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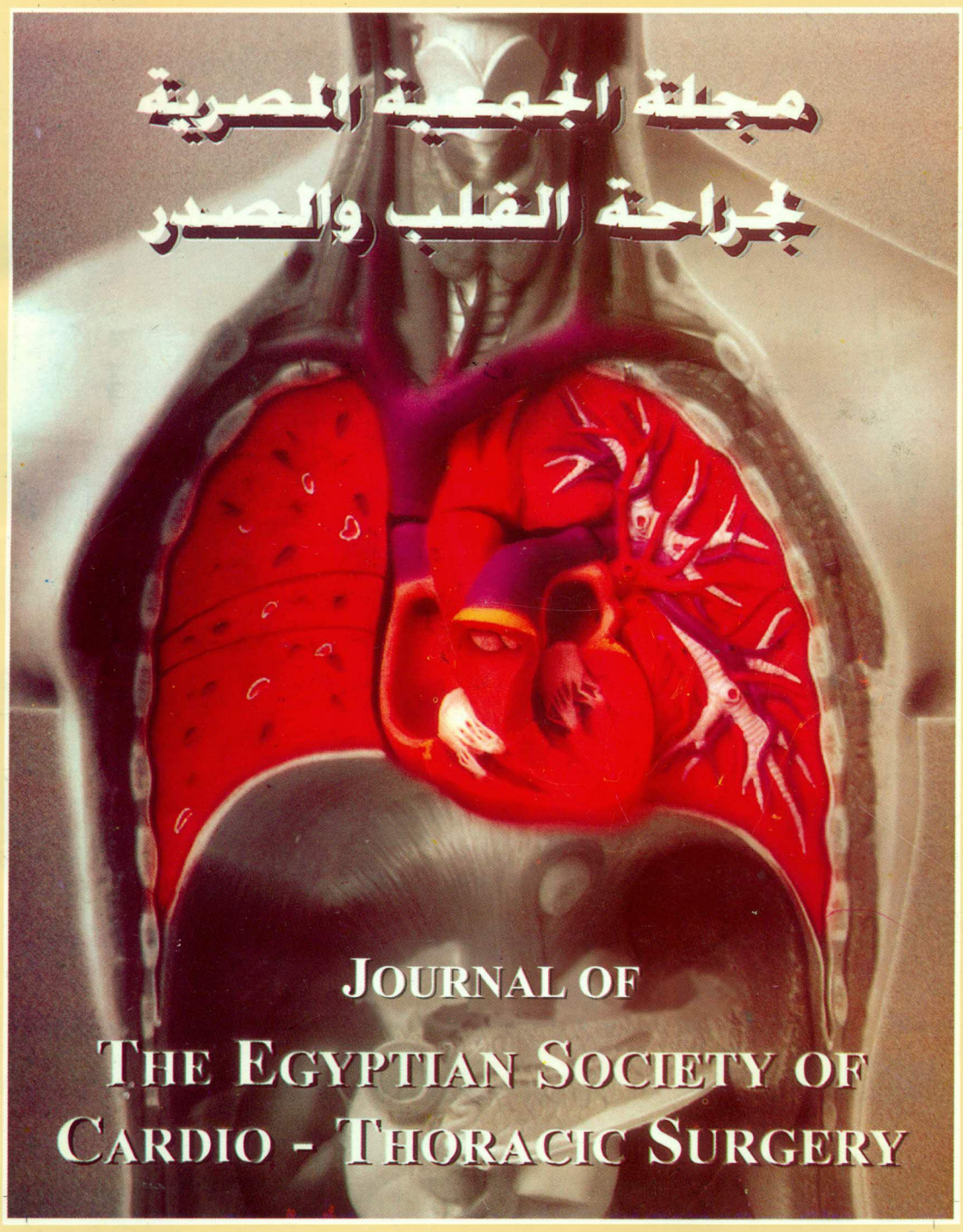

JOURNAL OF THE EGYPTIAN SOCIETY OF CARDIO - THORACIC SURGERY

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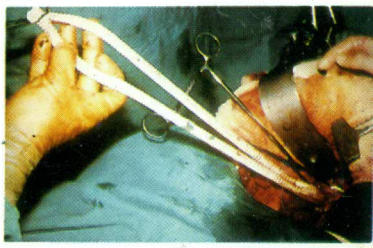

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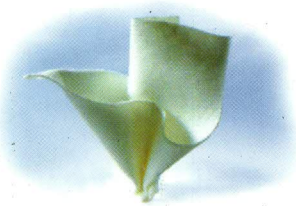

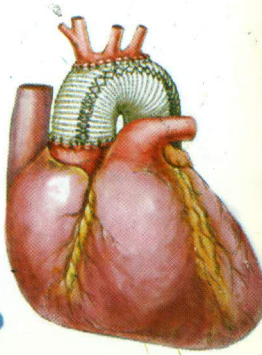

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Information for authors

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Surgical Management of Ebstein's Anomaly: A 22 - Year Experience

Abstract

From May 1975 to February 1997, 24 patients with Ebstein's anomaly underwent surgical treatment. Ages ranged from 5 to 45 years (median 17.5 years, mean 17.58 years). In 54% tricuspid valve reconstruction was possible and, in 38% a prosthetic valve usually a bioprosthesis was inserted. In 8% a bidirectional cavo pulmonary anastomosis was performed. There were 2 hospital deaths (8.43%).

Follow up was obtained in all patients who survived the operation. postoperative reduction in heart size was marked. atrial arrhythmias were reduced and late postoperative exercise testing showed a significant improvement in performance. Postoperative echocardiography revealed that tricuspid valve function was good among the patients who underwent valve reconstruction with significant increase in the left ventricular volume and ejection fraction.

Two of the tweleve patients (16.5%) who underwent valve reconstruction required reoperation 5 and 12 years late with reoperation free rate is 83.33±15.12% at 5 years and 10 years. Among 9 patients who underwent tricuspid valve replacement, 3 bioprosthetic valves required replacement 8 to 11 years after implantation with reoperation free rate is 100% at 5 years and 37.5± 28.64% at 10 years.

Follow up functional evaluation is in progress and is complete in 90% of the patients. Of those followed up more than one year after operation 95% were in NYHA functional class I or 11

4 patients had a total of 6 successful pregnancies with deliveries of normal children with no serious pregnancy related maternal complications.

We conclude that surgical repair of Ebstein's anomaly is indicated for those patients who are in NYHA class 111 or IV and for selected other patients who are showing clinical deterioration. whenever possible we prefer valve reconstruction using valvouloplasty and anuloplasty which is based on available utilizable valve leaflet tissue.

S.Azab, M.D. A. El Kerdany,M.D, A. El Nori, M.D., T. El-Saygh, M.D. A. Darwazah, M.D. FRCS.

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INTRODUCTION

Ebstein's anomaly is a rare cardiac malformation that usually affacts the tricuspid valve. It is characterized by downword displacement of the origin of the septal or posterior tricuspid leaflets or both into the right ventricle and the leaflets are variably deformed. The severity of Ebstein's anomaly is extremely variable not only in its anatomy but also in the clinical presentation (1).

Although patients with Ebstein's who are in NYHA Functional class I or II have a relatively good term prognosis with their natural evolution and can benefit from

- *From Cardiothoracic department-Ain Shams University Hospital.*

medical treatment (2), yet the surgical treatment is indicated in patients who are in NYHA class III or IV and other patients who are not responding to medical treatment.

The surgical repair of Ebstein's anomaly is based on the reconstruction of a monocusp valve by the use of the anterior leaflet of the tricuspid valve which is usually enlarged and is the least abnormal leaflet in this anomaly

Unfourntually , some patients with Ebstein's anomaly are not good candidates for valve repair due to associated abnormalities of the anterior leaflet and tricuspid valve replacement should be considered. In this series we describe our experience with operative treatment of this rare anomaly for more than 20 years at Ain Shams University Hospitals.

Materials and Methods

From May 1975 to February 1997, Twenty four consecutive patients with Ebstein's anomaly underwent surgical repair at Ain Shams University Hospitals. Indications for operation included patients with NYHA functional class 111 or IV, patients with severe cyanosis, progressive cardiomegaly or history of paradoxical embolization.

The ages ranged from 5 to 45 years (mean 17.58 years). Cardiothoracic ratio ranged between 0.55 and 0.93 and the hematocrite values ranged between 45 and 70%. The basic rhythm was sinus rhythm in 22 patients with prolonged PR interval in 20% of the cases and right bundle branch block in 65% and atrial fibrillation in 2 patients. Six of our patient (25%) exhibited a tachyarrhythmia (supra ventricular tachycardia and in 2 patients a WPW pattern were seen.

The diagnosis of Ebstein's anomaly was made by complete echocardiographic study in all patients except for the first 3 patients who underwent cardiac catheterization. Also by using the Doppler studies, the tricuspid regurgitation could be estimated accurately in the majority of patients. Associated cardiac defects diagnosed by echocardiography are listed in table (1)

Operative finding

In the majority of our patients (22 patients) both septal and posterior leaflets were downword displaced and the point of maximum displacement was the commissure between these two leaflets. This displacement divided right ventricle into proximal or atrialized part and functional (ventricularized) portion which lied distal to the displaced valve. In 16 patients, the anterior leaflet of the tricuspid valve was enlarged and elongated (Sail like) and It was diffusely thickened in the rest of the patients.

Right atrium was enormously dilated in most of the patients together with atrial septal defect found in 18 patients, patent formon ovale in 4 patients. Also tricuspid anulus was markedly dilated in majority of patients and on testing the valve, It showed severe regurgitation in 20 patients and moderate regurgitation in the rest of the patients .

Surgical Technique

Our surgical technique for patients with Ebstein's anomaly consists of:

— Plication of the atrialized portion of the right ventricle

— Valve reconstruction using valvuloplasty when feasible

— Valve replacement if the repair is not feasible or not satisfied.

— ASD closure using pericardial patch except for patent foramen ovale which was closed directely

— Repair of the associated defects during the same operation.

In 13 patients (54%), we managed to reconstruct tricuspid valve using Danielson technique with ventricular plication and annuloplasty. (Figure 1)

The ventricular plication suture are placed through the atrilized right ventricle using a series of interrupted mattress sutures (ethibond with double teflon pledgets). These sutures when they are tied, they oblitrate the atrialized - portion of right ventricle and bring the base of the anterior tricuspid leaflet up to the right atrial-right ventricular junction.

The epicardial arteries should be inspected after each plication suture is placed to avoid large branchs of right coronary artery or posterior descending artery. The tricuspid valve repair was completed in all patients by posterior annuloplasty. The posterior aspect of the annulus was first narrowed with the annuloplasty suture and then further oblitrated by additional interrupted mattress sutures with teflon pledgets. The tricuspid valve was tested after completion of the procedure using 50 ml's syringe bulb with saline under pressure and the valve was replaced if significant regurgitation was found.

This reconstructive technique was not possible in 9 patients and Tricuspid valve was replaced using a biopresthetic valve in 6 patients and mechanical valve (st. Jude medical prosthesis) in 3 patients. In order to avoid injury to the A-V bundle. the suture line was shifted well posterior to the A-V node area and the coronary sinus in 6 patients (Barnard,s technique). A permenant pacemaker was inserted with the valve replacement in one patient who had a congenitally corrected TGA with Ebstein's anomaly of the left A-V valve and congenital heart block.

A Bidirectional superior Cavo-pulmonary anastomosis was performed in 2 patients as they had significant pulmonary infundibular stenosis and the right ventricular cavity was estimated to be small for biventricular repair.(Hypoplastic right ventricle).

Postoperative follow up:

Complete follow up was obtained for all patients who survived the operation except for one patient who was missed after 3 years follow up. Folow up ranged from 1 to 252 months with an average of 74.67 ± 69.61 months and cumulative follow up of 149.3 patients - years.

Patients are followed by clinical examination and repeated chest x ray . Two-dimensional echocardiographic and Doppler studies were performed in all patients before discharge, 6 months postoperatively and every year.

Statistical analysis:

Results was presented as mean ± standared deviation, chi - square test was used to compare qualitative data and the unpaired student test was used to compare quantitative data among patient's groups. Pearson's test was used to find the significance of relation between qualitative and quantitative variables. Willcoxon

Table (1): Associated anomalies with Ebsteim's disease.

Associated defects	Number N
Atrial septal defect	18
Ventricular septal defect	3
Pulmonary stenosis (valvular and mild subvalvular)	2
Congenitally corrected transposition of great arteries with Ebstein anomaly of the left side A-V valve	4
Bilateral superior vena cavae	2

(Gehan) test was used to compare actuarial survival curves.

Results

In Table (2), the total qurgical experience of Ebstein;s anomaly is illustrated tricuspid valve was reconstructed in 13 patients (54%) using Danielson repair with plication of the atrilized right ventricle and annuloplasty. Another patient had valve repair first but the valve showed severe incomptence when tested and it was replaced with a bioprosthetic valve(Hancok tissue valve size 35. In 8 patients tricuspid valve was replaced in addition to another patient with failed repair. Among those 9 patients who underwent valve replacement, 6 patients received bioprosthetic valves (Carpentier Edwards or Hancock tissue valve) and in 3 patients mechanical valves (st. Jude medical valve) were inserted. There was only one case with complete heart block after valve replacement early in our series.

Two deaths (8.4%) occured within 30 days of operation, the first patient died 4 days postoperatively with progressive low cardiac output and arrythmia after he had tricuspid valve repair. He had a massive preoperative cardiomegaly & his postoperative echocardiographic examination revealed a moderate tricuspid incomptence with poor right and left ventricular functions.

The second patient who died 25 days postoperatively was diagnosed to have congenitally corrected transposition of the great arteries with Ebstein's anomaly of the left atrioventricular valve. He was operated upon at age of 45 years and his valve was replaced with a st.Jude medical valve but his postoperative course was stormy with prolonged mechanical ventillation and low cardiac output. He died on his 25th postoperative day. Repeated echocardiographic examination in the postoperative period showed progressive systemic ventricular dysfunction.

Reoperation for tricuspid valve replacement were required in two patients (Table 3) out of the 12 patients who survived tricuspid valve repair which represents a total incidence of 16.6% in a follow up extending to 20 years. In the first

Table (2): Total surgical experience of Ebstein's anomaly repair.

No.	Preoperative data			Postoperative data		
	Age (Yr)	NYHA	Operation	length of follow up (Yr)	NYHA	Comments
1	17	IV	replacement	22	II	Reop. age 28 for tissue valve failure
2	23	III	replacement	20	I	Reop. age 33 for valve failure
3	20	II	replacement	lost in follow up 3 ys P.O	-	-
4	21	IV	reconstruction	13	I	Reop. age 33
5	13	III	reconstruction	1.5	I	-
6	5	IV	Bidirectional Glen's	1.5	I	-
7	18	III	replacement	4	I	-
8	8	III	reconstruction	0.5	II	-
9	9	IV	reconstruction	1.5	I	-
10	18	IV	reconstruction	hospital death	I	-
11	21	III	replacement	10	I	-
12	25	II	replacement	9	II	-
13	45	IV	replacement	hospital death		
14	17	III	reconstruction	12	II	Reop. age 25 for tissue valve failure
15	10	III	reconstruction	10	I	Reop. age 20
16	11	IV	Bidirectional Glen's	7	II	
17	18	IV	reconstruction	8	I	
18	19	III	reconstruction	10	I	
19	17	III	reconstruction	9	I	
20	13	IV	reconstruction	death 2 years postop. from congestive heart F. and arrythmia	-	-
21	21	IV	replacement	7	I	-
22	17	II	reconstruction	5	I	-
23	26	III	replacement	8	I	-
24	10	III	reconstruction	0.5	II	-

patient who was 10 years old a less than ideal repair was accepted as an alternative to valve replacement in the hope that the child would grow further before a valve prosthesis would be required. The child reached 15 years before valve replacement

Table (3): Reoperation after Ebsteins anomaly repair.

No	The initial operation	Age (Ys)	Reoperation	Operative finding	Interval Ys
1-	Valve Rectonstruction	10	Valve replacement Bioprosthesis	dilatation of an anulus	5
2-	" "	21	Valve replacement st. Jude valve	Dilatation of anulus & valve incomptence	12
3-	Valve replacement bioprosthesis (C.E.valve)	21	Valve re-replacement bioprosthesis (C.E.valve)	Primary tissue valve failure	11
4-	Valve replacement (bioprosthesis)	23	Valve re-replacement (st. Jude valve)	"	9
5-	Valve replacement (C.E valve)	17	Valve re-replacement (st.Jude valve)	"	8

C.E: Carpentier Edward.

was necessary. The second patient who had valve repair very early in 1984, he required valve replacement 12 years after repair because of progressive dilatation of the tricuspid annulus and right ventricle.

Out of the 8 patients who survived the tricuspid valve replacement in the initial operation, 3 patients required valve re-replacement due to bioprosthetic valve degeneration 8 to 11 year after the operation (table: 3) All five patients survived reoperation and are now in NYHA class 1 or II So, out of the 22 hospital survivors, 5 patients were reoperated (22.7%). The reoperation-free rate is 92.31±7.39% at 5 years, 52.75±23.4% at 10 years and 26.37 ±22.02% at 19 years.

The reoperation free rate of valve replacement group is 1 00% at 5 years and 37.5 ± 28.64% at 10 years (P non - significant)

The reoperation free rate of valve repair group (13 patients) is 83.33 ± 15.12 % at 5 years and 10 years (Figure 2).

