of myasthenia, all patients had undergone a careful neurological check up prior to surgery that included physical examination, chest CT, and positive electromyography test.

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, incidence of thymoma, pre-and postoperative pulmonary functions, operating time, duration of respiratory ventilation, length of stay in the intensive care unit and overall length of hospitalization, and postoperative

complications.

Clinical assessment of the severity of the disease:

The respective levels of symptoms were graded according to the modified Osserman classification (Osserman and Genkins, 1971) (8):

-Class I indicating ocular myasthenia only,

-Class IIa representing mild generalized myasthenia with ocular involvement.

-Class IIb denoting moderately severe generalized myasthenia with ocular involvement and mild bulbar symptoms.

-Class IIc combining acute severe myasthenia, developing over a period of weeks or months and showing severe bulbar symptoms, with late onset severe myasthenia, showing severe bulbar involvement and gradual development from class I and II.

The patients were divided randomly into two groups:

Group A included patients who underwent thymectomy through a sternotomy.

Group B included patients who underwent thymectomy through a manubriectomy.

Pulmonary functions were performed using Sensormedix 2200 pulmonary function Lab. Flow volume loop, pre-and postbronchodilator was performed for every patient before surgery. FVC=Forced Vital Capacity (FVC), Forced Expiratory Volume in the first second (FEV1), Peak Expiratory Flow Rate (PEFR), Peak Inspiratory Flow Rate (PIFR) were chosen as major airway function indices, and the mean forced

expiratory flow during the middle half of the forced vital capacity (FEF 25-75) represented the small airway function.

Preoperative 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.

During anesthesia, the administration of muscle blocking agents was avoided. Intravenous opioids were used cautiously, because inadequate analgesia can lead to severe postoperative respiratory compromise. As regards prophylactic antibiotics, no aminoglycosides or tetracyclines or penicillins were used as they can potentiate the myasthenic effects. Instead cephalosporines were used (Schalke, 1998) (9).

The operation was performed under general anesthesia using a single lumen tube.

In both groups the maximal resection of the thymus gland and ectopic tissue was deemed mandatory for surgical success and improvement of the disease, and every effort was done to achieve it.

Patients were extubated in the operating room if possible.

After surgery, all patients were taken directly from the operating room to the intensive care unit. In the postoperative period, the patients were administered intravenous neostigmine, based on their preoperative total daily dose of pyridostigmine in a ratio of 1:60 neostigmine to pyridostigmine.

Patients were changed from intravenous neostigmine to oral pyridostigmine as soon as they were able to take medications by mouth.

The following variables were monitored postoperatively. hemodynamic and

respiratory parameters, and the duration of postoperative intubation and ventilation.

Ten days postoperatively pulmonary functions were performed according to the preoperative scheme.

Statistics

Associations between qualitative variables were tested using Chi-square and Fisher's exact test.

The Student's t-test for equality of means with 2-Tail significance was also used. All values are presented as mean + standard deviation (SD), and the standard error of mean was calculated, and p values were used, where the level of significance was set at $p < 0.05$.

Results

There were 32 females and 18 males with age ranging from 5 to 41 years, with a mean of 25 ± 9.6 years. Twenty-one of the patient, were in Osserman classification IIa, 26 were in class IIb, and 3 were in class IIc.

None of the patients had either thoracic deformity or any disease of the heart or of the respiratory organs. Radiological signs indicative of pleuropulmonary disease were also absent in all the cases. Group I included 26 patients who underwent thymectomy through a sternotomy. The mean age of the patients in this group was 24.8 ± 10.5 (5 - 41) years. They were 19 females and 7 males. Thirteen of the patient were in Osserman classification 2a, and 12 were in class 2b, and 1 was in class 2c.

Group II included 24 patients who underwent thymectomy through a manubriotomy. The mean age of the patients in this group was 25.2 ± 9.2 (12 - 41) years. They were 13 female and 11 males. Eight of the patients were in Osserman classification 2a., 14 were in class 2b, and 2 were in class 2c.

Table (1): Preoperative data in 50 patients with myasthenia gravis for thymectomy.

Preoperative Variable	All (N = 50)	Sternotomy group (N=26)	Manubriotomy group (N=24)	P-value
Age range at onset of disease (Year) Mean \pm SD	4-38 22.1 \pm 8.9	4-38 21.5 \pm 9.6	8-34 22.7 \pm 8.2	P>0.05
Duration range of disease (month) Mean \pm SD	2-108 35.1 \pm 32.3	2-108 40.3 \pm 35.6	2-84 29.4 \pm 27.9	P>0.05
Age range at operation (year) Mean \pm SD	5-41 25 \pm 9.6	5-41 24.8 \pm 10.5	12-41 25.2 \pm 9.2	P>0.05
Sex (Female: Male)	32:18	19:7	13:11	P>0.05
Incidence of thymoma (%)	3 (6%)	1 (3.8%)	2 (8.3%)	P>0.05
Level of symptoms Osserman classification: Class I (%)	0	0	0	P>0.05
Class II a (%)	21 (42%)	13 (50%)	8 (33.3%)	
Class II b (%)	26 (52%)	12 (46.2%)	14 (58.3%)	
Class II c (%)	3 (6%)	1 (3.8%)	2 (8.3%)	
Pyridostigmine (%) Range (mg/day) Mean \pm SD	100% 60-360 223.2 \pm 82.2	100% 180-360 228.4 \pm 61.2	100% 60-360 217.5 \pm 101.3	P>0.05
Steroid (%) Range (mg/day) Mean \pm SD	10 (20%) 0-60 7.6 \pm 17.6	4 (15.3%) 0-30 4.6 \pm 11.0	6 (24.9%) 0-60 10.8 \pm 22.6	P>0.05

As displayed in Table 1, there were no significant differences in patient profile in both groups as to patient age at onset of the disease or at operation, duration of the disease, sex ratio, rate of thymoma, preoperative level of symptoms, or preoperative medication.

When we compared the respiratory functions of both groups preoperatively (Table 2), we found no significant differences between the two groups.

Table 3 shows the intraoperative data for

both groups as regards removal of pericardial fat, and opening the right or left pleura, where it became evident that through the manubriotomy approach less has been resected, and the pleurae are less frequently opened.

Striking differences could be demonstrated in table 4 as regards need for postoperative intubation, length of postoperative ventilation, and length of ICU stay, showing a statistically significant improvement in these items in the manubriotomy group.

Table (2): Respiratory function preoperatively in 50 patients with myasthenia gravis for thymectomy.

Respiratory Functions	All N = 50	Sternotomy N = 26	Manubriotomy N = 24	P-value
FVC (%)	58-100 69.6±10.5	58-84 67.2±6.7	58-100 72.33±13.12	P>0.05
FEV1 (%)	58-115 70.8±13.9	58-79 67±5.4	60-115 75±18.5	P>0.05
PEFR (%)	45-89 61.6±9.5	45-69 60±6.3	54-89 63.3±11.9	P>0.05
PIFR (%)	49-70 58.3±5.5	49-67 58.5±5.2	52-70 58.1±5.9	P>0.05
FEF 25-75 (%)	50-83 58.6±8.1	50-64 57.5±3.9	50-83 59.8±11	P>0.05

FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the first second; PEFR = Peak Expiratory Flow Rate; PIFR = Peak Inspiratory Flow Rate; FEF 25-75 = mean forced expiratory flow during the middle half of the forced vital capacity.

Table (3): Intraoperative data in 50 patients with myasthenia gravis for thymectomy.

Intraoperative Data	All N = 50	Sternotomy N = 26	Manubriotomy N = 24	P-value
Left pleura opened (%)	17 (34%)	13 (50%)	4 (16.7%)	0.013
Right pleura opened (%)	17 (34%)	17 (65%)	0 (0%)	<0.001
Pericardial fat removed (%)	20 (40%)	18 (69.2%)	2 (8.3%)	0.008
Thymoma present (%)	3 (6%)	1 (3.8%)	2 (8.3%)	P>0.05

Table (4): Postoperative data in 50 patients with myasthenia gravis after thymectomy.

Postoperative Data	All N = 50	Sternotomy N = 26	Manubriotomy N = 24	P-value
Postoperatively Intubated (%)	10 (20%)	6 (23.1%)	4 (16.7%)	P>0.05
Postoperatively Ventilated (%)	4 (8%)	4 (15.4%)	0 (0%)	0.045
Postoperative Ventilation time range (hours) Mean ± SD	0-173 12.6±95.2	0-173 24.3±58.6	0	0.044
ICU stay range (hours) Mean ± SD	48-456 142.4±95.2	48-456 169.7±110.7	72-240 111.4±62.8	0.03

Table (5): Respiratory function postoperatively in 50 patients with myasthenia gravis after thymectomy.

Respiratory Functions	All N = 50	Sternotomy N = 26	Manubriotomy N = 24	P-value
FVC (%)	59-102 70.6±10.4	59-81 67.2±5.5	63-102 74.3±13	0.01
FEV1 (%)	59-116 72.5±13.6	59-80 69.2±5.1	62-116 76.0±18.5	P>0.05
PEFR (%)	59-90 66.2±7.9	59-69 65.1±3.8	59-90 67.3±10.7	P>0.05
PIFR (%)	42-67 52.5±5.5	42-57 49.9±4.3	49-67 55.2±5.6	0.001
FEF 25-75 (%)	52-96 63.4±10.6	52-70 60.9±4.7	53-96 66.0±14.2	P>0.05

FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the first second; PEFR = Peak Expiratory Flow Rate; PIFR = Peak Inspiratory Flow Rate; FEF 25-75 = mean forced expiratory flow during the middle half of the forced vital capacity.

Table (6): Postoperative mortality and morbidity in 50 patients with myasthenia gravis after thymectomy.

	All N = 50	Sternotomy group N = 26	Manubriotomy group N = 24
In-hospital mortality	0	0	0
Abnormal wound healing	8 (16%)	3 (11.5%)	5 (20.8%)
Mediastinitis	2 (4%)	2 (7.7%)	0
Pneumonitis	6 (12%)	4 (15.4%)	2 (8.3%)
Phrenic palsy	1 (2%)	1 (3.8%)	0

Ten days postoperatively pulmonary functions were performed (table 5) and showed that the FVC and PIFR were significantly higher postoperatively in the manubriotomy group than in the sternotomy group. At the same time all other pulmonary function tests performed showed better values in the manubriotomy group, although not statistically significant. The mean FEV1% increased from the preoperative value 70.8% to a postoperative value of

72.50% with a p-value < 0.001.

The respective complication rates are depicted in table 6. It is obvious that the trend is towards a higher complication rate in the sternotomy group as regards development of mediastinitis, pneumonitis, and phrenic palsy.

There was no hospital mortality in either approach.

Discussion

Thymectomy is recognized currently as standard effective therapy complementing the medical management of patients with generalized myasthenia gravis (Bril et al, 1998) (10), but the optimal surgical approach remains controversial (Jaretzki, 1997) (11).

Maximal thymectomy

The beneficial effect of thymectomy is thought to be maximized by the removal of all thymic tissue, including ectopic thymic tissue (Bulkley et al, 1997(12), Masaoka et al, 1996 (13); Jaretzki et al, 1988)(14).

Anatomic studies (Jaretzki and Wolff, 1988 (15); Masaoka et al, 1975 (16) have proven that islets of ectopic thymic tissue can be present in mediastinal and cervical fat. Thus, the extended transsternal approach and the transcervical-transsternal approach have been advocated to maximize the completeness of thymectomy and improve results. Jaretzki and associates in 1988 (14) stressed in their original work on the fact, that their aim was not a "total", but a "maximal" thymectomy, because ectopic microscopic thymic always remains in the myasthenic patients in spite of all efforts of the surgeons. Through their "maximal" thymectomy through the "extended" transsternal approach, they reported very good long term results in their patients with a 46% remission rate.

Other surgeons however (De Filippi et al, 1994 (17); Cooper et al, 1988 (18) , prefer the less invasive transcervical approach because they believe that it also allows performance of a complete thymectomy.

Bril and colleagues recently reported in 1998 (10) an excellent long-term remission rate (45%) with the improved transcervical thymectomy, advocated by Cooper and

associates in 1988 (18) , which matches the results after en bloc transcervical-transsternal "maximal" thymectomy of Jaretzki et al, 1988 (14) with their long-term remission rate of 46%.

The partial sternum-splitting (manubriotomy) technique seemed to be a rational compromise between the extended incisions for cervicomediastinal thymectomy, which is very invasive, and the limited incision for transcervical thymectomy, which might not allow for a complete thymectomy. Gracey and associates in 1984 (19) reported about thymectomy through a manubriotomy with good immediate postoperative results. They stated that only 9.4% of their patients needed postoperative mechanical ventilation, and that these were preoperatively in Osserman classes IIb and IIc, with significant bulbar symptoms.

As there are several reliable approaches that allow thymectomy to be accomplished on the basis of different philosophies, it seems logical to assume that a less invasive but still radical approach, which is Video-assisted thoracoscopic (VATS) thymectomy is desirable and may facilitate the goal of early thymectomy (Mineo et al, 2000) (20). It combines the minimal surgical trauma of the transcervical approach and the excellent visualization of the anterior mediastinum of the transsternal approach, and its first results are encouraging (Mineo et al, 2000 (20) . Mack et al, 1997) (21) .

Pulmonary Status after thymectomy

Evaluation of preoperative pulmonary functions in myasthenic patients is considered vital by different authors, as these might indicate the necessity for postoperative mechanical ventilation, and for special precautions postoperatively for prevention of postoperative pulmonary complications (Naguib et al, 1996 (22); Baraka, 1992 (23)).

Frequent monitoring of vital capacity is useful but should not substitute for clinical evaluation of the patient's weakness ability to protect the airway, and the trend in arterial blood gases (Matthay, 1995)(24) . There are four particularly helpful risk factors in predicting the need for postoperative mechanical ventilation in patients undergoing thymectomy: duration of myasthenia gravis, history of chronic respiratory disease, pyridostigmine dosage above 750 mg/day, and preoperative vital capacity of less than 2.9 litres (Leventhal et al, 1980) (25) . Loach considered a vital capacity below 2,0 liters as a prediction for the need of postoperative mechanical ventilation. (Loach et al, 1975) (26) . This could not be correlated with our results as we excluded patients with associated pulmonary pathology and the presence of myasthenic crisis, and none of our patients needed pyridostigmine in a dose higher than 360 mg/day.

On the other hand, the value of pulmonary functions for the prediction of postoperative mechanical ventilation has been questioned by various authors, who considered these predictors as lacking the necessary sensitivity (Brussel, 1998) (27) .

The fact is, patients with myasthenia gravis face major pulmonary problems as part of their disease process, as the myasthenic forced vital capacities are significantly lower than those for normal subjects (Litchfield and Noroian, 1989) (28) . Due to expiratory weakness, cough efficacy is reduced and may lead to postoperative pulmonary complications (Younger et al, 1984) (29). The preoperative data of the patients in our study have demonstrated the same findings in the form of a FVC of 69.6% and all FEVI of 70.8% of predicted values.

The risk of postoperative respiratory insufficiency was estimated to be 50% higher for patients after transsternal thymectomy (Drachman, 1994) (30) .

This increased risk with median sternotomy for thymectomy is related to impaired pulmonary mechanics after a major chest incision. Splinting of the chest, damage to the phrenic nerves, mediastinal infection, a higher pain medication requirement, and postoperative pulmonary complications such as atelectasis and pneumonia have all been cited as disadvantages to the transsternal approach (Wechsler and Olanow, 1980) (31) .

The data from our study show that the postoperative pulmonary status of the patients undergoing thymectomy through a manubriotomy approach was significantly better than those who had a sternotomy approach. This was reflected by the necessity of postoperative ventilation, the duration of postoperative ventilation, and the duration of ICU stay.

The pathophysiology of myasthenia gravis entails the autoimmune mediated binding of antibodies to the acetylcholine receptors, followed by their lysis by complement-mediated factors. Striking clinical improvement may occur after thymectomy without change in measurable immune parameters, including the absence of change in serum levels of auto antibodies (Roberts and Kaiser, 1998) (32). This observation can explain the significant improvement in the pulmonary function parameters in this study, namely the FEVI done 10 days postoperatively. Despite the expected deterioration in FVC and FEVI due to pain following sternotomy or manubriotomy. The mean FEVI % increased from 70.8% to 72.5% with p-value < 0.001. An explanation to this early

postoperative improvement in the pulmonary functions is the optimization of therapy during the postoperative intensive care unit stay.

Ten days postoperatively pulmonary functions showed that the FVC and PIFR were significantly higher postoperatively in the manubriotomy group than in the sternotomy group. At the same time the Forced Expiratory Volume in the first, second (FEV1); the Peak Expiratory Flow Rate (PEFR), and the mean forced expiratory flow during the middle half of the forced vital capacity (FEF 25-75) showed better values in the manubriotomy group, although not statistically significant.

Mortality and Morbidity after thymectomy

In our study, as well as in recent other studies, no mortality was encountered irrespective of surgical approach (Detterbeck et al, 1996 (33) . Yim et al, 1995 (34) ; DeFilippi et al, 1994 (17) . Frist et al, 1994 (35)). Morbidity rates have differed, depending on the approach chosen for thymectomy:

Owing to its less invasive nature, transcervical thymectomy is rarely accompanied by major complications (DeFilippi et al, 1994 (17). Cooper. et al, 1988 (18) . Cooper and co-workers reported in 1988 (18) a wound infection rate of 1.5% and one case of postperi. cardiotomy syndrome, whereas DeFilippi. and associates in 1991 (17) found no major complications.

Video-assisted thoracoscopic surgery has only recently appeared on the scene. In terms of postoperative morbidity, the preliminary figures after thoracoscopic thymectomy seemed to be slightly higher at the beginning compared to those after transcervical thymectomy. Yim and associates in 1995 (34) gave a complication rate of 12.5% for pneumonia. In 2000

however, Mineo and associates (20) reported no major morbidity, but only minimal chest pain in 6.5% of patients related to the trocars at 6-month follow-up.

As argued by the proponents of the transsternal approach, diminished morbidity rates after transcervical and thoracoscopic thymectomy are unlikely to compensate for the perceived disadvantage of leaving behind thymic tissue in the anterior mediastinum which is not readily accessible through these approaches (Machens et, al, 1998) (36) .

Unlike transcervical thymectomy, transsternal thymectomy with extensive resection of the parathymic fat pad carries a substantial risk of nerve damage. In myasthenic patients with already compromised respiratory muscle function, nerve palsies may amount to catastrophic injuries (Jaretzki et al, 1988) (11) .

Several investigators reported on the postoperative complications after transsternal 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% to 16% in the form of sternal fistula, wound infection, seroma, and hematoma, keloid formation, and defective wound healing. Atelectasis and Pneumonia occurred at a rate of 8-14%. thrombosis related complications occurred at a rate of 12.7% (Machens et al, 1998 (36) ; Spath et al, 1987) (37) .

Jaretzki and associates in 1988 (14) rated the risk of postoperative empyema, deep sternal wound infection, sternal wound dehiscence, chylothorax, and pulmonary embolism at 1% each.

As regards postoperative complications in our sternotomy approach group, the incidence was similar to the reviewed literature reports, with mediastinitis being 7%, pneumonitis 15.4%, and phrenic nerve

palsy 3.8%. This was higher than in the manubriotomy group, where mediastinitis was not encountered, the incidence of pneumonitis was reduced to 8.3% and phrenic nerve palsy did not occur, which make the complications with the mediastinotomy approach very near to those reported in the literature for the cervical approach and for the Video-assisted thoracoscopic surgery. All these mentioned complications affect indirectly the pulmonary status of the patients, which is of specific concern for the myasthenic patterns who may have global respiratory muscle weakness (Black and Hyatt, 1971) (4).

Conclusion

Our data indicate that thymectomy through a manubriotomy, which allows extensive removal of ectopic thymic tissue in addition to the thymus through a less invasive approach than a full sternotomy, is associated with a significantly smoother postoperative course and less pulmonary complications, when compared with thymectomy through a full sternotomy. On the other hand it allows a more extensive removal of ectopic thymic tissue from the mediastinum, which a cervical approach would not be able to reach, thus improving the long-term remission rate of the myasthenic patients.

Thus, thymectomy through a manubriotomy should be the method of choice for surgical treatment of myasthenia gravis, until the long-term results of Video-assisted thoracoscopic surgery prove it as efficient in addition to being less invasive.

References

- 1- Blaugrund SM, Rosin HB, Genkins G, and Osserman KE. Studies in myasthenia gravis. The role of thymectomy and controlled ventilation. *Ann Otol Rhinol Lar* 73: 618, 1964.
- 2- Black L, Hyatt R. Maximal static respiratory pressures in generalized neuromuscular disease. *Am Rev Respir Dis*; 103:641, 1971.
- 3- Gibson GJ, Pride NB, Newsom Davis J, Loh LC. Pulmonary mechanics in patients with respiratory muscle weakness. *Am Rev Respir Dis* 115: 389, 1977
- 4- Estenne M, Heilpom A, Delhez L, Yernault J, De Troyer A. Chest wall stiffness in patients with chronic respiratory muscle weakness. *Ant Rev Respir Dis* 128: 1002, 1983.
- 5- Rochester DF, Arora NS. Respiratory muscle failure. *Med Clin North Am* 67: 573, 1983.
- 6- Radwan L, Strugalska M, Kozirowski A. Changes in respiratory muscle function after neostigmine injection in patients with myasthenia gravis. *Eur Respir J* 1: 119, 1988
- 7- Kirsch JR, Diringer MN, Borel CO, Hanley DF, Meriitt WT, Bulkley GB. Preoperative lumbar epidural morphine improves postoperative analgesia and ventilatory function after transsternal thymectomy in patients with myasthenia gravis. *Crit Care Med* 19: 1474, 1991.
- 8- Osserman KF, Genkins G. Studies on myasthenia gravis. Review of a twenty-year experience in over 1200 patients. *M Sinai J Med* 38: 4 97, 1971.
- 9- Schalke B. Therapeutic concepts in the treatment of myasthenia gravis. *Z Herz, Thorax-, Gefaßchir* 12: 282, 1998.
- 10- Bril V, Kojic J, Ilse, WK, Cooper. ID.

- Long-term clinical outcome after transcervical thymectomy for myasthenia gravis. *Ann Thorac Surg*, 65:1520, 1998.
- 11- Jaretzki A III. thymectomy for myasthenia gravis: analysis of the controversies regarding technique and results. *Neurology* 48 (Suppl 5): S52, 1997.
 - 12- Bulkley GB, Bass KN, Stephenson GR, Diener-West M, George S, Reilly P, Baker R, Drachman D. Extended cervicomediastinal thymectomy in the integrated management of myasthenia gravis. *Ann Surg* 226:324, 1997.
 - 13- Masaoka A, Yamakawa Y, Niwa H, Fukai I, Kondo S, Kobayashi M, Fujii Y, Monden Y. Extended thymectomy for myasthenia gravis patients: a 20-year review. *Ann Thorac Surg* 62:853, 1996.
 - 14- Jaretzki A III, Penn AS, Younger DS, Wolff M, Olarte NR, Lovelace I?,E., Rowland LP. "Maximal" thymectomy for myasthenia gravis. *Results. J Thorac Cardiovasc Surg* 95:747, 1988.
 - 15- Jaretzki A III, Wolff M. "Maximar" thymectomy for myasthenia gravis. *Surgical anatomy operative techniques. J Thorac Cardiovasc Surg* 96:711, 1988.
 - 16- Masaoka A, Nagakoa Y, Kotabe Y. Distribution of thymic tissue at the anterior mediastinum: current procedure in thymectomy. *J Thorac Cardiovasc Surg* 70:747, 1975.
 - 17- DeFilippi VJ, Ricluman DP, Ferguson MK. Transcervical thymectomy for myasthenia gravis. *Ann Thorac Surg* 57:194, 1994
 - 18- Cooper JD, Al-Jilaihawa AN, Pearson FG, Humphrey JG, Humphrey HE- An improved technique to facilitate transcervical thymectomy for myasthenia gravis. *Ann Thorac Surg* 45:242, 1988.
 - 19- Gracey D, Diverlie M, Howard F Jr, Oayne W. Postoperative respiratory care after transsternal thymectomy in myathenia gravis. A 3-year experience in 53 patients. *Chest* 86: 67, 1984
 - 20- Mineo T, Pompeo E, Lerut T, Bernardi G, Coosemans W, Nofroni. I. Thoracoscopic Thymectomy in Autoimmune Myasthenia: Results of Left-Sided Approach. *Ann Thorac Surg* 69: 1537, 2000
 - 21- Mack MJ, Scruggs GR, Kelly KM, Shennib H, Landreneau RJ. Video-assisted thoracic surgery: has technology found its place? *Ann Thorac Surg* 64:211, 1997.
 - 22- Naguib M, Dawlatly A, Ashour M, Bamgboye E. Multivariate defeminants of the need for postoperative ventilation in myasthenia gravis. *Can J Anaesth* 43: 1006, 1996.
 - 23- Baraka A. Anaesthesia and myasthenia gravis. *Can J Anaesth* 39: 476, 1992.
 - 24- Matthay M. Acute hypercapnic respiratory failure: Neuromuscular and obstructive diseases. In *Chest medicine*. Eds Georg R, Light R, Matthay M, Matthay R. 3rd edition. Williams & Wilkins. Baltimore, Philadelphia, Hong Kong, London. P 578, 1999.
 - 25- Leventhal S, Orkin F, Hirsh R. Prediction of the need for postoperative mechanical ventilation in myasthenia gravis. *Anesthesiology* 53: 20, 1980
 - 26- Loach A, Young A, Spalding J. Postoperative management after thymectomy. *BMJ* 1: 309, 1975
 - 27- Brussel T. Anesthetic management of

- patients with myasthenia, gravis. Z Herz, Thorax, Gefäßchir 12: 271, 1998
- 28- Litchfield M, Noroian. E. Change in selected pulmonary functions in patients diagnosed with myasthenia gravis. J Neurosci Nurs 21: 375, 1989.
- 29- Younger D, Braun N, Jaretzkj A III, Penn A, Lovelace R. Myasthenia gravis: determinants for independent ventilation after transsternal thymectomy. Neurology 34: 336, 1981.
- 30- Drichuman DB. Myasthenia gravis. N Engl J Med 330: 1797, 1994.
- 31- Wechsler A, Olanow C. Myasthenia gravis. Surg Clin North Am 60: 946, 1980.
- 32- Roberts J, Kaiser L. Acquired lesions of the mediastinum. In Fishman's pulmonary diseases and disorders. Ed: Fishman A, Elias J, Fishman J, Grippi M, Kaiser 1, Senior R. 3rd edition. McGraw Hill New York, London, Tokyo, Toronto. P 1525, 1998.
- 33- Detterbeek F, Scot W, Howard J Jr, Egan F, Keagy B, Starek J, Mill 14, Wilcox B. One hundred consecutive thymectomies for myasthenia gravis. Ann Thorac Surg 62: 242, 1996.
- 34- Yim A, Kay R, Ho J. Video-assisted thoracoscopic thymectomy for myasthenia gravis. Chest 108: 1440, 1995.
- 35- Frist W, Thirumalai S, Doehring W, Stewart J, Stewart, J, Fenichel G, Bender H Jr. Thymectomy for the myasthenia gravis patient: factors influencing outcome. Ann Thorac Surg 57:334, 1994.
- 36- Machens A, Busch C, Emskotter Th Izbicki J. Morbidity after transsternal thymectomy for myasthenia gravis. A changing perspective? Thorac Cardiovasc Surg 46: 37, 1998.
- 37- Spath G, Brinkmann A, Huth C, Wietholter H. Complications and efficacy of transsternal thymectomy in myasthenia gravis. Thorac Cardiovasc Surg. 35: 283, 1987.

SAFETY OF ORAL ANTICOAGULATION THERAPY DURING PREGNANCY IN PATIENTS WITH MECHANICAL MITRAL VALVES

ABSTRACT

In order to evaluate the safety of oral anticoagulants on gravid patients and their offsprings, 27 females with mitral (\pm aortic) St. Jude mechanical valves were prospectively followed-up during 29 pregnancies. Sixteen patients were anticoagulated with phenindione and 11 (39.3%) received, in addition, 225 mg dipyridamole, given in 3 divided portions. The target INR was 2.5-3.5 in the former and 2-2.5 in the latter mode of therapy. A fortnight before delivery, intravenous heparin therapy was substituted.

There were no maternal complications, apart from a single nonfatal postpartum hemorrhage (3.7%). The outcome of pregnancy was: 24 mature babies (82.8%), 3 prematures (9.7%) and 2 cases of stillbirth (6.4%). Outcome was dose-related: being 55.8 ± 17.9 mg/d for mature babies and 82.5 ± 11.2 mg/d for prematures and stillbirths ($P=0.03$). Combined therapy allowed receiving smaller phenindione doses and was less associated with prematurity and stillbirth, compared to monotherapy ($P>0.05$).

The use of phenindione (\pm dipyridamole) provided a safe and an effective anticoagulation therapy during pregnancy. As the likelihood of fetal complications appeared to be dose-related, patients should receive the smallest dose necessary to achieve the target INR.

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INTRODUCTION

The most suitable anticoagulation regimen for pregnant patients with mechanical cardiac valves is still controversial. Two regimens have been recommended: either oral anticoagulation therapy throughout pregnancy except 3-4 weeks prior to planned delivery, or heparin during the first trimester followed by oral anticoagulation as in the first alternative (1,2). The aim of this prospective study was to evaluate the outcome of pregnancy in patients receiving phenindione (Dindivan®) therapy, with or without dipyridamole throughout pregnancy.

Material and Methods

In the period between January 1991 and January 1998, we prospectively followed-up 29 pregnancies in 27 women with St. Jude mechanical mitral (\pm aortic) valve prostheses. Table (1) shows the patients' demographics at the beginning of pregnancy. According to the year of the operation, patients operated upon before September 1995 were anticoagulated with phenindione alone, while those operated upon at a later date received, in addition, 275 mg dipyridamole, given in 3 divided portions. The maximum allowed daily dose of phenindione was 100 mg. The target INR

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was 2.5-3.5 in the monotherapy group and 2-2.5 in the combined therapy group of patients.

Patients were followed-up at our department's anticoagulation clinic on a monthly basis. An echocardiographic study, a complete blood picture as well as renal and hepatic profiles were arranged for every patient bimonthly.

Two weeks before the expected time of delivery, patients were hospitalized at the maternity hospital and were shifted to heparin therapy. A loading dose of 5000 IU units was initially given intravenously, followed by a continuous IVI of 20-30 IU/kg/h through a syringe pump; so as to keep the APTT between 1.5-2 times the control. Heparin was discontinued at the onset of labor and reinitiated -together with the patient's initial oral antithrombotic therapy- 24 hours after delivery. Once the targeted INR was reached, heparin therapy was discontinued. On the other hand, emergency Cesarean section was arranged for mothers presenting with premature labor while phenindione therapy was still in effect.

Statistical study: Data were analyzed with the SPSS software for windows (release 7.5, 1996). Differences between categorical variables were assessed by Chi-square contingency analysis or Fischer's exact test as indicated. Continuous variables were expressed as means (\pm sd) and were analyzed by the non-parametric Mann and Whitney test. A P-value of ≤ 0.5 was considered significant.

Results

Both pregnancy and delivery were

hemodynamically well tolerated by all mothers. The bimonthly-arranged investigation battery showed no significant changes from that recorded at the onset of pregnancy. The daily phenindione dose varied from 12.5 to 100 mg with a mean value of 62.5 ± 21.9 mg. The achieved INR varied from 1.5 to 3.4 with a mean value of 2.3 ± 0.36 . Unsurprisingly, and through targeting a lower INR range, patients on combined therapy received smaller daily phenindione doses (55.7 ± 21.9 , range: 12.5-87.5 mg) compared to those received by patients on phenindione monotherapy (66.7 ± 21.4 , range: 25-100 mg; $P>0.05$). No oral anticoagulant-related complications were recorded throughout pregnancy, delivery or postpartum period. Delivery was vaginal in 27 pregnancies (93.1%) and by emergency Cesarean section in 2 cases due to premature onset of labor. In another case (3.4%), the patient has developed postpartum hemorrhage necessitating blood transfusion and delaying the re-initiation of heparin therapy.

Twenty-seven healthy babies were born (93.1%): 26 were mature (82.8%) and 3 were premature (10.3%). We had 2 cases of stillbirth (6.9%), however, no spontaneous abortion, intrauterine fetal death, neonatal death, embryopathy or central nervous system abnormalities were recorded. Both cases of stillbirth and 2 out of the 3 premature babies belonged to the monotherapy group of patients ($P>0.05$). As, shown in figure 1, pregnancy outcome was significantly related to the mean daily dose of phenindione; being 58.3 ± 21.4 mg for mature babies and 82.5 ± 11.2 mg for prematures and still births ($P=0.03$).

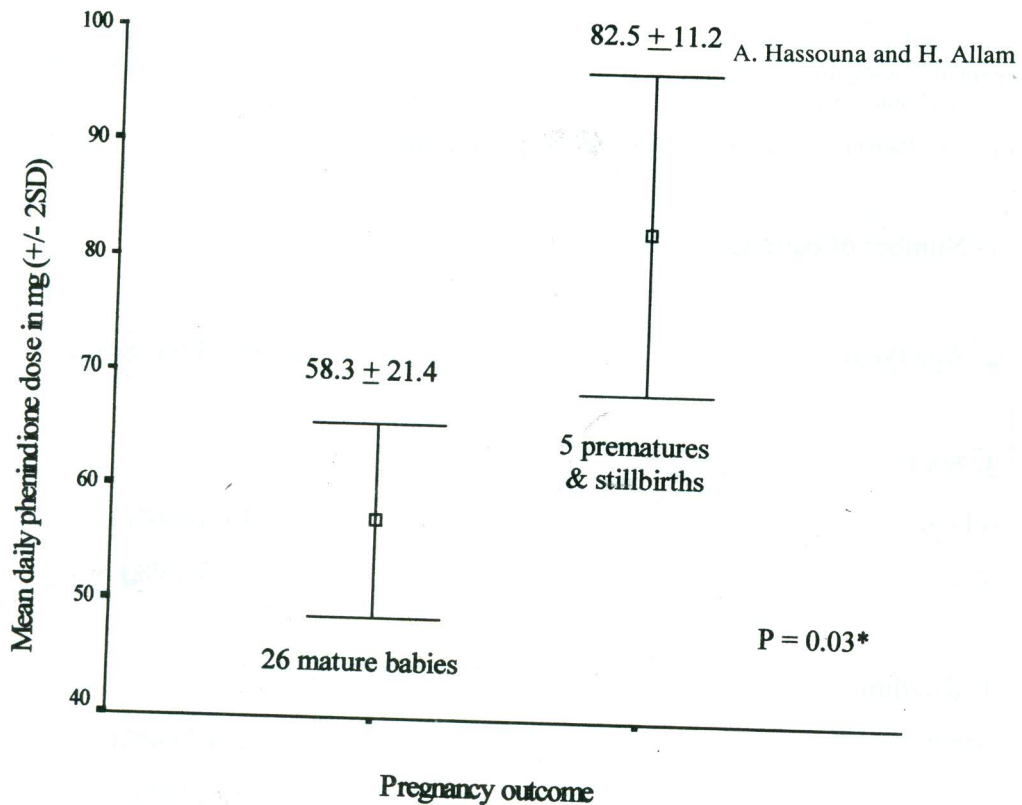


Figure (1): Pregnancy outcome as related to mean daily phenindione dose. Values are presented as mean \pm 2 SD, * = Mann and Whitney test.

Discussion

Although women with mechanical cardiac valves can generally tolerate pregnancy and delivery, the use of oral anticoagulants still represents a double jeopardy to both: the mother and the fetus. Physiologically, pregnancy is a hypercoagulable state, which may favor the likelihood of maternal thromboembolism (3). Moreover, coumarin derivatives are alleged to increase fetal wastage by bringing the risks of warfarin embryopathy during the first trimester, central nervous system damage throughout pregnancy and neonatal bleeding when their fetal anticoagulant effect is furtherly sharpened by the trauma

of delivery (4).

Maternal outcome: heparin has been suggested to replace oral anticoagulants for being able to achieve effective anticoagulation; while being safe due to the inability of its large molecule to cross the placenta. However, the use of use of subcutaneous heparin so as to prolong the APTT to 1.5-2.5 times the control was associated with as much as 5.4% rate of fatal maternal valve thrombosis (5). Moreover, comparative studies have demonstrated statistically significant higher rates of mechanical valve thrombosis, thromboembolic events (5,6) and bleeding (5) in patients on subcutaneous heparin,

Table (1): Patients demographics at the beginning of pregnancy.

1- Number of patients	27
2- Age (years)	25.9 ± 3.9 (18-32)
3- NYHA functional class	
-class I	18 (66.6%)
-class II	9 (33.3%)
4- Rhythm	
-sinus	19 (70.4%)
-AF	8 (29.6%)
5- Position of prosthesis	
-mitral	21 (77.7%)
-mitral and aortic	6 (22.2%)
6- Duration of implantation (years)	2.9 ± 1.1 (1-6)

Values are presented as numbers (%) or mean ± SD (range).

compared to those receiving oral anticoagulants. In view of these data, oral anticoagulant therapy throughout pregnancy appeared to be safer for the mother. In our

study, no oral anticoagulant-related complications have been recorded and the single bleeding episode was a case of postpartum hemorrhage, when the patient

was just being weaned from heparin therapy.

Fetal outcome: there is a general agreement on the salutary role of heparin during the last 2-4 weeks of pregnancy (4,5, 7-9). Through its short duration of action, the use of heparin avoids the delivery of an anticoagulated infant, subjected to the trauma of vaginal delivery. In our study, patients were hospitalized during the last 2 weeks of pregnancy and oral antithrombotic therapy was replaced by continuous IV heparinotherapy. As previously recommended (5), emergency Cesarean section was carried out in 3 patients, where labor prematurely developed while the mother's phenindione therapy was still in effect. Following these guidelines, no fetal hemorrhagic complications were observed in any of our cases.

In fact, the heart of the debate is the type of anticoagulant therapy that should be followed during the first trimester and the main points of judgement are the associated rates of fetal wastage and the likelihood of congenital malformations. Fetal wastage was suggested to be due to placental hemorrhage and detachment during effective anticoagulation; a complication that may follow oral anticoagulants as well as heparin therapy (4,5). A collective review however, showed a slightly better fetal outcome in patients on subcutaneous heparin (4).

The risk of congenital malformation associated with the use of oral anticoagulants in gravid patients is estimated to be between 4-5% (4-6); representing an important medico-legal disadvantage for their use during pregnancy (5). While the reported incidence of coumarin embryopathy varied from 0% (4,8,10) to as much as 9% (6,9), no phenindione-related congenital malformations have ever been reported (11), to the best of our knowledge. The effect of intensity of anticoagulation has been verified by Cotrefu and coll. and no

fetal complications or embryopathy were recorded among patients receiving a small dose of warfarin (<5 mg / day) throughout pregnancy (10). In our study, the mean INR achieved (2.3 ± 0.36) was within the target range recommended by the major European and American societies (1,2) and the prevalence of prematurity and stillbirth were significantly related to phenindione dose ($P=0.03$). These data suggested that patients must receive the smallest dose of oral anticoagulants necessary to achieve the targeted INR, so as to decrease the likelihood of fetal complications.

Adjuvant antiplatelet therapy: In patients with mechanical mitral valves, several studies have shown that the use of adjuvant antiplatelet therapy permitted to target a lower INR range and was associated with less thromboembolic events, compared to the use of oral anticoagulants alone (12-14). However, the effect of antiplatelets on pregnancy outcome is a subject of debate (7-9). Sareli and co-workers have reported significant fetal loss with the use of warfarin and dipyridamole in a small series of 11 patients (9). On the other hand, in a large study on 47 pregnancies, the incidences of spontaneous abortion and stillbirth associated with the use of such combination (8) were well comparable to those reported with the use of oral anticoagulants alone (4,6). In our study, no fetal loss was reported among the 11 patients who were receiving phenindione and dipyridamole throughout pregnancy. Until a large randomized study is conducted to compare pregnancy outcome in patients receiving monotherapy to that of patients benefiting from combined therapy, the exact effect of antiplatelets will remain unclear.

In Conclusion

The use of phenindione (\pm dipyridamole) was a safe and an effective prophylaxis against thromboembolism for pregnant

patients with mechanical mitral (\pm aortic) valve prostheses. In the absence of drug-induced major side effects, toxicity or congenital malformations, phenindione can provide an attractive alternative to the more commonly used coumarin derivatives. As the likelihood of fetal complications appeared to be dose-related, patients should receive the smallest dose necessary to achieve the target INR.

References

- 1- Ad Hoc Committee of the Working Group on Valvular Heart Disease: guidelines for prevention of thromboembolic events in valvular heart disease: Official document of the European Society of Cardiology. *J. Heart Valve Dis* 1993; 2: 398-410.
- 2- Committee on management of Patients with Valvular Heart Disease. ACC/AHA Guidelines for the management of patients with valvular heart disease. Executive Summary. A report of the American College of Cardiology / American Heart Association Task Force on Practice Guidelines. *J heart Valve Dis* 1998; 7: 672-707.
- 3- Schafer AT. The hypercoagulable states. *Ann Inter Med* 1985; 102: 814-28.
- 4- Sbarouni E and Oakley CM. Outcome of pregnancy in women with valve prostheses. *Br Heart J* 1994; 71: 196-201.
- 5- Salazar E, Izaguire R, Verdejo J, Mutchinick O. Failure of adjusted doses of subcutaneous heparin to prevent thromboembolic phenomena in pregnant patients with mechanical cardiac valve prostheses. *J Am Coll Cardiol* 1996; 27: 1698-703.
- 6- Hanania G, Thomas D, Michel PL, Garbarz E, Age C, Millaire A, Acar J. Pregnancy in patients with heart valve prosthesis. A French retrospective cooperative study (155 cases). *Arch Mal Coeur Vaiss* 1994; 87 (4): 429-37.
- 7- Elkayam U. Anticoagulation in pregnant women with prosthetic heart valves: A double jeopardy. *J Am Coll Cardiol* 1996; 27 (7): 1704-6.
- 8- Pavankumar P, Venugopal P, Kaul U, et al. Pregnancy in patients with prosthetic cardiac valve. A 10-year experience. *Scand J Thorac Cardiovasc Surg* 1988; 22 (1): 19-22.
- 9- Sareli P, England MJ, Berk MR, et al. Maternal and fetal sequelae of anticoagulation during pregnancy in patients with mechanical heart valve prosthesis. *Am J Cardiol* 1989; 63: 1462-5.
- 10- Cotrufo M, De Luca TSL, Calabro R, Mastrogianni G, Lama D. Coumarin anticoagulation during pregnancy in patients with mechanical valve prostheses. *Eur J Cardiothorac Surg* 1991; 5: 300-5.
- 11- Jenkins BS and Braimbridge MV. Management of anticoagulant therapy in patients with prosthetic heart valves. *Thorax* 1971; 26 (2): 206-11.
- 12- Hayashi JI, Nakazawa S, Oguma F, Miyamura H, Eguchi S. Combined warfarin and antiplatelet therapy after St. Jude Medical valve replacement for mitral valve disease. *J Am Coll Cardiol* 1994, 23, 672-7.
- 13- Kontozis L, Skudicky D, Hopley MJ, Sareli P. Long-term followup of St.

Jude Medical prosthesis in a young rheumatic population using low-level warfarin anticoagulation: an analysis of the temporal distribution of causes of death. *Am J Cardiol* 1998, 81 (6), 736-9.

14- Pouleur 14, Buyse M. Effects of

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dipyridamole in combination with anticoagulant therapy on survival and thromboembolic events in patients with prosthetic heart valves. A metanalysis of randomized trials. *J Thorac Cardiovasc Surg* 1995; 110: 463-72.

PULMONARY LYMPHANGIOLEIOMYOMATOSIS A RARE DISORDER PRESENTED WITH BILATERAL SPONTANEOUS PNEUMOTHORAX

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INTRODUCTION

Simultaneous bilateral pneumothorax is rare (1), and most frequently follows trauma or iatrogenic injury. It may occur following venipuncture or catheterization of the internal ingular or subclavian vessels (2), and has also been reported following tracheostomy and mediastinoscopy (3,4). While spontaneous pneumothorax is not uncommon, it is bilateral in less than 5% of cases (5). Lymphangioleiomyomatosis is a rare disease affecting young women of childbearing age with fewer than 100 cases documented in the literature by 1994 (6). The disease is characterized pathologically by diffuse atypical smooth muscle proliferation within the pulmonary interstitium surrounding and within airways, blood vessels, and lymphatic channels. It may involve the lungs, mediastinum, or abdomen in combination or separately (7). We report a female patient, with both pulmonary and extrapulmonary lymphangioleiomyomatosis, who had presented with bilateral spontaneous pneumothorax.

Case Report:

A 34 year old Indonesian, nonsmoker woman referred to the Thoracic Surgical Unit at King Fahad Specialist Hospital, Kingdom of Saudi Arabia, because of bilateral spontaneous pneumothorax. The history of chest problems started in the previous two months when she sustained

three attacks of pneumothorax on the right side and two attacks on the left side. Prior to this period the patient was completely asymptomatic with insignificant past medical or surgical history.

On examination, the patient had normal vital signs without cyanosis. There was increased resonance on percussion with reduced breath sounds over both lung fields. Chest X ray showed bilateral pneumothoraces more on the left side. Blood gases were within normal range on room air. Bilateral intercostal drains were inserted. CT scan of the chest showed diffuse small air cysts in the different lobes of both lungs (Fig. 1). Pulmonary function tests were of a mild restrictive nature. The left lung became fully expanded in a week time while the right continued to leak air with partial collapse.

Exploration of the right hemithorax revealed a diffusely distributed well defined, thin walled cysts ranging in diameter from a few millimeters up to 5 cm Lung cystectomy with pleurodesis was performed. Postoperatively the lung had full expansion without air leak. Two weeks later the same procedure was done on the left side due to recurrence of air leak. The histopathology of removed material showed mesenchymal tissue consisting of proliferating spindle cells with interspaced endothelial lined vascular spaces and lymphatics. The spindle cells have oval nuclei with blunt ends and drawn-out amphophilic cytoplasm (Fig. 2).

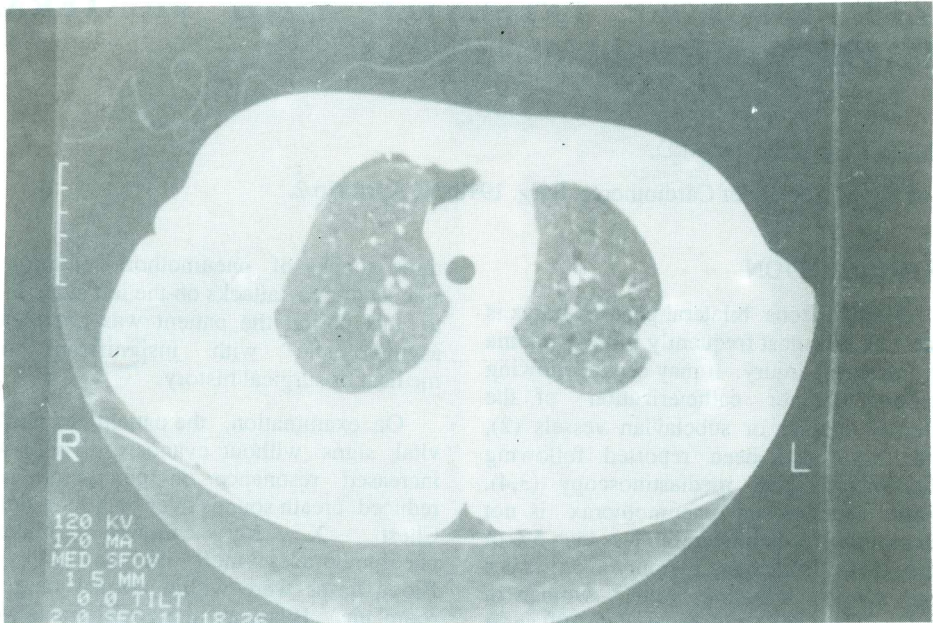


Fig. (1): CT Scan of the chest, showing multiple small thin walled cysts distributed uniformly in both lungs with residual right anterior pneumothorax.

Based on the above pathological findings, a diagnosis of pulmonary lymphangioleiomyomatosis was made. Abdominal CT (Fig. 3) revealed right renal mass measuring 7X5 cm in the upper pole of the right kidney, which gave the same histopathological features on FNAC. The patient was doing fine postoperatively during the short-term follow up without any complication. Two months later the patient travelled back home and was lost for further follow up.

Discussion

Lymphangioleiomyomatosis is a rare idiopathic disease, affects young females of childbearing age, characterized by smooth

muscle proliferation of smooth muscle cells in the walls of small airways, venules, and lymphatics of the lung, as well as mediastinal and retroperitoneal lymphatics, either individually or in combination (6,7). This results in lymphatic obstruction and chylothorax, vascular disruption with haemoptysis and airway obstruction with formation of multiple bullae and hyperinflation. The clinical picture is of progressive dyspnoea, pneumothorax, chylothorax and haemoptysis. Our patient developed a multifocal lesion affecting both lungs and right kidney.

In one series, pneumothorax was the presenting feature of

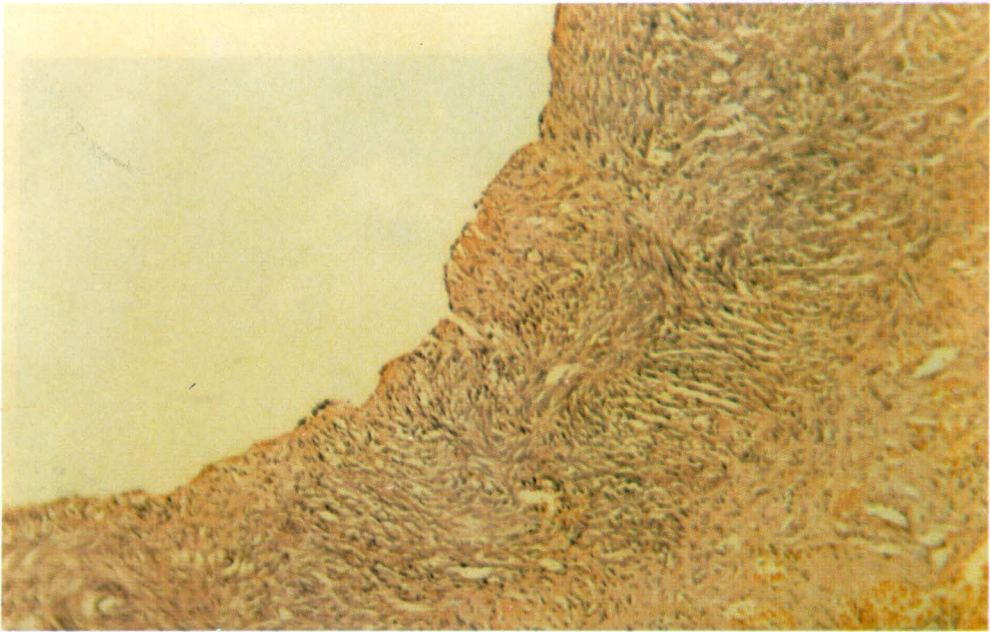


Fig. (2): Low-power view of the lung showing a dilated lymphatic vessel which is lined by flat endothelial cells with proliferation of smooth muscles around (hematoxylin-eosin, $\times 100$).

lymphangioliomyomatosis in 21% of cases, and developed at some time during the illness in 43% of cases (8). Others have found pneumothorax even more commonly present in 53% of cases at presentation, and 81% during the course of the illness (9). While unilateral pneumothorax occurring spontaneously in a young, apparently healthy female is most likely to be idiopathic, the same does not apply for pneumothorax occurring bilaterally, and in these circumstances, lymphangioliomyomatosis should be considered high amongst the diagnostic possibilities. Bilateral spontaneous pneumothorax was the only presentation of our patient although she had both pulmonary and extrapulmonary involvement. The prevalence of recurrent pneumothorax has

been addressed in the literature. Carrington et al (7) reported four patients who had 22 documented episodes of this complication. Our patient developed 7 episodes of pneumothorax on both sides of the chest before the disease entity was clarified.