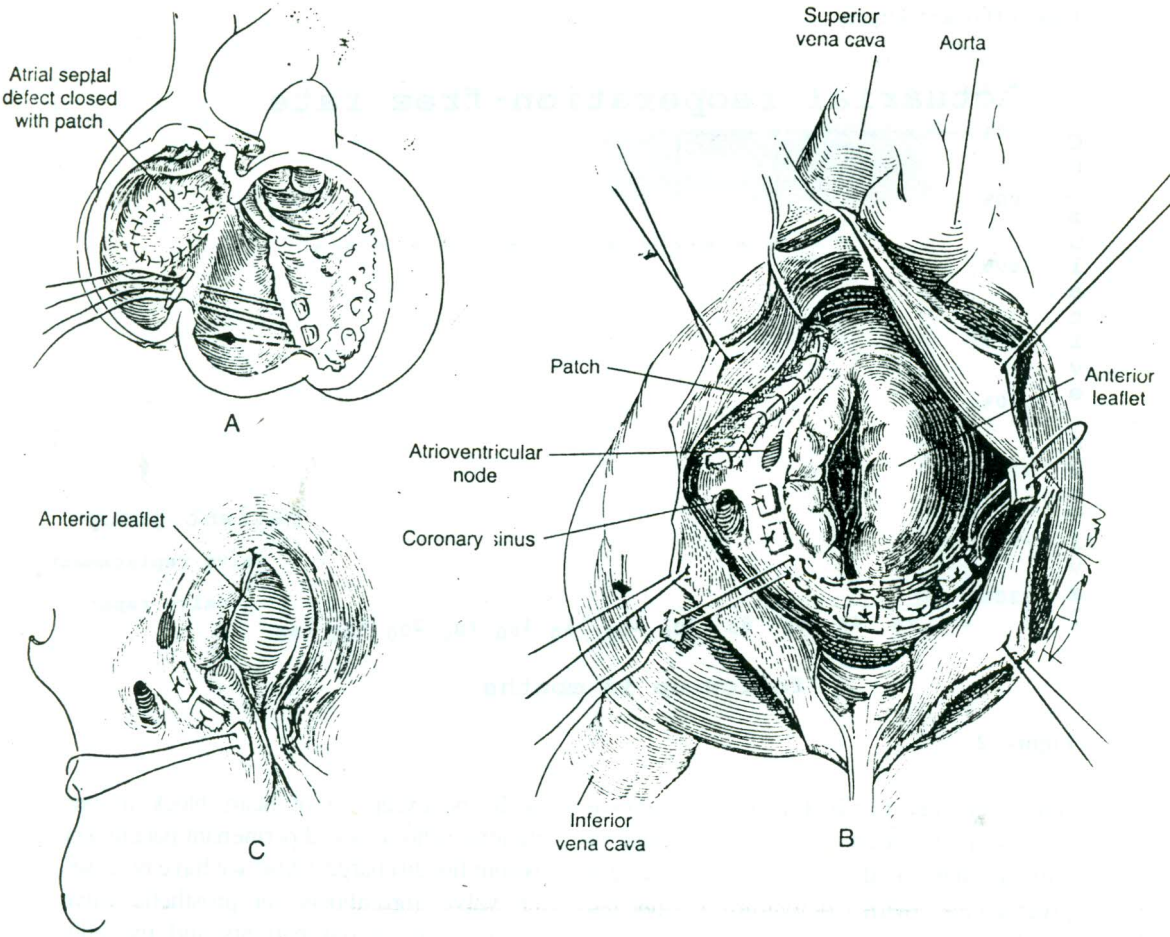

Fig. (1): Repair of the tricuspid valve in Ebstein's anomaly using Danielson's technique.
-A series of interrupted mattress sutures are placed which oblitrate the atrialized portion of the right ventricle and bring the base of the anterior leaflet up to the right atrial-right ventricular function.
-As sutures were tied; this oblitrated the atrialized part of the right ventricle. (From Castaneda et al 1994) (3) .

A detailed follow up survery is in progress. To date follow up of 20 of the 22 operative survivors (91.1%) has been obtained, There have been one late death due to congestive heart failure. The survival rate for all patients is 91.11 ± 6% at 252 months (Fig.3).

For the valve repair group (13 patients) the survival rate is 91.67 ± 7.9% and the survival rate of valve replacement group (9 patients is 8 8.24 ± 11.1 % (P non significant).

Of survivors followed -up-more than 1 year after operation, 90% were in NYHA

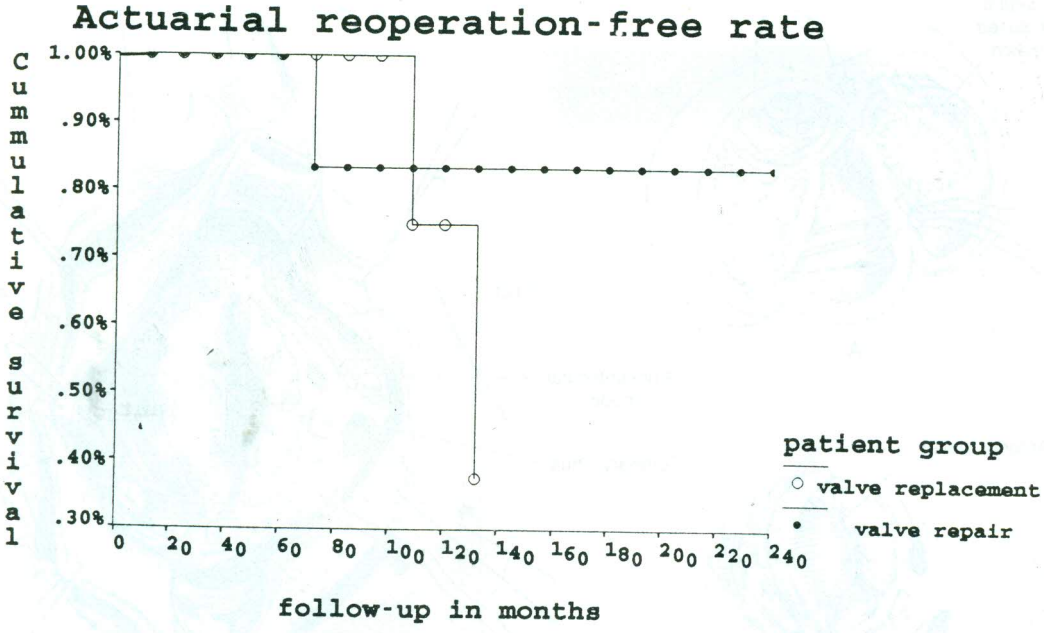

Figure (2):

functional class I or II.(Fig. 4) Postoperative reduction in heart size was marked, 4 patients have had a total of 6 successful pregnancies with deliveries of normal children, Serial echocardiography during the follow up showed that the patients who had valve reconstruction have achieved either complete tricuspid valve comptence (6 patients) or only mild incomptence (5 patients). on the other hand, there was only one patient in which his echocardiographic examination showed a moderately severe incomptence and this patient died 2 years postoperatively from congestive heart failure and arrhythmia.

No. valve - related complications occured in the valve replacement group with the exception of heart block in one patient who recieved permenant pacemaker before his discharge. Also we have no cases of valve thrombosis or prosthetic valve endocarditis in our patients and the only indication for valve re-replacement was primary tissue valve failure in 3 patients (Table 3).

Improvement in rhythm or conduction disturbances was observed in most of the patients. In one patient atrial fibrillation spontaneously converted to sinus rhythm. In another patient WPW episodes have not recurred since the operation although the accessory conduction was not interrupted during the operation. Another 4 patients had a reduction in the frequency of arrhythmia episodes.

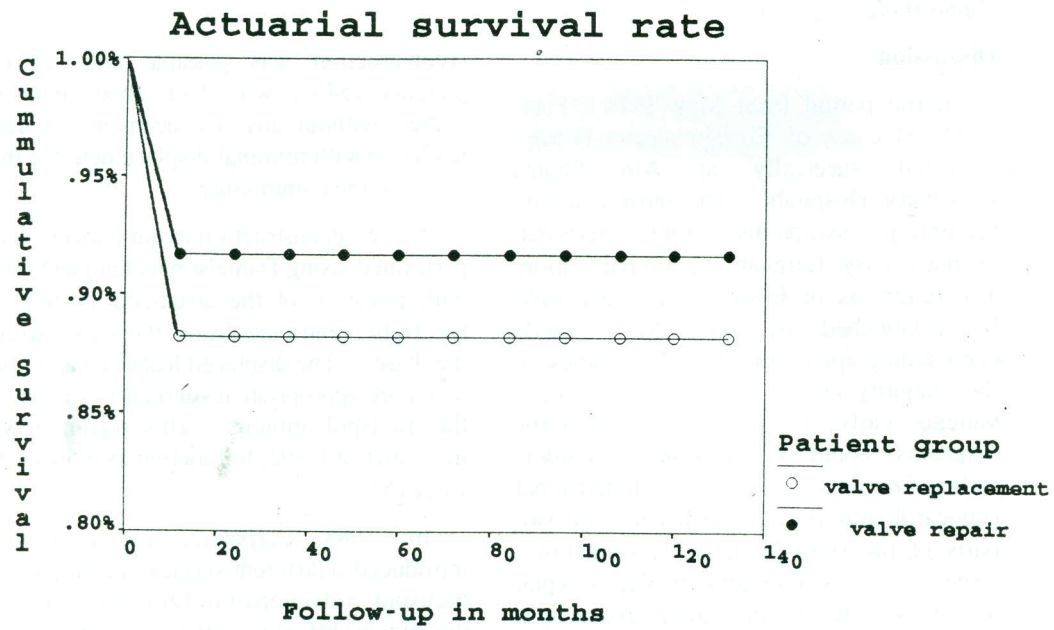

Figure (3):

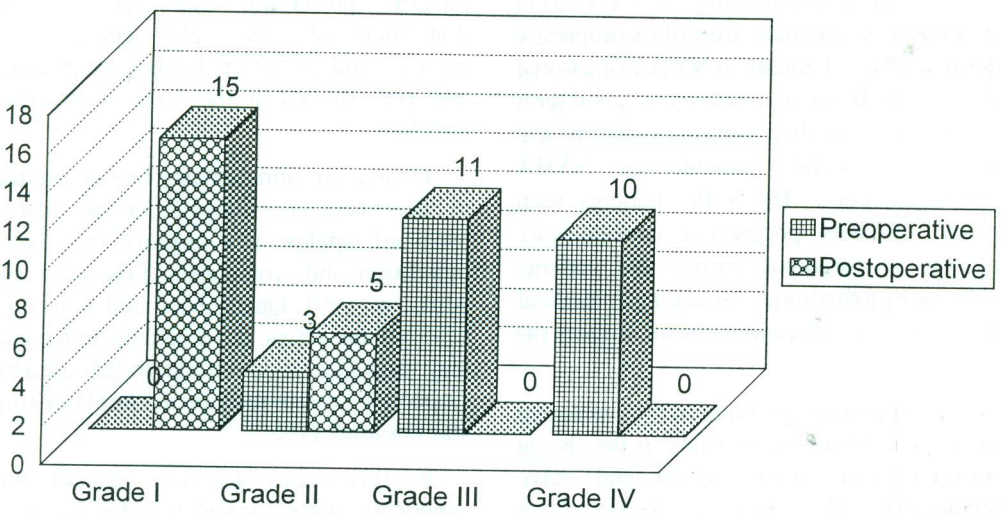

Figure (4): Improvement in NYHA functional class after repair of ebstein's malformation of the tricuspid valve

Discussion

In the period from May 1975 to Febr. 1997, 24 cases of Ebstein's anomaly were corrected surgically at Ain Shams University Hospitals . The most common presenting symptoms were exertional dyspnea, easy fatiguability and palpitation. The diagnosis of Ebstein's anomaly could be established by 2-D, M - mode echocardiography and Doppler studies in the majority of our patients except for 2 patients early in our series where the diagnosis could be confirmed by cardiac catheterization. Two - dimensional echocardiography can visualize the two parts of the right ventricle separated by a large anterior leaflet and displaced septal leaflet (4). It is important to assess right and left ventricular functions on which the prognosis of the repair dependes.

The indications for surgical intervention in Ebstein's anomaly are still incompletely defined (5). Patients in NYHA functional class 1 or II have a relatively good term prognosis with their natural evolution. On the other hand, patients in NYHA functional class III or IV, patients with severe cyanosis, progressive cardiomegaly history of paradoxic emboli and patients with tachyarrhythmias refractory to medical treatment are all candidates for surgery (4) (6).

The important problem in the corrective surgery of Ebstein's anomaly is the choice between valve reconstruction and valve replacement (7). Since the repair of an incomptent tricuspid valve in patients with Ebstein's anomaly relies on the anterior leaflet, this leaflet should be studied with particular care. In our series, the valve reconstruction was possible only in 13 patients (54%) who had good anterior leaflet without any displacement for that leaflet or with minimal displacement for the leaflet at the commissure.

Valve reconstruction in our patients was performed using Danielson technique(5) (8) with plication of the atrialized portion of the right ventricule from the apex toword the base. The displaced leaflet come to lie at a more appropriate level relative to rest of the tricuspid annulus. This repair allows the anterior leaflet to function as monocusp valve (5).

In 1988, Carpentier and co-worker introduced a different surgical technique for tricuspid valve repair in Ebstein's anomaly, the major difference relative to the classic Danielson's procedure is that plication is performed in a circumferntial fashion thereby preserving the apex to-base dimension of the right ventricle, the anterior and posterior leaflats are detected and repositioned at the level of tricuspid annulus.

Finally an annuloplasty ring is inserted to decrease the diameter of the dilated tricuspid anulus and improve the leaflet opposition and comptence of the valve, (9) Also in 1991 Quaegebeur and coworker reported on series of 10 patients in whome they used a technique similar to that used by carpentier except than an annuloplasty ring was not used. (10)

In this series we have no personal experience with carpentier technique or its modification by Quaegebeur and Danielson technique is still our technique of choice to reconstruct tricuspid valve in patients with Ebstein's anomaly.

In our series the tricuspid valve was not suitable for reconstruction in 42% of patients and the valve was excised and prosthetic valve was inserted. The anterior leaflet was too deficient to function adequately as a monocusp valve. In Ebsteinis anomaly, the prosthetic valve is either sutured to the anatomic anulus or the Barnard's technique is performed (11).

Other surgeons used different techniques to reduce the risk of complete heart block after tricuspid valve replacement like Milgalter et al (1991) and Yamazaki et al (1993) who used a pericardial patch to bridge the conduction tissue during tricuspid valve replacement. In our series, we used to put the prosthesis in the anatomical position in 4 patients and complete heart block developed in one patient (25%). In the other patients the suture line was placed on the atrial side of the coronary sinus and AV node to avoid injury to conduction system. (Barnard's technique) (11) with no cases of complete heart block. Other investigators reported different rates of heart block after tricuspid valve replacement witch ranged between 0% (5) to 70% (1).

A stent-mounted gluteraldhyde-preserved porcine bioprothesis may be considered optimal in most patients with Ebstein's malformation but it is subjected to the usual problems of a biopresthesis (6) (14).

In patients with normal hearts, mechanical valves in tricuspid position have a higher incidence of malfunction and thrombosis than they have in aortic or mitral position. However mechanical valves have functioned better in patients with Ebstein's anomaly, perhaps because the right ventricles are larger and there is less tendency for fibrous tissue ingrowth into the prosthesis. In our series and in other (6) bioprosthetic valves seem to last longer in tricuspid position in Ebstein's anomaly compared with their performance in heart with normal ventricular anatomy. In smaller children in whom the right sided atrioventricular valve is severly dysplastic and right ventricular volume is prohibitive prosthetic replacement is not always possible. To over come this problem some surgeons reported the use of stentless sermilunar homograft replacement of tricuspid valve in Ebstein's malformation as an alternative in the management of a certain difficult subset of patients (15).

In this series, we preferred to insert a bioprosthetic valves for the females in the childbearing age and 4 patients had a total of 6 successful deliveries with no serious pregnancy heart disease were seen in the offspring (0%).

Other investigators (16) studied the effect of Ebstein's anomaly on pregnancy and they reported that pregnancy in women with Ebstein's anomaly is well tolerated but they reported 4% incidence of congenital heart disease in the offspring.

Indications for plication of the atrialized ventricle at the time of tricuspid valve replacement are controversial (15). In our series plication of the atrialized ventricle was performed routinely when the tricuspid valve was reconstructed as it was an integral part of the annuloplasty portion of the repair and we didn't do any plication for the patients who had tricuspid valve replacement except for one patient who had a very big atrialized portion. This is in coincidence with Barbero-Marcial et al (1979) who reported that plication may be considered with tricuspid valve replacement

only when the atrialized portion of the ventricle is very thin walled and aneurysmal. In the literature there is suggestion that omission of plication compromises right ventricular function postoperatively (I) (15) .

Jugdutt et al., (1977) and Danieleon, (1982) attributed the low cardiac output state of their patients who underwent tnicuspid valve replacement to the fact that they had distinict atrialized chamber that were left unplicated.

In contrast to this Caralps et al, (1981) reported a good right ventricular function for their patients without plication of the atrialized portion of the ventricle.

In our series, we had 2 hospital deaths (8.4%) which does not differ too much from other investigator like Danielson et al (1992) who reported (6.3%) hospital mortality and Van son et al (1995) who reported an early hospital death of 10.0% of their cases.

The first patient in our series died from progressive low cardiac output and arrythmia due to severe preoperative cardiomegaly. Danielson et al 1992 showed that increasing cardiomegaly is associated with increasing ventricular fibrillation. They recommended the use of intravenous Lidocaine prophylactically for the first 48 hours postoperatively in the high risk patients as the ventricular fibrillation and ventricular arrythmia were the main cause of death in their patients.

The second patient who died early after surgery in our group had a corrected T.G.A, with Ebstein's anomaly of the systemic atrio ventricular valve. He was referred to us for surgery at age of 45 ys and by that time his systemic ventricle showed significant dysfunction which became more worse after surgery until he died 25 days after operation. Van-son et al 1995 recommended early surgical intervention for patients with corrected T.G.A and Ebstein's anomaly to preserve systemic ventricular function.