Over the years, many therapeutic options have been tried. In the early literature, symptomatic or palliative treatment (pleurectomy, tube thoracostomy, thoracic duct ligation) was used extensively (10). Within the past decade, research on estrogen and progesterone receptors in the proliferating smooth cells (11, 12) has resulted in the investigation of hormonal manipulation therapy for lymphangioliomyomatosis. Various treatment modalities have been proposed,

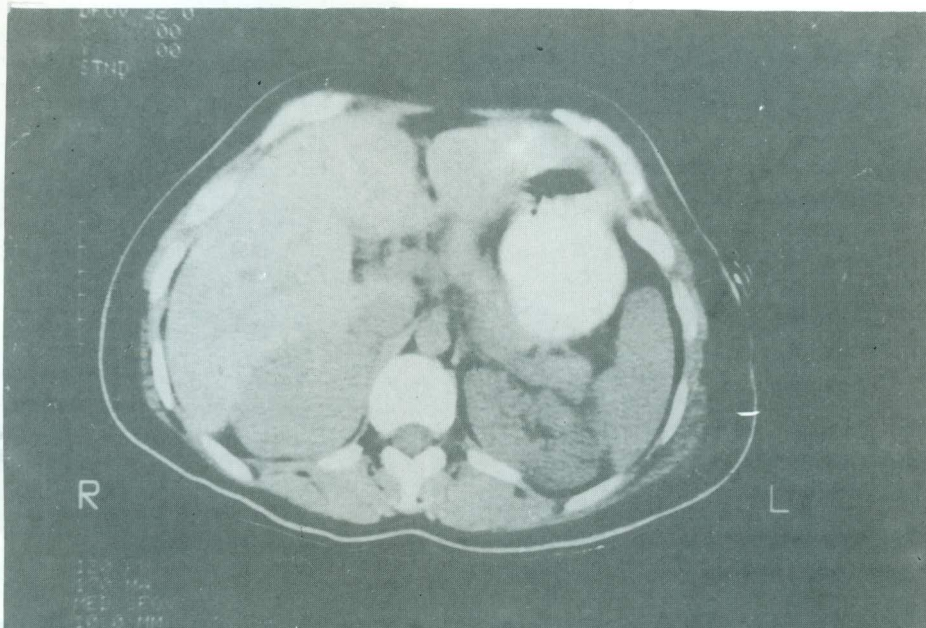


Fig. (3): CT Scan of the abdomen, demonstrating a homogenous soft tissue mass involving the upper pole of the right kidney.

including oophorectomy, antiestrogen (Tamoxifen) therapy, as well as administration of luteinizing hormone releasing agonists (9,13,14). However, the success and utility of these types of therapy have been equivocal. Recently, lung or combined heart-lung transplantation has been suggested as a therapeutic option for lymphangioleiomyomatosis. Few cases have been reported in the literature, and those procedures performed appear to have been successful (15 -17). However recurrence of lymphangioleiomyomatosis in an allograft lung after single lung transplantation has been reported (17). Although it is considered as a symptomatic or palliative treatment, bilateral pleurodesis proved to be

all effective palliative treatment in our patient at least for the short term follow up.

From the review of literature and management of this case, it is clear that LMA is considered as an unclear disease that can affect more than one organ in the body. Treatment of complications is indicated especially when it is life threatening as bilateral spontaneous pneumothorax. However, more research work is required to identify the etiology of this disease for definitive treatment.

FIG. 1. CT Scan of the chest, showing multiple small thin walled cysts distributed uniformly in both lungs with residual right anterior pneumothorax.

FIG. 2. Low-power view of the lung showing a dilated lymphatic vessel which is lined by flat endothelial cells with proliferation of smooth muscles around (hematoxylin-eosin, x 100).

FIG. 3. CT Scan of the abdomen, demonstrating a homogenous soft tissue mass involving the upper pole of the right kidney.

References

1- Donovan JP: Bilateral spontaneous pneumothorax: a rare entity. *Ann Emerg Med* 1987; 16: 1277-1280.

2- Arnold S, Peathers RS, and Gibbs E: Bilateral pneumothoraces and subcutaneous emphysema. A complication of internal jugular venipuncture. *BMJ* 1973; 1: 211-212.

3- Parkin SD: A case of bilateral pneumothorax after tracheostomy. *J Laryngol Otol* 1965; 79: 457-461.

4- Furgano FA, and Saldman LJ: Bilateral tension pneumothorax associated with mediastinoscopy. *J Thorac Cardiovas Surg* 1972; 63: 329-333.

5- Melton III LJ, Hepper NGG, and Offord KP: Incidence of spontaneous pneumothorax in Olmsted county, Minnesota: 1950 to 1974. *Am Rev Respir Dis* 1979; 120: 1379-1382.

6- Firotiz-Abadi A, Higgins JP: Pulmonary lymphangioleiomyomatosis. *Pathol* 1994; 26: 138-140.

7- Carrington CB, Cugell DW, Gaensler EA, et al: Lymphangioleiomyomatosis: physiologic-pathologic-radiologic correlations. *Am Rev Respir Dis* 1977, 116: 977-995.

8- Corrin B, Leibow AA, and Friedman PJ: Pulmonary

Lymphangioleiomyomatosis. *Am J Pathol* 1975,79: 348-367.

9- Taylor JR, Ryu J, Colby TV, and Raffin TA: Lymphangioleiomyomatosis: Clinical course in 32 Patients. *N Engl J Med* 1990, 323:1254-1260.

10- Shuman RL-Engelman R, and Kittle CF: Pulmonary lymphangioleiomyomatosis. *Ann Thoracic Surg* 1979; 27:70-75.

11- Berger U, Khaghani A, Pomerance A, Yacoub NW, and Coombes RC: Pulmonary lymphangioleiomyomatosis and steroid receptors: an immunocytochemical study. *Am J Clin Pathol* 1990, 93: 609-614.

12- Ohori NP, Yousem SA, Sonmez-Alpha E, and Colby TV: Estrogen and progesterone receptors in lymphangioleiomyomatosis, epithelioid hemangioendothelioma of the lung. *Am J Clin Pathol* 1991, 96: 529-535

13- Adamson D, Heinrichs WL, Raybin DM, and Raffin TA: Successful treatment of pulmonary lymphangioleiomyomatosis with oophorectomy and progesterone. *Am Rev Respir Dis* 1985, 132: 916-921

14- Rossi GA, Balbi B, Oddera S, Lantero S, and Ravazzoni C: Response to treatment of the luteinizing-hormone-releasing hormone in a patient with pulmonary lymphangioleiomyomatosis. *Am Rev Respir Dis* 1991, 143: 174-176.

15- Sleiman C, Mal H, Jebrak G, et al: Pulmonary lymphangioleiomyomatosis treated by single lung transplantation. *Am Rev Respir Dis* 1992, 145: 964-966.

16- Wellens F, Estenne M, de Francquen P,

Goldstein J, Leclerc JL, and Primo G:
Combined heart-lung transplantation for
terminal pulmonary
lymphangioliomyomatosis. J Thorac
Cardiovasc Surg 1985, 89: 872-876

17- Nine JS, Yousem SA, Paradis IL,
Keenan R, and Griffith BP:
Lymphangioliomyomatosis:
Recurrence after lung transplantation. J
Heart Lung Transplant 1994, 13: 714-
719.

MANAGEMENT OF PATENT DUCTUS ARTERIOSUS IN THE PREMATURE INFANTS: LIGATION VERSUS PHARMACOLOGIC TREATMENT

ABSTRACT

Between January 1995 and January 1999, a hemodynamically significant patent ductus arteriosus (PDA) associated with cardiopulmonary compromise presented in 112 premature infants who underwent pharmacologic (indomethacin) and/or surgical ductal manipulation. The PDA was closed by surgical ligation in 59 cases, and by pharmacologic means in 53 cases. Pharmacologic treatment was initially tried in 90 infants with a failure rate of 37 cases (41 %) who subsequently treated by surgical ligation. The average birth weight was 1,616 gm in the surgical group versus 1,631 gms. in the pharmacologic group, and the average gestational age was 30 weeks in the surgical group versus 32 weeks in the pharmacologic group. Among the infants who underwent surgical ligation there were 6 postoperative complications (10.2%), and 4 cases of hospital mortality (6.8%). Among the infants treated with indomethacin there were 28 post-treatment complications (52.8%), and 7 cases of hospital mortality (13.2%). The average post-treatment ventilatory support was prolonged in the pharmacologic group (38 days versus 16 days in the surgical group), as well as the total hospital stay (49 days in the pharmacologic group versus 39 days in the surgical group). Our data suggest that surgical ligation of hemodynamically significant PDA yields a more predictable result with low morbidity and mortality.

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INTRODUCTION

It is well documented that closure of hemodynamically significant patent ductus arteriosus in the face of cardiopulmonary dysfunction can result in a reduction in morbidity and mortality (1-3). In 1963, Powell (4) first reported surgical ligation of a patent ductus arteriosus in a preterm infant. Several reports have shown that surgical ligation is an effective and definitive procedure that is associated with low morbidity and mortality in the premature infants (2,5-7). Since the introduction of indomethacin (prostaglandin synthetase inhibitor) for pharmacological closure of the PDA in 1976 (8), there has

been controversy over the use of medical versus surgical therapy (7,9-12). The purpose of this report is to review our results of the surgical and pharmacological management of a hemodynamically significant PDA in premature infants.

Material and Methods

Between January 1995 and January 1999, 112 premature infants with a birth weight under 2,500 gm and gestational age less than 37 weeks underwent treatment of a hemodynamically significant patent ductus arteriosus at King Fahad Specialist Hospital in Buraydah, Kingdom of Saudi Arabia. The criteria for a hemodynamically significant PDA included: 1. Hyperdynamic

circulation, 2. bounding peripheral arterial pulses, 3. systolic or continuous murmur, 4. radiographic evidence of cardiomegaly and pulmonary congestion, and 5. echocardiographic evidence of a large PDA (enlarged left atrium and increased left atrial/aortic dimensions or ratio, and left to right shunting in contrast echocardiography). The average birth weight for the entire group was 1,623 gm (range 800 to 2,400 gm). The average gestational age was 30 weeks (range 26 to 36 weeks). Sixty-two infants (55.4%) were males and 50 infants (44.6%) were females.

Fifty-nine infants were treated surgically. Criteria for surgical ligation of the PDA in these neonates include deterioration of pulmonary function in infants with contraindications (22 Infants, i.e. 37.3%) or failure to indomethacin therapy (37 infants, i.e. 62.7%). All infants were receiving therapy with digitalis, diuretic drugs, and restriction of fluids.

The ductual ligation procedure was carried out in a heated (28°C) operating room approximately 50 meters from the Newborn Intensive Care Unit (NICU) and on the same floor. The infant was transported to the operating room in an infant incubator. During the procedure, the infant's body temperature was maintained above 36.2°C with an underlying heating pad and, at times, an overhead radiant heater. The infant is positioned on the right side and a small 3 to 5 cm posterolateral transpleural thoracotomy incision was used to enter the chest through the fourth intercostal space. The PDA was ligated with two No. 2/0 silk sutures. Then the chest was closed in layers with size 10 or 12 intercostal tube connected to an underwater seal. The total time away from the NICU ranged from 40 to 75 minutes. Upon return

to the unit, mechanical ventilation was resumed.

Ninty infants were treated initially with indomethacin. The initial dose was 0.2 mg/kg i.v. over 30 minutes and if necessary was repeated every 8-12 hours for a maximum three doses. The response to indomethacin therapy was manifested by disappearance of murmurs, improvement of congestive heart failure, and absence of any residual blood flow through the ductus by echocardiography. Fifty-three infants (59%) responded successfully to indomethacin treatment, while 37 infants (41%) did not respond to indomethacin and shifted to surgical treatment.

A comparison was made between the surgical and pharmacologic treated groups of infants. The presenting clinical features of both groups are similar, as are the methods of diagnosis, ventilatory support, and intensive care monitoring. The duration of ventilatory support, total hospital stay, early postoperative morbidity and mortality, and late follow-up complications were compared.

Statistical Package for the Social Science (SPSS) for windows, version 7.5, was used for data entry, editing, recoding and analysis. T-test was used for comparison of quantitative data and chi-square was used for comparison of qualitative data.

Results

Surgical Ligation:

Of the 59 premature infants who underwent surgical ligation 34 (57.6%) were males and 25 (42.4%) were females. The average gestational age was 30 weeks (range 26 to 36 weeks). The average birth weight was 1,616 gm (range 800 to 2400

Table (1): Comparison of 59 patients who underwent ligation and 53 patients treated with indomethacin.

Factor	Surgical group (n = 59)	Pharmacologic group (n = 53)	P-value
Gestational age (weeks)	30 (\pm 3.5)	32 (\pm 2.4)	P = 0.014*
Birth weight (grams)	1,616 (\pm 517)	1631 (\pm 490)	P = 0.781
Sex (male/female)	34 (57.6%) / 25 (42.4%)	28 (52.8%) / 25 (47.2%)	P = 0.26
Pre-treatment ventilation (number of infants)	42 (55.3%)	34 (44.7%)	P = 0.63
Pre-treatment BPD	8 (13.6%)	9 (17%)	P = 0.2
Post-treatment ventilation (days)	16 (\pm 8.8)	38 (\pm 14.4)	P = 0.001*
Hospital stay (days)	39 (\pm 12.6)	49 (\pm 19.2)	P = 0.004*
Early complications	6 (10.2%)	28 (52.8%)	P = 0.00001*
NEC	2 (3.4%)	10 (18.9%)	P = 0.003*
ICH	1 (1.7%)	5 (9.4%)	P = 0.003*
Mortality	4 (6.8%)	7 (13.2%)	P = 0.25
Follow-up complications	1 (1.7%)	2 (3.8%)	P = 0.4

* P-value is significant when it is < 0.05

gm). Preoperative ventilation was required in 42 infants (55.3%). Preoperative problems include bronchopulmonary dysplasia (BPD) in 8 infants (13.6%), renal impairment in 3 infants (5.1%), gastrointestinal bleeding in 3 infants (5.1%), and intracranial hemorrhage (ICH) in 2

infants (3.4%). Indications of surgical interference include, (1) indomethacin failure in 37 infants (62.7%), and (2) contraindication to indomethacin in 22 infants (37.3%). The mean age at operation was 10 days (range 1 to 21 days), and the mean body-weight was 1633 gm (range 800

to 2,40 gm).

Fifty-five infants (93.2%) survived following surgical ligation of their PDAs and were discharged from the hospital after an average stay of 39 days (range 7 to 71 days). Four infants (6.8%) died postoperatively, two infants (3.4%) died of septicemia, one (1.7%) died because of pulmonary insufficiency, and one (1.7%) died of necrotizing enterocolitis (NEC). Six infants (10.2%) developed postoperative problems which include pneumothorax in two infants (3.4%), necrotizing enterocolitis in two (3.4%), wound infection in one (1.7%), right pleural effusion in one (1.7%), and intracranial hemorrhage (ICH) in one infant (1.7%). The mean postoperative ventilation was 11 days (range 1 to 39 days). Seven infants (12%) were able to be extubated within one week of the ductal ligation. The remaining infants required ventilatory support for an average of 18 days (range 8 to 42 days).

The last follow-up of this group of patients included 51 of the total 59 patients as 4 infants died in the early postoperative period and 5 patients were lost to follow-up. These patients were followed from 5 to 47 months (mean 22 months). Fifty patients were developing normally in relation to their gestational age. One patient had neurologic abnormalities in the form of microcephaly, psychomotor retardation, and mild-to-moderate quadriplegia. All of the 51 patients had normal chest roentgenograms except late changes of bronchopulmonary dysplasia (moderate linear streaking of both lung fields) in those who had already this problem preoperatively and survived the operation (7 patients), however subsequent chest films have shown improvement or clearing of these changes.

Pharmacologic Management

Ninty premature infants were treated initially with indomethacin. Fifty-three infants (59%) responded to indomethacin, while 37 infants (41%) failed to respond to the full dose of this pharmacologic treatment and converted to surgical ligation. Of these 37 failures 35 infants did not show any response at all to indomethacin, while 2 infants had initial response as proved both clinically and echocardiographically, then reopening of the ductus presented 5 and 7 days later with the full picture of hemodynamically significant ductus which required surgical ligation.

Of the 53 infants responded to indomethacin treatment there were 28 (52.8%) males and 25 (47.2%) females. The mean gestational age was 32 weeks (range 27 to 36 weeks), and the mean birth weight was 1,631 gm (range 1,050 to 2350). Thirty-four infants (64%) required ventilatory support prior to the initiation of pharmacologic treatment, 9 of them (17%) had already bronchopulmonary dysplasia. Ventilatory support was necessary for all average of 38 days (range 17 to 76 days). Eighteen infants (34%) received one dose of indomethacin, 19 infants (36%) received two doses, and 16 infants (30%) received three doses. Twenty-eight infants (52.8%) developed complications to pharmacologic treatment. Complications of indomethacin include necrotizing enterocolitis in 10 infants (18.9%), renal impairment in 9 (17%), intracranial hemorrhage in 5 (9.4%), and gastrointestinal bleeding in 4 infants (7.5%). Seven infants (13.2%) died following indomethacin treatment. The cause of death in these infants include pulmonary insufficiency in 3 infants (5.7%), necrotizing enterocolitis in 3 (5.7%), and intracranial hemorrhage in one infant (1.9%). Forty-six (86.8%) infants survived

following indomethacin management and were discharged from the hospital after an average stay of 49 days (range 24 to 103 days).

Fourty-one of the 53 patients in this group were evaluated in the last follow-up, as 7 infants died in the immediate postoperative period and 5 patients were lost for the follow-up. The mean follow-up period for this group was 20.4 months (range from 3 to 45 months).Thirty-nine patients were developing normally in relation to their gestational age. One patient had neurologic abnormality and another patient developed mild retrolental fibroplasia. Chest roentgenograms showed late changes of bronchopulmonary dysplasia in those 8 patients who had already this problem preoperatively and survived to the last follow-up, however subsequent chest films have shown improvement or clearing of these changes.

We compared between the surgically and pharmacologically treated groups of infants from the statistical point of view. We found that there is no statistically significant difference between the two groups regarding birth weight, sex, requirement for mechanical ventilation prior to start of treatment, rate of bronchopulmonary dysplasia, mortality rate, and late follow-up complications. On the other hand, there is a significant difference regarding the gestational age (30 weeks in the surgical group versus 32 weeks in the pharmacologic group), duration of post-treatment mechanical ventilation (16 days in the surgical group versus 38 days in the pharmacologic group), total hospital stay (39 days in the surgical group versus 49 days in the pharmacologic group), and complications of treatment (10.2% in the surgical group versus 52.8% in the pharmacologic group). Although the mortality rate is high in the pharmacologic group (13.2% versus 6.8% in the surgical

group), however it is not statistically significant difference (Table 1).

Discussion

It is generally acknowledged that occlusion of a hemodynamically significant patent ductus arteriosus is of benefit in premature infants. The two main methods for accomplishing this have been surgical ligation and the use of indomethacin, a prostaglandin synthetase inhibitor (13). In recent reports, surgical ligation is recommended as the initial therapy for PDA in premature infants (7,11,13-16). Numerous reports have documented the success of operative ductal closure, with very low morbidity and mortality (2,7,11,16-19). However, direct comparisons between surgical and pharmacologic treatment have shown diverse results, which are difficult to apply clinically (11,20-23).

Pharmacologic manipulation of the PDA using indomethacin also has been shown to be effective(22,23), although it is associated with failure rate tip to 43% (13,14,24,25). In this study the failure rate of indomethacin is 41% (37 out of 90 infants). We reported in this study 2 cases of recurrent PDA which represent 3.6% of the total number of infants who responded initially to indomethacin (55 infants). In a study done by Weiss et al (26) they found that 12% of the premature infants developed reopening of their ductus after initial response to indomethacin. Failure is thought to be related to low birth weight (25-29), severity of cardiopulmonary compromise (15), and route of administration (28,29). In addition, several reports have shown that among those infants who respond to indomethacin administration, those of lower birth weight and those who received indomethacin at an earlier post-natal age more frequently experience a recurrence of

their symptomatic PDA (30-32). The birth weights in the recurrent 2 cases in this study were 900 and 1050 gm and they received indomethacin on third and fifth day of age respectively.

The advantage of indomethacin therapy is control of PDA without the attendant risks of surgical intervention. The disadvantages are: 1. contraindication of indomethacin therapy in infants with renal impairment, sepsis, coagulopathy, intracranial haemorrhage, and liver failure; 2. questionable efficacy in infants weighing less than 1,000 gm; 3. temporary ductus closure with reopening; 4. renal impairment, necrotizing enterocolitis and other as yet unknown, long term effects of indomethacin therapy (24,25,33). Edmunds has suggested that indomethacin may also affect the development of the fetal brain although longterm clinical follow-up is pending (34).

In this study 22 infants (37.3% of the surgical group) were found to have contraindication for indomethacin therapy. Eight infants (13.6%) had renal impairment. 5 infants (8.3%) had gastrointestinal bleeding, 4 infants (6.8%) had intracranial hemorrhage, 3 infants (5%) had necrotizing enterocolitis, and 2 infants (3.4%) had thrombocytopenia. Almost the same result was reported by Gersony et al., who found 38% of their patients had contraindications to indomethacin therapy (20).

In this study twenty-eight infants (52.8%) developed complications with the use of indomethacin treatment. These complications include necrotizing enterocolitis in 10 infants (18.9%), renal impairment in 9 infants (17%), intracranial hemorrhage in 5 infants (9.4/1), and gastrointestinal bleeding in 4 infants (7.5%). Almost the same complications were reported by others (24,25,33).

The surgical technique for ligation of PDA in the neonate has been well established.

However, the reported morbidity and mortality rates of large series are highly variable (2,3,17-19). Wagner et al reported the surgical results for 268 infants enrolled in the National Collaborative Study and found that the intraoperative and early postoperative complication rates were 26% and 57%, respectively (3). However, more recent studies reported lower morbidity and mortality rates (35-38). In this study there was no major intraoperative complications. Severe fluid restriction prior to ligation often resulted in marked hypotension following anesthetic induction and during ligation. This was corrected by rapid intravenous fluid administration. In addition, during retraction of the lung, the trans-Cutaneous Po₂ often fell. This was corrected by temporary release of lung retraction, ventilation of both lungs and then expeditious ductal ligation. Seven infants (11.9%) developed postoperative complications. The postoperative complications of PDA ligation include pneumothorax in two infants (3.4%), NEC in 2 infants (3.4%), intracranial hemorrhage in one infant (1.7%), superficial wound infection in one infant (1.7%), and right pleural effusion in one infant (1.7%).

Review of the data from this study and by comparison of the two modalities of treatment revealed that there was no statistically significant difference in mortality rate although the percentage was higher in the indomethacin group (Table 1). Overall postoperative complications were significantly higher in the indomethacin group as well as duration of postoperative ventilation and total hospital stay. In a comparative study done by Mavroudis et al, mid Grosfeld et al (4,39), they concluded

that NEC as a complication was significantly higher in the indomethacin group as well as the overall mortality. However, they found that intraventricular hemorrhage (IVH) was significantly higher in the surgical group. It was reported that the most severe complication of surgery was IVH owing to sudden hypertension induced by ductal ligation. Both experimental and clinical studies have shown that sudden increases in diastolic blood pressure and cerebral blood flow can occur with ductal ligation (40-42). However, using a strict medical protocol, Strange et al (43) found no IVH among 20 infants after ductal ligation.

Long-term follow-up revealed no significant difference between the two modalities of treatment. Neurologic impairment and retrolental fibroplasia as a long-term follow complications have been reported in this series of patients as well as other series (1,44).

We conclude that surgical ligation of hemodynamically significant PDA yields a more predictable result with low morbidity and mortality. A review of the literature and the data from our patient series, which shows a 42% failure rate of indomethacin, has let us to adopt a surgical approach to closure of a hemodynamically significant PDA.

References

- 1- Nelson RJ, Thibeault DW, Emmanouilides GC, and Lippinann M: Improving the results of ligation of patent ductus arteriosus in small preterm infants. *J Thorac Cardiovasc Surg* 1976; 71: 169-178.
- 2- Mikhail M, Lee W, Toews W, et al: Surgical and medical experience with 734 premature infants with patent ductus arteriosus. *J Thorac Cardiovasc Surg* 1982; 83: 349-357.
- 3- Wagner HR, Ellison RC, Zierler S, et al: Surgical closure of patent ductus arteriosus in 268 preterm infants. *J Thorac Cardiovasc Surg* 1984; 87: 870-875.
- 4- Powell ML: Patent ductus arteriosus in premature infants. *Med J Aust* 1963; 2: 58-60.
- 5- Brandt B III, Marvin WJ, Ehrenhaft JL, Heitz S, and Doty DB: Ligation of patent ductus arteriosus in premature infants. *Ann Thorac Surg* 1981; 32: 167-172.
- 6- Ghosh PK, Lubiner J, Mogilnar M, et al: Ligation of patent ductus arteriosus in very low birth-weight premature neonates. *Thorax* 1985; 40: 533-537.
- 7- Perez CA, Bustorff-Silva JM, Villasenor E, Fonkalsrud EW, and Atkinson JB: Surgical ligation of patent ductus arteriosus in very low birth-weight infants: is it safe? *Am Surg* 1998; 64: 1007-1009.
- 8- Friedman WF, Hirschklau MJ, Printz MP, and Kirkpatrick SE: Pharmacologic closure of patent ductus arteriosus in the premature infant. *N Engl J Med* 1976; 295: 526-529.
- 9- Cotton RB, Stahlman MT, Kovar 1, and Catterton WZ: Medical management of small preterm infants with symptomatic patent ductus arteriosus. *J Pediatr* 1978; 92: 467-473.
- 10- Mahoney L, Carnero V, Brett C, et al: Prophylactic indomethacin therapy for patent ductus arteriosus in very low birth-weight infants. *N Engl J Med* 1982; 306: 506-510.
- 11- Robie DK, Waltrip T, Garcia-Prats JA, Pokorny WJ, and Jaksic T: Is surgical ligation of patent ductus arteriosus the

- preferred initial approach for the neonate with extremely low birth weight? *J Pediatr Surg* 1996; 31: 1134-1137.
- 12- Pokharel R, Hisano K, Yasufuku M, Ataka K, Okada M, Yoshimoto S, Nakamura H: Ligation of medically refracted patent ductus arteriosus (PDA) in an extremely low body weight premature infant. *Surg Today* 1998; 28: 1290-1294.
 - 13- Palder SB, Schwartz W, Tyson KRT, and Marr CC: Management of patent ductus arteriosus: a comparison of operative V pharmacologic treatment. *J Pediatr Surg* 1987; 22: 1171-1174.
 - 14- Trus T, Winthrop AL, Pipe S, et al: Optimal management of patent ductus arteriosus in the neonate weighing less than 800 g. *J Pediatr Surg* 1993; 28: 1137-1139.
 - 15- Zerella JT, Spies RJ, Deaver DC III, Dailry WJR, Haple DCE, and Trump DS: Indomethacin versus immediate ligation in the treatment of 82 newborns with patent ductus arteriosus. *J Pediatr Surg* 1983;18: 835-841.
 - 16- Trus T, Winthrop AL, Pipe S, Shah J, Lailger JC, and Lati GY: Optimal management of patent ductus arteriosus in the neonate weighing less than 800g. *J pediatr Surg* 1993; 28: 1137-1139.
 - 17- C.assady G, Crouse DT, Kirklin JW, et al: A randomized controlled trial of very early prophylactic ligation of the ductus arteriosus in babies who weighed 1000 gms or less at birth. *N Engl J Med* 1989; 320: 1511-1516.
 - 18- Coster DD, Gorton ME,, Grooters RK, Thieman KC, Schneider R-F, and Soltanzadeh H: Surgical closure of the patent ductus arteriosus in the neonatal care unit. *Ann Thorac Surg* 1989; 48: 386-389.
 - 19- Pokorny WJ, Adams JM, McGill CW, et al: Ligation of patent ductus arteriosus in the neonatal intensive care unit. *Mod Probl Paediatr* 1985; 23: 133-142.
 - 20- Gersony WM, Peckham GJ, Ellison RC, Miettinen OS, and Nadas AS: Effects of indometliacin in premature infants with patent ductus arteriosus: results of a national collaborative study. *J Pediatr* 1983; 102: 895-906.
 - 21- Mavroudis C, Cook LN, Fleischaker JW, et al: Management of patent ductus arteriosus in the premature infant: indomethacin versus ligation. *Ann Thorac Surg* 1983; 36: 561-566.
 - 22- Merritt TA, White CL, Jacob J, et al: Patent ductus arteriosus treated with ligation or indomethacin: a follow up study. *J Pediatr* 1979; 95: 588-611.
 - 23- Merritt TA, DiSessa TG, Feldman BH, et al: Closure of patent ductus arteriosus with ligation or indomethacin: a consecutive experience. *J Pediatr* 1978; 93: 639-646.
 - 24- Alpert BS, Lewins MJ, Rowland DW, et al: Plasma indomethacine levels in preterm newborn infants with symptomatic patent ductus arteriosus: clinical and echocardiographic assessment of response. *J Pediatr* 1979; 95: 578-582.
 - 25- Ivery HH, Kattwinkel J, Park TS, and Krovetz LJ: Failure of indomethacine to close persistent ductus arteriosus in infants weighing under 1000 grams. *Br Heart J* 1979; 41: 304.-307.

- 26- Weiss H, Cooper B, Brook M, Schluter M, and Clyman R: Factors determining reopening of the ductus arteriosus after successful clinical closure with indomethacin. *J Pediatr* 1995; 127: 466-471.
- 27- Cooke RWI, Pickering D: Poor response to oral indomethacin therapy for persistent ductus arteriosus in very low birthweight infants. *Br Heart J* 1979; 41: 301-303.
- 28- Smith IJ, Goss I, Corigdon PJ: Intravenous indomethacin for patent ductus arteriosus. *Arch Dis Child* 1984; 59: 537-541.
- 29- Yaffe SJ, Friedman WF, Rogers D, et al: The disposition of indomethacin in preterm babies. *J Pediatr* 1980; 97: 1001-1006.
- 30- Heymann MA, Rudolph AM, and Silverman NH: Closure of the ductus arteriosus in premature infants by inhibition of prostaglandin synthesis. *N Engl J Med* 1976; 295: 530-537.
- 31- Halliday HL, Hirata T, Brady JP: Indomethacin therapy for large patent ductus arteriosus in the very low birth weight infant: results and complications. *Pediatrics* 1979; 64: 154-159.
- 32- Mellander M, Leheup B, Lindstrom DP, et al: Recurrence of symptomatic patent ductus arteriosus in extremely premature infants treated with indomethacin. *J Pediatr* 1984; 105: 138-143.
- 33- Nagaraj HS, Sandhu AS, Cook L, et al: Gastrointestinal perforation following indomethacin therapy in very low birth weight infants. *J Pediatr Surg* 1981; 16: 1003-1007.
- 34- Edmunds LH: Operation or indomethacin for the premature ductus. *Ann Thorac Surg* 1978; 26: 586-589.
- 35- Rajadurai VS, Yu VYH: Intravenous indomethacin therapy in preterm neonates with patent ductus arteriosus. *J Pediatr Child Health* 1991. 27: 370-375.
- 36- Buchheit JQ, Stewart DL: Clinical comparison of localized intestinal perforation and necrotizing enterocolitis in neonates. *Pediatrics* 1994, 93: 32-36.
- 37- Kosloske AM: Indications for operation in necrotizing enterocolitis revisited. *J Pediatr Surg* 1994; 29: 663-666.
- 38- Giacoia GP, Azubuiké K, Taylor JR: - Indomethacin and recurrent ileal perforation in a preterm infant. *J perinatol* 1993; 4: 297-299.
- 39- Grosfeld JL, Chaet M, Molinari F, Engle W, Engum SA, West KW, Rescorla FJ, Scherer LR: Increased risk of necrotizing enterocolitis in premature infants with patent ductus arteriosus treated with indomethacin. *Ann Surg* 1996; 224: 350-355.
- 40- Senesson SE, Lundell BPW, Herin P: Changes in intracranial arterial blood flow velocities during surgical ligation of the patent ductus arteriosus. *Acta Pediatr Scand* 1986; 75: 36-42.
- 41- Perlman JAt Hill A, Volpe JJ: The effect of patent ductus arteriosus on flow velocity in the anterior cerebral arteries: ductal steal in the premature newborn infant. *J Pediatr* 1981; 99: 767-771.
- 42- Marshall TA., Marshall F Jr, Reddy PP: Physiologic changes associated with ligation of the ductus arteriosus in preterm infants. *J pediatr* 1982; 101:

749-754.

- 43- Strange MJ, Myers G, Kirklin JK, et al:
Surgical closure of patent ductus does
not increase the risk of intraventricular
hemorrhage in the preterm infant. J
Pediatr. 1985; 107: 602-604.
- 44- Gay JH, Daily WJR, Meyer BHP,
Trump DS, Cloud DT, and Molthan
NE: Ligation of the patent ductus
arteriosus in premature infants: report
of 45 cases. J pediatr Sturg 1973; 8:
677- 683 ..

PHARMACOLOGICAL TREATMENT OF INTERNAL THORACIC ARTERY GRAFTS WITH VASODILATORS, IS IT REALLY BENEFICIAL? A RANDOMIZED DOUBLE-BLIND, PLACEBO-CONTROLLED, CLINICAL STUDY

ABSTRACT

The internal thoracic artery (ITA) is by far the conduit of choice for coronary artery bypass grafting (CABG). To avoid spasm of this arterial graft, and to increase its flow, many vasodilator preparations have been used either intraluminally or topically by many surgeons. To figure out the best vasodilating preparation to get maximum flow after ITA harvesting, we have performed a randomized double blind, placebocontrolled study in thirty patients submitted for elective, first time CABG. These patients were randomly divided into five groups. Free flow of the in situ ITA conduit was measured twice, the first measurement was performed just after dividing the distal end of the graft after its harvesting, the second measurement was taken after wrapping the ITA graft in a swab soaked with the solution of one of the commonly used vasodilating drugs, papaverin 2mg/ml, nitroglycerin 1mg/ml, verapamil 0.5mg/ml, nitroprusside 0.5 mg/ml, and normal saline 0.9%. In all five groups, free flow of the ITA graft increased significantly with time. However, we have found no statistically significant differences between the different treatment groups regarding the second flow measurement ($P=0.2$). We concluded that optimum harvesting and handling techniques of ITA pedicle is sufficient for adequate flow. If we achieve this, there would be no need for further pharmacological preparations to treat ITA graft. We suggest that preparation of ITA by topical vasodilators is not significantly superior to placebo in terms of ITA flow.

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INTRODUCTION

The internal thoracic artery (ITA) is by far the ideal conduit for CABG, due to its proven efficacy and long-term patency rate (1,2). However, being a viable arterial graft, ITA conduit has the potential for vasospasm during its takedown with insufficient early graft flow, this might cause perioperative morbidity and mortality (3,4). In order to overcome this serious problem, many surgeons have tried several vasodilator drugs either topically or intraluminally for pharmacological and/or mechanical

dilatation of ITA graft (5,6). Most of the studies regarding the effect of topical vasodilators were performed in vitro following different mechanical manipulations (7,8). This study was designed to assess the effectiveness of the most commonly used vasodilators to inhibit vasospasm and to maximize ITA flow before ITA-left anterior descending (LAD) anastomosis.

Patients and Methods

Thirty consecutive patients scheduled for elective first time CABG were randomly

chosen and divided into five treatment groups. This study was performed at Mayo Clinic, Rochester, USA, over a three months period.

Vasodilator drugs were prepared in sealed bottles and coded in the pharmacy. Both surgeons and O.R. staff were blinded to the drug type.

Surgical procedure

The left ITA was harvested as a pedicle from the level of the subclavian vein down to its bifurcation into musculophrenic and superior epigastric arteries, using diathermy and metal clips. Three minutes after systemic heparinization in a dose of 300mg/kg, and after checking the activated clotting time (ACT), the ITA was divided before its bifurcation. Free flow was measured by letting the cut end of the artery to bleed in a graded glass jar for half a minute then we calculated the follow per minute. Then, a Bulldog closed the distal end of the ITA graft, and the artery was wrapped in gauze soaked with one of the solutions of our study. The graft was then left to lie beneath the sternal border for 15 minutes to get maximum pharmacological effect of the preparation. During this time we make the necessary purse sutures in the aorta and right atrium for cannulation, then routine cannulation was performed.

The second measurement was taken just before commencing cardiopulmonary bypass (CPB). CPB then was established and core temperature was reduced to 28 degrees Celsius. For myocardial preservation, we used St. Thomas cold crystalloid cardioplegia by ante grade route, and topical iced saline slush. In all patients left ITA was anastomosed to LAD and that was the last distal anastomosis to be done.

Systemic rewarming was performed just

after securing the ITA-LAD nastomosis. We don't use vasopressors or vasodilators during CPB.

The free flow of the ITA graft was measured allowing the free end of the graft to bleed in a graded container for thirty seconds and then the value was corrected to get blood flow /minute. First measurement was taken just after the distal end was divided (after systemic heparinization), then the ITA graft was wrapped in a swab soaked with the pharmacological preparation. The ' second measurement was taken twenty minutes later just before establishing CPB and after trimming the distal end of the graft to make it ready for anastomosis. The mean arterial pressure was recorded.

The tested drug solutions were Papaverin 2mg/ml, nitroglycerin 1mg/ml, verapamil 0.5mg/ml, nitrgprusside 0.5mg/ml, and normal saline 0.9%. All solutions were arbitrary chosen and were applied at room temperature (18-21 degrees).

Statistical Analysis

Our results were expressed as mean + standard error. In order to analyze statistically significant differences in mean continuous parameters such as age, body surface area (BSA), number of grafts, time, etc. between the five groups, analysis of variance was done using the Duncan multiple comparison option. A non-parametric analysis of Kruskal, Wallis was done due to sample size restrictions in the subgroups.

Paired t-test was performed to analyze statistically significant differences between first and second flow measurements specific for each group.

P-value less than or equal to 0.05 were considered statistically significant.

Table (1): Patients clinical characteristics and hemodynamic data

Factor	Group I Normal saline	Group II Papaverine	Group III Verapamil	Group IV Nitroglycerine	Group V, Sodium nitroprusside	P- value
Male/Female	5/1	3/0	3/1	6/3	5/3	
Age	66 ± 3.9	62 ± 5.5	54.8 ± 3.8	67.9 ± 2.4	65.6 ± 3.5	1.0
No. of grafts	3.5 ± 0.2	2.9 ± 0.2	3.1 ± 0.3	3.6 ± 0.3	3.4 ± 0.2	0.4
MAP1 (mm Hg)	72.5 ± 2.9	76.5 ± 4.0	82.9 ± 3.2	78.0 ± 3.3	76.1 ± 3.9	0.2
MAP2 (mm Hg)	77.8 ± 2.5	73.4 ± 3.6	79.8 ± 3.7	73.6 ± 2.7	73.5 ± 2.3	0.4
CPB time (min)	103.6 ± 4.5	101.6 ± 5.6	103.3 ± 6.7	104 ± 8.1	102.6 ± 7.9	1.0
X clamp time (min)	62.4 ± 3.4	63.1 ± 4.5	57 ± 4.5	63.3 ± 4.3	64.9 ± 5.2	0.8
CPB Q, (l/min)	4.4 ± 1.8	4.7 ± 1.9	4.9 ± 1.8	4.9 ± 1.5	4.8 ± 1.1	0.3

BSA = body surface area; MAP 1,2 = mean arterial blood pressure in first and second free flow measurements; CPB = cardiopulmonary bypass time; X clamp = cross clamping time; Q = flow. P±values were calculated from Kruskal ± Wallis test.

Table (2): ITA flow rates before and after treatment

Time	Group I Normal saline	Group II Papaverine	Group III Verapamil	Group IV Nitroglycerine	Group V, Sodium nitroprusside	P- value*
First flow	38.8 ± 9.7	42.3 ± 8.5	41.1 ± 8.0	39.2 ± 11.0	40.63 ± 5.25	0.5
Second flow	85.4 ± 15	81.9 ± 5.7	78.3 ± 9.1	83.6 ± 24.0	98.5 ± 12.35	0.2
P- value**	0.002	0.0004	0.0001	0.03	0.0001	

* P-values calculated from Kruskal - Wallis test.

* P-values calculated from paired t-test.

Results

Demographic, hemodynamic and CPB data of the five groups are shown in Table 1. No statistically significant differences were detected between the groups with respect to

age, BSA, number of grafts, time intervals between the two flow measurements, bypass time, cross clamping time, and CPB flow. Mean arterial pressure (MAP) during the time of the first and second ITA flow

measurements was not significantly different either within or between groups.

In all five groups the second free flow measurement was significantly higher compared to the flow immediately after division of the distal end of ITA pedicle ($P < 0.002$, 0.0004 , 0.0001 , 0.03 , and 0.0001 respectively.) (Table 2) However, there were no statistically significant differences between the five groups. None of the patients have showed clinical picture of ITA spasm in this study.

Discussion

This study supports the observations of others (3, 9, 10) that ITA flow is usually low just after its takedown. Most probably this is due to the vasospasm induced by mechanical manipulations of arterial grafts, as well as the physical factors such as diathermy (11, 12). This study shows that with time, the spasm is relieved and the arterial graft dilates and ITA flow increases significantly with no significant advantage of topical application of vasodilators over placebo.

These findings differ from those of other reports noting that topical use of similar vasodilators have shown significant increase in ITA graft flow over saline (10) However there is a study that showed that topical vasodilators have no effect on ITA flow and the only factor increasing the flow was time (8). However, Our study differs from the works performed by others in being a randomized double blind, placebocontrolled study.

The ITA graft was wrapped in drug - soaked swab for a period of twenty minutes and we believe that this is enough to get maximum benefit of the medication used; this has been confirmed by another report (4). There was previously published

evidence that if free flow of the ITA graft is at least 100ml/min, post-anastomotic flow would be equivalent to that of a vein graft (13, 14). Of course provided that the anastomosis was done optimally. However, accepting a free flow of at least 50ml/min does not protect against hypoperfusion (13, 14). So, it is very important to optimize ITA graft flow before deciding to use it as a pedicled graft.

In our study, all groups including the control saline group, achieved satisfactory flow in the range of 78 ± 9 to 98 ± 12 ml/min. There was no clinical evidence of hypoperfusion during the perioperative period. Our results coincide with the findings of other studies (8). However, Cooper and co-workers have reported satisfactory flow of ITA graft after treating it with nitroprusside (10).

Clinical comparative studies on the effect of various vasodilators used to increase ITA flow are few (8, 10). Most of the studies have been performed in vitro (5, 7, 15, 16). Jett et al. has shown that experimental inhibition of the contraction of precontracted ITA rings was best achieved with nefidipine, sodium nitroprusside and papaverine, with the least or no effect achieved with nitroglycerin (7). On the Other hand He and co-workers found that glyceril trinitrate was more potent than papaverine in relaxing precontracted ITA rings, while nefidipine took a longer time to achieve this relaxation (12). Our data shows that verapamil and sodium nitroprusside, both of which are known to have direct and indirect effects to relax smooth muscles (7), were not superior to treatment with saline to improve ITA graft blood flow. We explain this by the fact that ITA grafts undergo spontaneous recovery and dilatation with time, putting in mind that mean arterial

pressure and cardiac output is satisfactory.

It is well known that arterial grafts undergo vasoconstriction that may be triggered by mechanical stimulation, as well as various vasopressor substances, besides, low cardiac output states is a well known cause for spasm of arterial grafts (17). It is widely accepted that the endothelium of the ITA spontaneously releases significant amounts of nitric oxide (NO) that plays an important role in arterial vasodilatation. Moreover, NO production can be stimulated by a variety of vasoactive substances. It has been suggested that blood vessels with intact endothelium react poorly to vasoconstrictors, whereas they contract strongly when endothelium is damaged or lost (17, 18). One possible explanation for the salutary effect of time on ITA flow is that after the first mechanical or physical insult that might take place during ITA takedown, if the endothelium is intact, a time related recovery would take place. Probably due to release of endothelial relaxing factor.

We believe that using a higher drug dosage of vasodilators (than the doses we used in this study) to achieve more potent effect on ITA flow is unnecessary and might affect hemodynamics.

In conclusion, this study has shown that careful harvesting and gentle handling of ITA pedicle is sufficient to achieve adequate flow prior to its anastomosis to the LAD, we believe that there is no need for further pharmacological treatment of the ITA graft. However, if the ITA-LAD anastomosis is performed very early after harvesting the ITA, i.e. before the artery has enough time to dilate and recover spontaneously from its initial spasm, vasodilators may be beneficial in this situation.

References

- 1- Loop F.D., Lytle B.W., Cosgrove D.M., Stewart R.w., Goormastic M., Williams G.W., Golding L.A., Gill C.C., Taylor P.C., Sheldon W.C. Influence of the internal mammary graft on 10 year survival and other cardiac events. *New Engl J Med* 1986; 314: 1-6.
- 2- Lytle B.W., Loop F.D., Cosgrove D. M., Ratliff N.B., Easley K., Taylor P.C. Long-term (5-12 Years) Serial studies of internal mammary artery and saphenous vein coronary bypass grafts. *J Thorac Cardiovasc surg* 1985; 89: 248-258.
- 3- Barner H.B. Blood flow in the internal mammary artery. *Am Heart J* 1973; 86: 570-571.
- 4- Sabaru M.R., McClung J.A., Fass A., Red G.E. Early postoperative spasm in the left internal mammary bypass artery. *Ann Thorac Surg* 1987; 44: 195-200.
- 5- Green G.E. Techniques of internal mammary-coronary artery anastomosis. *J thorac Cardiovasc surg* 1979; 78: 455-459.
- 6- Mills N.M., Bringaze W.L. Preparation of the internal mammary artery graft: Which is the best method?. *J Thorac Cardiovasc Surg* 1989; 98: 73-79.
- 7- Jett G.K., Guyton R.A., Hetcher C.R., Abel P.W. Inhibition of human internal mammary artery constrictions. *J Thorac Cardiovasc Surg* 1992; 104: 977-982.
- 8- Sasson L., Cohen A.J., Hauptman E., Schachner A. Effect of topical Vasodilators on internal mammary Arteries. *Ann Thorac Surg* 1994; 59: 494-496.
- 9- Canzer C.C., Dame N.A. Ultrasonic assessment of internal thoracic artery graft flow in the revascularized heart. *Ann Thorac surg* 1994; 58: 135-138.

- 10- Cooper G.J., Wilkinson G.A. Overcoming perioperative spasm of the internal mammary artery. Which is the best Vasodilator?. *J Thorac Cardiovasc Surg* 1992;104:465-468.
- 11- Frierson J.H., Bigelow J.C., Duke D.J., Mahoney T.M., Dimas A.P. Treatment of perioperative mammary artery spasm with nifedipine. *Am Heart J* 1993; 125: 884-886.
- 12- He G.W., Rosenfledt F.L., Buxton B.F., Angus J.A. Reactivity of human isolated internal mammary artery to constrictor and dilator agent. *Circulation* 1989; 80 (2): 141-150.
- 13- Jones E.I., Lattuf O.M., Weintraub W.S. Catastrophic consequences of internal mammary artery hypoperfusion. *J Thorac Cardiovasc Surg* 1989; 98: 902-907.
- 14- Louagie Y.A.G., Haxhe J.P., Buch M., Sehoevaerds J.C. Intraoperative electromagnetic flow meter measurement in coronary artery bypass grafts. *Ann Thorac Surg* 1995; 57: 357-364.
- 15- Chester A.H., Panda R., Borland A.A., Tadjkarimi S., Schyns C.J., Oonell G.S., Yacoub M.h. Effect of application of papaverine on contractile response of internal mammary artery. *Br J Surg* 1994; 81: 527-531.
- 16- Fonger J.D., Yang X.M., Cohen R.A., Haudenschild C.C., Shemin R.J. Impaired relaxation of the human mammary artery after temporary clamping. *J Thorac Cardiovasc Surg* 1992; 10: 971-996.
- 17- He G.W., Yang C.Q., Starr A. Overview of the nature of vasoconstriction in arterial grafts for coronary operation. *Ann Thorac Surg* 1995; 59: 676-683.
- 18- Yang Z., Lyscher T.F. Biological and Vasomotor properties of the internal thoracic artery.. role of the endothelium. In: Angelini G.D., Brian A.J., Lyscher T.F., eds. *Arterial conduits in myocardial revascularization*. UK: Arnold Publishers, 1996: 23-31.

MANAGEMENT OF STERNAL WOUND INFECTION AFTER STERNOTOMY FOR OPEN HEART SURGERY

ABSTRACT

No one can deny that mediastinitis is a catastrophic complication of open heart surgery, occurring in 0.4 to 5% of cases. A total of 3178 patients were operated upon in our department in Ain-Shams University over a period of 3 years. Sixty four of them suffered from mediastinitis with an incidence of 2%. To study the risk factors for mediastinitis the patients were divided into 2 groups, group (1) (infection group) (n=64) and group (2) (control group) (n=3114).

To evaluate the results, morbidity and mortality in the infection group (1) (n=64), this was further subdivided into subgroup (A) (patients with superficial wound infection) (n=28) and subgroup (B) (patients with deep wound infection) (n=36).

By statistical analysis it was found that the following were the risk factors for mediastinitis in our patients: age, NYHA class, (P<0.001 for each, highly significant), diabetes mellitus, respiratory insufficiency, reexploration for bleeding (P<0.01 for each, highly significant), duration of use of inotropic drugs (P<0.05, significant). Staphylococcus aureus organism was responsible for 43.4% of all infections in our patients.

The strategy of treatment of infected patients comprised antibiotics according to culture and sensitivity with frequent dressing of wound.

In more deep infections debridement was adopted with removal of necrotic tissues, curettage and sternal closure by stainless steel wires using the "Boncheck technique" and cautious irrigation by povidone-iodine (Betadine) for 2-10 days according to patient status followed by saline and garamycin for 2 days as a wash.

In more aggressive infections muscle flap transposition (as pectoralis major or rectus abdominis muscles) were used or omental flap transposition as these flaps has an advantage of promoting wound healing in the presence of bacterial contamination due to rich blood supply in the used flaps.

The overall mortality in our infection group of patients was 18.75% which parallels other groups of patients in the literature. It was proved statistically that high mortality rate was associated with MVR, MVR with DeVega repair of tricuspid valve, AVR, DVR with DeVega repair of tricuspid valve, CABG, Fallot repair and aortic aneurysm operations.

On the other hand, DVR, VSD repair and mitral valve re-replacement had a low mortality rate. Hence, we can conclude that: - Careful preoperative preparation, meticulous and rapid surgical technique and careful hemostasis are usually required to reduce the incidence of mediastinitis.

- Treatment of early cases of mediastinitis by strong antibiotics according to culture and sensitivity, and the rapid and early surgical intervention reduces morbidity and mortality.

- Surgical intervention is in the form of debridement, the use of diluted povidone-iodine (Betadine) for mediastinal irrigation cautiously as it might cause iodine toxicity and constrictive pericarditis.

Also, proper reclosure of sternum by "Boncheck technique" and the muscles and skin as a full thickness stimulates fibrosis and improves stability of sternum.

Finally, the use of muscle and omental flaps transposition is a new line of surgical treatment that should be implemented in aggressive and severe deep sternal wound infections.

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INTRODUCTION

No one can deny that mediastinitis is a catastrophic complication of open heart surgery, occurring in 0.4 to 5% of cases (1). Patients who undergo median sternotomy continue to suffer morbidity and death from sternal wound complications. Major complications are divided practically into two groups: Sternal dehiscence alone and major sternal or mediastinal infection with or without associated sternal dehiscence. The associated mortality rate in adults is 13% to 33% (2,3). Many risk factors for these complications have been proposed; however, risk factors between institutions have differed and occasionally conflicted. Mediastinitis is defined as "clinically significant infection involving the mediastinum, below the sternum with purulent drainage and positive bacterial cultures (4)".

Materials and Methods

Three thousand-one-hundred and seventy eight patients underwent open heart surgery through a median sternotomy, including mitral (MVR), aortic (AVR) or double valve replacement (DVR), mitral or double valve replacement with DeVega repair of tricuspid valve, coronary artery bypass grafts, mitral valve re-replacement, congenital heart operations as repair of Fallot and ventricular

septal defect (VSD) repair, and aortic aneurysm surgery. These open heart procedures were performed in the cardiothoracic surgery departments in Ain-Shams University hospital and Ain-Shams Specialized hospital during the period from March 1st 1995 till the end of February 1998. Of these 3178 cases sixty four suffered from mediastinitis (Mediastinitis incidence is 2%).

The following factors were considered as risk factors for mediastinitis and were viewed for the affected patients: Age, gender, preoperative New York Heart Association (NYHA) class, presence of diabetes mellitus, previous sternotomy, duration of bypass, aortic cross clamp time, respiratory insufficiency, re-exploration for bleeding, type of organism causing the infection, duration of mechanical ventilation and inotropic drugs in intensive care unit (ICU).

General plan for patients undergoing open heart surgery.

All patients were scrubbed with povidone-iodine (Betadine) and were shaved from chin to knee or ankle (according to the operation) on the night prior to operation.

The operative field was scrubbed and painted with povidone-iodine solution, and adhesive disposable drapes were applied to

all surfaces of the operative field prior to draping.

Prophylactic broad-spectrum antibiotics were used in all patients prior to operation and continued for 7 days postoperatively. Claforan, Cephobid, Fortum, Augmentin Mandol, Rocephin were used as monotherapy or in combination with other antibiotics as Unasyn, Nebcin (with monitoring of kidney function) in the assigned doses according to the body weight of the patient. Strong forms of mediastinitis were treated mostly with Vancomycin and Tienam with other antibiotics according to culture and sensitivity from the wound culture, guided by creatine level to monitor the kidney function for Vancomycin administration.

Surgical technique performed

The operative approach in all patients was through a median sternotomy with cardiopulmonary bypass and systemic hypothermia (25°-28°C). Also, local hypothermia using crushed ice was used. Modified blood cardioplegia has been routinely used in all patients in the form of a bag of 500 ml hypothermic hyperkalemic cardioplegia solution with 150 ml of its content being voided out and replaced by blood of patient through aortic root at a temperature of 34°C immediately after going on bypass and starting the systemic blood cooling. Also, 10 meq of KCl is added to this first dose of cardioplegia. If an additional dose was required so the above procedure was repeated apart from the fact that the replaced blood would be supplied from the heart-lung machine rather than from the aortic root of the patient being operated upon. Sixty four patients developed mediastinitis following open cardiac procedures in our studied series. The patients were prospectively and retrospectively studied.