In this series, the arrythmia was a major cause of death in 2 patients (early and late deaths). These 2 patients had a frequent attacks of tachyarrhythmia preoperatively but they didn't have an electrophysiological studies preoperatively as they were operated upon early in this series when the facilities for mapping was not avilable.

Many investigators concluded that abnormal atrioventricular conduction pathway whenever present are responsible for serious tachyarrhythmias and should be interrupted surgically in all cases (5) (8).

Driscoll and coworker (1988) reported that on maximum exercise testing for their patients who underwent repair of Ebstein's anomaly, they showed significant increase in work performance, exercise duration and maximum oxygen uptake. Danielson et al 1992 showed that oxygen consmption in their patients increased from a mean of 47% of predicated value before operation to a mean of 72% of predicted value after operation.

In our series, the majority of the patients showed also marked improvement in their exercise tolerance and NYHA functional class inspite the fact that most of our patients have had a significant preoperative cardiomegaly and advarced NYHA functional class (111 or IV).

In Conclusion

— Surgical repair of Ebstein's anomaly is indicated for those patients who are in class III or IV and for selected other patients who are showing clinical deterioration.

— Whenver possible, we prefer valve Reconstruction to valve replacement

— For tricuspid valve replacement, the bioprosthetic valve is the valve of choice especially for females in the childbearing age

— Repair of the Ebstein's anomaly is associated with improvement in exercise tolerance and NYHA functional class and reduces the supraventricular arrythmias.

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Surgical Treatment of D-Transposition of the Great Arteries in Neonates and Infants. A Pioneer Egyptian Experience and A Protocol to Start With

ABSTRACT

In this study, we intended to initiate a protocol for management of transposition of the great arteries (TGA) in our center in Cairo University Paediatric Hospital (CUPH) according to our conditions and available facilities. We have chosen to start by the Senning operation for infants with TGA+IVS, then adding the arterial switch procedure (ASO) for young infants with TGA+VSD (without banding). Gaining experience in this we started to tackle neonates with TGA + IVS doing the (ASO).

Accordingly, from January 1993 to December 1995, 52 patients were operated upon ; 13 neonates with TGA+IVS (group I) and 39 infants ; 4 with TGA+VSD (group II) and 35 with TGA + IVS (group III). (ASO) was performed for group I and II (17 patients) with 41.1% mortality while the Senning operation was performed for group III (35 patients with 28.6% mortality).

The total mortality was 34.6% . Causes of death after the (ASO) included LV failure (3), coronary-related problems (2) and septicaemia (2). I.C.U stay was 12.5 ± 1.9 days. Mortality after the Senning operation was due to RV failure (4), pulmonary venous obstruction (2) and septiaemia (4). I.C.U stay was 9.1 ± 2.8 days.

Late follow up for the (ASO) patients showed trivial mild mitral and aortic incompetence that disappeared with diuretics and digoxin, while 4 patients were presented 6 months after the Senning operation with severe RV decompression and tricuspid regurgitation and were kept on heavy doses of diuretics and digoxin. Pulmonary venous obstruction was presented in one patient a year after surgery in a very bad shape and he died before re-intervention.

Assessment of our protocol showed a success in the policy that we adopted; an overall gradual decline in the total annual mortality from 49.4% after the first year down to 25.9% after the third year which reflects improvement in the learning curve in 3 areas; better patient selection, perioperative management and gaining more experience as regards surgical techniques.

Our conclusion is that the ASO is still the best solution in dealing with neonates with TGA+IVS as well as TGA+VSD. Our future policy is to start tackling infants with TGA+IVS with the rapid 2-stage (ASO) despite the apparent higher mortality after (ASO) in our study, taking into consideration the better long-term survival after (ASO) according to many recent studies. meanwhile, keeping the Senning procedure when the (ASO) can not be done.

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BACKGROUND

Transposition of the great arteries (TGA) is not a rare entity among congenital heart diseases. It is the commonest congenital heart disease causing congestive heart failure in the first year of life (1). Although, first described by Baillie in (1797), the first surgical interference was done 150 years later in 1950 by Blalock and Hanlon performing closed atrial septectomy, followed by Rashkind's balloon atrial septostomy that opened the way for palliation (2). A real breakthrough was achieved by Senning in 1958 (3) when he described his first total corrective technique through switching the venous pathways. Other techniques were adopted later, yet none satisfied the dream of an anatomical as well as physiological solution for the problem until Jatene in 1975 (4), described his technique of switching the great arteries with translocation of the coronary arteries. In the same year, Yacoub recorded successful cases (5).

Several protocols have been suggested, since then , to choose the timing and type of repair, yet they are changeable according to the different techniques adopted in each center. Corrective surgery can be performed as early as the first day of life to take the advantage of an already prepared left ventricle due to the high pulmonary vascular resistance in cases of intact septum and before the development of pulmonary vascular disease in cases with VSD

In this study, we aimed at evaluating our selected protocol for management of simple transposition of the great arteries, as well as transposition with ventricular septal defect (TGA+VSD), taking into consideration the limitations we face and available facilities in our center.

Policy, Patients and Methods

At the beginning of our learning curve, we had to build up experience for the whole team (cardiologists, anaesthetists, perfusionists, surgeons and intensivists) to deal with neonates and infants with such complex anomaly.

Our chronological policy proceeded as follows:-

I-The problem of delayed referral of infants for surgery obliged us to plan for physiological correction (Senning operation).

II-Later, we started the arterial switch operation (ASO) with selected suitable, relatively good candidates with TGA + VSA in infancy.

III-Next, ASO could be performed in neonates with simple TGA.

Accordingly from January 1993 to December 1995, 52 patients diagnosed as a transposition of the great arteries were operated upon at "Cairo University Paediatric Hospital (CUPH). They were 38 males (73%) and 14 females (27%). Age ranged from 7 days up to 13 months with a mean of 153 ± 100 days. Twenty five percent were neonates (13 cases) with an age ranging from 7 : 30 days (mean = 19.8 ± 7.7 days) and 75% were infants (39 cases); the age of which ranging from 2: 13 months (mean = 6.7 ± 2.4 months).

Their body weight ranged from 2.5 : 10 kg (mean 5.4 ± 2 kg) (Table 1); that of neonates ranged from 2.5 : 4 kg (mean 3.3 ± 0.5 kg), while that of infants ranged from

5 : 10 kg (mean = 6 ± 1.8 kg). Most patients were found around the 50th percentile of growth curves .

• **Our protocol of this study depended on:**

Echocardiographic diagnosis and assessment:

I- Preoperatively:

a - Associated anatomical findings as atrial septal defect (ASD), ventricular septal defect (VSD), patent ductus arteriosus (PDA), aortic coarctation (CO).

b - Left ventricular end diastolic diameter percentage (LVEDD%).

c - Left ventricular end diastolic volume percentage (LVEDV%).

d - Septal position: type I : Rightward displacement, Type II : centered position and type Ill: leftward displacement.

e - Atrio-ventricular (A-V) valve status: incompetence or straddling

f - Semilunar valve status: (incompetence or stenosis)

g - Coronary patterns: according to Yacoub nomenclature (,5)

h - Left ventricular outflow obstruction (LVOTO)

II- Postoperatively:

ICU echocardiography was used to assess preloading conditions of the heart taking in account any change in septal position, right atrial filling and LV contractility. Following the senning operation, SVC, IVC or pulmonary venous obstruction could be assessed as well as RV conlractility.

Cardiac catheterization and angiography:

Our policy was to catheterize all infants. while for neonates this was reserved only for echo suspicion of unusual coronary pattern. Of concern were: aortic oxygen saturation, left ventricular and right ventricular peak systolic pressures (LVP & RVP), assessment of LVOT and delineating coronary pattern.

Exclusion criteria:

These were obtained from echo and catheter data

A - General exclusion criteria:

1.Complex TGA (e.g. with juxtaposition of atria appendages, TGA with univentricular heart or with double outlet right or left ventricles ... etc).

2. L - TGA.

3. Corrected TGA.

4. D - TGA with LVOTO.

5. Associated aortic arch abnormalities, e.g. coarctation.

B- For Senning operation : (SEN op.)

1. Tricuspid incompetence

2. Straddling A - V valve

C- For Arterial Switch Operation (ASO)

1. Septal position type Ill

2. LVp / RVp ≤ 70% (in catheterized patients)

3. Semilunar valvular incompetence

4. Cases of simple transposition older than 30 days

Accordingly, 17 patients (32.7%0 were eligible for the (ASO) of which 4 infants with TGA + VSD (32.5%) and 13 neonates with simple TGA, while 35 infants were candidates for Senning operation (Table 2).

During initial assessment of the patients, the majority needed initial **preoperative management** and procedures according to their clinical status on admission, for control of chest infection and or heart failure, and resumption of good feeding prior to the operation.

Non invasive oxymetric assessment was done for all patients together with echocardiographic study to assess patency and efficiency of the present communications. Oxygen saturation below 70% was an indication of further management; medical; using prostaglandin E 1 infusion (PGE1), interventional; performing Balloon atrial septostomy (BAS) whether under fluoroscopy or recently under echocardiographic guidance (6), or surgical; performing a Blalock - Hanlon atrial septectomy (BHS).

Anaesthesia

Anaesthesic regimen had undergone some modifications; induction was performed with fentanyl 50 µg/kg and pancuronium 100 µg/kg and after the beginning of by-pass, additional 10 µg/kg/dose of fentanyl and a 100 µg/kg/dose of pancuronium to maintain their plasma level. On rewarming, an additional 15 µg/kg/dose of fentanyl and 100 µg/kg/dose of pancuronium were given.

Perfusion technique

Using membrane oxygenator primed with freshly donated, non-citrated blood. Intermittent conventional haemofiltration during by-pass to mantain haematocrite around 35. Modified haemofiltration was used at the end if there is low haemoglobin, myocardial oedema or development of arrhythmia.

Operative Techniques:

I - The Senning Operation: (SEN op.)

In reconstruction of pulmonary venous chamber, besides the commonly used **direct technique (D);** Suturing the remaining edge of right atriotomy to the rightward edge of left artiotomy above the right pulmonary veins, and the separate **intervening pericardial patch technique (SP),** we standardized the dimensions of an **in-situ pedicled pericardial patch technique (PP)** *which is trapezoid in shape; the narrow base of which is formed of the pericardial reflection over pulmonary veins and is equal to the diameter of both veins together, the wide free edge of the patch is about 2 times the length of the base which equals the distance from the base to the free edge of the patch. (illustration 1).*

II - The Arterial Switch Operation: (A.S.O)

Of concern was the following:

1. The ascending aorta was transected about 1 cm distal to the origin of coronary arteries.

2. Coronary explantation in U-shaped scallops which were filled by a single pantalon-like fresh pericardial patch.

3. The pulmonary artery was transected proximal to its bifurcation.

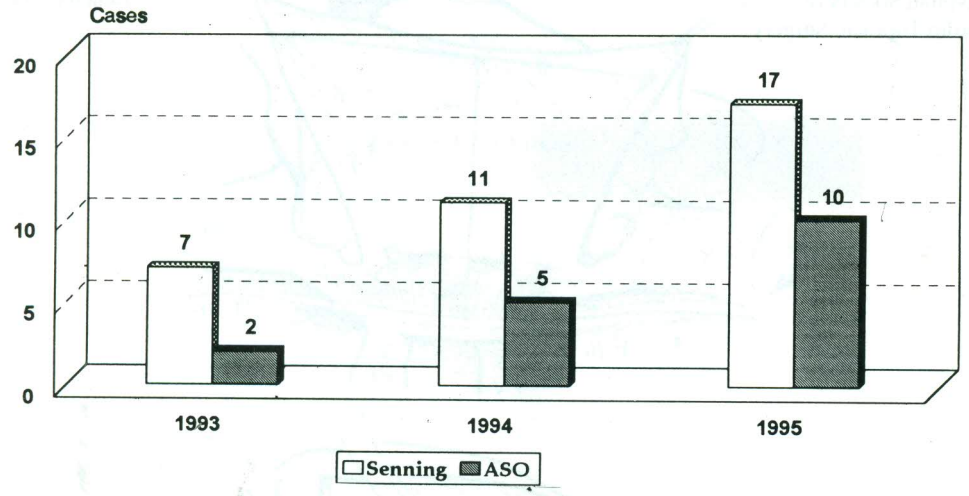

Fig. (1): Senning and Arterial Switch operation (ASO) (Annual cases).

Evaluation of operative protocol included the following points:-

1. Modification in operative technique (if any).

2. Regression of ischaemic time.

3. Operative haemodynamic measurement and postoperative echo diagnosis for morbidity and mortality related factors.

4. ICU stay and late follow-up.

Statistical Analysis

Descriptive statistics were obtained using Kwikstat and Statgraph program. All statistical tests were carried out at 0.05 significance level. Quantitative data were reported as the mean ± the standard deviation while qualitative data were reported as frequency and percentage. Statistical analysis was performed using a one-way analysis of variance and if significant, the analysis of data was followed by T test to detect statistically significant difference. It should be noted that (P) value was replaced by the (t) value since the material size was smaller than 30 in 2 of the three groups.

Results

During the period of the study we operated upon 52 patients that were divided into 3 groups according to their age and pathological characteristics:

- **Group I** which included 13 neonates (25%) with simple TGA for which the Arterial Switch procedure (ASO) was performed.
- **Group II** which included 4 infants (7.7%) with TGA and VSD that was managed by the A.S.O and,
- **Group III** which included 35 infants (67.3%) with simple TGA where the Senning operation was performed.

Table (3) shows the demographic characteristics of each group.

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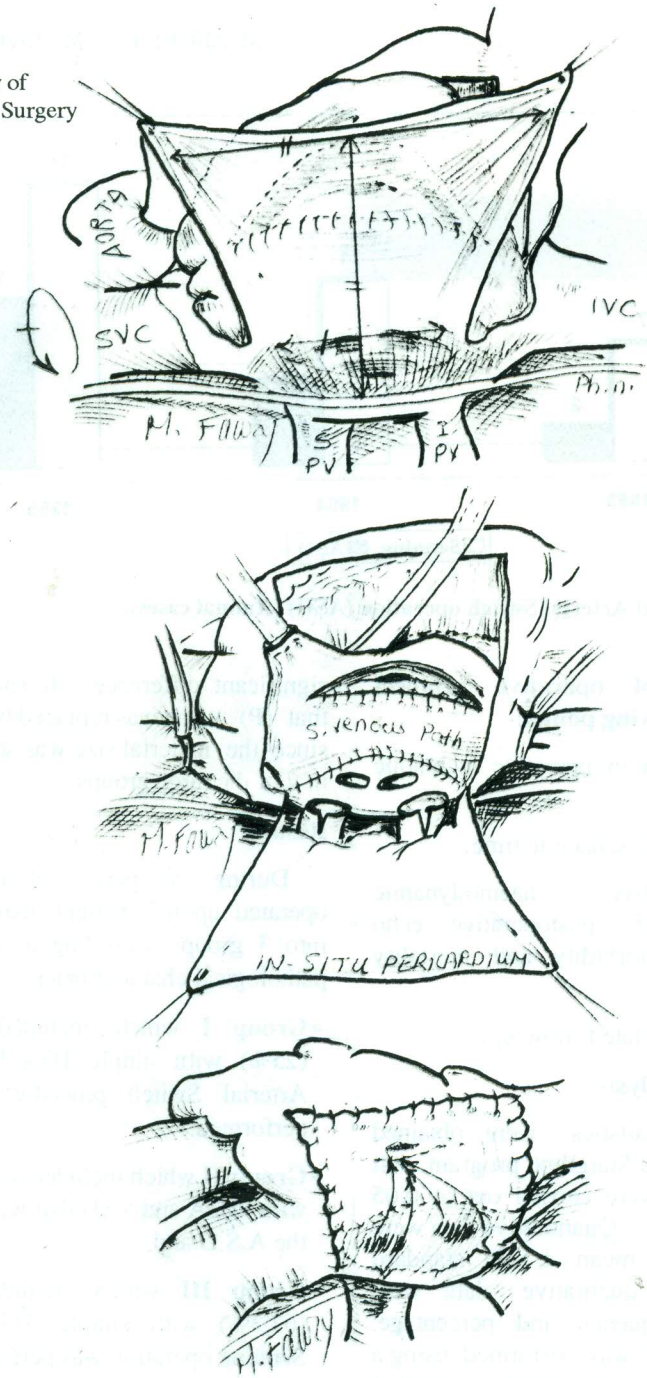

III. 1: Pedicled Pericardial Technique In SENNING Op. (Surgeon's View)
SVC: Superior vena cave, IVC: inferior vena cave, SPV: superior pulmonary, vein, IPV: inferior pulmonary vein, Ph. N: phrenic nerve.