In order to evaluate the subject of mediastinitis we have divided the patients into 2 groups twice. Firstly into group (1&2) to study the risk factors of mediastinitis (Table 2) and secondly into subgroup (A&B) to evaluate the difference between superficial and deep wound infection in our study group of infected patients (Table 4).

Group (1) comprises the infection group [number of patients (n=64)] and group (2) represents the control group (n=3114) with both groups (1&2) representing the total number of patients in our study (n = 3178).

Group (1) (n=64) was further subdivided into subgroup A (n=28) representing patients with superficial wound infection and subgroup B (n=36) with deep infections (unstable sternum).

The condition in patients of subgroup (A) (superficial wound infection) (n=28) started 6 days postoperatively. Those patients had a stable sternum, serosanguinous or purulent discharge from the subcutaneous tissue (not communicating with mediastinum under the sternum). They had low grade fever and their general condition was relatively good. Such group of patients was managed conservatively with a combination of 2 antibiotics, to be adjusted later according to culture and sensitivity, frequent wound dressing (twice or more) daily. Then finally curettage and secondary stitches under local anesthesia.

However, the condition in subgroup (B) (deep wound infection patients) was different (n=36), where the patients had continuous high fever and marked leucocytosis. The sternum was unstable and dehiscent in all cases, mostly sucking air with cough and respiration, denoting communication between mediastinum and the open air. This condition was evident

after the 7th to 10th postoperative day. There was always frank pus soaking the patient's dressings.

This group of patients was managed by starting a combination of 2 strong antibiotics, as soon as the condition was diagnosed, to be adjusted later according to culture and sensitivity. Surgical intervention by debridement of wound was adopted very soon after diagnosis, curettage of infected sternal edges, excision of pyogenic membrane found and necrotic tissue (this was sent for culture and sensitivity), with povidone-iodine (Betadine) wash (0.5% solution in normal saline at a rate of 100 ml/hr for 2-10 days), closed circuit irrigation and drainage (by placing a single thin line for inflow and a single wide diameter drain for drainage) and sternal closure by the "Boncheck technique" where sternal halves reapproximation is done by two longitudinal stainless steel wires (one in each half) to be twisted together at the end of the repair (Fig.4). Five or six transverse stainless steel wire sutures are used after that, passing outside the longitudinal sutures. All the muscle and tissue bulk above the sternum with the skin were closed as a one layer with interrupted mattress tension sutures with prolene, also interrupted simple mattress sutures using prolene was applied. Stitches were removed on the 8th and 12th day respectively.

It is to be noted that in 7 cases the patients needed debridement followed by muscle flap transposition including pectoralis major (Fig.5) and rectus abdominis muscle flap combined. In addition, two patients needed omental flap transposition together with debridement. Using the transposition flap techniques, those were indicated and done either due to

failure of debridement and closed circuit irrigation technique or due to severity of the infection from the start.

It is to be noted that muscle flap transposition technique has an advantage of promoting wound healing in the presence of bacterial contamination due to rich blood supply in the used flaps (5).

Mediastinal irrigation is continued for 2 to 10 days, according to patient status. Usually when the discharge became clear, with subsidence of temperature and improvement of leucocytosis, the wash with Betadine was discontinued and replaced by free saline and garamycin for two days as a wash after which the irrigation was stopped. Then the drains were removed two days later.

Results

Tables 1,2,3,4,5,6 and 7 represent the different results obtained in our study over 3 years period. The following results are obtained using different statistical analysis:

* Table (1) represents the total number of cases with mediastinitis (n=64) in accordance to the different operative procedures done (Fig. 1). By Z-test, it was found that each operation in relation to the total of other operations is highly significant ($P<0.001$). Hence, by Z-test it was found that the frequency of infection in all operative procedures in group (1) is the same.

* Table (2) shows the different risk factors studied in both group (1) (infection group, n=64) and group 2 (control group, n=3114) with the following results:

- By comparing each of the risk factors in groups (1 and 2) using the Chi-square test it was found that (Table 5):

Table 1: Total No. of cases with mediastinitis and the different operative procedures done in group (1)

Operative procedure	No. of patients	Percent (%)	P value
1) MVR	7	10.9	P<0.001 HS
2) MVR and DeVega repair of tricuspid valve	3	4.7	P<0.001 HS
3) AVR	8	12.5	P<0.001 HS
4) DVR (MVR and AVR)	9	14	P<0.001 HS
5) DVR and DeVega repair of tricuspid valve	14	21.9	P<0.001 HS
6) CABG	8	12.5	P<0.001 HS
7) Fallot repair	7	10.9	P<0.001 HS
8) VSD repair	3	4.7	P<0.001 HS
9) MV re-replacement	3	4.7	P<0.001 HS
10) Aortic aneurysm operations	2	3.1	P<0.001 HS
Total	64		

From table (5) we conclude that in our study group of patients (group 1), the following factors were proved to be risk factors:

- 1) Age HS P<0.001
- 2) NYHA class HS P<0.001
- 3) Diabetes mellitus HS P<0.01
- 4) Respiratory insufficiency HS P<0.01
- 5) Re-exploration for bleeding HS P<0.01
- 6) Duration of use of inotropic drugs S P<0.05

While, the following factors were not proved to be risk factors in group (1) (NS P>0.05).

Gender, previous sternotomy, obesity, bypass time, aortic cross clamp time and duration of mechanical ventilation.

Table (3) represents the type of organism causing infection (Fig.3) where:

By Z-test, on comparing each causative organism with the total of other organisms it was found that:

- 1) For staphylococcus aureus (staph.

Table (2): Risk factors for mediastinitis (Total n = 3178)

Risk factor	Infection group (1) (n=64)	Control group (2) (n=3114)
A) Preoperative		
1) Age		
< 50 yrs	26	1923
≥ 50 yrs	38	1191
2) Gender		
Male	42	1846
Female	22	1268
3) NYHA class		
< 3	15	1762
≥ 3	49	1352
4) Diabetes mellitus		
No	24	642
Yes	40	2472
5) Previous sternotomy		
Yes	3	168
No	61	2946
6) Obesity		
< 85 kg	43	1912
≥ 85 kg	21	1202
B) Perioperative and Postoperative		
1) Bypass time		
< 120 min	31	1861
≥ 120 min	33	1253
2) Aortic cross-clamp time		
< 90 min	36	1982
≥ 90 min	28	1132
3) Respiratory Insufficiency		
Yes	18	477
No	46	2637
4) Re-exploration for bleeding		
Yes	9	158
No	55	2956
5) Duration of mechanical ventilation in ICU		
< 24 hrs	52	2493
≥ 24 hrs	12	621
6) Duration of use of inotropic drugs		
< 24 hrs	18	1362
≥ 24 hrs	46	1752

Table (3): Type of organism causing infection

Organisms obtained by culture	No. of patients (n = 64)	Percent (%)
1) Staphylococcus aureus	28	43.4
2) KLEBSIELLA	8	12.5
3) Pseudomonas Pyocyaneus	7	10.9
4) E. coli	5	7.8
5) Negative culutres (non-bacterial)	16	25

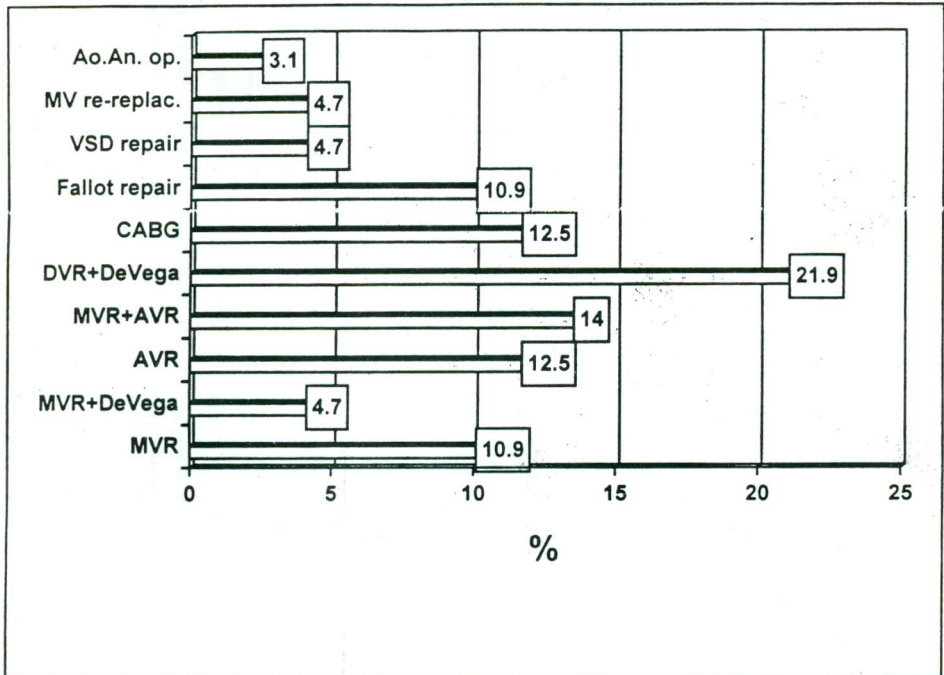


Fig. (1): Comparison between the different operative procedures

Table (4): The operative procedures done in relation to subgroups (A & B) and the mortality rates

Operative procedure	Subgroup (A) (n=28 pts) (pts with superficial wound infection)				Subgroup B (n=36 pts) (pts with deep infections (unstable sternum))				Total		
	No. of pts	%	Mor-tality	%	No. of pts	%	Mor-tality	%	No. of pts	Mor-tality	%
1) MVR	3	10.7	0	0	4	11	1	25	7	1	14.3
2) MVR+DeVega repair of tricuspid valve	1	3.6	0	0	2	5.5	1	50	3	1	33.3
3) AVR	3	10.7	0	0	5	13.8	2	40	8	2	25
4) DVR (MVR + AVR)	4	14.3	0	0	5	13.8	1	20	9	1	11.1
5) DVR + DeVega repair of tricuspid valve	5	17.9	0	0	9	25	3	33.3	14	3	21.4
6) CABG (Coronary artery bypass grafting)	3	10.7	0	0	5	13.8	2	40	8	2	25
7) Fallot repair	5	17.9	0	0	2	5.5	1	50	7	1	14.3
8) VSD (Ventricular septal defect) repair	1	3.6	0	0	2	5.5	0	0	3	0	0
9) Mitral valve re-replacement	2	7.1	0	0	1	2.8	0	0	3	0	0
10) Aortic aneurysm operations	1	3.6	0	0	1	2.8	1	100	2	1	50
11) Total	28		0	0	36		12	33.3	64	12	18.75

Pts. = patients.

Table 5: Results of risk factors

Risk factor	Group 1	Group 2	Chi-square	P value
A) Preoperative				
1) Age < 50 yrs ≥ 50 yrs	40.63 59.38	61.75 38.25	11.804	HS P<0.001
2) Gender Male Female	65.63 34.38	59.28 40.72	1.047	NS P>0.05
3) NYHA class < 3 ≥ 3	23.44 76.56	56.58 43.42	27.950	HS P<0.001
4) Diabetes mellitus No Yes	37.50 62.50	20.62 79.38	10.791	HS P<0.01
5) Previous sternotomy Yes No	4.69 95.31	5.39 94.61	0.062	NS P>0.05
6) Obesity < 85 kg ≥ 85 kg	67.19 32.81	61.40 38.60	0.887	NS P>0.05
B) Perioperative and Postoperative				
1) Bypass time < 120 min ≥ 120 min	48.44 51.56	59.76 40.24	3.339	NS P>0.05
2) Aortic cross-clamp time < 90 min ≥ 90 min	56.25 43.75	63.65 36.35	1.481	NS P>0.05
3) Respiratory Insufficiency Yes No	28.13 71.88	15.32 84.68	7.822	HS P<0.01
4) Re-exploration for bleeding Yes No	14.06 85.94	5.07 94.93	10.177	HS P<0.01
5) Duration of mechanical ventilation in ICU < 24 hrs ≥ 24 hrs	81.25 18.75	80.06 19.94	0.056	NS P>0.05
6) Duration of use of inotropic drugs < 24 hrs ≥ 24 hrs	28.13 71.88	43.74 56.26	6.222	S P<0.05

Where: P > 0.05 = NS (Non-Significant)
P < 0.001 = HS (Highly Significant) or

P < 0.05 = S (Significant)
P < 0.01 = HS (Highly Significant)

Table 6:

Operative procedure	P value
1) MVR	P> 0.05 NS
2) MVR and DeVega repair of tricuspid valve	P> 0.05 NS
3) AVR	P> 0.05 NS
4) DVR (MVR and AVR)	P> 0.05 NS
5) DVR and DeVega repair of tricuspid valve	P> 0.05 NS
6) CABG	P> 0.05 NS
7) Fallot repair	P _≤ 0.05 S
8) VSD repair	P> 0.05 NS
9) MV re-replacement	P> 0.05 NS
10) Aortic aneurysm operations	P> 0.05 NS

Table 7:

Operative procedure	P value
1) MVR	P> 0.05 NS
2) MVR and DeVega repair of tricuspid valve	P> 0.05 NS
3) AVR	P> 0.05 NS
4) DVR (MVR and AVR)	P< 0.05 S
5) DVR and DeVega repair of tricuspid valve	P> 0.05 NS
6) CABG	P> 0.05 NS
7) Fallot repair	P> 0.05 NS
8) VSD repair (No mortality)	-----
9) MV re-replacement (No mortality)	-----
10) Aortic aneurysm operations	P> 0.05 NS
11) Total	P< 0.01 HS

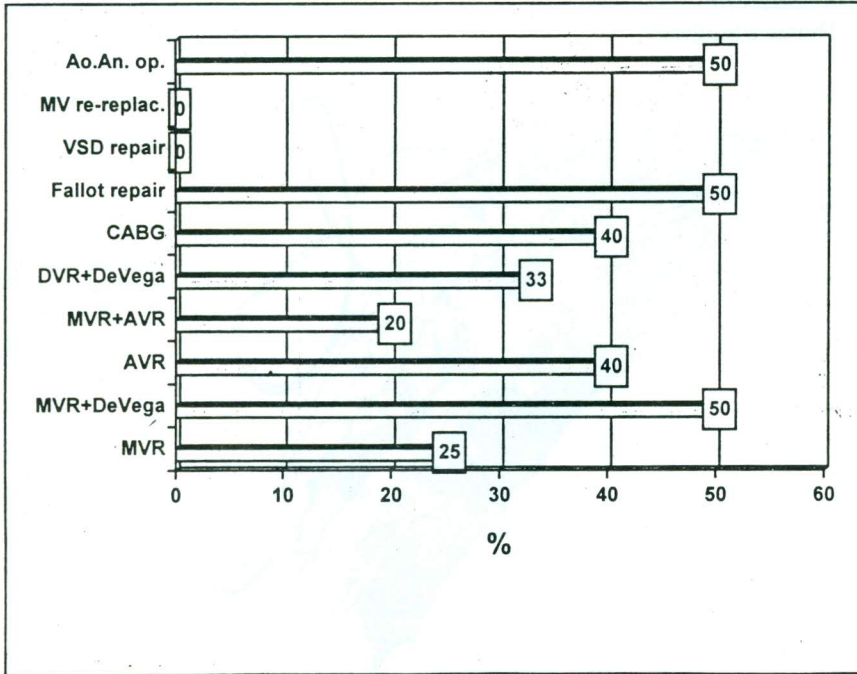


Fig. (2): Mortality rate among deep infection patient group (group-B)

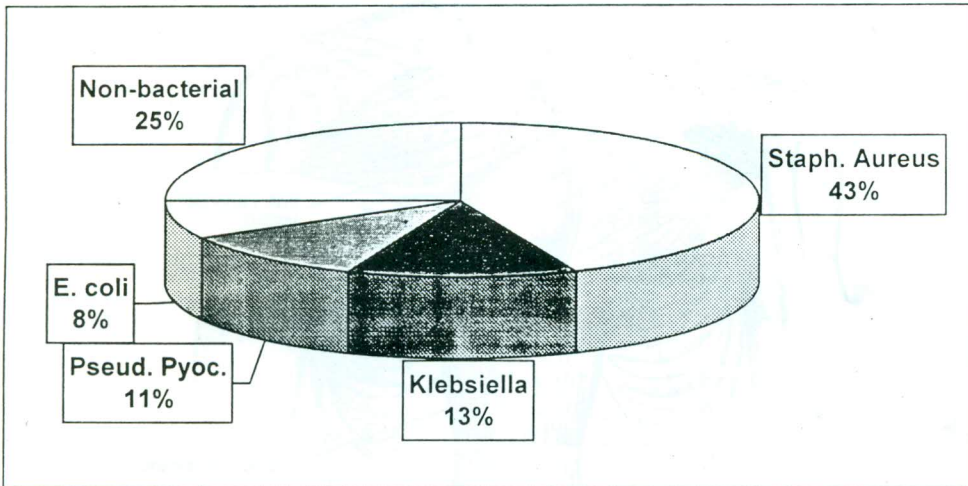


Fig. (3): Pie-chart showing the different types of causative organisms

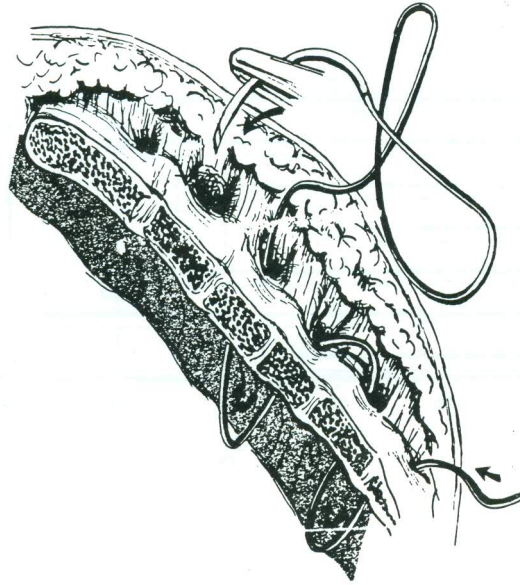


Fig. (4): Lateral reinforcement of the sternum is begun at its distal end, passing the wire around the ribs until the manubrium is reached.

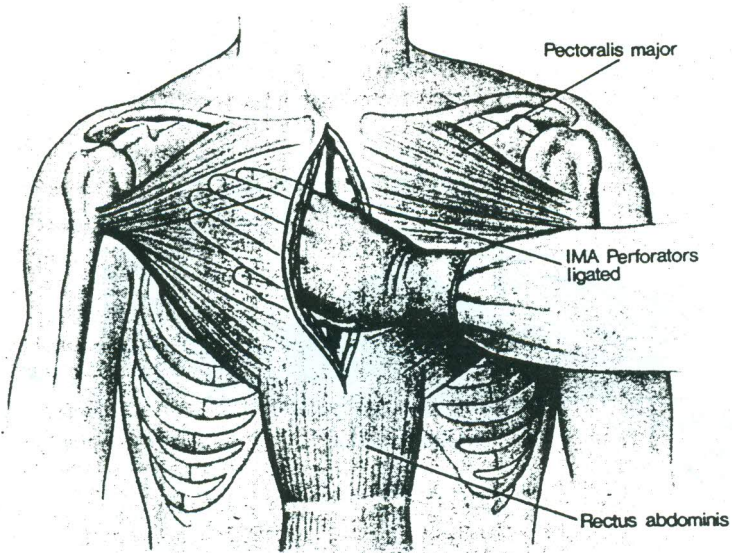


Fig. (5): After ligation of IMA perforators, the pectoralis major muscle is bluntly elevated from the anterior chest wall. The rectus muscle is left undisturbed.

aureus) $P > 0.05$ NS.

2) For klebsiella $P < 0.001$ HS.

3) For pseudomonas Pyocaneus, $P < 0.001$ HS.

4) For E.coli, $P < 0.001$ HS.

5) For negative (Non-bacterial) cultures $P < 0.001$ HS.

Hence, by Z-test infection caused by staphylococcus aureus is equivalent to that caused by all other organisms together. Thus, staph. aureus is responsible for 43.4% of all infections among group (1).

Table (4) shows the operative procedures done and the associated numbers and percentage of patients with superficial (subgroup A, $n=28$) and deep (subgroup B, $n=36$) wound infections and the mortality rates (Fig.2).

On comparing between subgroup (A and B) as regards which is more prevalent (superficial or deep infection) in each subgroup the following results were obtained (Table 6)

So, there is a non-significant difference ($P > 0.05$) between the superficial (subgroup A) and deep infection (subgroup B) among all the operative procedures except for the Fallot repair where there is a significant difference ($P \leq 0.05$) regarding the superficial in comparison to deep infection.

On comparing between the mortalities among subgroup (B) it was found that:

By Z-test, it was found that low mortality rate was associated with numbers 4 (DVR), 8 (VSD repair), 9 (mitral valve replacement) and 11 (the total of studied sample), while high mortality rate was associated with numbers 1 (MVR), 2 (MVR + DeVega repair of tricuspid valve), 3 (AVR), 5 (DVR with DeVega repair of tricuspid valve), 6 (CABG), 7 (Fallot repair)

and 10 (Aortic aneurysm operations).

It is to be noted that subgroup (A) (superficial infection patients) had no mortality (0%).

Discussion

In spite of careful preoperative preparation, adequate hemostasis, and good surgical technique, midline sternotomy infection occurs in a small subset of patients undergoing cardiac procedures (6).

Sternal and mediastinal infections after cardiac operations are dreaded complications that cause substantial morbidity and mortality (7). The incidence of mediastinitis in the infection group (1) is (64/3178) 2%. This incidence is in agreement with other authors (2.1%) (8).

It is slightly higher than in that series (1.4%) (1) and less than this series (2.7%) (9) and far less than that series (5%) (10).

The principle of mediastinitis itself could be explained in our series by the hot climate in our country in addition to the possibly low hygienic standard in an appreciable percentage of our patients. However, the lower incidence of mediastinitis in our series could be possibly attributed to the fact that nowadays in our department all the surgeons and working staff adopt strict measures regarding scrubbing, draping the patient in the operating theatre, sterilization and handling of instruments and all matters dealing with the patient.

As mentioned before, our series of patients had 3178 cases done over a period of 3 years. Those cases were principally divided into 2 groups, group (1) ($n=64$) infection group and group (2) ($n=3114$) control group. Group (1) (infection group) was further subdivided into 2 subgroups, subgroup (A) ($n=28$) superficial wound infection patients and subgroup (B) ($n=36$) (deep wound infection patients).

By reviewing table (2) and the results of this section to determine the different risk factors in our series and by using the Chi-square test to analyze the data (Table 5), it was evident that the following were proved to be risk factors for mediastinitis in our series of patients: Age, NYHA class ($P < 0.001$, highly significant for each). Also, diabetes mellitus, respiratory insufficiency and re-exploration for bleeding ($P < 0.01$, also highly significant for each).

Finally, duration of use of inotropic drugs ($P < 0.05$, significant).

On the other hand, gender, previous sternotomy, obesity, bypass time, aortic cross-clamp time and duration of mechanical ventilation were not proved to be risk factors in group (1) ($P > 0.05$, non-significant).

On the contrary, some authors considered obesity as a risk factor for mediastinitis (11).

These results are in agreement with others (1,12). Our results could be explained on the basis of that for preoperative factors age and patients with diabetes mellitus the infection happened in many of the elder sector of population with compromised immunity. Also, the respiratory insufficiency patients usually have smoking history, and evidence of COPD (chronic obstructive pulmonary disease) as evidenced by radiographic investigations.

Our results also coincide with another series (12) again in that a cluster of postoperative factors contribute to mediastinitis as re-exploration for bleeding and the continued and prolonged use of parenteral inotropic drugs and subsequently longer intensive care unit (ICU) stay.

On the contrary, the previous

sternotomy, intraoperative factors as prolonged bypass and aortic cross clamp time and postoperative prolonged duration mechanical ventilation in ICU were proved to be significant risk factors in the latter series (12), in contradiction to our series of infection patients which was not.

This could be attributed to the fact that the population of patients with those particular complications was low in number in our series.

By reviewing table (3), pie-chart in (Fig.3), the different types of organisms causing infection could be observed. We can conclude that staphylococcus aureus was responsible for 43.4% of all infections among group (1). This incidence is less than the series of some authors (59.6%) (13).

This result could be explained on the basis of the hot climate in our country in addition to the lower hygienic standard in a big percentage of patients in the latter series. These conditions are better nowadays thus the less incidence in our series compared to the latter. This coincides also with the results of other authors (1) where staph. aureus was the organism with the highest incidence 8/28 (28.6%) in that series yet it is lower than that in our series.

The deep sternal wound infection is more aggressive and fatal than superficial wound infections as appears from our results in table (4) with different statistical analysis among subgroup (A) and subgroup (B), and among the population of subgroup (B) itself with the deep wound infection.

The reported incidence of mortality has a wide range extending from 10-71% as reported by some authors (9,14).

On reviewing (Table 4), it was found that mortality among subgroup (A)

(superficial wound infection) was 0%, while among subgroup (B) (deep wound infection) was 33.3%, while the overall mortality among group (1) (infection group) including both subgroups (A & B) was (12/64) (18.75%).

This mortality rate is better than in other groups (52%) (1), (23.4%) (13) and (24%) (15). This could be explained by better scrubbing, draping, sterilization and handling of instruments in the theatre than before.

However mortality in our series was more than others as (14%) (16,17), yet the latter figure parallels our figure (18.75%). This could be attributed to following almost the same precautions in dealing with the patient.

Treatment in our series, as mentioned before, comprised various surgical techniques including debridement and irrigation with povidone iodine together with muscle flap transposition when indicated by pectoralis major (Fig.5) and rectus abdominis muscles and also omental flap transposition. It is to be noted that muscle flaps are thought to work by two basic methods as shown by some authors (18) that musculocutaneous flaps demonstrate ability to survive a bacterial inoculation and control infection. The muscle flaps bring a rich network of blood supply to an area of bone that is infected and poorly vascularized.

This line of management parallels other authors in literature (17) who adopts a similar regimen of treatment where he adopts an open method where debridement, open packing until a (clean) wound develops, and then exercising options of secondary closure or use of flaps to fill the space with or without a skin graft.

In the closed method, he usually allows irrigation for 3 to 5 days (In our centre we

usually use povidone-iodine for 2-10 days according to severity of infection and then we usually shift to saline wash together with garamycin for 2 or 3 more days) or until the effluent becomes sterile. He uses irrigants as antibiotic solutions, saline or dilute povidone-iodine. The latter is probably used most frequently because of its effectiveness and because of reports that continuous mediastinal lavage with antibiotics may predispose the patient to fungus infection and antibiotic toxicity.

However, caution in povidone-iodine treatment is necessary because constrictive pericarditis and iodine toxicity have been reported. Our lines of treatment also parallel other patients series (19,20), hence, careful preoperative preparation, meticulous and rapid surgical technique and careful hemostasis are usually required to reduce the incidence of mediastinitis.

Also, treatment of early cases of mediastinitis by strong antibiotics according to culture and sensitivity and the rapid and early surgical intervention reduces morbidity and mortality. It was proved that the following are risk factors for mediastinitis in our series: Age, NYHA class, diabetes mellitus, respiratory insufficiency, re-exploration for bleeding and duration of use of inotropic drugs.

Also, debridement, the use of diluted Povidone-iodine for mediastinal irrigation with caution, due to its reported side effects from prolonged use and proper reclosure of sternum by "Boncheck technique" (Fig.4) and the muscle layer and skin by the previously-mentioned technique as a full thickness stimulates fibrosis and improves stability of sternum.

The use of muscle flap transposition as pectoralis major (Fig.5) and rectus abdominis muscles, and omental flap are new lines of surgical treatment that should be implemented in aggressive and severe

deep sternal wound infections.

References

- 1- Rutledge, R.; Applebaum, R.F. and Kim, B.J.: Mediastinal infection after open heart surgery. *Surgery*; 1985; 97:88-92.
- 2- Ottino, G.; DePaulis, R.; Pansini, S.; Rocca, G. et al.: Major sternal wound infection after open-heart surgery: a multivariate analysis of risk factors in 2579 consecutive operative procedures. *Ann. Thorac. Surg.* 1987; 44:173-179.
- 3- Sarr, M.G.; Gott, V.L. and Townsend, T.R.: Mediastinal infection after cardiac surgery. *Ann.thorac.surg.* 1984; 38:415-423.
- 4- Cheung, E.H.; Craver, J.M.; Jones, E.L.; Murphy, D.A.; Hatcher, C.R. and Guyton, R.A.: Mediastinitis after cardiac valve operations. Impact upon survival. *J. Thorac. Cardiovasc.*, 1985; 90:517-522.
- 5- Herrera, H.R.; Mark, E. and Ginsburg A.: The pectoralis major myocutaneous flap and omental transposition for closure of infected median sternotomy wounds. *Plastic and Reconstructive Surg.* 1982; 70:465.
- 6- Majure, J.A.; Albin, R.E.; O'Donell, R.S., et al.: Reconstruction of the infected median sternotomy wound. *Ann. Thorac. Surg.* 1986; 42:9-12.
- 7- Nishida, H.; Grooters, R.K.; Soltanzadeh, H.; Thieman, K.C.; Schneider, R.F. and Kim, W.P.: Discriminate use of electrocautery on the median sternotomy incision. A 0.16% wound infection rate. *J. Thorac. Cardiovasc. Surg.*; 1991; 101:488-494.
- 8- Demmy, T.L.; Park, S.B.; Liebler, G.A.; Burkholder, J.A.; Maher, T.D.; Benckart, D.H.; Magovern, G.J. Jr. and Magovern, G.J.: Recent experience with major sternal wound complications. *Ann. Thorac. Surg.*; 1990; 49:458-462.
- 9- Serry, C.; Bleck, P.C.; Javid 5 H.; Hunter, J.A.; Goldin, M.D.; Delaria, G.A. and Najafi, H.: Sternal wound complications-Management and results. *J. Thorac. Cardiovasc. Surg.*; 1980; 80:861-866.
- 10- Sanfelippo, P.M. and Danielson, G.K.: Complications associated with median sternotomy. *J. Thorac. Cardiovasc. Surg.*; 1972; 63:419-423.
- 11- The Parisian Mediastinitis Study Group: Risk factors for deep sternal wound infection after sternotomy: A prospective, multicenter study. *J. Thorac. Cardiovasc. Surg.*; 1996; 111: 1200-1207.
- 12- Newman, L.S.; Szczukowski, L.C.; Bain, R.P. and Perlino, C.A.: Suppurative mediastinitis after open heart surgery. A case control study of risk factors, *Chest*; 1988; 94:546-553.
- 13- Bassiouny, M.; El-Saegh, M.M.; Ali, M.A. and Shoeb, A.: A new approach for management of postoperative mediastinitis, *Egyptian. J. Surg.*; 1988; 7 (2): 25-28.
- 14- Cullifod, A.T.; Cunningham, J.N. Jr.; Zeff, R.H.; Isom, O.W.; Teiko, P. and Spencer, F.C.: Sternal and costochondral infections following open heart surgery. A review of 2,594 cases. *J. Thorac. Cardiovasc. Surg.*; 1976; 72:714-726.
- 15- Bor, D.H.; Rose, R.M.; Modlin, J.F.; Weintraub, R. and Friedland, G.H.: Mediastinitis after cardiovascular

- surgery. *Rev. Infect. Dis.*; 1983; 5:885-897.
- 16-Thurer, R.J.; Bognolo, D.; Vargas, A.; Isch, J.H. and Kaiser, G.A.: The management of mediastinal infection following cardiac surgery: an experience utilizing continuous irrigation with povidone-iodine. *J. Thorac. Cardiovasc. Surg.*; 1975; 68:962-968.
- 17-Loop, F.D.I; Lytle, B.W.; Cosgrove, D.M.; Mahfood, S.; McHenry, M.C.; Goormastic, M., Stewart, R.W.; Golding, L.A.R. and Taylor, P.C.: Sternal wound complications after isolated coronary artery bypass grafting: Early and late mortality, morbidity and cost of care. *Ann. Thorac. Surg.*; 1990; 49:179-187.
- 18-Chang, N. and Mathes, S.J.: Comparison of the effect of bacterial inoculation in musculocutaneous and random pattern flaps. *Plast. Reconstr. Surg.*; 1982; 70:1-9.
- 19-Molina, J.E.: Primary closure for infected dehiscence of the sternum. *Ann. Thorac. Surg.*; 1993; 55:459-463.
- 20-Jeevanandam, V.; Smith, C.R.; Rose, E.A.; Malm, J.R. and Hugo, N.E.: Single-stage management of sternal wound infections. *J. Thorac. Cardiovasc. Surg.*; 1990; 99:256-263.

THE CARBOMEDICS 'TOP-HAT' SUPRAANNULAR PROSTHESIS AS A SALVAGE TO THE SMALL AORTIC ANNULUS PROBLEM

ABSTRACT

The Carbomedics "Top-Hat" supraannular prosthesis (introduced in 1993) is a new valve that tries to solve the problem of small aortic annulus. A total of 148 patients underwent aortic valve replacement by open heart surgery in our department in Ain-Shams University over a period of one year. In order to evaluate this new valve and its hemodynamics in relation to the small aortic annulus problem, our 148 patients were divided into 2 groups: group (A) (n=62) (study group) whose patients had the Carbomedics "Top-Hat" supraannular prosthetic valve implanted, and group (B) (n=86) (control group) whose patients had different types of standard aortic prosthetic valves implanted. Our study group (A) (n=62) had an average age of 31.14 ± 14.1 (range 16 to 68 years). Preoperatively in group (A), 18 patients (29%) were in NYHA class II, 38 (61.3%) in class III and 6 (9.7%) were in class IV. All patients in our study group (A) were diagnosed and followed up after 3 months from operation by echocardiography exclusively.

By statistical analysis, many results were evaluated. By "Sperman Correlation Test", it was found that there is a significant inversely proportional correlation between the aortic annulus and postoperative pressure gradient as the "Correlation Coefficient" ($r = -0.90578$). Also, there is a significant inversely proportional relationship between the body surface area and postoperative pressure gradient, where ($r = -0.65182$).

By comparing between preoperative and postoperative data within group (A) it was found that there is a highly significant (HS) difference ($P < 0.001$) by using the student t-test, for each of pressure gradients (pr.gr.), ejection fraction (EF), end-diastolic diameter (EDD) and end-systolic diameter (ESD), having each an average of 35.636 ± 20.235 , 0.0364 ± 0.03 , 5.772 ± 5.66 and 6.454 ± 3.82 , respectively. Also, comparing preoperative and postoperative NYHA classes in group (A) yielded a significant (S) difference ($P < 0.05$) by using the chi-square test, where (Chi-Square = 8.12).

Using the student t-test, comparison between group A and B regarding improvement of patients showed that there is a highly significant difference (HS) ($P < 0.001$) for each of pr.gr. difference and ESD difference, having an average of (group A= 50.09 ± 15.51 , group B= 35.12 ± 14.26), and (group A= 13.58 ± 7.65 , group B= 15.02 ± 6.31), respectively.

Also, the same principle was applied to each of the EF difference and EDD difference who had a significant (S) difference ($P < 0.05$), where each had an average of (group A= 7.09 ± 7.16 , group B= 6.51 ± 6.55) and (group A= 8.944 ± 9.43 , group B= 21.2 ± 10), respectively.

By comparing the average of body surface areas (BSA) in our patients, the patients with a "Top-Hat" prosthesis had significantly (HS, $P < 0.001$) smaller BSA for each of the three sizes (19, 21 and 23mm) than that of patients for whom an intraannular standard

prosthesis was used. Thus in practice, BSAs being equal, a larger "Top-Hat" prosthesis can be used.

The mortality in our study group (A) was 4 patients (4/62) (6.25%) which is reasonable and parallels other authors in literature.

In conclusion, the "Top-Hat" supraannular Carbomedics prosthesis is a useful alternative and salvage in the small aortic annulus. It shows favourable hemodynamic properties due to the gain of a 2mm or 4mm increase in valve size, compared to standard bileaflet intraannular valves.

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J. of Egypt. Society of Cardiothorac. Surg. 1998, VI April No 2.

INTRODUCTION

There is a directly proportional relationship between the diameter of the aortic valve and the body surface area (BSA) of the patient. In general, BSA values lower than 1.7m^2 are highly predictive of a small aortic annulus and thus indicate the need of a 19mm prosthesis (1,2).

Some authors showed that various 19mm standard prostheses of the latest generation result in substantial obstruction of the left ventricular outflow tract and less marked reduction in hypertrophy of the left ventricle compared with larger prostheses. Thus, the solutions to the problem of a small aortic annulus are to design a small prosthesis with better hemodynamics, to implant a larger prosthesis by aortic root enlargement, or to modify the sewing cuffs to take advantage of supraannular implantation (3).

Device description

The Carbomedics "Top-Hat" supraannular prosthesis (introduced in 1993) is a standard Carbomedics valve in which the cuff has been transferred to the inflow level of the valve. As a result, the prosthesis

sits above the annulus rather than within it. The valve housing protrudes into the aortic root like a top hat (4).

The "Top-Hat" valve provides an adaptation of the bileaflet valve that permits a device 2mm to 4mm larger in diameter to be inserted in the supraannular position within the aortic sinuses (This device was approved for market release by the US Food and Drug Administration on September 29, 1993). The cuff rests on top of the aortic valve annulus, and the valve housing protrudes into the aortic root like a top hat, so that structural components of the valve sit above the annulus rather than within the annulus (Fig.3a,b) (5). This feature allows a size advantage of up to 5mm over other mechanical valves. The outside diameter of the supraannular valve has been minimized with the use of the modified, titanium stiffening ring, and pyrolytic carbon valve components to reduce potential interference with coronary blood flow and aortotomy closure. The knitted polyester sewing ring has a thin, reinforced brim at the inflow end of the valve. The original carbomedics bileaflet valve features of recessed pivot design, radiographic visibility, low-noise level, and valve rotatability are all retained.

The valve comes with its own sizer (Fig. 4a,b) (3). The lower cylindrical section is inserted into the annulus, and it represents the inner diameter of the prosthetic valve orifice. The upper profile portion of the sizer replicates the size and shape of the valve and sewing cuff above the annulus and assesses proper clearance for the coronary ostia. Although the sizer allows for an estimate of clearance of the coronaries away from the valve housing, sizing is normally carried out in the cardioplegia-arrested heart. When the aorta redestends with blood, the walls of the sinuses move away from the valve (5).

Materials and Methods

One hundred and forty eight patients underwent aortic valve replacement by open heart surgery through a median sternotomy in the cardiothoracic surgery department at Ain-Shams University hospital and Ain-Shams Specialized Hospital over a period of one year starting January 1st 1997 till the end of February 1998. Sixty two patients had the Carbomedics "Top-Hat" supraannular prosthetic valve implanted (group A) whereas eighty six patients had different types of standard aortic prosthetic valves implanted (group B). This is a prospective study.

Of these 148 patients 81(54.7%) were males and 67(45.3%) females. Group A (n=62) comprised 43(69.4%) males and 19(30.6%) females whereas in group B (n=86), there were 68(79%) males and 18(21%) females. The study group (A) (n=62) had an average age of (31.14±14.1) (range, 16 to 68 years).

In the preoperative period, 18 patients (29%) were in New York Heart Association (NYHA) class II, 38(61.3%) in class III and 6(9.7%) were in class IV.

Primary aortic valve replacement was

performed on 54(87.1%) cases and repeat valve replacement, on 8 cases (12.9%). Forty-two patients (67.7%) were in sinus rhythm, 18(29%) were in atrial fibrillation, and 2(3.3%) had a pacemaker due to heart block.

All 62 patients in our study group (group A) were diagnosed by echocardiography exclusively. The available Doppler echocardiographic unit in our Cardiothoracic Surgery Department, Ain-Shams University, was used (Type Hewlett-Packard 77021:H-P Co, Palo Alto Calif.). Both two-dimensional and Doppler echo studies were used.

The preoperative left ventricular ejection fraction in the study group A ranged between (0.34 and 0.66) with an average of (0.519±0.087).

The preoperative end diastolic diameter (EDD) ranged between 41 and 82 millimetre (mm) with an average of 60.45±11.85, also the preoperative end systolic diameter (ESD) ranged between 32 and 64mm with an average of 47.772±9.298.

Also, in group (A) the preoperative peak pressure gradient ranged between 42 and 126mmHg with an average of 66.818±21.656. Also, in group (A) the preoperative aortic annulus diameter ranged between 19 and 25mm with an average of 21.272±1.881, while the body surface area (BSA) in group (A) ranged between 1.2 and 2.6m² with an average of 1.759±0.333.

Isolated aortic valvulopathy (Table 1) was diagnosed in 39 patients (62.9%) in our study group, mitral and aortic valvulopathy in 19 patients (30.6%) and mitral, aortic, and tricuspid valvulopathy in 4 patients (6.5%).

The aortic lesion in group A was pure stenosis or a double lesion with preponderance of stenosis in 47 patients

(75.8%) and insufficiency in 15 patients (24.2%). The cause of the valvular disease in group A was rheumatic in 51 patients (82.3%), degenerative in 8 patients (12.9%), infective endocarditis on native valve in 1 patient (1.6%) and in previous aortic valve replacement patients due to paravalvular leak in 1 patient (1.6%) and valve thrombosis in another (1.6%). One patient only had a concomitant coronary artery disease and coronary artery bypass grafting was done to him by a saphenous venous graft to his left anterior descending artery.

Surgical technique performed

The operative approach in all patients was through a median sternotomy with cardiopulmonary bypass and systemic hypothermia (25°-28°C). Also, local hypothermia using crushed ice was used. Modified blood cardioplegia has been routinely used in all patients in the form of a bag of 500ml hypothermic hyperkalemic cardioplegia solution with 150ml of its content being voided out and replaced by blood of patient through aortic root at a temperature of 34°C immediately after going on bypass and starting the systemic blood cooling. Also, 10 meq of KCl is added to this first dose of cardioplegia. If an additional dose was required so the above procedure was repeated apart from the fact that the replaced blood would be supplied from the heart-lung machine rather than from the aortic root of the patient being operated upon.

After aortotomy, aortic valve was resected and sizing was performed by using the supraannular sizer in each patient of the study group (A). The aortic prosthesis was implanted in the supraannular position. Pledgets were placed in the aortic surface of

the native aortic ring while knots, in the aortic aspect of the prosthetic sewing cuff.

Twenty one patients (33.9%) received size 19mm of the supraannular Carbomedics (Top-Hat) aortic prosthetic valve, while 24 (38.7%) received size 21mm, 15 (24.2%) received size 23mm and only 2 (3.2%) received size 25mm.

The postoperative intensive care unit (ICU) stay ranged from 24 hrs to 4 days. All patients received the usual oral anticoagulant therapy (Dindevan or Marevan) controlled by the prothrombin time (P.T.) (normal= 13 seconds) to be usually double the normal P.T. or with a recommended international normalized ratio (INR) ranging between 2.5 and 3.5.

The postoperative echocardiographies were done for surviving patients out of the 62 patients in group (A), after 3 months from the operation using the same device as the preoperative echocardiographies.

Results

The postoperative left ventricular ejection fraction in group (A) ranged between 0.38 and 0.68 with an average of 0.555 ± 0.098 . The postoperative EDD ranged between 40 and 72mm with an average of 54.681 ± 10.339 and postoperative ESD ranged between 28 and 58mm with an average of 41.318 ± 8.909 .

By using the "Sperman Correlation Test", statistical analysis of the data provided the different clinical characteristics for the study group (A) (n=62) where if the correlation coefficient (r) is negative (-), so there is an inversely proportional relationship between the 2 subjects. On the contrary, if the correlation coefficient is

Table (1): Different operative procedures done

Operation	Group A		Group B	
	No	%	No.	%
AVD	39	62.9	51	59.3
AVD+MVD (DVD)	19	30.6	29	33.7
DVD+Tric.VD	4	6.5	6	7

Where: AVD = Aortic valve disease; MVD = Mitral valve disease, DVD = Double valve disease; Tric. VD = Tricuspid valve disease.

Table (2): Number of patients in different valve sizes with their BSAs and postoperative pr.gr.

Group A (n=62)

Valve size (mm)	19	21	23	25
No. of patients	21	24	15	2
Percent (%)	33.9	38.7	24.2	3.2
BSA (m ²)	1.2-1.8	1.4-2.1	1.6-2.3	1.7-2.6
Pr. Gr. (mmHg)	35-43	29-36	19-25	22 and 23

Group B (n=86)

Valve size (mm)	19	21	23	25
No. of patients	27	33	26	0
Percent (%)	31.4	38.4	30.2	0
BSA (m ²)	1.3-2.2	1.4-2.5	1.7-2.6	0
Pr. Gr. (mmHg)	38-49	32-39	22-28	0

Where: No. = number, BSAs = Body surface areas, Pr.Gr. = pressure gradient.

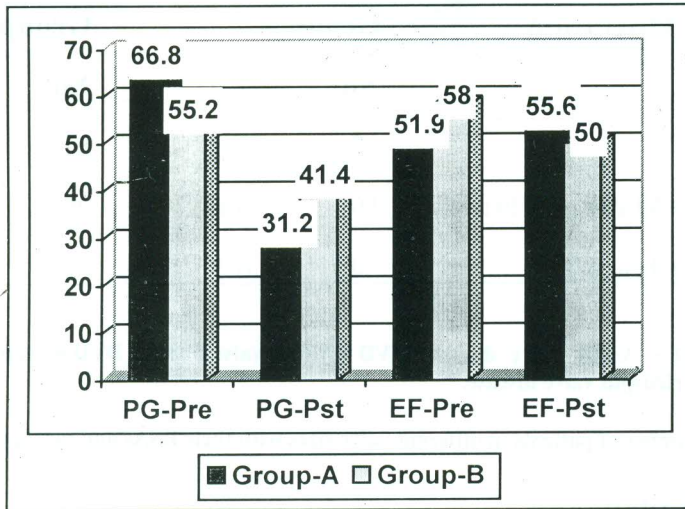


Fig. (1): Comparison between group-A and group-B regarding EF and PG pre and post mean values.

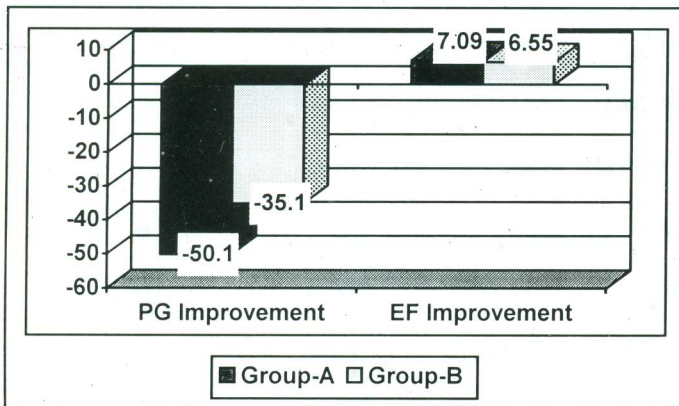


Fig. (2): Comparison between group-A and group-B regarding improvement in the EF and PG.

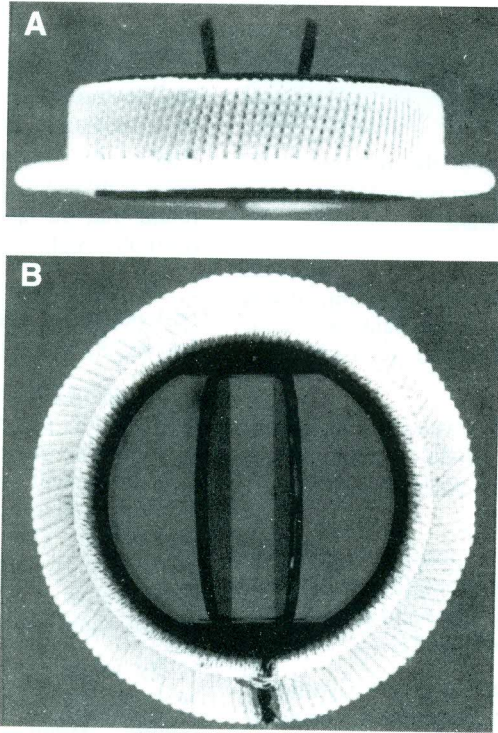


Fig. (3): The carbomedics "Top Hat" supraannular aortic prosthesis. A. Profile view B. Overview.

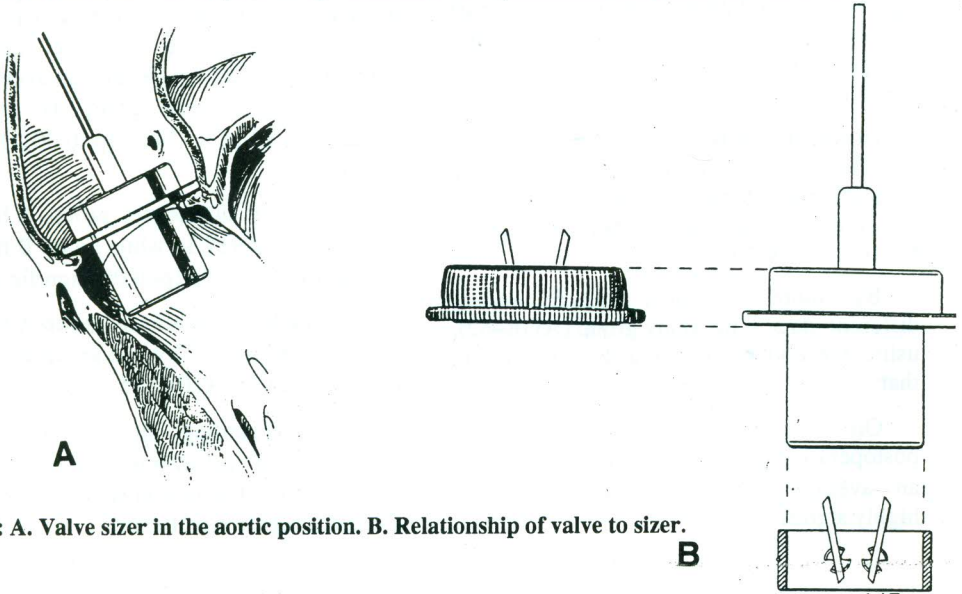


Fig. (4): A. Valve sizer in the aortic position. B. Relationship of valve to sizer.

positive (+), hence there is a directly proportional relationship between the 2 subjects.

If (r) is <0.36048 the relationship is nonsignificant but if (r) is >0.36048 so, the relationship is significant.

So, on comparing the aortic annulus with the postoperative pressure gradient, it was found to be a negative significant correlation (inversely proportional) to each other ($r = -0.90578$).

There was a negative significant (inversely proportional relationship) between BSA and postoperative pr.gr., ($r = -0.6512$).

There was a positive significant correlation (directly proportional) between preoperative NYHA class and preoperative pressure gradient ($r = 0.77071$).

Also, there was a positive significant correlation (directly proportional) between preoperative pressure gradient and preoperative EDD ($r = 0.65528$). A positive significant correlation (directly proportional) between preoperative pressure gradient and preoperative ESD was also detected ($r = 0.73919$).

However, there was a negative non-significant correlation (inversely proportional) between the postoperative pressure gradient and postoperative ejection fraction ($r = -0.29737$).

By more statistical analysis among different data in the study group (A) ($n=62$), using the student t-test (Fig. 1), it was found that:

On comparing the preoperative and postoperative pressure gradients, there was an average of 35.636 ± 20.235 ($P < 0.001$, highly significant).

On comparing between the preoperative and postoperative EF, there was an average of 0.0364 ± 0.03 ($P < 0.01$, highly significant). Also, by comparison between the preoperative and postoperative EDD, it was found that the average was 5.772 ± 5.66 ($P < 0.001$, highly significant).

On comparing between preoperative and postoperative ESD, the average was 6.454 ± 3.82 ($P < 0.001$, highly significant).

By using the Chi-square test, comparison between the preoperative and postoperative NYHA class in group A yielded that the column percent for NYHA classes II, III and IV preoperatively were 28.57, 73.68 and 50 respectively. On the other hand, it was 71.43, 26.32 and 50, respectively for postoperative NYHA (Chi-square=8.12, $P < 0.05$, significant difference).

By using the student t-test, comparison between the study group (A) ($n=62$) and control group B ($n=86$) regarding improvement (symbolized by the difference between the preoperative and postoperative average in each item) (Fig.2), it was found that: Regarding the pressure gradient difference (D), group (A) had an average of 50.09 ± 15.51 while group B had, an average of 35.12 ± 14.26 ($p < 0.001$, highly significant).

For the EF difference, group A had an average of 7.09 ± 7.16 while group B had an average of 6.51 ± 6.55 ($p < 0.05$, significant).

For the EDD difference, group A had an average of 8.944 ± 9.43 , while group B had an average of 21.2 ± 10 ($P < 0.05$, significant).

Finally regarding the ESD difference group A had an average of 13.58 ± 7.65 , while group B had an average of 15.02 ± 6.31 ($P < 0.001$, highly significant).

The mortality in our study group (A) was 4 patients out of 62 (6.25%) within the three months of follow-up. Two cases with double valve replacement with DeVega repair of tricuspid valve died, one intraoperatively due to pump failure and inability to go off-bypass and the second due to low cardiac output in the 2nd postoperative day. The third case was aortic valve re-replacement (due to valve thrombosis) and died of uncontrolled postoperative bleeding on the night of the operation.

Finally, the fourth case was aortic valve replacement in an old male aged 68, and died of cerebral embolism on the sixth postoperative day.

Discussion

The presence of a small aortic root presents a difficult problem to the surgeon. However, the use of supraannular prosthesis as Carbomedics "TopHat" allows the use of a larger size than would be possible for a prosthesis implanted in the intraannular position of aortic valve. Aortic valve replacement with a small aortic prosthesis may lead to unacceptable gradient in adult patients (6).