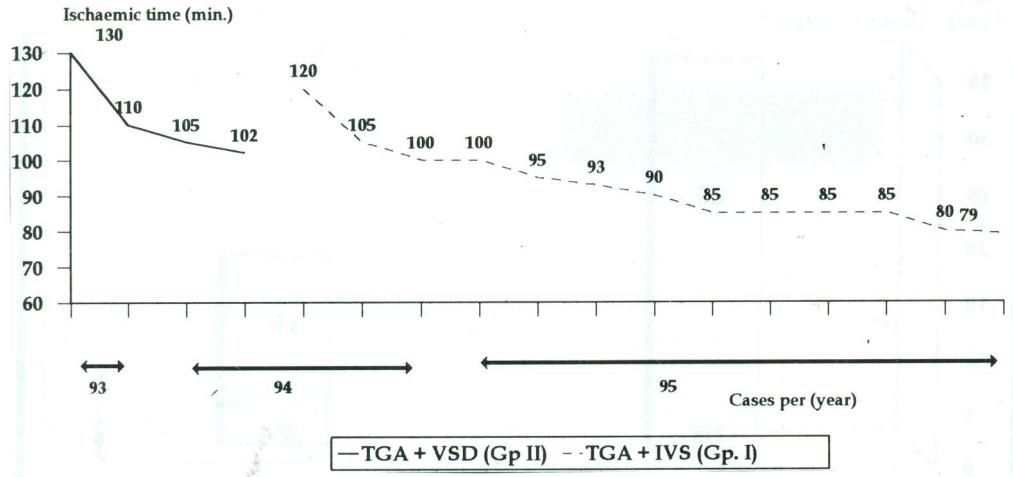

Fig. (2): Ischaemic time in cases of A.S.O

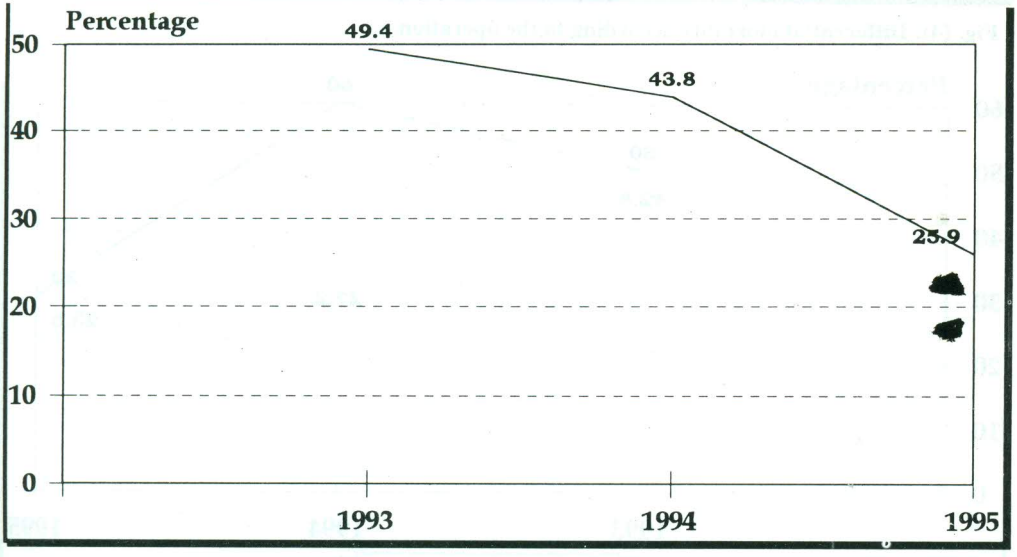

Fig. (3): Annual Mortality (Total).

Echocardiographic assessment was done for all patients to detect the anatomical and functional characteristics and to check for the presence of any of the exclusion criteria denoted in our protocol. The data obtained are summarized in table (4) for each group separately.

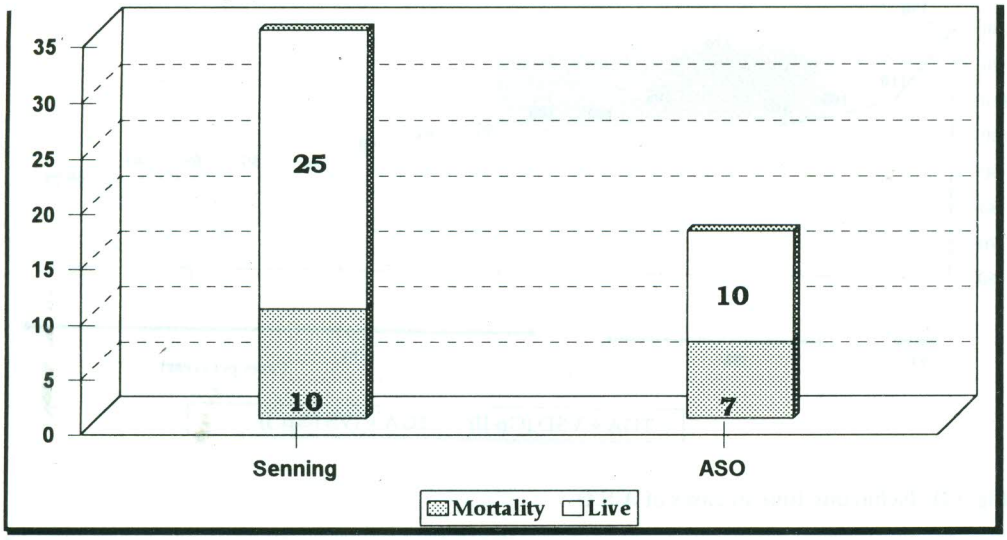

Fig. (4): Differential mortality according to the operation.

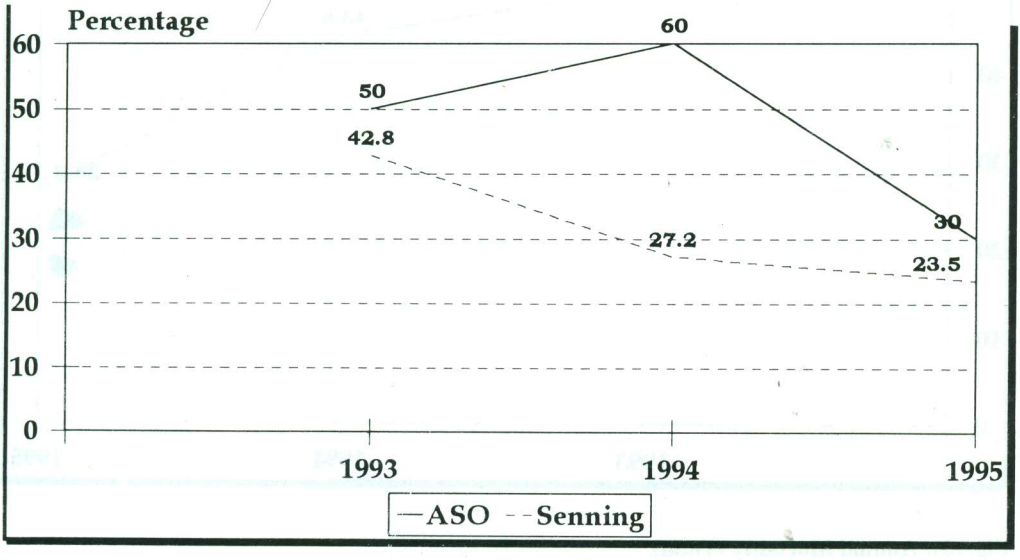

Fig. (5): Annual Mortality (Differential).

Thirty-six infants were subjected to cardiac catheterization and angiography, while only 4 of the 13 neonates (30.7%) were catheterized. Data obtained are included in table (5).

Sixty percent of the patients necessitated preoperative management; three patients had chest infection (5.8%), while heart failure had to be controlled in other 3 patients (5.8%).

Table (1): Demographic data of the patients studied

		Minimum	Maximum	Mean ± S.D
Age		7 days	13 months	153 ± 100 days
Weight		2.5	10	5.4 ± 2
Height		40	80	60.2 ± 9.5
B.S.A.		0.18	0.54	0.33 ± 0.09
Sex	Male	38 (73%)		
	Female	14 (17%)		

Table (2): Operative techniques of each group.

Pathology	Simple TGA	TGA + VSD	Simple TGA
Age category	(Neonates)	(Infants)	
Number	13	4	35
Operation	ASO		Senning

Table (3): Demographic data of studied cases.

	Group I	Group II	Group III
Age	20.8 ± 9.3 (d)	5.3 ± 2.8 (m)	6.3 ± 1.6 (m)
Weight	3.3 ± 0.5	6.3 ± 1.5	6.1 ± 1.7
Height	49.1 ± 4.2	64.8 ± 12.7	63.7 ± 7.1
B.S.A.	0.24 ± 0.03	0.40 ± 0.08	0.36 ± 0.079

Table (4): Echocardiographic data.

	Group I	Group II	Group III
ASD	9/13 (69%)	-	15/25 (42.9%)
VSD	-	4/4 (100%)	-
PDA	3/13 (23%)	-	-
Coarctation		-	-
LVEDD	2.5 ± 0.1	3.4 ± 0.2	1.9 ± 0.3
LVEDD Exp.	2.9 ± 0.1	3.3 ± 0.1	3.2 ± 0.1
LVEDD%	86 ± 2.6	103.5 ± 4.4	61.1 ± 8.2
LVEDV	23.1 ± 2.5	49.7 ± 2	12.2 ± 4.6
LVEDV Exp.	28.2 ± 3.6	46.7 ± 9.4	19.7 ± 6.1
LVEDV %	83.8 ± 8.9	99 ± 9.7	63.4 ± 19.4
RV	0.77 ± 0.1	1.4 ± 0.4	1.1 ± 0.4
Septal position	I: 9/13 (69.2%)	2/4 (50%)	-
	II: 4/13 (30.8%)	2/4 (50%)	-
	III: -	-	35/35 (100%)
AV valve	Normal	Normal	Normal
S.L. valve	-	-	-
Coronary pattern	A: 10/13 (69.2%)	A: 4/4 (100%)	32/35 (91.4%)
	B: 2/13 (15.4%)		2/35 (6.3%)
	D: 1/13 (7.7%)		1/35 (2.9%)
LVOTO	-	-	-

LVEDD Exp = Expected left ventricular end diastolic diameter
LVEDV Exp = Expected left ventricular end diastolic volume
S.L. = Semilunar

Table (5): Catherter data.

	Group I (4/13)	Group II (1/4)	Group III (35)
O_2 saturation	72.5 ± 9.6	65	40.5 ± 5.2
LVP	85.5 ± 6.6	90	82.2 ± 4
RVP	83 ± 0.08	0.72	50 ± 0.7
LV/RV P.	65.1 ± 5.6	71	62 ± 4.3
Coronary P.	as echo	as echo	as echo
LVOTO	absent	absent	absent

LVP = Left ventricular peak systolic pressure.
RVP = Right ventricular peak systolic pressure.

Table (6): Initial procedures

	Group I	Group II	Group III
O_2 sat. before	65.1 ± 5.6	72.5 ± 1.3	63 ± 4.3
B.A.S	4/13 (30.8%)	-	16/35 (45.7%)
PGE1	3/13 (23.1%)	-	-
B-H. septectomy	-	-	4/35 (11.4%)
O_2 sat. after	72.2 ± 1.7	-	80.2 ± 4.5

O2sat = Oxygen saturation.
B.A.S. = Balloon atrial septostomy.
PGE1 = Prostaglandin E1
B.H. septectomy = Blalock - Hanlon Atrial septectomy.

Table (7): Mortality related after the Senning operation.

	Age (m)	Technique	RV dimension	Ischemia	T. of death
RV failure	12	D	1.2	62	2
	10	D	1.8	72	7
	10	S.P	1.9	60	13
	12	P.P	1.9	80	16
Pulmonary venous obstruction	5	D	0.7	63	9
	10	D	1.9	75	4
Septicaemia	10	P.P	1.8	70	15
	8	S.P	1.0	75	9
	9	S.P	1.2	60	15
	7	P.P	1.2	65	13
Mean ± S.D.	9.3 ± 2.2		1.45 ± 0.45	68.2 ± 7.1	10.3 ± 4.9
Statistical Significance	S.S	S.S	S.S	N.S	N.S

D: direct
S.P.: separate patch
P.P: Pedicled pericardium
S.S: Statistically significant
N.S: Non-significant
Note: Additional late mortality of pulmonary venous obstruction is not included.

Initial procedures were necessary in 16 patients (30.8%) to improve O_2 saturation. Table (6).

Operative Results

Analysis of operative techniques:

Total interventions done 52, patients, 35 Senning operation (infants, group III). ASO (4 infants : group II and 13 neonates group I). Fig (1) shows the annual number of cases of each technique.

Evaluation of Senning operation:

a) Reconstruction of the pulmonary venous pathway from the pulmonary venous compartment to the tricuspid valve and right ventricle was done by 3 techniques, 20

Table (8): Mortality and morbidity related factors for the Arterial Switch petients.

	Age (d)	Coronary	Ischemic time	LV/RV pressure ratio	Time of death	Comments
Coronary problems	19	D	105	0.85	6 h	
	22	A	100	-	12 d	LAD & CX 2 separate ostia
Delayed sternal closure	7	A	90	-	-	
	8	A	85	-	-	
+ infection	25	A	100	-	14 d	Septicemia and D.I.C.
	30	B	120	0.87	15 d	
L.C.O.P.	30	A	95	0.89	15 d	
	*8 m	A	110	-	14 d	
	*4 m	A	130	0.72	14 d	
	10 d	B	93	0.7	-	Undergone peritoneal dialysis and recovered
	28 d	A	85	-	-	
Mean ± S.D.	49 ± 70.6		1012 ± 14.3	0.81	12 ± 5.3	
Significance	N.S	S.S	S.S	N.S	N.S	

*** TGA + VSD**
S.S. Statistically significant
N.S. Non-signicant

patients (57.4%) by the direct technique (D), 5 patients (14.3%) had reconstruction with a separate pericardial patch interposition, and in the last 10 patients (28.6%) we shifted to our standardized pedicled pericardial patch technique.

b) Haemodynamics measurements revealed no significant obstruction in both systemic and pulmonary venous compartments. SVC pressure reading ranged from 14 : 17 cm H_2O with a mean of 15 ± 0.2 cm H_2O, while IVC pressure recording ranged from 12:15 cm H_2O (mean = 13 ± 0.3 H_2O). Right appendicular pressure reading ranged from 5:10 cm H_2O (mean =7 ± 1cm H_2O).

c) Mortality:

Ten patients died in this group (28.6 %), the causes of death were:

1. Right ventricular failure : 4 patients (11.4%) and they died after 2, 7, 13, and 16 days respectively.

2. Pulmonary venous obstruction : was experienced in 2 patients and they died 9 and 4 days after operation respectively.

3. Septicemia: 4 patients (11.4%), and they died after a mean duration of (13 ± 2.8 days).

d) I.C.U. Stay: ranged from 2 (including a dead patient) to 16 days with a mean of 9.1 ± 2.8 days . Table (7) shows mortality related factors for each patient separately.

e) Late Follow up:

Within the following 2 years, 4 patients were presented with severe right ventricular decompensation with tricuspid regurgitation. They were kept on daily diuretics and digoxin. Patient no. 19 presented 1 year after surgery with pulmonary venous obstruction, he was managed medically as his state could not allow surgical interference and he died after 6 months.

Evaluation of Arterial Switch Operation:

We performed arterial switch operation for 4 infants with TGA + VSD (group II) and 13 neonates with simple TGA (group 1) with a total mortality of 7 patients (41%) (Fig. 4). Five from group I (38.5%) and 2 from group II (50%).

a) Regression of ischemic time: is shown in Fig. 2.

b) Morbidity and Mortality Table (8).

c) ICU Stay : ranged from one day (died the first postoperative day) to 15 days (mean 11.8 ± 3.9) in group I and 10 : 14 days (mean 12.5 ± 1.9 days) in group II. Table (8) shows mortality related factors in these patients.

d) Late Follow up

Patients were kept on minimal dose of diuretics for 6 months after surgery. Trivial mild aortic and mitral regurgitation was experienced in 3 operated neonates. This disappeared after 6 months with diuretics and lanoxin that was stopped later. No supravalvular pulmonary stenosis was experienced in the follow - up period (approximately one year). All patients returned to their percentile growth pattern.

DISCUSSION

Choice of protocol

Before the start of this study, lots of questions had to be answered to choose the suitable policy, putting into consideration the condition of our community, the quality of patients we receive and the experience and facilities of our center. These questions were:

a. How should we start ? with arterial switch operations (ASO) or with an atrial type of repair ?

b. In what type of pathology ? simple T.G.A or those with V.S.D ? c . At what age ? Neonates or infants ?

d. If with (ASO); with one or two-stage (ASO)

e. And if with atrial switch; with Mustard or Senning operation ?

Indeed, the answer of one question may be leading to the rest, yet we were confronted with the following facts and observations derived from previous large scale studies concerning both techniques as well as early and late outcome:

There are many anatomic considerations suggesting the morphologically left ventricle (LV) to be a better systemic pump than the morphologically right ventricle (RV) being formed almost entirely of the sinus or pumping portion (no conus).

Phylogeneticalíy, the (LV) is the ancient "professional" pump. With more compact myocardium (stratum compactum), a double coronary and a double conduction system and guarded by the mitral valve with well balanced papillary muscles, better designed to occlude a circular systemic A-V orifice (7) .

Moreover, the theoretical and practical advantages of anatomic correction over physiological repair (Mustard or Senning) ; in terms of lower incidence of arrhythmia and a normal systemic ventricle and a normal A-V valve function, have been supported in many mid-term (8-9) as well as early reports of late follow-up studies (10).

This would favour the ASO as opposed to an atrial switch operation. Yet, we preferred to start dealing with this complex anomaly in infancy by the simpler atrial type of repair, senning operation was chsen since it has less incidence of arrhythmia although the two stage repair could solve the problem of patients with TGA + IVS beyond the neonatal period, we were not in favour of this; as shunt control and debanding procedure will increase the risk of the second stage procedure in the absence of prior experience of one stage arterial switch operation at the beginning of our study.

The physiological repair (atrial switch operation) still has a role in a limited number of patients; where anatomic problems (e.g. coronary artery anatomy, seminular valvular incompetence or stenosis) may contraindicate arterial switch operation. In addition, the presence of neonatal disease could lessen the opportunity of a one-step-ASO because of delay (11). Moreover, the rapid two-stage policy; i.e, performing the banding then the total correction 2 weeks later; necessitates performing the first stage closer to the neonatal period (12).

Concerning age, surgical treatment for both TGA + IVS and TGA + VSD was recommended by many investigators to be done in the early neonatal period (11) . On the contrast we preferred to start ASO in infants with TGA + VSD, avoiding the neonatal period and its problems meanwhile, getting acquainted to the technique, we started to operate upon neonates with simple form of TGA near the middle of the second year of our experience.