Other means were suggested to deal with the problem of small aortic annulus as surgical enlargement of aortic root, and aortic homografts. However, problems like bleeding for the first and durability as well as availability of the second limit their use to some extent. Also, the use of porcine stentless bioprostheses is a newer alternative for dealing with the small aortic root, however, their durability is still not yet known (7,8).

Our concern in this study focuses upon the value of using supraannular "Top-Hat" Carbomedics valve in small aortic annulus patients. So, over a period of one year 148 patients had different procedures involving

aortic valve replacements. Those patients were divided into 2 groups, the study group A (n=62) with supraannular "Top-Hat" Carbomedics aortic valves implanted, and the control group (B) (n=86) with the standard intraannular aortic valve being implanted.

Concerning the study group (A), the previously mentioned results describe the different relations of data together and their evaluation as those results by the "Sperman Correlation Test". The most important of those results was the inversely proportional relationship between the aortic annulus and post-operative pressure gradient (a negative significant correlation with $r = - 0.90578$).

Hence, the smaller the aortic annulus and its prosthesis size (Table 2), the higher the postoperative pressure gradient and vice versa. Thus on using a supraannular aortic valve as "Top-Hat" gives lower pressure gradient than that given by a standard intraannular valve in the same size of annulus. This agrees with the series of some authors (4). The difference between the two prostheses does not affect the valve areas for each size, but it does allow the opportunity to implant a larger size in each patient. This opinion is also supported by the fact that patients in whom a 19mm intraannular prosthesis is implanted, can be considered to have a poorer prognosis because of the persistence of high transvalvular gradients and the inability to substantially reduce left ventricular hypertrophy (9,10).

Bech and co-workers (11) concluded that the echocardiographic measurement of the aortic annulus diameter is a fairly sensitive method to identify patients receiving a small prosthesis. Moreover the predictive accuracy is dependent upon training as well as image quality.

The comparison of the average BSAs (Body surface Areas) in our series shows

that patients with a "Top-Hat" prosthesis had a significantly ($P < 0.001$, highly significant) smaller BSA for each of the three sizes (19, 21 and 23mm) than that of patients for whom an intraannular standard prosthesis was used. In practice, this means that BSAs being equal, a larger "Top-Hat" prosthesis can be used. These analyses must be looked at carefully because of the characteristics of the groups studied although they do suggest that the use of a prosthesis designed specifically for supraannular implantation constitutes an especially interesting advantage in patients with small aortic annulus.

By using the student t-test, comparison between the different preoperative and postoperative parameters in the study group (A) yielded a highly significant change ($P < 0.001$) for the following parameters, pressure gradient (average 35.636 ± 20.235), EF (average 0.0364 ± 0.03), EDD (average 5.772 ± 5.66) and ESD (average 6.454 ± 3.82). Also, by comparing the preoperative and postoperative NYHA class using the Chi-square test there was a significant change $P < 0.05$ (Chi-Square=8.12). These results are explained by the excellent hemodynamic changes of the supraannular "TopHat" prosthetic valve on the patient as regards his left ventricular function, pressure gradient and NYHA class.

In order to evaluate the above results more, the student t-test was used to compare between the study group A and control group B regarding improvement. It was found that it was highly significant ($P < 0.001$) for pressure gradient difference and ESD difference between the 2 groups. The improvement was only significant ($P < 0.05$) regarding EF difference and EDD difference between the 2 groups.

Hence, these results could be attributed

to the great hemodynamics of supraannular "Top-Hat" Carbomedics valve with its advantage of having one size in favour of the "Top-Hat", as coincides with the results of some workers (4).

However, on the contrary as the modification of the "Top-Hat" prosthesis alters only the sewing cuff, the results should not vary in regard to those published for the Carbomedics standard prosthesis (12,13).

Mild insufficiency is a common finding in most normally functioning prosthetic heart valves, labelled as "physiological insufficiency" (14).

Mortality in this study group comprised only 4 cases (6.25%). This is in agreement with the series of some authors (8.7%) (5) and (7.3%) (15), but opposes the very low mortality in another series (3.9%) (4). This less percent in mortality could be explained on the basis of the higher number of patients in that series ($n = 127$) compared to our study group ($n = 62$).

Conclusions

The "Top-Hat" supraannular Carbomedics prosthesis is a useful alternative in the small aortic annulus. It shows favourable hemodynamic properties due to the gain of a 2mm or 4mm increase in valve size, compared to standard bileaflet intraannular valves.

References

- 1- Chambers J.: Echocardiography and the small aortic root. *J. Heart Valve Dis.* 1996; 5 (Suppl.3): 264-268.
- 2- Franzen, S.F.; Huljebrant, I.E.; Konstantinov, I.E.; Nylander, E. and Olin, C.L.: Aortic valve replacement for aortic stenosis in patients with small

- aortic root. *J. Heart Valve Dis.* 1996; 5 (Suppl.3): 284-288.
- 3- Gonzalez-Juanatey, J.R.; Garcia-Acuna, J.M.; Vega, M.; et al.: Influence of size of aortic valve prostheses on hemodynamics and change in left ventricular mass: implications for the surgical management of aortic stenosis. *J. Thorac Cardiovasc. Surg.* 1996; 112:273-280.
 - 4- Bernal, J.M.; Martin-Duran, R.; Rabasa, J.M. and Revuelta, J.M.: The Carbomedics "Top-Hat" supraannular prosthesis. *Ann. Thorac. Surg.* 1999; 67:1299-1303.
 - 5- Roedler, S.; Moritz, A.; Wutte, M.; Hoda, R. and Wolner, E.: The Carbomedics "Top-Hat" supraannular prosthesis in the small aortic root. *J. card. Surg.* 1995; 10: 198-204.
 - 6- Barner, H.B.; Labovitz, A.J. and Fjone, A.C.: Prosthesis valves for the small aortic root. *J. Card. Surg.*; 1994, 9 (Suppl.): 154-157.
 - 7- Walther, T.; Falk, V.; Diegeler, A.; et al.: Stentless bioprostheses for small aortic root. *J. Heart Valve Dis.* 1996; 5 (Suppl. 3): 302-307.
 - 8- Sintek, C.F.; Fletcher, A.D. and Khonsari, S.: Small aortic root in the elderly: use of stentless bioprosthesis. *J. Heart Valve Dis.*, 1996; 5 (Suppl. 3): 308-313.
 - 9- Kratz, J.M.; Sade, R.M.; Crawford, F.A. Jr.; Crumbley, A.J. III and Stroud, M.R.: The risk of small St. Jude aortic valve prostheses. *Ann. Thorac. Surg.*, 1994; 57:1114-1119.
 - 10-Sim, E.K.W.; Orszulak, T.A.; Schoff, H.V. and Shub, C.: Influence of prosthesis size on change in left ventricular mass following aortic valve replacement. *Eur. J. Cardi.o-thorac. Surg.*,- 1994; 8:293-297.
 - 11-Bech-Manssen, O.; Caidahl, K.; Myken, P.S.; Kizellman, I.I.; Larsson, S. and Wallentén, I.: Preoperative echo prediction of small prosthesis size. *J. Heart Valve Dis.* Mar., 1996; 5 (2):128-135.
 - 12-Copeland, J.G. III; Sethi, G.K.; North American team of clinical investigators for the Carbomedics prosthetic heart valve: Four-year experience with the Carbomedics valve: the North American experience. *Ann. Thorac. Surg.*, 1994; 58:630-638.
 - 13-Bernal, J.M.; Rabasa, I.M.; Gutierrez-Garcia, F.; Morales, C.; Nistal, J.F. and Revuelta, I.M.: The Carbomedics valve: experience with 1049 implants. *Ann. Thorac. Surg.* 1998; 65:137-143.
 - 14-Chambers, J.; Monaghan, M. and Jackson, G.: Colour flow Doppler mapping in the assessment of prosthetic valve regurgitation. *Br. Heart J.* 1989; 62:1.
 - 15-Knez, I.; Machler, H.; Rehak, P.; Oberwaider, P.; Anelli-Monti, M.; Dacar, D. and Rigler, B.: Concomitant procedures in the small versus standard aortic root. *J. Heart Valve Dis.* 1996; 5 (Suppl.III): S294-S301.

URGENT CORONARY ARTERY REVASCULARIZATION

ABSTRACT

In recent years, urgent coronary artery bypass grafting (CABG) has become an important part of most cardiac surgery programs. Surgeons nowadays can anticipate an operative mortality of about 5% for such patients. Our current study was conducted to evaluate results and outcome of urgent CABG and try to find out the possible methods to reduce postoperative mortality and morbidity. The internal mammary artery (IMA) is the conduit of choice for CABG in many institutions.

This study included 30 patients who underwent urgent CABG in our cardiothoracic surgery departments at Ain-Shams and Specialized hospitals. This is a prospective study, starting January 1997, with a follow up period (average 24 months) for the whole population.

The mean age for patients was 50.3 years (range 23 to 66 years). The majority were of the male gender, with 20 males (67%) and 10 females (33%).

All patients were referred to the hospital suffering from angina pectoris and all preoperative data were recorded to each patient. All diagnostic cardiac tools were conducted to each patient as 12 lead ECG, chest radiogram, echocardiography and cardiac catheterization. All operative data were recorded and postoperative events were carefully observed and evaluated meticulously. Most of our patients (33%) were in group V according to classification related to ejection fraction (EF), (23%) in group IV, (26%) in group III, 15% in group II and non had (EF) less than 30%. Decision making for surgery was done within 4 hours from the diagnosis for patient condition as emergency or as urgent if after that.

There were 92 distal anastomoses for CABG done in our series with a mean of 3.1 anastomoses per patient (range 2-5). There were 44 grafts for LAD-Diagonal systems, 22 for circumflex system and 26 to right system. There were 18 single saphenous venous grafts and 3 sequential grafts.

Regarding perioperative morbidity, it was found that overall incidence of sternal wound infection in our series was 10%, with superficial and deep wound infections having 6.6% and 3% respectively.

For perioperative myocardial infarction (PMI), 4 patients (13.3%) had new Q-waves in ECG. There were statistical difference in incidence of PMI among patients before and after urgent CABG ($P < 0.01$, highly significant; $P < 0.001$, highly significant and $P < 0.05$, significant) as regards cardiac enzymes CPK, CK-MB and LDH respectively. R-waves changes were significant ($P < 0.05$) while Q-waves were not ($P > 0.05$).

Two patients had intraaortic balloon pumps (IABP). There were no serious postoperative pleuropulmonary complications. However, radiologically, 3 patients (10%) had postoperative atelectasis and 9(30%) had pleural effusion and 1(3%) had pneumothorax.

Twenty-eight patients had undergone urgent or emergency CABG (93%). The overall incidence of perioperative mortality in the whole study was 6.6%, with 2 mortalities. However, results of late follow up showed that 2 patients died with a mortality rate of 13%.

Hence, postoperative mortality has acceptable results in patients undergoing urgent CABG. We thus recommend surgical consultations to evaluate patients with acute coronary artery ischemia, also the use of arterial conduits for such patients. Finally, urgent or emergency CABG can be performed in all critical patients to save the viable myocardium and to help those patients who are at risk, with no fear of increased mortality or morbidity especially with the new surgical techniques and updated methods of myocardial preservation.

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INTRODUCTION

No-one can deny that in recent years, urgent coronary artery bypass grafting (CABG) has become an important subject of most cardiac surgery programs. Thus urgent CABG can be used effectively to salvage most patients who are at risk. The concept of rapid reperfusion to save jeopardized, but still viable, ischemic myocardium is fast gaining clinical acceptance (1).

The operative mortality for urgent CABG shows that the general impression is that it only carries out moderate risk, with evidence to indicate that surgeons anticipate an operative mortality of 5% for such patients. However, in patients with severe left ventricular failure caused by ischemic cardiomyopathy, the superior long-term survival treatment has been shown to be CABG (2).

The internal mammary artery (IMA) is a very important conduit for CABG and is routinely used in many institutions (3). The IMA is preferred by many surgeons for direct coronary artery revascularization, as the superior long-term patency of the IMA compared with the reversed saphenous vein graft is well-established. Hence, it has been

chosen by some surgeons as the bypass conduit of choice. Other conduits that could be used for CABG include the right gastroepiploic artery (RGEA), inferior epigastric artery (IEA) and radial artery (RA)(4).

Patients and Methods

This study comprised 30 patients who underwent urgent CABG in the department of cardiothoracic surgery, Ain-Shams University Hospital and Ain-Shams Specialized Hospital. All patients were operated upon using pedicled IMA grafts and reversed saphenous vein grafts (SVGs) as a single or sequential grafts. This study was conducted in a prospective manner, starting January 1997.

The following diagnostic and interventional procedures were performed for every patient.

A) Preoperative data

All patients were referred to the hospital suffering from angina pectoris. The following data were recorded for each patient:

- Age, sex, height and weight.
- Body surface area (BSA), determined

by the Dubois nomogram.

- Angina class according to the Canadian cardiovascular society classification was scored for every patient (5).

- Type of medication received especially platelet inhibitors and anticoagulant drugs.

- Analysis of risk factors as:

1. Family history of coronary artery disease (CAD)

2. History of smoking.

3. Hypercholesteremia (if cholesterol level was above 6.5 mmol/L)

4. Hypertension (if diastolic pressure was above 90mmHg).

5. Obesity.

6. Chronic obstructive pulmonary disease (COPD) as evidenced in radiograms.

7. Diabetes mellitus (DM).

The patients had routine chest radiograms, twelve-lead electrocardiogram (ECG), laboratory investigations including complete blood picture with hemoglobin, serum creatine and bilirubin and cardiac enzymes as lactate dehydrogenase (LDH), creatine phosphokinase (CPK), creatine phosphokinase-MB, aspartate aminotransferase (ASAT) and alanine aminotransferase (ALAT) were measured as soon as the patient arrived in intensive care unit (ICU). Also, catheterization data were recorded where all patients underwent left sided ventriculography and coronary angiography.

For coronary angiography: Stenosis greater than 50% of luminal diameter was considered to be of hemodynamically significant importance.

For ventriculography: Left ventricular function (LVF) was quantitated by LV score

as developed by the coronary artery surgical study (CASS) It was performed in the right anterior oblique projection. Five segments were analyzed (anterobasal, anterolateral, apical, diaphragmatic and posterobasal). A numerical score was assigned to these segments into four classes (Normal; moderate hypokinesia = class I; severe hypokinesia = class II, akinesia = class III; dyskinesia with or without aneurysm = class IV). The total score was obtained by adding the values assigned to each segment. A total score of 5 means a normal LVF. A score of 15 or more implies a severe LV dysfunction.

Left ventricular end diastolic pressures (LVEDP) were grouped according to some authors (7) into:

- Normal LVEDP less than 12mmHg.

- Moderately elevated: LVEDP between 13-18mmHg.

- Markedly elevated: LVEDP more than 18mmHg.

B) Intraoperative data

The collected data comprised bypass time in minutes (min.), aortic cross clamp time (min.), number of distal anastomoses, cardiac output (COP) and cardiac index (CI) before and at the end of bypass, type of cardioplegia used and the need for inotropic support.

C) Postoperative data

Postoperative course of all patients was evaluated with regard to perioperative mortality and morbidity. Perioperative mortality (POM) was defined as "any death occurring within the first 30 days after operation". Morbidity was defined as one or more of the following: Cardiac complications as postoperative myocardial infarction (PHI) where ECG shows new Q waves that equal 4 or more milliseconds

with significant elevation of cardiac enzymes more than twice normal values, low cardiac output and new atrial fibrillation. Sternal wound infections whether superficial or deep, pleuropulmonary complications as pleural effusion, atelectasis or prolonged mechanical ventilation of 2 or more days, the incidence of postoperative blood, the patient was re-explored for bleeding when more than 800ml was lost in 1st 2 hours in ICU or when 1000ml was lost within 3 hours after operation. Central nervous system (CNS) complications as stroke and renal complications as oligemia and renal failure. Hospital stay was recorded for patients.

D) Follow up results

Patients were followed after hospital discharge. Deaths were interpreted as cardiac or non-cardiac related.

Patients admitted to the hospital were subject to decision of operation within 4 hours from diagnosis as urgent or emergency. Routine bypass was established, then distal anastomoses with vein grafts were performed by the use of continuous 7/0 prolene suture. Proximal aorta-SV anastomoses were performed by the use of continuous 6/0 prolene suture with the use of side occlusion clamp after removing the aortic clamp. The IMA-coronary anastomoses were performed by the use of continuous 7/0 prolene suture.

Sequential grafting for left anterior descending artery (LAD) and diagonal arteries was used in 3 cases (10%). Valve replacement was done in addition to CABG in 2 cases, one mitral and the other aorta (6.7%). CABG was performed in 3 cases on beating heart (10%). Redo-coronary was

performed in one case (3.3%) using venous grafts only.

One patient was re-explored (3.3%) due to postoperative bleeding. Pump failure was treated by the use of inotropic drugs as dopamine with or without adrenaline. Postoperative hypertension was controlled nicely using sodium nitroprusside at a dose of 1.5 to 8 microgram/kg/minute. All patients received combination of routine antibiotics as cephalosporin or semisynthetic penicillin. Patients stayed in the intensive care unit (ICU) for about 48 hours (hrs) after which they were discharged to ward. Anti-platelet drugs in the form of aspirin 1/2 gram/day and persantin 75mg three times daily were prescribed for the majority of patients.

The aim of our work was to study the outcome of urgent CABG and possible method to reduce postoperative mortality and morbidity, improve the results and to find out the optimum time of surgical intervention.

Results

The mean age for the whole population was 50.3 years (range 23 to 66 yrs). The majority of the patients were of the male gender, with 20 males (67%) and 10 females (33%).

Preoperative clinical discrete variables for the whole population are shown in table (1)

Twenty seven patients (90%) presented with typical chest pain, 10 (%) with a history of previous myocardial infarction (M1), one of whom had a recent MI 18(60%) with a history of dyspnea on exertion, 3 (10%) with atypical chest pain,

Table (1): Preoperative clinical discrete variables for the whole population:

Variables	Number	Percentage (%)
1- Gender:		
Male	20	67
Female	10	33
2- Risk factors:		
Obesity	7	23
Hypertension	18	60
NIDDM	10	33
IDDM	8	27
Previous MI	10	33
Previous PTCA	1	3
Hypercholesteremia	6	20
F.H. of IHD	10	33
Current smoking	19	63
COPD	2	6
3- CCS angina class:		
a- Class II	18	60
b- Class III	9	30
c- Class IV	3	10
4- Anti-anginal drugs:		
β blockers	25	63
Nitrates	13	43
Calcium antagonists	19	63
Anti-platelet drugs	25	83

NIDDM = Non insulin dependent diabetes mellitus.

IDDM = Insulin dependent diabetes mellitus.

F.H. of IHD = Family history of ischemic heart disease.

COPD = Chronic obstructive pulmonary disease.

CCS = Canadian Cardiovascular Society.

Table (2): Patients classification according to ejection fraction (EF).

Group	Ejection fraction (EF)	Number	Percentage (%)
Group I	Less than 30	0	0
Group II	30 - 39	5	16
Group III	40 - 49	8	26
Group IV	50 - 59	7	23
Group V	More than 59	10	33

Table (3): Shows the preoperative catheterization data for the whole population.

Variables	Number and Percentage
Extent of coronary disease:	3 (10%)
Two-vessel disease	22 (73%)
Three-vessel disease	5 (17%)
Four-vessel disease	8 (26%)
LMCA more than 50% stenosis:	
LVWM score (CASS):	
Normal 5	6 (20%)
Mild depression 6-10	14 (46.6%)
Moderate 11-15	7 (23%)
Severe depression 16-30	3 (10%)
LVEDP:	
Normal \geq 12mmHg	8 (26%)
Moderate 13-18mmHg	16 (53%)
Marked elevation \geq 18mmHg.	6 (20%)

3 (10%) with pain at rest, 1(3%) with a history of rheumatic fever.

Preoperative coronary angiography revealed that the LAD was significantly affected (more than 70% obstruction) in 26 patients (86.7%). The circumflex (Cx) in 19(63.3%), the obtuse marginal (OM) in 5(16.6%), the right coronary (Rt.C.) in 20(66.6%), the first diagonal (D1) in 6(20%) and the left (Lt.) main coronary artery was critically occluded in 8(26.6%) as shown in figure (Fig.1). (Cath. = catheter).

The patients were classified into 5 groups according to the value of the ejection fraction as shown in Table (2):

Most of our patients (33%) were in group V, (23%) in group IV, (26%) in group

III, (15%) in group II and non of our patients had EF less than 30%.

Left ventricular end-diastolic pressure (LVEDP) was recorded for every case, the distribution of its value is shown in (Fig.2).

In 9 cases (30%) LVEDP. ranged from 10-15mmHg, while in 23% of cases, it was in the range of 15-20mmHg. Values ranging from 20-25, 25-30 were present in 13% and 6% respectively. LVEDP was nearly normal (5-10mmHg) in 27% of cases.

- The different operative procedures are shown in Fig. (3) as a pie-chart.

The preoperative catheterization data for the whole population is shown in table (3).

In 3 patients (10%) two bypass grafts

Table (4): Perioperative mortality, perioperative morbidity and hospital stay for the whole population

Variables	Number	Percentage (%)
Perioperative mortality	2	6.6
Deep sternal wound infection	1	3
Superficial sternal wound infection	2	6.6
Perioperative MI	4	13
Ischemia	4	13
Arrhythmia	3	10
Packed RBCs	7	23
FFP	4	13
Autotransfusion	0	0
Pleural effusion	9	30
Mechanical ventilation ≥ 48 hours	4	13
Atelectasis	3	10
Respiratory infection	4	13
IABP	7	23
Leg wound infection	5	17
Urinary tract infection	5	17
Hospital stay	12.5	---

MI = Myocardial infarction; Packed RBCs = Packed red blood cells FFP = Fresh frozen plasma; IABP = Intra-aortic balloon pump.

were done, three bypass grafts were done in 22 patients (73%) and 4 bypass grafts in 5 patients (17%). This is illustrated in Fig. (4).

The operative results included a total number of 92 distal anastomoses for CABG performed in the 30 patients operated upon; with a mean number (no.) of 3.1 anastomoses per patient (range 2-5). There were 44 grafts for the LAD-Diagonal systems, 22 grafts to Cx coronary artery system and 26 grafts to the right coronary artery system. There were 18 single SVGs and 3 sequential grafts. The mean bypass time was 86 minutes (min.) and mean aortic cross-clamp time was 43.7 min.

Table (4) shows the perioperative

mortality, morbidity and hospital stay for the whole population (n = 30).

The overall incidence of perioperative mortality in the whole study was 6.6%. One case died intraoperatively due to pump failure and arrhythmia. While another case died postoperatively after 7 days due to shock lung, low cardiac output and multisystem failure.

Evaluation of perioperative morbidity showed that the overall incidence of sternal wound infection (both deep and superficial) was 10%. The incidences of superficial and deep wound infections were 6.6% and 3%, respectively.

Regarding perioperative myocardial

Table (5A):PMI (Enzymes changes, CPK)

CPK	Increase postoperatively	Normal postoperatively	Total
Increase preoperatively	11	12	23 (23%)
Normal preoperatively	2	3	5 (18%)
Total	13 (46%)	15 (54%)	28

Chi-square : $P < 0.001$, highly significant.

Table (5B):PMI (Enzymes changes, CK-MB)

CK-MB	Increase postoperatively	Normal postoperatively	Total
Increase preoperatively	7	14	21 (75%)
Normal preoperatively	0	7	7 (25%)
Total	7 (25%)	21 (75%)	7 (25%)

Chi-square : $P < 0.001$, highly significant.

Table (5C): PMI (Enzymes changes, LDH)

LDH	Increase postoperatively	Normal postoperatively	Total
Increase preoperatively	12	10	22 (79%)
Normal preoperatively	2	4	6 (21%)
Total	14 (50%)	14 (50%)	28

Chi-square : $P < 0.05$, significant.

Table (5D): PMI (ECG changes, R-waves progression)

R-waves	Good postoperatively	Poor postoperatively	Total
Good preoperatively	9	3	12 (43%)
Poor preoperatively	12	4	16 (57%)
Total	21 (75%)	7 (25%)	28

Chi-square : $P < 0.05$, significant.

Table (5E): PMI (ECG changes, Q waves)

Q waves	positive postoperatively	Negative postoperatively	Total
Positive preoperatively	2	6	8 (29%)
Negative preoperatively	2	18	20 (71%)
Total	4 (14%)	24 (86%)	28

Chi-square : $P > 0.05$, non-significant.

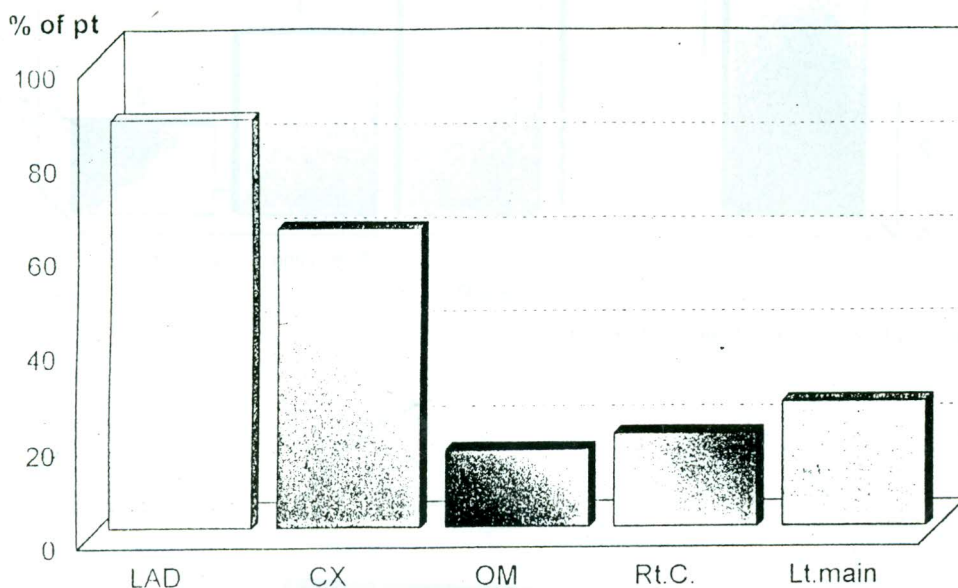


Fig. (1): Shows preoperative cath. Data.

infarction (PMI), four patients (13.3%) had new Q-waves in the ECG. In these 4 cases, enzymes and echo data were also abnormal and supported the diagnosis of new infarctions. There were statistical differences in the incidence of PMI among the patients before and after urgent CABG ($P < 0.01$, highly significant, $P < 0.001$, highly

significant and $P < 0.05$, significant) as regards cardiac enzymes CPK, CK-MB and LDH respectively. R-waves in 12 lead ECG were significant ($P < 0.05$). As regards Qwaves, they were not significant ($P > 0.05$) as shown in table 5 (from A till E), which illustrate perioperative myocardial infarction (PMI).