Echocardiographic assessment alone helped us to shorten the decision making period for neonates so as not to lose the golden period of repair as soon as possible, while cardiac catheter was preserved for cases of uncertain coronary anatomy, when LV function is questionable or to rule out the possibility of pulmonary vascular disease in cases with V.S.D. The LV/RV pressure ratio of at least (0.7) was taken as a safe figure ; in agreement with Castaneda (13) and other reporters; although others have mentioned the possibility to go down

to a ratio of (0.3) in neonates of 1.5 kg body weight (14) .

We believe that initial management was mandatory for infants and neonates with T.G.A especially with intact septum by putting the baby in a better form, mainly improving hypoxaemia with the resultant effect on all body systems. This was mediated through different procedures starting from an effective medical treatment till the ability to perform echo-guided bed-side balloon atrial septostomy in the I.C.U to obtain adequate atrial communication which allows better O_2 delivery with O_2 saturation of at least 70% (14) . This way of handling such babies matches well with what was recommended by other investigators (6,14,15) .

To obtain better surgical results, we tried to avoid technical-related complications of both techniques mentioned in the literature. In ASO, we used the U-shaped scallop technique for coronary explantation (13). Extensive epicardial mobilisation of the proximal coronary arteries to avoid coronary kink (10) . We used the single "pantalon like" pericardial patch technique to fill the site of coronary explantation to avoid supravalvular stenosis(16,17) .

To avoid supravalvular aortie stenosis, we used to excise a segment of the distal aorta enough to avoid kink but not too large to avoid tension of the suture line (10) .

The main technical improvement that we adopted in the Senning operation, to avoid future pulmonary venous obstruction, was the use of a pedicled pericardial patch. The idea itself was mentioned by Tonkin and associate (18) in 1983, describing the modified Shumacker's technique to use an in situ pericardial patch in the "MUSTARD" operation to make use of the still viable patch which is amenable to further growth. The same idea was used by Castaneda (12), performing the Senning operation in neonates and young infants where a separate patch technique would result in accelerated stenosis due to the enormous rate of cardiac growth at that age with fibrosis of the multiple suture lines around the "dead" pericardial patch. Our modification really aimed at standardizing the dimensions of the patch used as mentioned in text. We feel that this makes the use of the pedicled pericardial patch a rather "safe" technique instead of depending on objective views as it allows free passage of blood yet without redundancy that may impede the forward blood flow and hence low cardiac output.

II - Protocal Evaluation

Analysis of the total mortality in this study (34.6%) in terms of annual mortality shows a gradual decline from 49.4% in 1993 down to 25.9% in 1995 Fig (3). This looks similar to other centers' reports describing their early experience in dealing with transposition of the great vessels. Yamaguchi described the 1st 6 year experience in 6 centers in Japan from 1982 (8). He mentioned a 60% mortality in the first year, going down to 13% after 6 years. A similar report of Wernovsky (10) shows an initial mortality of 14 : 27% going down to 5% after 9 years of experience.

Further analysis in terms of differential mortality according to the type of operations performed in our study (Fig. 4,5) shows a rather steady, gradual decline of annual

mortality after the Senning operation despite doubling the number of cases, thus reflecting an improvement in the learning curve. Whereas, the abrupt increase in mortality with the arterial switch operation could be explained by the addition of another factor in the second year ; that is dealing with neonates. Plotting the two curves together in (Fig. 5) could explain the slow decline in the curve in Fig (3) dealing with the annual mortality.

We studied different incremental risk factors for death and complications after both techniques in our study (Senning and ASO). The most statistically significant factors after Senning operation were older age at operation, preoperative RV diameter % and the technique of pulmonary venous; pathway reconstruction Table (7). Ninety percent of complications took place in patients older than 6 months. This could be explained by the development of right ventricular failure and the occurrence of general sepsis that correlated well with increased mean ICU stay in days for these patients (13 ± 2.8 d) in comparison to 9.1 ± 2.8 d for the rest in the same group. This is to the contrary of what has been often found in the past that a "younger" age at repair is a real risk factor for death after the actual repair and was identified in a multi-institutional study in the Congenital Heart Surgeons Society, some institutions have achieved good results with the Senning atrial switch repair even when performed in the first two weeks of life with a hospital mortality of 4%. Several institutions attest to the likelihood that young age can no longer be considered a risk factor for deaths after the atrial switch repair, thus supporting our results.

In our study, 50% of complicated patients had RV diameter > 1.8 cm, that is 140% of normal in relation to age. This correlated well to the development of RV failure. The response of RV function to exercise was not assessed in our study yet those with diameter > 140% of normal were received later with RV dysfunction. This figure was taken as a single parameter for possible post operative RV changes (or deterioration) in our cases. This correlates well with deteriorated ejection fraction in other multicentric studies; studying RV changes after the Senning operations (2).

Mechanical problems in pulmonary venous pathways were totally eliminated in our study after using pedicled pericardial patch technique. Direct technique of repair was claimed to be the cause of these problems especially when performed at an older age; 75 % of infants with mechanical problems were older than 6 months and all had their repair using the direct technique.

In comparison, other factors as, ischaemic time was not statistically significant being 68.2 ± 7.1 min for complicated cases and 67.9 ± 5.2 min for the rest of the group. A striking difference in our study is the absence of active arrhythmia in the Senning group although their incidence may reach up to 4.7% after this technique which is still less in comparison to the Mustard operation which is considered by itself as an independent risk factor for the development of arrhythmia (11). Thus, it was excluded from our protocol. Serial ECG readings were taken to exclude arrhythmia in our study. No active arrhythmia were noticed, to necessitate the use of Holter monitoring.

As regards the arterial switch operations, we observed that the most significant risk factors for death and complications were abnormal coronary

artery pattern, age at repair and the ischemic time, in agreement with many reporters (2,8). In our study, all patients with abnormal coronary pattern were complicated after the procedure, no matter what type of distribution. However, coronary- related problems (ischemia, infarction) constituted only 50% of causes of mortality. The occurrence of these problems correlated well with longer ischemic time; being 104.5 ± 11.5 min while that of the whole group was 92.1 ± 11.2 min. Some reporters, like Yamaguchi refers these complications to the mere type of distribution, mainly type B,C Yacoub, where he considered them to be a relative contraindication to do the arterial switch procedure (8).

In our study, ischaemic time correlated well also to the development of other complications; being 101.2 ± 14.3 min for complicated babies, compared to 92.1 ± 11.2 min for non complicated babies. Seventy five percent of patients with delayed sternal closure had citrated blood/plasma priming fluid, 90% only had haemofiltration their ischaemic times being 100, 120 minutes respectively at the beginning of the experience. Table (8).

However, with both techniques, septicaemia was the leading cause of death (6 out of died 17 patients) : i.e. 35.3% of the total mortality. It correlates well with ischemic time, I.C.U stay and accordingly, indirectly with the age at repair and RV function after the Senning operation. Elimination of this factor alone would have resulted in mortality of 21 % instead of 34.6%.

Another institutional risk factors that is still valid in our study; is "center experience". This would be evaluated by the interval in years after the first case of the technique as well as the number of cases performed during this period. Our experience is a 3-year-old one and constitutes only 52 cases divided between the two techniques. This could need further years to go down with the ischaemic time, mortality rate and age at repair to accepted levels.

Conclusion

Analysis of data showed the success of the protocol we adopted to eliminate many high risk factors that could abort the trial to initiate a learning curve in dealing with transposition of the great arteries. Our future policy will be towards overcoming the problem of delayed referral of infants which adds a patient-specific risk factor to the procedure. This could be achieved by increasing the awareness of medical staff to time-related prognosis in dealing with the problem so that babies should be sent once diagnosed; before losing the optimal time of anatomic correction.

We intend to extend the use of Arterial Switch operation in neonates with intact ventricular septum being the gold standard for management despite the high mortality in our study, which still coincides with other reports of early experience of the technique (8,13). We aim at improving the learning curve in terms of better ischaemic time, lower mortality rate in this pathology before we start dealing with neonates with TGA + VSD using the arterial switch. Shifting to rapid-two-stage arterial switch operation will enable us, thus to tackle the problem of babies with TGA+IVS where a one-stage procedure is not possible. The

sound long-term survival after this policy observed by many reporters (8, 10, 16) in comparison to the Senning operation encourages us to use it in the near future.

And so long the problem of delayed referral of babies exists, the Senning operation should be kept for babies received late, or in whom the left ventricle seems unsuitable or failed to be prepared.

The gradual decrease of such mechanical complications of pulmonary venous pathway using a pedicled pericardial patch encourages us to keep this technique.

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Doppler Echocardiographic Assessment of Mitral Prosthetic Valves

Abstract

Doppler echocardiographic characteristics of mechanical and tissue mitral prostheses: Starr-Edwards, Bjork-Shiley, Hall-Medtronic and Hancock were compared in 110 patients with clinically normal valve function. Starr-Edwards prostheses had significantly higher Vmax and PG (P<0.001) as compared to other mitral prostheses. A significant large EVA was found in Hall-Medtronic and Hancock mitral prostheses in comparison with Starr-Edwards (P<0.01 and P<0.01 respectively), as well as Hall-Medtronic vs. Bjork-Shiley mitral prostheses (P<0.05). MR was found in 20% of Hancok tissue valves and 35% of Bjork- Shiley valves. A significant reduction of EVA and PI was found in Starr-Edwards and Bjork-Shiley prostheses implanted > 10 years ago (P<0.01) as compared to those implanted <10 years ago. In conclusion, Doppler indices, especially EVA and PI are very useful and sensitive parameters of prosthetic mitral valve function. Reduction of PI may be the first sign of subclinical prosthetic valve dysfunction. Hall -Medtronic prosthesis appears to have the most optimal hemodynamics.

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INTRODUCTION

Several noninvasive techniques including phonocardiography, M-mode and two-dimensional echocardiography and cinefluoroscopy have been used to assess prosthetic valve function (1). However, Doppler echocardiography is superior over other noninvasive techniques because it allows quantitative assessment of valve function. It is safe, easily repeatable and provides haemodynamic data that closely correlate with parameters obtained by invasive procedures (2,3,4,5). The purpose of our study was to compare Doppler flow characteristics and pressure gradients of various normally functioning mechanical and tissue prosthetic valves implanted in mitral position.

Texas Heart Institute and Mansoura University Hospitals

Material and Methods

The study group consisted of 110 patients with prosthetic mitral valves selected from Texas Heart Institute outpatient clinics during their routine postoperative follow-up during the period from February 1995 to August 1995. All patients had normally functioning mitral prostheses as defined by absence of symptoms or clinical evidence of mitral stenosis or regurgitation. Their age ranged from 30 to 74 years (mean 49.3 ± 19.3); there were 32 men and 78 women. Ninety-five patients had mechanical mitral valves: 30 had Starr-Edwards, 47 Bjork-Shiley and 18 Hall-Medtronic, while 15 patients had Hancock bioprostheses. Patients with Starr-Edwards and Bjork-Shiley valves were divided into two groups: A) with valves implanted less than, and B) with valves implanted more than 10 years ago.

Doppler echocardiographic studies were performed using pulsed and continuous Doppler ultrasound (Advanced Technology Laboratories (ATL), Ultramark 8). The records were taken on video tapes in all patients. Trans-prosthetic flow was examined with the transducer positioned at the cardiac apex from a four-chamber echocardiographic view, with sample volume positioned at the left ventricular side of the valve plane and approximately parallel to the atrioventricular flow. To obtain adequate pulsed Doppler tracings in the case of Bjork-Shiley valve, the sample volume was placed at the major orifice, in the case of Starr-Edwards valve alongside the ball at the sewing ring, in the case of Hall-Medtronic valve on both sides of the open disk and in the case of Hancock valve centrally, between the tips of the mitral leaflets.

Peak diastolic flow velocity (Vmax), peak pressure gradient (PG), effective valve area (EVA), performance index (PI) and presence of mitral regurgitation (MR) were assessed for each valve.

Vmax was measured in meters per second (m/s). PG was calculated using the modified Bernoulli equation:PG = $4xVmax^2$, the gradient being expressed in millimeters of mercury (mmHg). EVA was calculated using the pressure half-time (PHT) method described for the native mitral valve (6): EVA = 220/PHT, the valve area was expressed in square centimeters (cm^2). PI was calculated as the ratio between EVA and manufacturer's orifice size. All calculations were an average of three cardiac cycles for patients in sinus rhythm, and five cardiac cycles if atrial fibrillation was present. The presence of MR was assessed from the apical view in all types of examined prostheses and in the case of metallic prostheses left parastemal long axis view was also employed. If MR was present the extent of the regurgitant jet was mapped in the left atrium by pulsed Doppler. Jets that measured up to 1.5 cm into the left atrium were considered mild MR. Patients with regurgitant jets that measured more than 1.5 cm were excluded from this study.

Statistical analysis: comparison of Doppler indices for various mitral valve prostheses was done using the Student t test.

Results

Demographic and clinical parameters of patients with mitral valve prostheses are shown in Table 1. Most of patients were women (71%) and had Bjork-Shiley prostheses (41%). Figure 1 shows a flow velocity envelop across the mitral valve obtained with pulsed Doppler by placing the sample volume in the left ventricle, in an apical view, in a patient with a normally functioning Bjork-Shiley mitral prosthesis. The flow pattern resembles that of a normal native mitral valve.

Doppler indices for various types of mitral valve prostheses are shown in Table 2 and Figure 2. Starr-Edwards and Bjork-Shiley mitral prostheses implanted >10 years ago have significantly reduced EVA

Table 1:Demographic and clinical parameters in patients with mitral valve prostheses (n=110):

Parameter	Number(%)
Age (years)	
< 60	96 (87)
> 60	14 (13)
Sex	
male	32 (29)
female	78 (71)
Prosthetic valve type	
Starr-Edwards: A	10 (9)
B	20 (18)
Bjork-Shiley: A	32 (29)
B	15 (14)
Hall-Medtronic	18 (16)
Hancock	15 (14)

A = valves implanted <10 years; B = valves implanted >10 years.

Table 2: Doppler indices for 110 mitral prosthetic valves with clinically normal functions.

Valve type		Vmax (m/sec)	PG (mm Hg)	EVA (cm^2)	PI	MR
Starr-Edwards	A	1.70±0.45[4]	11±5[4]	1.8±0.5[2]	0.65±0.05	25%
	B	2.10±0.45	15±6	1.4±0.4[1]	0.59±0.02[1]	23%
Bjork-Shiley	A	1.50±0.45[4]	9 ±5[4]	2.2±0.8[3]	0.64±0.02	35%
	B	1.65±0.45	14±6	1.7±0.4[1]	0.60±0.02[1]	33%
Hall-Medtronic		1.40±0.35[4]	8±2[4]	2.6±0.8[2,3]	0.68±0.02	30%
Hancock		1.42±0.35[4]	8±4[4]	2.4±0.5[2]	0.65±0.04	20%

A = prostheses implanted less than 10 yeras ago; Vmax=peak diastolic flow velocity; PG= peak pressure gradient; EVA = effective valve area; PI= performance index; MR= mitral regurgitation; [1]p<0.01 B vs A group; [2]p<0.01, Hall-Medtrotic and Hancock valves vs Starr-Edward; 3p<0.05 Hall-Medronic vs Biork-Shiley valves; 4p<0.01 Starr-Edwards vs all other valves.

(p<0.01) as compared with valves implanted <10 years ago.

Discussion

The diastolic flow pattern across a prosthetic mitral valve is very complex and depends on left atrial pressure, cardiac output, compliance of the left ventricle, heart rate at the time of the study, patient's age, presence and severity of mitr al

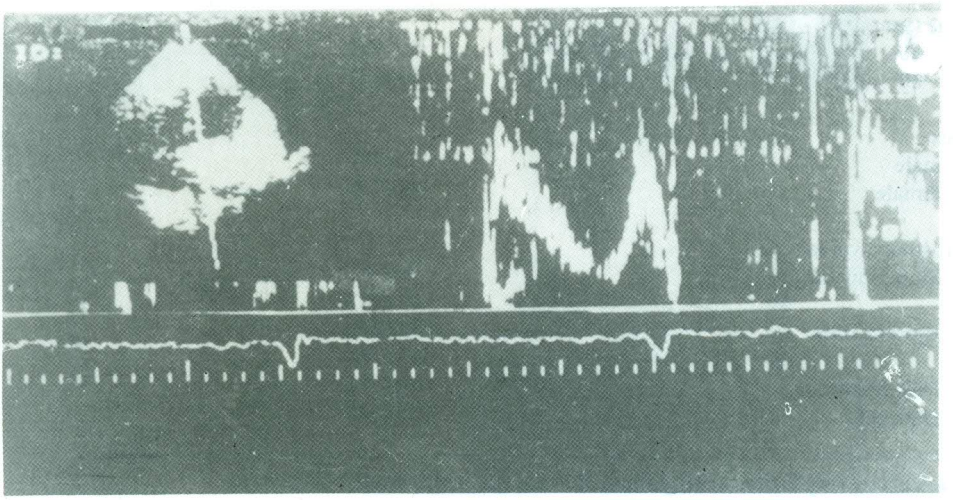

Fig.1: Pulsed Doppler echocardiography in a patient with normally functioning Bjork-Shiley prosthesis. Inset shows Doppler sample volume in the left ventricle, in the apical 4-chamber view, beneath the prosthetic valve. The flow pattern resembles that of a normal native mitral valve. An early peak occurs in the beginning of diastole followed by a rapid fall. A second peak corresponding to atrial systole occurs in patients in normal sinus rhythm.

regurgitation, mechanical properties of the prosthesis, its size and orientation as well as on the place of sample volume and location of the transducer. Because of the influence of these factors, a wide range of Doppler calculated effective valve areas for each type and size of mitral prostheses has been reported (2,4,7,8,9).

In comparison with other mitral valves included in our study, Starr-Edwards prostheses had significantly higher Vmax and PG ($p < 0.001$), probably caused by a peripheral flow pattern in Starr-Edwards valves during occlusion of the prostheses. Similar findings were reported by Williams and Labovitz, 1985 (7).

Comparing Starr-Edwards and Bjork-Shiley valves implanted more than 10 years ago (15.5 ± 2.1 and 12.5 ± 2.1 respectively) with those implanted less than 10 years ago, significant reduction of EVA and PI in both types of prostheses were found ($p<0.01$), although patients had no clinical signs of valve dysfunction. The most probable cause of reduced EVA regarding the time elapsed from valve implantation is tissue overgrowth. None of Starr-Edwards or Bjork-Shiley prostheses implanted less than 10 years ago had PI less than 0.60, while in 4 patients with prostheses for more than 10 years PI ranged from 0.52-0.55. This finding suggests that PI is reduced before clinical signs of prosthetic valve

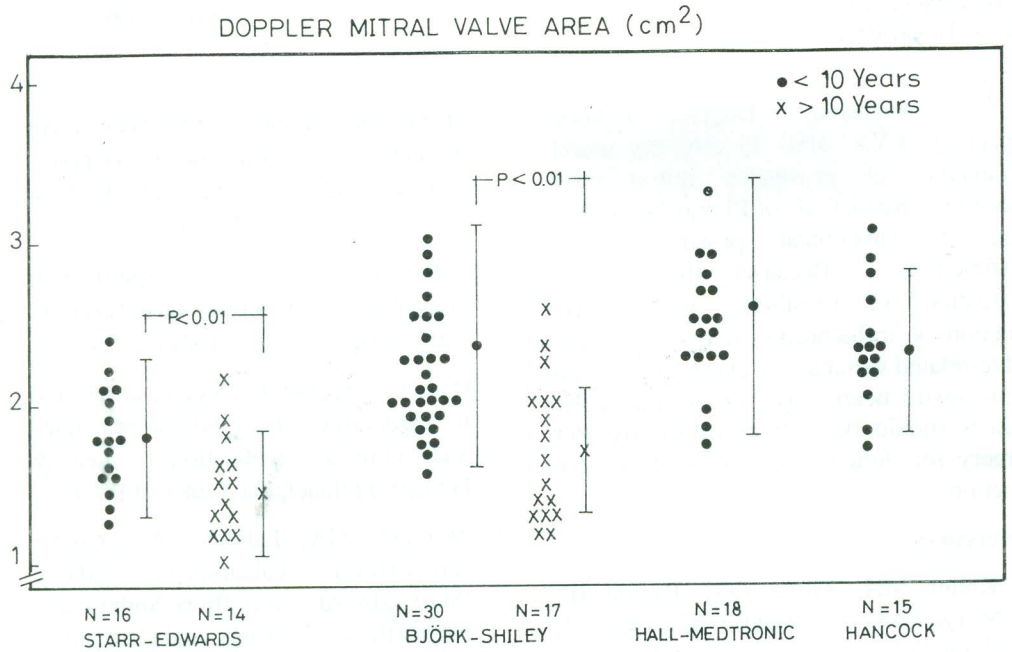

Fig.2: EVA ranged widely for each type of normally functioning mitral prostheses.

dysfunction occur. Patients with reduced PI must be carefully followed-up and if any sign or symptom of heart failure develops they must be considered as candidates for surgery. Significant changes of Doppler indices regarding the time elapsed from valve implantation were also observed by Gibbs,1987 (5)

Hall-Medtronic and Hancock mitral prostheses compared with Starr-Edwards, had significantly larger EVA ($p<0.01$ and $p<0.01$, respectively), as well as Hall-Medtronic vs. Bjork-Shiley mitral prostheses ($p<0.05$). We found no significant difference between tilting disc mitral valves and Hancock bioprostheses. Hall-Medtronic prostheses showed a better performance, this may be a direct consequence of its design that enables unimpeded transvalvular flow on both sides of the open disc (7).

In our study mild MR was found in 35% of normally functioning Bjork-Shiley valves and 30% of Hall-Medtronic valves. As tilting disc prostheses have been designed with a minor degree of regurgitation (2-7% of the stroke volume) to permit washout around the disc, this mild regurgitation was considered trans-valvular and inherited (2, 10). In 20% of Hancock bioprostheses mild regurgitant jets were found. It probably caused by incipient leaflet degeneration and does not mean valve dysfunction. Although Starr-Edwards valves have no static regurgitation, mild regurgitant jets were found in about 25% of the patients and we speculate that it is probably caused by valve orientation or by pannus formation.

In conclusion, Doppler indices, especially EVA and PI are very useful parameters of prosthetic mitral valve function. Reduction of PI may be the first sign of subclinical prosthetic valve dysfunction. Because the Doppler evaluation of prosthetic mitral valve function is influenced by many patient and valve-related variables, in every patient with a prosthetic heart valve the basal Doppler indices should be determined shortly after surgery for longitudinal follow-up of valve function.

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Right Ventricular Function Before and After Closed Mitral Valvotomy "Surgical & Echocardiographic Study "

Abstract

We studied 82 patients who had mitral stenosis and referred to closed mitral valvotomy beacuse of disabling cardiac symptoms in cardiothorcic surgery department Tanta university. Their ages ranged from 16 to 32 years, twenty eight patients were males and 54 patients were females. We classified our patients twice, according to post operative pulmonary artery pressure and according to post operative clinical improvement. We found that mitral valve area before commissurotoy was 0.87 ± 0.2 cm^2 and became 2.1 ± 0.5 cm2 post operatively which is considered to be statistically significant as P < (0.05). The more the increase in mitral area the more is the improvement in post operative right ventricular EF % (RV-EF%) as in patients in whom mitral valve area increased less than 0.5 cm^2 had pre & post operative RV EF% 36.5± 7.2 and 36.8 ± 8.1 which is statistically insignificant, while in patients with mitral valve area increased more that 1 cm^2 have pre & post operative Rv-EF% 42.1 ± 8.4 of 48.4 ± 9.9% which is statistically significant .

Mean RV.EF% preoperatively in the whole group was 43.3 ± 8.7 and became post operatively 48.4 ± 6.2% which again statistically significant .

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INTRODUCTION

Pulmonary hypertension causes an afterload systolic pressure exceeding 70 mmHg represents a serious impedence to emptying of the right ventricle and when this level is exceeded in patients with rheumatic heart disease right ventricular end diastolic and right atrial pressure often rises (1).

Increase in pulmonary artery pressure results in hypertrophy and dilatation of the right ventricle with decrease in right ventricular ejection fraction (2).

The thin walled right ventricle usually works against a low afterload and is not suited to handle increased afterload (3) .

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Accordingly, it has been suggested that right ventricular function is primarily afterload dependant and several clinical studies reported a strong inverse correlations between right ventricular ejection fraction and pulmonary artery pressure (4).

Patients and Methods

The studied population consisted of 82 patients who had mitral stenosis and referred to surgery because of disabling cardiac symptoms. Their ages ranged from 16 to 42 years (mean age was 26.7 ± 4.2 years). Twenty eight patients were males and 54 patients were females.

Inclusion criteria :

1) Symptomatic mitral stenosis inspite of adequate medical treatment and operated upon by closed mitral valvotomy .

2) Having pulmonary hypertension as diagnosed by echo-Doppler examination .

Exclusion criteria :

1) Patients with calcific mitral stenosis as diagnosed by echocardiography requiring mitral valve replacement .

2) Patients with atrial fibrillation, history of embolization or left atrial thrombus requiring open mitral commissurotomy .

3) Patients in whom adequate echocardiographic data could not be obtained .

All patients were subjected to the following :

(1) preoperative and 4 weeks post operative studies :

1- Thorough history and clinical examination .

2- Electrocardiography for signs of right sided hypertrophy .

3- M-mode, two-Dimensional and Doppler echocardiography to detect :-

a) Mitral valve area (M.V.A).

b) Pulmonary artery pressure .

c) Rt. ventricular ejection fraction .

d) Tricuspid incompetence .

{II} Operative studies

* Left anterolateral thoracotomy was used in the Lt. 5th intercostal space .

* Assessement of the mitral valve as regards;

- Its size by surgeon's finger.

- Condition of cusps whether healthy, mildly fibrotic or heavily fibrotic .

- Presence or abscence of calcification .

- Presence or abscence of pre valvotomy regurgitation .

* Valvotomy was done either by :-

a- Finger dilatation .

b- Trans ventricular using Tubb's dilator.

* Assessement post valvotomy as regards; mitral valve orifice, presence of post valvotomy incompetence.

The operative results of valvotomy was assessed by surgeon's finger and classified according to Brock 1952 into .-

Excellent : If the valve orifice is fully opened or both commissures fully splitted.

Good : If one commissure full opened and the other to the point of critical tendon insertion OR both divided to behind the point of critical tendon Insertion.

Fair results : If only one commissure opened.

Poor results : If neither commissure spotted to behind the point of critical tendon insertion.

Assessement of Rt Ventricular Ejection fraction

Patients were examined in the left lateral decubitus. An apical 4 chambre view was obtained with the transducer positioned at the point of maximal cardiac apical impulse and angled toward the right shoulder .

While recording the apical 4 chamber view care was taken to obtain the maximal right ventricular size. Both end systolic and end diastolic frames were taken at end-expiration with the position of the transducer not changed.

Simpson's rule was used to determine the volumes of the resulting end systolic and end diastolic frames, utilizing computer system by which the right ventricular body was divided into a number of slices one or two millimeters in thiclness.

The volumes of these slices were estimated and summated. Volumes of three beats were measured and averaged for each patient. Righ ventricular ejection fraction RV-EF% was determined using this formula

$$RV\ EF\% = \frac{EDV\text{-}ESV \times 100}{DV}$$

Where EDV = end diastolic volume, ESV = end systolic volume(5)

Results

We classified our Patients twice :

1) First classfication according to post operative pulmonary artery pressure, into 2 groups.

Group I : including those patients who had systolic pulmonary artery pressure < 70, fifty patients were present in this group.

Group II : including those patients who had systolic PAP > 70 and 32 patients were present in this group.

2) Second classification according to post operative clinical imporvement, into 2 groups.

Group III : including those patients who improved at least 2 functional classes post operatively, sixty patients were present In this group.

Group IV : including those patients who didn't improve 2 functional classes post operatively, 22 patients were present in this group.

[I] As. regard right ventricular election fraction (RVEF%):

The preoperative RV-EF% of the whole patients was 43.3 ± 8.7% (32-56%).

In group I : mean RV-EF% was 45.6±6.2% (42-56%).

In group II : mean RV-EF% was 39.2±5.1% (32-54%).

The post operative RV-EF% of the whole patients was 48.4±6.2% (43-58%).

In group I: Mean RV-EF% was 49.7±9.2% (44-58%).

In group II : Mean RV-EF% was 45.1 ± 7.1% (34-56%).

There is statistically significant improvement in mean RVEF% in overall patients and in each group post operatively as $p<0.05$.

[II] As regard estimated PAPs :

Overall patients showed mean of 67.4 ± 20.2 preoperatively and 44.5 ± 18.2 post operatively with P value < 0.05 i.e statistically significant Improvement in P.A.Ps post operatively.

In group I : Mean PAPs preoperatively is 51.8 ± 13.3 and post operatively 37 ± 10. 1. P value < 0.05 .

In group II : Mean PAPs preoperatively is 84.4 ± 16.2 and post operatively 56.6 ± 20. 1. P value < 0.05.

Table 1: Effect of change in mitral valve area on right ventricular ejection fraction.

Preop. RVEF% Mean ± SD	Post op. RVEF% Mean ± SD	Difference	P value
M.V.A increased < 0.5cm2 (n=5 patients)			
36.5 ± 7.2	37.8 ± 8.1	1.03	> 0.05
M.V.A increased 0.5 - 1 cm2 (n=20 patients)			
41.6 ± 7.8	47.8 ± 6.2	6.2	< 0.05
M.V.A increased >1 cm2 (n=57 patients)			
42.1 ± 8.4	48.4 ± 9.9	6.3	< 0.05

< 0.05 = Statistically significant difference.
> 0.05 = Statistically non significant difference.

Table 2: Effect of change of M.V.A on P.A.P

Preop. P.A.P Mean ± SD	Post op. P.A.P Mean ± SD	Difference	% change	P value
M.V.A increased < 0.5cm2 (n=5 patients)				
50.5 ± 19.1	47.9 ± 21.3	2.6	5.1%	> 0.05
M.V.A increased 0.5 - 1 cm2 (n=20 patients)				
43.5 ± 8.9	32.9 ± 13	10.6	24.3%	< 0.05
M.V.A increased >1 cm2 (n=57 patients)				
48.8 ± 9.1	30.1 ± 6.2	18.7	38.3%	< 0.05

Table 3: Operative evaluation of mitral valve.

Grade	No. of patients	%
Excellent & good	52	63.4
Fair	23	28
Poor	7	8.5

* **All the 7 patients with poor operative results had increase post operative M.V.A. by echocardiography < 0.5 cm2.**

Table 4: Distribution of functional class before and after closed commissuratomy.

Functional class	Preoperative		post operative	
		%		%
0	-	0	24	29.2
I	-	0	38	65.5
II	4	2.4	11	18.9
III	40	48.7	5	8.6
IV	38	46.3	4	6.8

{III} <u>As regard mitral valve area M.V.A:</u>

Mean M.V.A, estimated by pressure half time method, before commisurotomy was 0.87 ± 0.2cm2 (range : 0.6 - 1.lcm2).

Post operatively mean M.V.A showed increase to 2.1±0.5 cm2 (range 1- 2.9 cm^2) the difference from the preoperative value was statistically significant (P<0.05)

As regard the changes In mean M.V.A within each of the two groups there was also significant increase in M.V.A.

In group I mean M.V.A was 0.88 ± 0.12 cm^2 before operation and become 2 ± 0.32 cm2 post operatively.

In group II : mean M.V.A was 0.86 ± 0.34 cm2 before operation and become 2.2 ± 0.41 cm2 post operatively .

Table 5: The comparison between the clinically improved group and the clinically not improved group.

	Clinically improved group III	Clinically not improved group IV	P value
Mean RV EF	50.2 ± 7.8	43.1 ± 6.2	< 0.05
Mean PAP	41 ± 9.8	54 ± 16.1	< 0.05
Mean M.V.A	2.4 ± 0.6 cm^2	1.8 ± 0.4cm^2	< 0.05

There is statistical significant difference between group III and IV as regard RVEF, P.A.P. M.V.A as p vlue <0.05 in each item.

* All the 7 patients with poor operative results had increase post operative M.V.A by echocardiography < 0.5 cm^2.

* Twenty patients out of 23 who had fair operative results had increase post operative M.V.A by echocardiography > 0.5 cm-1 cm2 & 3 patients had M.V.A > 1 cm2 .

* All patients who had excellent or good operative results had increase post operative M.V.A > 1 cm2 by echocardiography .

There is statistical significant difference between group III and IV as regard RVEF, P.A.P. M.V.A. as p value < 0.05 in each item .

Discussion

In the present study the preoperative RVEF% was 43.3 ± 8.7% and became post operatively 48.4±6.2%. There is statistical significant improvement in mean RVEF% in overall patients. It can be noticed that.the depressed preoperative right ventricular ejection fraction in many patients is a reversible process provided that the pulmonary artery pressure regress significantly after surgery,this is applicable in our study as the preoperative value of PAP was 67.4±20.2 and became 44.5±18.2 postoperatively. On the other hand It was found that the more the mitral valve area increased the more is the improvement In the P.A.P & RTVEF%. In patients with mitral valve area increased less than < 0.5cm2 there is no significant difference between pre & post operative Rt VEF% & P.A.P while in patients with mitral valve area Increased more than 0.5cm2 there is significant difference between the pre&post. RVEF% & P.A.P.

So the extent of valvotomy is an important factor In the outcome of operation and the patient performance after the operation, as there is statistical significant difference between group 3 & 4 in our study as regard mitral valve area,

mean PAP, mean RVEF, so the more the increase in MVA post operatively the more is the clinical performance, the decrease in mean PAP and the decrease in RVEF %.

Dicola et al (6) studied right ventricular ejection fraction in 14 patients with isolated mitral stenosis before and after corrective surgery, they found that right ventricular ejection fraction was depressed preoperatively in relation to the severity of mitral stenosis and it improved substantially after surgery from (35±8% to 45±9%).

Iskandrian et al (7) studied the right ventricular ejection fraction In patients with mitral valve disease and pulmonary hypertension before and 3 months after operation, they found that before surgery, ejection fraction was <50% in 88% of patients, after surgery ejection fraction was normalized in 19% of patients.

The determinants of right ventricular function in mitral valve disease are not well known (7).

Unfortuonately, the complex geometry of the right ventricle and the difficulty of measuring right ventricular wall thickness preclude analysis of systolic wall stress or afterload. One can speculate that afterload is increased in patients with high pulmonary artery pressure, although it is possbile that with severe hypertrophy, afterload could be normal (2).

Werko et al (8) reported the hemodynamic results of closed mitral valvotomy in 39 patients. The average pulmonary artery pressure was reduced from 55 to 43 mmhg within 6 weeks after operation. Our results are coinciding with those of Werko et al, in our study overall patients showed mean of 67.4±20.2 preoperatively of 44.5±18.2 post operatively.

The adequecy of valvotomy affects the decrease in pulmonary artery pressure post operativelly. In our study, the patients who had increase M.V.A less than 0.5 cm^2 had post operative decrease In P.A.P of 2.6mm Hg only, while patients who had increase In M.V.A more than 1cm^2 had post operative decrease In PAP of 18.7mm.Hg.