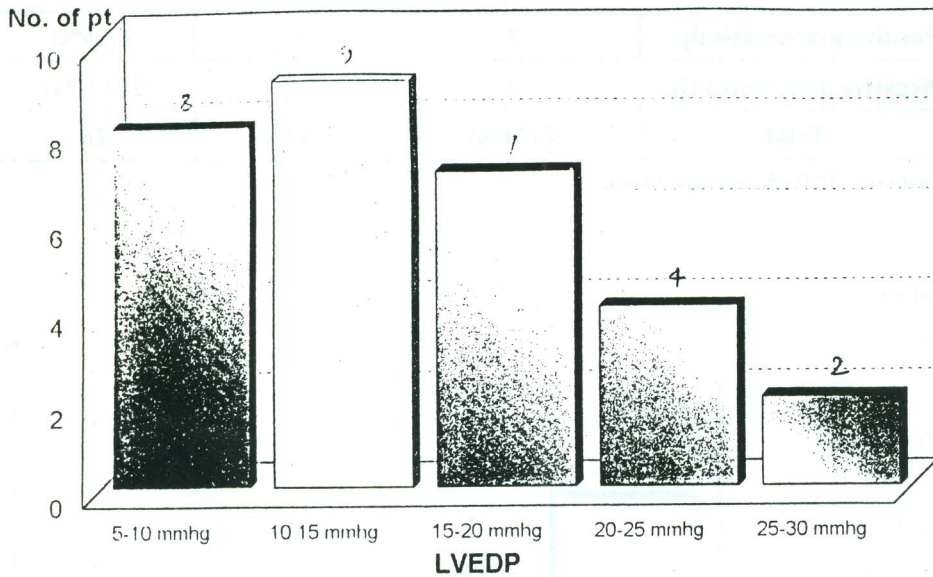


Fig. (2): Shows left ventricular end diastolic pressure.

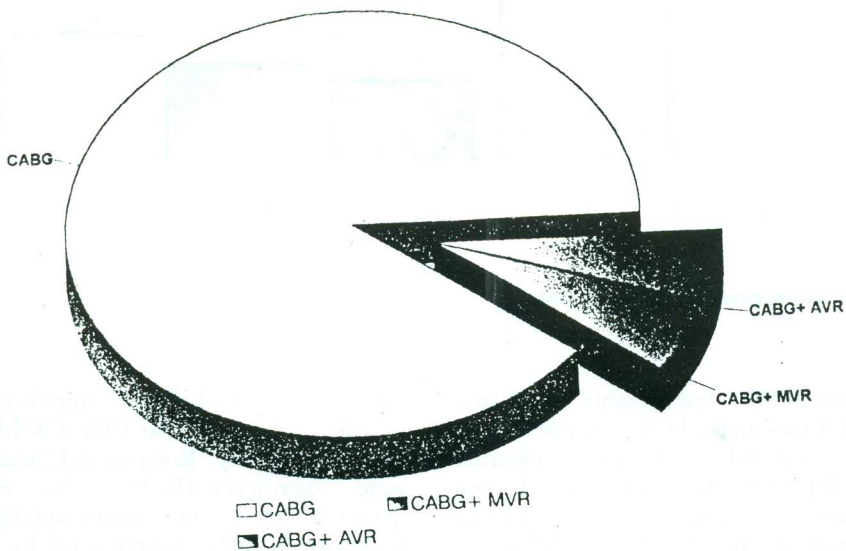


Fig. (3): Shows different operative procedures.

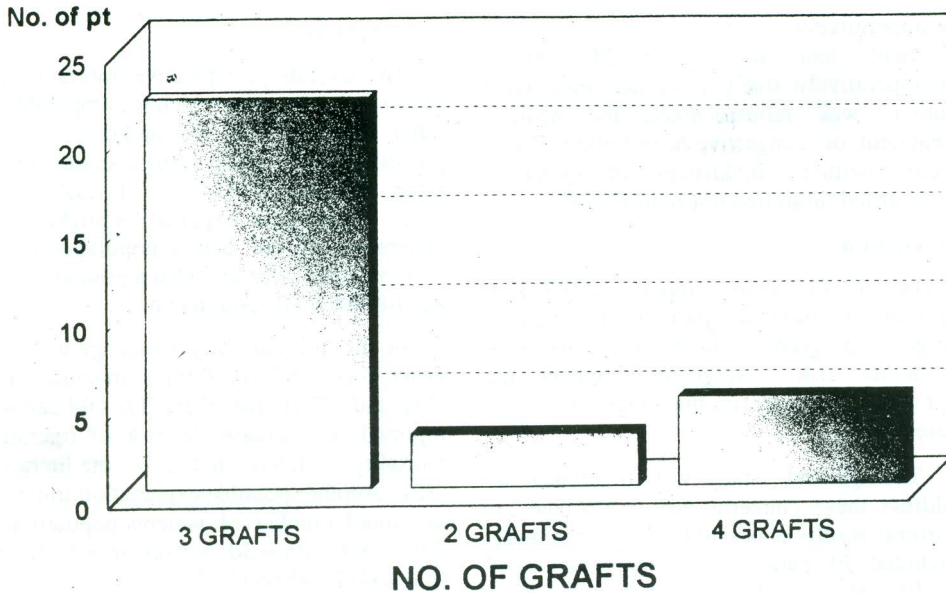


Fig. (4): Shows distribution of grafts among the whole population.

Three of those 4 patients were males, 2 of whom had history of previous myocardial infarction (M1). Two patients had a severely critical lesion in the left main coronary artery. Three patients experienced low cardiac index (CI) ($<1.5\text{ml}/\text{min}/\text{M}^2$) and needed high doses of inotropics and 2 patients had intraaortic balloon pump (IABP). Three patients had poor quality, small or intramural coronary vessels leading to incomplete revascularization in one patient and additional thromboendarterectomy in another.

Regarding ischemia, this was observed in 4 patients with a total incidence of 13%. Ischemia was observed on ECG without significant Q-waves or enzymes elevations.

Concerning bleeding and administered blood, the mean postoperative shed blood

loss in patients was 410ml (range = 40 - 1350ml). Only 1 patient required revision for bleeding. Seventy-seven percent of patients did not receive any blood or blood products.

There were no serious postoperative pleuropulmonary complications (respiratory failure) observed among the patients. Radiologically, 3 patients (10%) had postoperative atelectasis, 9(30%) had pleural effusion and only 1(3%) had pneumothorax. Four patients had atrial fibrillation (AF) or premature ventricular contractions (PVC) and 2 patients (7%) had CNS (central nervous system) troubles. The mean hospital stay time for all cases was 12.5 days.

Results of late follow up showed that 2 patients died (13%), one 12 months

postoperatively due to cerebrovascular accident and the other 24 months postoperatively due to a cardiac cause. One patient was rehospitalized for medical treatment of congestive heart failure. There were neither incidences of Q-waves myocardial infarction nor redo-CABG.

Discussion

In recent years, urgent CABG has become an important part of most cardiac surgery programs which only carries a moderate risk. Surgeons anticipate an operative mortality in the range of 5% of cases (1).

The present study was undertaken to address these concerns and to evaluate the current results of urgent CABG. This study included 30 patients who underwent urgent CABG at Ain-Shams University hospital cardiothoracic surgery department and at Ain-Shams Specialized hospital. This study was conducted in a prospective manner, starting January 1997.

This study included only those patients with coronary ischemia that was refractory to all other appropriate forms of therapy. The time from surgical consultation to initial incision in the operating theatre was almost less than 4 hours in all instances of those urgent or emergency cases and sometimes less than one hour in some cases.

The surgical CABG procedures were conducted using normothermia in all cases except in 3 (10%) performed on beating heart, with no significant difference between the latter and the blood cardioplegia used in the majority of cases.

The mean ischemic aortic cross-clamp time was 43.7 min. and bypass time was 86 min. These figures go with those reported in another series which were 34.1 min. and 68

min respectively.

The overall perioperative mortality rate in our series is 6.6%, which is comparable to other reports (7.6%) (8) and (8%) (9). On the other hand, these results contrast with other workers as (14.5%) (1) and (17%) (10). A possible explanation might be the differences in the patient population in our present study that included a younger mean age for the whole population.

In the present study, mean age was 50.3 years versus 67 years (yrs) in some series (11) and 72 yrs for others (1). Old age was reported to increase the risk of operative mortality in many studies in the literature (12). Another possible explanation might be the small number of patients population in this study ($n = 30$) versus ($n = 117$) and ($n = 444$) in others (1,11).

In our present series, mortality was present in those who had a preoperative severely depressed left ventricular function, large myocardial infarction and unstable hemodynamics. One patient died intraoperatively and another died postoperatively.

Regarding perioperative morbidity, deep sternal wound infection was found in one patient (3%) in our study group. This figure agrees with some authors (2.6%) (13) and (2%) (14) while other studies showed lower rates as (1.3%) (15). These results could be explained by the fact that results of our study group of patients were obtained in a small cohort of patients or might be due to local tissue destruction which is supported by some authors (16) who demonstrated an overall rate of 0.16% for sternal wound infection in 3118 patients. They attributed these results to their discriminate use of electrocautery.

Superficial wound infections occurred in

only 2 cases (6.7%) in our study group of patients. It was striking that this was observed in the inferior margins of sternotomy incisions and only in patients who underwent single IMA grafts. This was investigated by some authors (17) beforehand to understand the relationship between IMA harvesting and wound healing difficulties in inferior margins of sternotomy incisions where the cutaneous vascular perfusion in the sternal and xiphoid areas were studied by India ink injection in cadavers. They demonstrated an inherent paucity of nutrient supply to the inferior sternum and xiphoid areas. Hence, with the classic IMA harvesting beyond its distal bifurcation, the inferior sternal-xiphoid area which is already poorly vascularized even with an intact vascular anatomy, sustains additional lack of nutrient supply. Therefore, it may be more susceptible for necrosis and subsequent infection.

Many studies supported the finding that obesity (18) and diabetes mellitus (DM) (19) are predictors for sternal wound infections. The mechanisms for this are unknown for obesity. But for diabetes mellitus, this was attributed by some authors (12) to the increase of wound complications to the small vessels disease associated with DM, which decreases the potential of developing collateral blood flow after IMA mobilization.

In our present study, the mean postoperative shed blood loss was significantly lower after saphenous vein grafts (410ml) than after single IMA grafts (513ml). These data confirm that IMA surgery has a characteristic perioperative increased blood loss as reported by some authors (20).

Also, the relation between blood loss after saphenous vein (SV) and IMA grafts in our study shows that the risk of blood transfusion was the same. Donor blood was

required in 13% and 10% for SV and single IMA grafts respectively. An explanation might be that the patients receiving SV grafts in our study were older and were often females, who had a lower preoperative hematocrit, hemoglobin contents and body surface area than those receiving at least one IMA graft. These factors demonstrate a lower red cell volume. Some authors (21) demonstrated that red blood cell volume was the best predictor of need for blood transfusion after CABG.

In our study there were no serious postoperative pleuropulmonary complications. Nevertheless, 30% of our patients had postoperative radiologic evidence of pleural effusion and 10% of atelectasis. Some authors (22) suggested that pleurotomy with IMA harvesting was the cause of increasing postoperative pleural effusions. In contrast, other authors (23) observed no differences in incidence of postoperative pleural effusions between patients submitted to pleurotomy and those without pleurotomy showing pleural effusion rates of 80% and 81% respectively. They attributed the high incidence of pleural effusion without pleurotomy to unrecognized small openings in the pleura, which subsequently permit translocation of fluid from mediastinum to pleural space. These contradictory data support the fact that the origin of postoperative pleural effusion is multifactorial. Hence, this might be due to the fact that median sternotomy may damage the lymphatic channels in the anterior mediastinum or pleural effusion could be related to pericardial inflammation as reported by some authors (23) to be 70% of their patients by echocardiography. It is to be noted that only 3 patients out of 9(33.3%) with pleural effusion in our series required a prolonged postoperative chest tube drainage.

The genesis of atelectasis following CABG does remain controversial. In our

series of patients, the incidence of atelectasis was slightly higher in the patients submitted to pleurotomy (single IMA graft) than those with no pleurotomy (SV grafts) but the different percentages did not reach statistical significance. Similar observations were reported by some authors (24) with slightly higher non-significant increase of incidence of atelectasis in patients with pleurotomy (35%) than those without (23%).

This fact suggests that the effect of pleurotomy is partial and that the genesis of atelectasis is probably multifactorial as proposed by some authors (23) to be mechanical factors as retraction of left lower lobes, postoperative gastric distension or transient paresis of left hemi-diaphragm secondary to hypothermic injury to phrenic nerve.

For perioperative myocardial infarction (MI) a low incidence is reported usually although it varies between 0.4 and 10.3 % (25). This could be explained by the fact that criteria for diagnosis are not uniformly employed. These criteria include development of new pathologic Q-waves, QRS changes, increased CK-MB release, abnormal wall motion on echocardiography on left ventricular angiograms or uptake of technetium pyrophosphate scans.

In our present study, we used the most common criteria for diagnosis of perioperative MI which are new significant Q-waves and enzyme elevations supported by echocardiography findings. So, in our present study, new Q-waves MI occurred in 4 patients (13.3%). These results are consistent with some authors (10.3%) (25) and contrasted with data published by others (5.3%) (26). The differences in the results might be in the study populations.

Some authors (26) observed that

perioperative MI did occur almost 3 times more frequent in patients with preoperative ischemia than those without (6.9% and 2.5%, respectively). Several factors appear to increase the incidence of preoperative MI with the use of IMA grafts including the prolonged anesthesia time before the start of bypass which provides an opportunity for undiagnosed ischemia to occur which may result in preoperative MI. The issue of poor immediate flow with IMA surgery was attributed to the high incidence of preoperative MI after IMA surgery.

In our present study, preoperative MI was clinically significant. The postoperative course was benign in 3 patients, while 1 patient died. The slightly high preoperative MI rate might be due to the high percentage of poor quality vessels that led to thromboendarterectomy in 1 patient and incomplete revascularization in another.

Late follow up:

The goal of surgical treatment in patients with urgent CABG is to relieve ischemia in a very risky patient by establishing functioning grafts distal to critical stenosis.

Our follow up period was short (average 24 months for the whole population), yet due to the fact that revascularization clearly provides an excellent relief of symptoms, at the end of follow up in our series, relief of angina symptoms amounted 90% for patients. Also, no cardiac events (MI or need for redo-CABG) were observed among our patients.

It will probably be necessary to follow the patients for longer periods to show statistical differences in survival and events among patients. Based on the attrition rate of SV grafts with time, it requires at least 8 years until a statistical benefit from IMA grafts will probably be evident.

Conclusions

From this study, we can conclude that:

1- Postoperative mortality has acceptable results in patients undergoing urgent CABG. There is non-significant differences in postoperative mortality after SV grafts or single IMA grafts.

2- The incidence of sternal wound infections (superficial and deep) is higher in diabetic and/or obese patients undergoing IMA grafts. The risks of sternal wound complications should be carefully assessed in obese and diabetic patients.

3- IMA surgery in urgent CABG may lead to an increased postoperative blood loss but this is not of clinical significance if an extensive blood saving program is used.

4- There are no clinical significance in the incidences of pleuropulmonary complications among patients undergoing urgent CABG.

5- Perioperative MI has a slightly high incidence after urgent CABG (13.3%).

6- There were no clinical differences observed in the short-term follow up, with regard to clinical outcome.

7- Urgent or even emergency CABG can be carried out with only moderate risk, and the surgeon can anticipate mortality in the range of 5% for such patients, if those patients having re-operation are excluded and if one includes patients in a sufficiently stable condition to allow revascularization 12 to 24 hours after clinical deterioration.

8- Operative mortality in the range of 12% to 15% can be anticipated from surgical management of patients responding to true emergency CABG.

So, we recommend the following:

1- Surgical consultation to evaluate patients with acute coronary artery ischemia.

2- Use of arterial conduits for urgent or emergency CABG in selected patients whenever possible. Relative contraindications for this exist because of: old age, absence of conduits, hemodynamic instability, diabetes mellitus or the individual surgeon's preference.

3- Urgent or even emergency CABG can be performed in all critical patients to save the viable myocardium and to help those patients who are at risk, with no fear of increased mortality or morbidity especially with the new surgical techniques and updated methods of myocardial preservation.

References

- 1- Edwards, F.H.; Cohen, A.J.; Bellamy, R.F.; Thompson, L. and Weston, L.: Risk assessment in urgent and emergency coronary artery surgery. *Chest*; 1990; 97:1125-1129.
- 2- He, G.; Ryon, W.; Aguff, T.; Bowman, R. and Mack, M.: Risk factors for operative mortality and sternal wound infection in bilateral internal mammary artery grafting. *J. Thorac. Cardiovasc. Surg.*; 1994; 107:196-202.
- 3- Kitamura, S.; Inoue, K.; Kawachi, K.; Morita, R.; Seki, T.; Taniguchi, T. and Kawata, T.: Lower extremity ischemia secondary to internal thoracic coronary artery bypass grafting. *Ann. Thorac. Surg.*; 1993; 56:157-159.
- 4- Russo, P.; Orsuzulak, T.A.; Schaff, H.V. and Holmes, D.R.: Use of internal mammary artery for multiple coronary artery bypass. *Circulation*; 1986; 74 (Suppl. III): (111-48)-(III-52).
- 5- Campeau, L.: Grading of angina pectoris. *Circulation*; 1976; 54:522-523.
- 6- Chaitman, B.P.; Fisher, L.D. and Boursassa, M.G.: Effect of coronary

- artery bypass surgery on survival patterns in subsets of patients with left main coronary artery disease. Report of the Collaborative Study in Coronary Artery Surgery (CASS). *Am. J. Cardiol.*; 1981; 48:765-778.
- 7- Hammermeister, K.; Deruen, T. and Dodge, H.: Variable predictives of survival in patients with coronary disease. *Circulation*; 1979; 59:421-430.
- 8- Killen, D.; Hamaker, W. and Reed, W.: Coronary artery bypass following percutaneous transluminal coronary angioplasty. *Ann. Thorac. Surg.*; 1985; 40:133-138.
- 9- Varnauskas, E. and the European Coronary Surgery Study Group: Survival, myocardial infarction and employment status in a prospective randomized study of coronary bypass surgery. *Circulation*; 1985; 72 (Suppl. V):V-90-101.
- 10-Tector, A.J.; Schmahi, T.M. and Canino, V.R.: Expanding the use of internal mammary artery to improve patency in coronary artery bypass grafting. *J. Thorac. Cardiovasc. Surg.*; 1986; 91:9-16.
- 11 - Tomasco, B.; Cappiello, A.; Fiorilli, R.; Leccese, A.; Lupino, R.; Romiti, A. and Tesler, U.: Surgical revascularization for acute coronary insufficiency. Analysis of risk factors for hospital mortality. *Ann. Thorac. Surg.*; Sep. 1997; 64 (3):678-683.
- 12-Katz, N.; Hannan, R. and Wallace, R.: Cardiac operations in patients aged 70 years and over: Mortality, length of stay and hospital discharge. *Ann. Thorac. Surg.*; 1995; 60:96-101.
- 13-Cosgrove, D.; Lytle, B.; Loop, F.; Taylor, P. and Godmastic, M.: Does bilateral internal mammary grafting increase surgical risk? *J. Thorac. Cardiovasc. Surg.*; 1988; 29:633-638.
- 14- Grover, F.; Johnson, R.; Marshall, G.; Hammermeister, K. and Department of Veterans Affairs Cardiac Surgeons: Impact of mammary grafts on coronary artery bypass: Operative mortality and morbidity. *Ann. Thorac. Surg.*; 1994; 57:559-569.
- 15-Milano, C.; Kesler, R.; Archibald, N.; Sexton, D. and Jones, R.: Mediastinitis after coronary artery bypass graft surgery. Risk factors and long term survival. *Circulation*; 1995; 92:2245-2251.
- 16-Nishida, H.; Grooters, R.K.; Soltanzadeh, H.; Thieman, K.C.; Schneider, R.F. and Kim, W.P.: Discriminate use of electrocautery on the median sternotomy incision. A 0.16% wound infection rate. *J. Thorac. Cardiovasc. Surg.*; 1991; 101:488-494.
- 17-Francel, T.; Dufrense, C.; Baumgartner, W. and O'Kelley, J.: Anatomic and clinical consideration of an internal mammary harvest. *Arch. Surg.*; 1992; 127:1107-1111.
- 18-The Parisian Mediastinitis Study Group: Risk factors for deep sternal wound infection after sternotomy: A prospective, multicenter study. *J. Thorac. Cardiovasc. Surg.*; 1996; 111: 1200-1207.
- 19-Loop, F.; Lytle, B.; Cosgrove, D.; Mahfoods, M. and Taylor, P.: Sternal wound complications after isolated coronary bypass grafting: Early and late morbidity and cost of care. *Ann. Thorac. Surg.*; 1990; 49:179-187.

- 20-Henz, A.; Ramstram, J. and Nystrom, S.: Bilateral internal mammary artery for coronary revascularization: Early experience of 100 cases. *J. Thorac. Cardiovasc. Surg.*; 1989; 23:9-11.
- 21-Schonberger, J.; Woolley, S.; Tavilla, G.; Berreklow, E.; Bredee, J. and Wildevur, C.: Efficacy and safety of blood conservation program including low-dose aprotinin in routine myocardial revascularization. *J. Cardiovasc. Surg.*; 1996; 37:35-44.
- 22-Landymore, R. and Howell, F.: Pulmonary complications following myocardial revascularization with internal mammary artery graft. *Chest*; 1993; 104:434-437.
- 23-Hurlburt, D.; Myers, M.; Lefoce, M. and Goldbach, M.: Pleuropulmonary morbidity: Internal thoracic versus saphenous vein graft. *Ann. Thorac. Surg.*; 1990; 49: 959-964.
- 24-Wilcox, P.; Baide, E.; Hards, J.; Muller, N.; Dunn, L.; Pardy, R. and Pare, P.: Phrenic nerve function and its relation to atelectasis after coronary artery bypass surgery. *Chest*; 1988; 83:693-698.
- 25-King, S.B. and Talley, J.D.: Coronary arteriography and percutaneous transluminal coronary angiography changing patterns of use and results. *Circulation*; 1989; 79 (Suppl. I): 1-19-23.
- 26-Yusuf, S.; Sleight, P.; Held, P. and McMahon, S.: Routine medical management of acute myocardial infarction. Lessons from overviews of recent randomized controlled trials. *Circulation*; 1990; 82 (Suppl. II): (II-117)-(II-134).

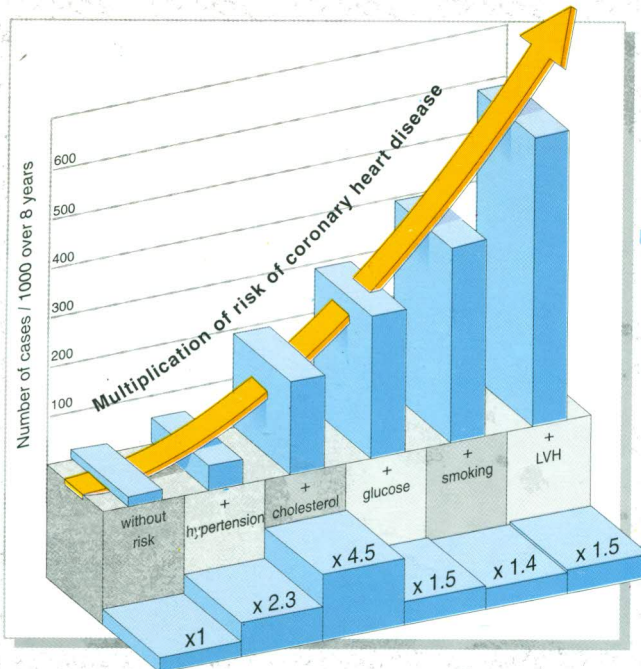
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1. Abbou CB et al. *Curr Med Res Opin*. 1985; 9 (7): 494-499.

2. Leonetti G et al. *Am J Cardiol*. 1990; 65 (17): 67-71.

3. Raggi U et al. *Hypertension*. 1985; 7 (6) (Part II): 157-160.

4. Rafferty EB et al. *J Cardiovasc Pharmacol*. 1993; 22 (suppl 6): 106-110.

5. Flack JR et al. *J Cardiovasc Pharmacol*. 1993; 22 (suppl 6): 75-77.

6. Kannel WB. *Am J Hypertens*. 1991; 4: 283-287.

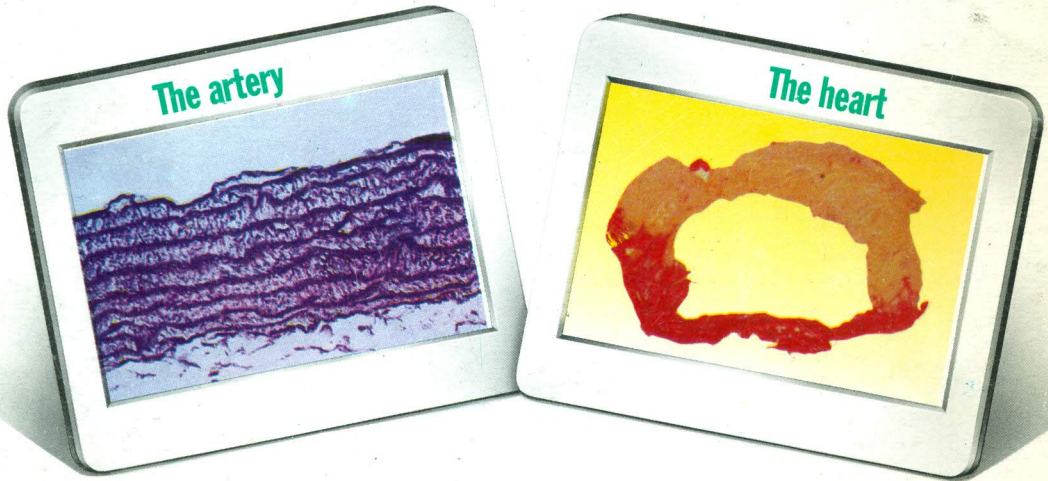


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1. SIHM I et al. *Eur Heart J*. 1993; 14(suppl) : 63 - 2. LEVY BI et al. *Circ Res*. 1988; 63 : 227-239 - 3. ASMAR RG et al. *J Hypertens*. 1988; (suppl 3) : S33-S39 - 4. MICHEL JB et al. *Circ Res*. 1988; 62 : 641-650
5. MORGAN TO et al. *Am J Hypertens*. 1993; 6 : 116 A - 6. MAC FADYEN RJ et al. *Br Heart J*. 1991; 66 : 206-211.

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