Werko et al (8) found that lack of post operative decrease in pulmonary pressure in 19 patients was due to inadequate valvotomy. These findings suggest that several mechanisms may contribute to the pulmonary arterial hypertension seen in patients with mitral valve disases.

- First mechanism is passive retrograde flow of elevated left atrial pressure and pulmonary venous pressure Into pulmonary arterial circuit. This mechanism resolves with left atrial decompression which is more with the more Is the opening of the mitral valve (9).

- Second mechanism is the reactive pulmonary vasoconstriction (10). This appears to be active mechanism induced by pulmonary venous hypertension and seems to resolve when pulmonary venous pressure is reduced by left atrial decompressions which again is more with the more in the opening of the mitral valve. These previous two mechanisms are reversible and are dependant on the extent of valvotomy as shown in our result and others.

The third mechanism is the induced morphologic changes in pulmonary vasculature (9) This mechanism results in an irreversible component of increased pulmonary artery pressure.

So the extent of closed mitral valvotomy will positevely infieunce the clinical performance of patients, the post operative

incrase In RTVEF% and the post operative decrease In systolic pulmonary artery pressure.

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Preoperative and Postoperative Nutritional Supplementation for Cardiac Malnourished. Patients Scheduled for Valve Replacement

ABSTRACT

Sixty cardiac patients (40 malnourished with cardiac cachexia and 20 well nourished) with a long history of Rheumatic valvular heart disease underwent open heart surgery for valvular replacement, were studied to determine the impact of a high- caloric liquid supplement before surgery and parenteral nutrition after surgery on preventing or minimizing catabolism and potential complication associated with open heart surgery.The experimental group of 20 malnourished patients with cardiac cachexia consumed blenderized food and a high-caloric dietary supplement providing 1500 Kcal/day. 15 days before surgery and parenteral nutrition in the form of dextrose and amino acids according to energy need using Harris-Benedict equation for one week after surgery (group II). The remaining 20 malnourished patients (group I) and well nourished patients (group III) consumed only blenderized foods before surgery and 2-3 days after surgery and served as control groups. The nutritional status of all patients was assessed 15 days, one day before surgery and one week after surgery. The results demonstrated that there were significant Improvement in anthropometric parameters and serum chemistry in group II as compared to group I, one day before surgery and one week after surgery. Also patients in group I required prolonged ventilatory support, regained ambulatory status later and had more postoperative complications than patients in group II and group III. The overall mortality in patients in group I was high than patients in group II and no mortality in group III. It was concluded that enteral nutritional supplementation 15 days before surgery and postoperative parenteral nutrition for one week improve the nutritional status of the malnourished cardiac patients underwent open heart surgery and decrease the incidence of potential complications and mortality.

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INTRODUCTION

Chronic protein-energy starvation has been frequently overlooked in patients with heart disease, since it was considered to be a protected organ during starvation (l) .

Cardiac cachexia is a common manifestation of chronic, severe rheumatic heart disease, especially when it involves the mitral valve. In a nutritional survey of 350 hospitalized patients, 50 patients with a primary cardiac diagnosis were-significantly malnourished. The incidence of malnutrition was higher than in those suffering from any other disease (2) The effects of malnutrition on cardiac performance were disregarded for many years, perhaps as a result of starling's statement that the heart and other vital Organs were not affected by starvation. Nevertheless, it was demonstrated that malnutrition has an adverse effect on cardiac performance. Semi-starvation produced a 17 percent decrease in heart volume and was associated with bradycardia, hypotension, reduced cardiac output, decreased heart work and decreased heart reserve (3).

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Cardiac cachexia is the term applied to the severe malnutrition that may accompany chronic congestive heart failure and that usually occur in New York Heart association (NYHA)) class Ill or IV individual. Hippocrates described such a patient:

"The flesh is consumed and become water, the abdomen fills with water, the feet and legs swell, the shoulders, clavicle,' chest and thighs "Melt away" (4) .

Anorexia is common in patients with congestive heart failure. It is associated with an inadequate diet that is deficient particularly, in calories, protein, thiamine and other vitamins. It contributes to the development of malnutrition, abdominal distress due to gastrointestinal hypomotility, which is possibly related to bowel wall edema; continuous dyspnea and iatrogenic factors contribute to the anorexic state (5) .

Two important mechanisms that are recognized as causes of cardiac cachexia, anorexia and malabsorption, would also be potentiated by tissue hypoxia and the characteristic "air hunger" of CHF. Pittman and Cohen have ascribed to anorexia a compensatory role in CHF. It prevents the increase of both total body oxygen consumption and splanchnic blood flow, which are associated with ingestion of a large meal (6) .

Despite many advances in medical therapeutics during the last half century heart disease remains the leadin cause of mortality and major morbidity (7) .

Aim of the Work

The aim of this study was to evaluate the preoperative and postoperative nutritional supplementation on preventing or minimizing catabolism and potential complications commonly associated with open heart surgery in patients with cardiac cachexia

Patients and Methods

Sixty cardiac patients [18 male (30%), 42 female (70%)] Aged 18 to 26 years (mean age 22 years) underwent open heart surgery for valve replacement at cardiothoracic surgery department, Tanta University Hospital. All patients underwent a history, physical examination, and routine laboratory studies.

The malnourished patients were selected according to the following inclusion 'criteria

I- Clinical history of recent weight loss exceeding 10% of the usual weight or an absolute weight of less than 15% below ideal body weight.

2- serum albumin of less than 3 g/dL.

Nutritional and metabolic profile were done for all patients after the medical regimen has reduced or eliminated edematous fluid accumulation.

Patients were divided into three equal groups each included 20 patients.

- Group I: included 20 cardiac malnourished patients not taken nutritional supplementation -

- Group II : Included 20 cardiac malnourished patients taken nutritional supplementation.

- Group III : Included 20 cardiac non-malnourished patients as a control group.

Table 1: Patients clinical data

	Age (yr)	Sex		Height (cm)	Weight (kg)	Type of surgery		
	M± SD	M	F	M± SD	M± SD	MVR	AVR	DVR
Group I	21.8±2.44	6	14	166.6±5.4	50.6±5.79	2	4	14
Group II	21.4±1.8	4	16	169.7±5.55	48.56±3.67	2	3	15
Group III	21.9±2.5	8	12	176.1±6.31	68.1±5.77	13	4	3

MVR: Mitral valve replacement
AVR: Aortic valve replcacement
DVR: Double valve replacement

For all patients the anthropometric parameters and serum chemistry were assessed before starting the nutritional supplementation two weeks preoperative (0 time), 1 day preoperative and one week postoperative.

*Anthropometric parameters.

- Height (cm)

- Weight (Kg).

-Arm Muscle circumference (AMC) (cm).

-Triceps skin fold (TSF)(mm).

*Serum chemistry.

- Albumin (g/dL).

-Transferrin (mg/dL).

-Total lymphocytic count (cell /MM3).

Anthropometric measurement were performed as described by Blackburn (2) Blood samples were obtained by a standard venipuncture technique.

* The following formulae were used in the study .

-To calculate how actual weight is related :

% reference body weight =

$$\frac{\text{actual weight}}{\text{reference body weight}} \times 100$$

- To calculate weight change

% Weight change =

$$\frac{\text{usual weight - actual weight}}{\text{usual weight}} \times 100$$

- Arm Muscle circumference (cm).

= 0.314 X triceps skin fold (mm)

-Total lymphocytic count (cell / mm3)

$$= \frac{\% \text{ lymphocyte X lecukocytes}}{100}$$

Predicted energy needs according to (Harris-Benedict equation).

For men =

66 + (13.7 x weight in kg) + (5 X height in cm) - (6.8 X age).

Table (2): Comparison of body weight (% of ideal), weight loss (% of usual) and somatic protein and fat compartment (M±SD).

	Group I	Group II	Group II
Body weight (% of ideal)			
0 time	70.32±5.43	71.51±5.97	93.95±5.82*
1 day pre-op.	68.75±5.82	75.45±4.37#	93.32±4.08*
1 week post-op.	65.64±6.16	78.73±6.01#	92.81±5.79*
Weight loss (% of usual)			
0 time	20.40±6.16	20.52±6.47	8.66±4.59*
1 day pre-op.	22.69±5.54	14.98±5.59#	9.81±4.74
1 week post-op.	23.83±5.4	10.78±4.79#	9.49±5.41
Triceps skin fold (mm)			
0 time	8.9±2.26	8.85±2.42	13.6±3.87*
1 day pre-op.	8.11±2.1	9.21±2.32	13.35±3.79*
1 week post-op.	8.01±2.1	9.25±2.38	13.2±3.85*
Arm muscle circumference (cm)			
0 time	2.79±0.65	2.78±1.05	4.27±0.96*
1 day pre-op.	2.54±0.73	3.20±0.82#	4.19±1.05*
1 week post-op.	2.46±0.49	3.28±0.89#	4.14±0.85*

*** Significant when group III compared to both group I and II (P < 0.05).**

 # Significant when group II compared to group I (P < 0.05).

For women =

65.- +(9.6 X weight in kg)+ (1.8 X height in cm) -(4.7 X age).

Feeding program

The feeding program for malnourished patients in group II started after early admission 15 days before surgery, we allowed the patients to eat the oral diet and we provided supplemental nutrients by means of fixed enteral solution. The nutrient solution was used is the fixed composition enteral formula, which is high in caloric density (1.5 Kcal/mL). In addition to a low water content,the high-caloric density formula has a relatively low sodium concentration and is complete with respect to all the essential nutrients. It has a moderate osmolality(400-650 mosm /kg). The patients were allowed to take 1000 mL/24 h. (1500 Kcal/24h.). The solution could be sipped or administered by nasogastric tube if anorexia prevented the patients to reach a hyperalimentation dose.

We used enteral feeding catheter (Flexi flow catheter) and an infusion feeding pump. The infusion period was 24 hours After completion of the cardiac procedure and the patients were stablized in the intensive care unit, the predicted energy needed which estimated according to Harris-Benedict equation was given as parentral solution via central line in the subclavian vein.

The solutions used were 50% dextrose in water and aminosterile 10%.

Nutritional goals

Protein: 1.5 g/kg /day

Calories: according to Harris-Benedict equation

Volume: up to 30 ml /Kg/day.

Sodium: as needed but not more than40 meq /day initially.

Potassium: as needed to *keep K+* > 3.5 meq/L and < 5.5 meq/L. Calcium , *we started with* 10 meq.

Magnesium: we started with 10 meq. **Chloride :** 60 meq /day.

Multivitamins : 10 mL

The volume restricted for nutritional support after surgery in the ICU as follow:

1000 mL on day 1

1250 mL on day 4

1500 ml on day 7

--The remaining 20 malnourished patients in group I and the well nourished patients in group III allowed to consume only blenderized food preoperatively and 2-3 days after surgery. while they received normal maintenance fluids immediately postoperatively for 2-3 days.

Statistical analysis of the data was done by using student (t) test. t values were compared with their tabulated probability values of 0.05 level of significance.

Results

Table (1)

Clinical data

Patients in group I had an age ranged between 18 to 26 years with a mean value of 21.8±2.44 years, their weight ranged between44.5 - 58 kg with a mean value of 50.6±5.79 kg and their height ranged between 160-175 cm with a mean value of 166±.6 5.4 cm. Two patients underwent mitral valve replacement (MVR), 4 aortic valve replacement (AVR) and 14 had double valve replacement (DVR).

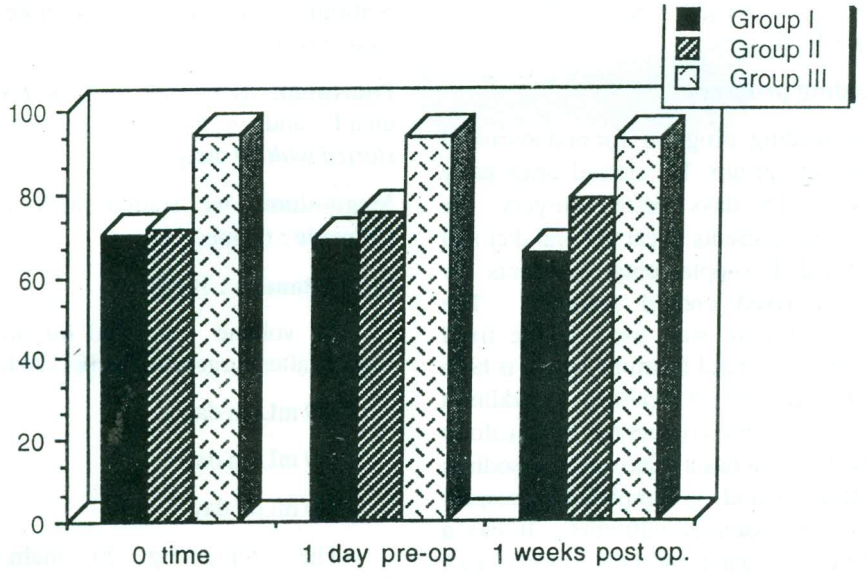

Fig. (1a) : Body weight (%of ideal)

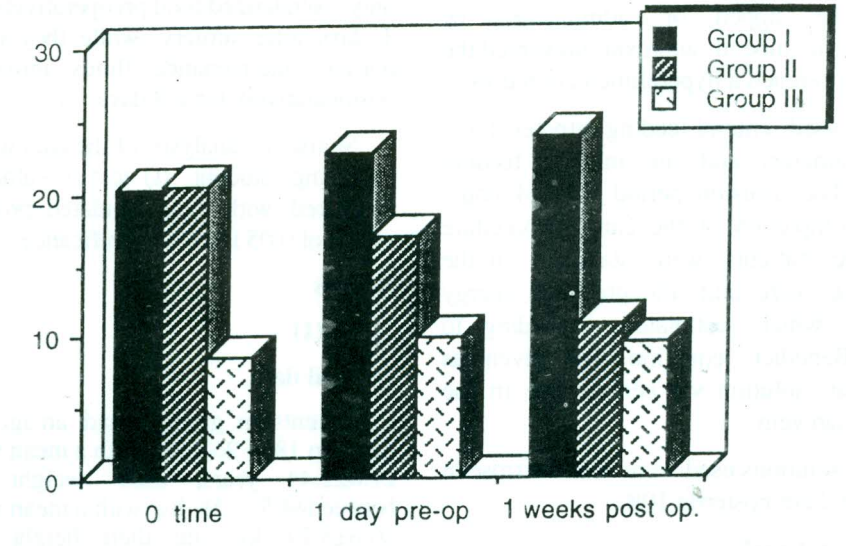

Fig. (1b) : Weight loss (% usual)

Fig.1: Comparison of body weight (% of ideal) weight loss (% of usual) and somatic protein and fat compartment (M±SD).

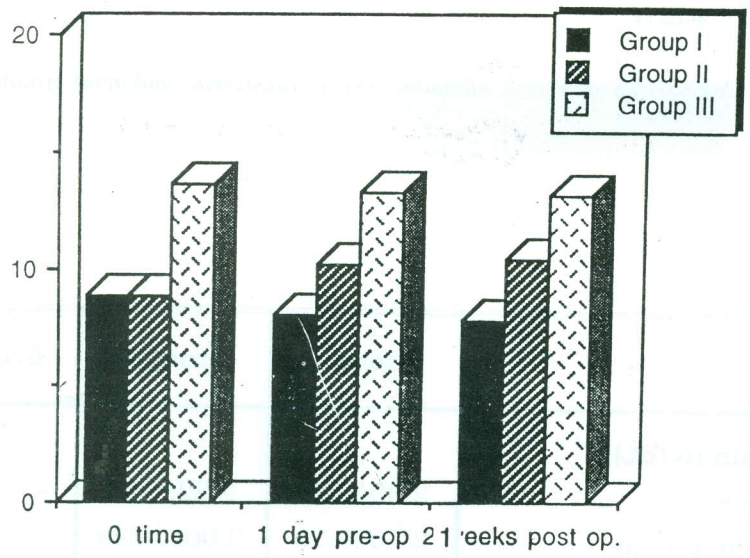

Fig.(1c) : Triceps skin fold (mm)

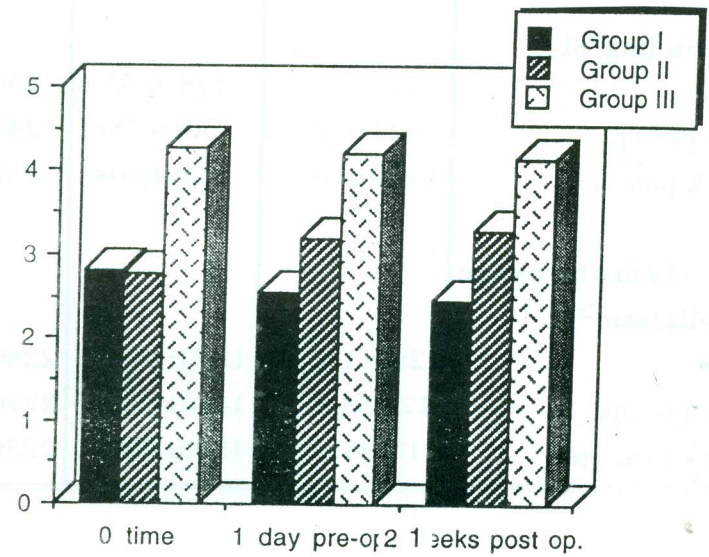

Fig. (1d) : Arm muscle cricumference (cm)

Fig.1: Comparison of body weight (% of ideal) weight loss (% of usual) and somatic protein and fat compartment (M±SD).

Table (3): Comparison of serum albumin, serum transferrin, and total lymphocytic count (M±SD).

	Group I	Group II	Group III
Albumin (G/dL)			
0 time	2.30±0.38	2.22±0.41	4.31±0.32*
1 day pre-op.	2.10±0.36	3.00±0.34#	4.25±0.25*
1 week post-op.	1.90±0.34	3.29±0.40#	4.05±0.32
Transferrin (mg/dL)			
0 time	130±7.50	128±6.95	250±6.96*
1 day pre-op.	124±6.20	150±5.75#	245±5.40*
1 week post-op.	120±6.45	165±4.60#	230±6.71*
Total lymphocytic count(cells/mm^3)			
0 time	1250±123.38	1240±203.46	2280±472.86*
1 day pre-op.	1200±69.04	1450±180.90#	2210±175.78*
1 week post-op.	1100±120.00	1500±206.70#	2230±392.55*

*** Significant when group III compared to both group I and II (P < 0.05).**

 # Significant when group II compared to group I (P < 0.05).

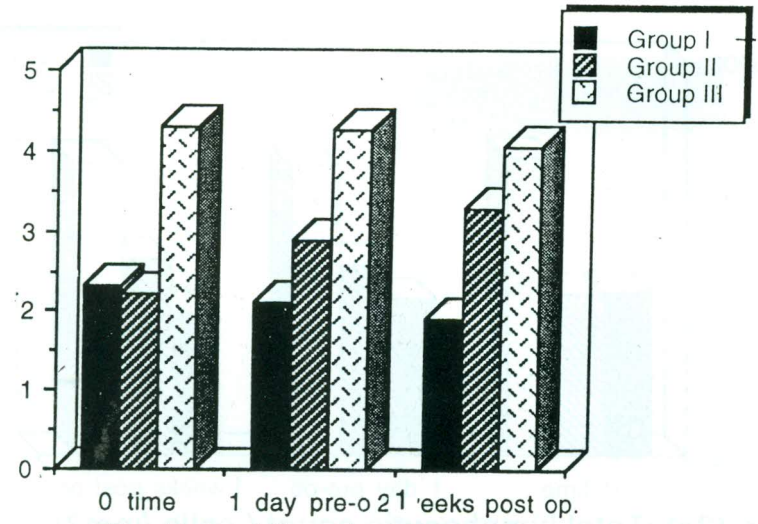

Fig. (2a) : Albumin (g/dL).

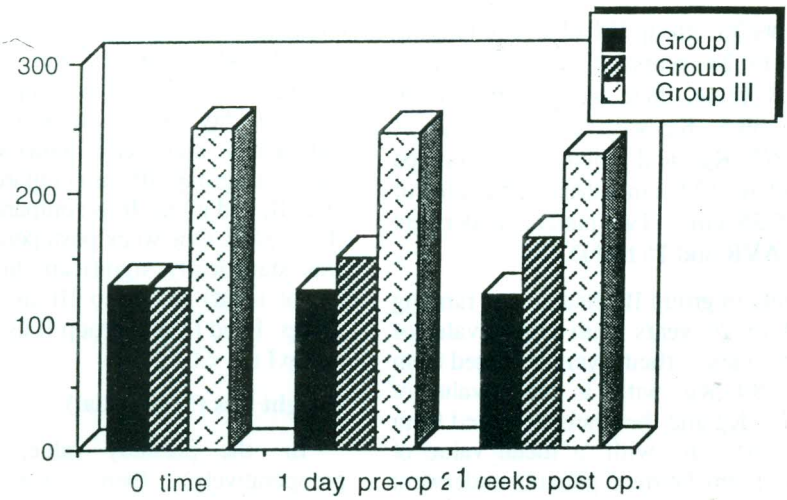

Fig. (2b): Transferrin (mg/dL).

Fig.2: Comparison of serum albumin serum transferrin and total lymphocytic count (M±SD)

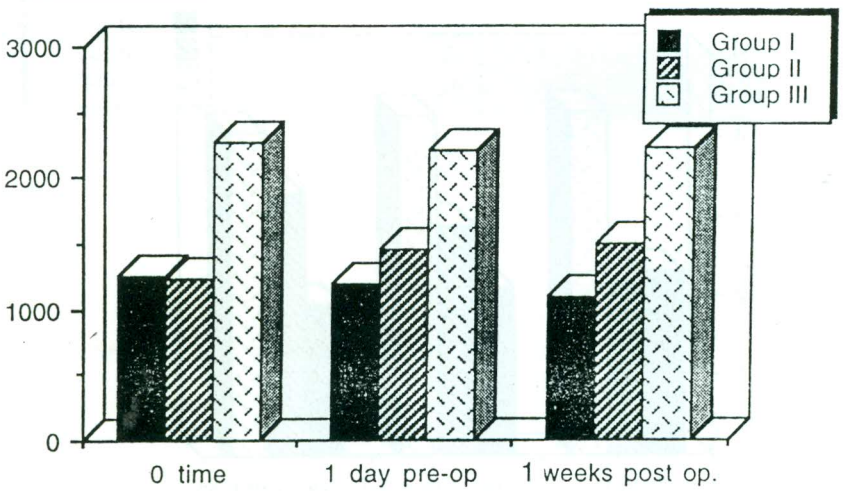

Fig. (2c) :Total lymphocytic count (cells /mm2).

Fig.2: Comparison of serum albumin serum transferrin and total lymphocytic count (M±SD)

Patients in group II had an age ranging from 18 to 24 years with a mean value. of 21.4 ±1.8 years, their weight ranged from 44.5 to 56.5 Kg with a mean value of 48.56±3.67 Kg and their height ranged from 160 to 177 cm with a mean value of 169.7 ±5.55 cm. Two patients underwent MVR, 3 AVR and 15 had DVR.

Patients in group III had an age ranging from 18 to 26 years with a mean value of 21.9±2.5 years , their weight ranged from 61.5 to 80 Kg with a mean value of 68.1±5.77 Kg and their height ranged from 167 to 185 cm with a mean value of 176.1±6.31 cm.Thirteen patients underwent MVR, 4 AVR and 3 had DVR.

Table (2) & Fig. (1)

Weight (% of ideal).

Two weeks preoperatively (0 time), there was statistically significant higher weight (% of ideal) in group III as compared to group I and group II ($P<0.05$),while there was insignificant difference in group II as compared to group I. One day before surgery, there was statistically significant higher weight (% of ideal) in group III as compared to group I and II, and group II as compared to group I ($P < 0.05$). One week postoperatively, there was statistically significant higher weight (% of ideal) in group III as compared to group I and II, and group II as compared to group I ($P < 0.05$).

Weight loss (% of usual).

In the prestudy value, (two weeks preoperatively) there was statistically significant lower weight loss (% of usual) in group III as compared to group I and II ($P < 0.05$), while there was insignificant difference when group II is comared to group I.

One day preoperatively, there was statistically significant lower weight loss

(% of usual) in group II and group III as compared to group I (P < 0.05), while there was insignificant difference in group III as compared to group II. One week postoperatively there was statistically significant lower weight loss (% of usual) in group II and group III as compared to group (P <0.05), while there was insiginificant difference in group III as compared to group II.

Table (4): Postoperative Complications

Complications	Group I	Group II	Group III
Acute renal failure	4	2	1
Pneumonia	2	1	0
Mediastinitis	3	1	0
Wound infection & delayed healing	4	1	0
Respiratory failure requiring tracheostomy	1	0	0
Intraoperative mortality	3	1	0

Triceps skin fold (TSF)

In the prestudy value, one day preoperatively and one week postoperatively, there was statistically significant increase in TSF in group III as compared to group I and II (P < 0.05), while there was insignificnt difference in group II as compared to group I.

Arm muscle eircumference (AMC).

In the prestudy value, one day before surgery and one week postoperatively, there was significant increase in AMC in group III. as compared to group I and group II ($P < 0.05$). While, there was insignificant difference in group II as compared to group I in the prestudy value, there was statistically significant increase in AMC one day preoperatively and one week postoperatively ($P < 0.05$).

Table (3) and Fig. (2)

Serum chemistry

In the prestudy value and one day before surgery, there were significant higher serum albumin and transferrin concentration in group III as compared to group 1 and group II ($P < 0.05$). While there was insignificant difference in group II as compared to group I in the prestudy value, there was significant increase in group II as compared to group I one day before surgery ($P < 0.05$). One week postoperatively, there was statistically significant higher serum albumin and transferrin concentration in group II and III as compared to group 1 ($P<0.05$) and there was no significance in group III as compared to group II.

Total lymphocytic count (TLC).

In the prestudy value and one day before surgery, there were significant increase in TLC in group Ill as compared to group I and II ($P<0.05$) and also there was significant increase in group II as compared to group I one day before surgery ($P < 0.05$). One week postoperatively, there was significant increase in group Ill as compared to group I and II ($P < 0.05$) and also there was significant increase in group II as compared to group I ($P<0.05$).

Table (4)

Postoperative complications

Postoperative complications, acute renal failure occured in 4 patients (20%) in group I, 2 patients(10%) in group II and 1 patients (5%) in group III. Pneumonia occured in 2 patients (10%) in group I and 1 patient (5%) in group Il. Mediastinitis occured in 3 patients (15%) in group I and 1 patient (5%) in group II. Wound infection and delayed healing occured in 4 patients (20%) in, group I and 1 patients (5%) in group II Respiratory failure requiring tracheostomy occured in 1 patients (5%) in group I. Intraoperative mortality occured in 3 patients (15%) in group I and 1 patient (5%) in group II while there was no mortality in group III.

Discussion

The term cardiac cachexia is used to describe the wasting that is seen in patients with heart failure secondary to valvular heart disease, coronary heart disease or cardiomyopathy. The cause of cachexia is thought to be multifactorial, decreased dietary intake and decreased cardiac output can lead to wasting of lean body mass and body fat stores. First these patients have limited reserve and their volume is critical to their metabolic management. Second, the hypermetabolism seen during acute injury may put an additional burden on the patients' stressed heart.

Our results demonstrated that there was statistically significant increase in weight (% of ideal) in group II one day before operation and one week postoperatively as compared to the prestudy value. Also our results show statistically significant

decrease in weight (% of ideal) in group I one day preoperatively and one week postoperatively as compared to the, prestudy value. In addition, our results show statistically, significant increase in body weight (% of ideal) in group II as compared to group I one day preoperatively and one week postoperatively. Also, there was statistically significant decrease in weight loss (% of usual) in group II and significant increase in group I one day preoperatively and one week postoperatively as compared to the prestudy values in both groups. In addition, there was statistically significant weight loss (% of usual) one day preoperatively and one week postoperatively in group I as compared to group II This indicates an improvement in the nutritional state in the malnourished group after hyperalimentation for two weeks preoperatively and one week postoperatively. Our results are in agreement with the results of Fischer et al (8) on the other hand, our results in contrary to the results of Abel et al., (9) who stated that postoperative hyperalimentation was ineffective in reversing the situation in malnourished cardiac patients. The difference in the results between our results and the results of Abel et al., may be due to, in Abel et. al study. They only use 5 days of postoperative hyperalimentation while in our study we use hyperalimentation for two weeks preoperatively and one week postoperatively, which gives us clinical significant changes in body weight and, this is in agreement with the results of Gibbon et al.(10)

Our results revealed sigificant decrease in triceps skin fold (TSF) in group I, one day preoperatively and one week postoperatively as compared to the prestudy value, while there was statistically significant increase in T'SF in group II one day preoperatively and one week postoperatively when compared to the prestudy value.

As regard to the arm muscle circumference (AMC) which is the best available measurement of protein calories malnuitrition there was statistically significant decrease in AMC in group I, one day preoperatively and one week postoperatively when compared with the prestudy value, also there was statistically significant increase in AMC in group II one day preoperatively and one week postoperatively. In addition there was significant increase in AMC in group II as compared to group I one day preoperatively and one week postoperatively. Our results are in agreement with those obtained by Fischer et al., (8) and Black burn et al., (2), while on the other hand our results differs from those cobtained by Abel et al.,(9) and Bristrian et al. (11)

Our results show that there were statistically siginficant decrease in serum albumin, and transferrin concentrations in group I one day preoperatively and one week postoperatively when compared to the prestudy Value. There were statistically significant increase in serum albumin and serum transferrin concentrations in group II one day preoperatively and one week postoperatively when compared with the prestudy value and when compared with the group I Our results are in agreement with the results of Fischer et al., (8) and Blackburn et al., (2). Our. results demonstrated that there was statisically significant, decrease in total lymphocytic count (TLC) in group I one day preoperatively and one week postoperatively when compared with the prestudy value, while there was significant increase in TLC in group II one day preoperatively and one week postoperatively when compared to

prestudy value and to group I and this indicate improvement in the immune state in malnourished patients after hyperalimentation, our results are in agreement with Fischer et al (8), Blackburn et al., (2) and Bistrian et al. (11)

Our results showed that malnourished patients in group I required longer ventilator support, regained ambulatory status later and had more postoperative complications than malnourished patients taking hyperalimention support in group II and than well- nourished patients in group Ill. The leading complication were acute renal failure in 4 patients .(20%), Pneumonia in 2 patients (10%), mediastinitis in 3 patients (15%) and respiratory failure requiring tracheostomy in one patient (5%). As a consequence of these complications, the overall mortality in group I was 3 patients (15%) as compared to one patient in group II and no mortality in the control group III, well nourished patients.

From this study we conclude that if the malnourished cardiac patients scheduled for open heart surgery for valve replacement were supplemented by enteral hyperalimentation for two weeks prior to surgery and by parenteral nutrition after surgery for one week, this regimen prepare the patient for stress of surgery and reduce potential complications.

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Influence of Hypothermic Cardiopulmonary Bypass on Hemodynamic Status and Systemic Oxygen Uptake

ABSTRACT

Fourteen patients undergoing hypothermic nonpulsatile cardiopulinonaiy bypass for open heart surgery were studied prospectively.The perfusion flow rate was 50 ml/kg/min and hemodilution was to 7.5 g% hemoglobin at stable hypothermia of 25°C. Arterial and mixed vcnous blood samples were taken simultaneously and analysed for oxygen tension, saturation, content, pH and base excess at prebypass, bypass and postbypass periods. The hemodynamic variables were concomitantly measured. Oxygen delivery, consumption and extraction ratio were calculated. The results showed a significant increase in the cardiac output and cardiac index associated with a decrease in systemic vascular resistance in the postbypass period. At prebypass period, oxygen delivery was 350.9±56 ml/min/m^2, oxygen consumption was 74.6±19.6 ml/min/m^2 and oxygen extraction ratio was 21.2±4. During the bypass period, these variables decreased to 188±19.1 ml/min/m^2, 24.13±4.4 ml/min^2 and 12.82±2.2 respectively. In the postbypass period, they increased to 543.2±106 ml/min/m^2 96±23 ml/min/m^2 and 24.2±5.2 respectively. Thus the immediate postoperative period is a period of stress to the patient as it represents the period of highest risk for decompensation

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INTRODUCI'ION AND AIM OF WORK

Since introduction of cardiopulmonary bypass (CPB) into clinical practice over Four decades ago, it has remained the mainstay technique that has enabled heart valve surgery and coronary artery bypassgrafting to be performed on hundreds of thousands of patients worldwide. Despite the importance of this fundamental and well established technique, there remains disagreement on basic physiologic aspects of its performance.

It is truly that CPB significantly alters bodily homeostasis as does no other type of major surgery. One of the most important physiological aspect concerning CPB is systemic oxygen uptake which is considered an indicator of its efficacy (1,2).

The aim of this study was to evaluate changes in the hemodynamic status and oxygen metabolism of the whole body before and during CPB, and also in the immediate postoperative period in patients undergoing cardiac operations using CPB with systemic hypothermia and hemodilution.

Patient and Methods

This study was performed on 14 patients with a mean age of 21.2±3.3 yr. and a medium weight of 57+0.6 kg undergoing open heart surgery for valvular diseases (3 patients with mitral valve insufficiency, 4 patients with double mitral valve lesion, 4 patients with aortic valve insufficiency and

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3 patients with double aortic valve lesion). The work was done in the Cardiothoracic Surgery Department of Assiut University Hospital in the period from January to July 1996 and approved by local ethics committee and informed consent was obtained. Thorough clinical examination, laboratory investigations and echo-cardiography [ESAOTE BIOMEDICA, SIM 7000 CFM] were performed for every patient.

Patients with severe hemodynamic disturbance as a result of tight mitral stenosis, atrial fibrillation and superimposed ischemic heart disease. and those with hepatic or renal disorders were excluded from the study, as they may have metabolic derangement. Patients who were receiving diuretic therapy or digoxin continue their treatment to the morning of the surgery. All patients were premedicated with 0.2 mg/kg morphine sulphate I.M. and 0.2 mg/kg diazepam orally one hour before operation.

Monitoring Means:

- Electrocardiogram leads 11 and V5, operating room monitor, siemens, U. S. A.

-Venous cannulation : Two large bore cannulae gauge (16) were inserted in the hand or forearm under local anaesthesia.

- Radial artery catheter (20) gauge after Allen's test.

- Swans ganz catheter quadrilumen 7 F and heparin coated (spectramed laboratories U.K.).

- Cardiac output computer (spectramed, hemodynamic profile computer model SP 1445).

- Temperature probes inserted into the esophagus and rectum.

Anaesthesia

Anaesthesia was induced with fentanyl 50 pig/kg combined with sodium thiopental 2-3 Mg/kg and pancuronium bromide 0.3-0.4 mg/kg. Intermittent inhalation of fluothane was supplemented to control the blood pressure as needed. Anaesthesia was supplemented during CPB by intermittent IV doses of fentanyl and pancuronium bromide.

CPB phase:

After heparinization of the patient with I.V. heparin 4 mg/kg and cannulation of aorta and superior and inferior vena cava, CPB was initiated using Macci Bubble oxygenator (adult type). The oxygenator was primed with 1500 ml of lactated Ringer's solution. The patients were perfused by a roller pump (Sarns 5000, Ann Arbor, MI) at a flow rate of 50 ml/kg/min at temperature 25°C and 70 ml/kg/min at core temperature above 30°C. The flow was monitored by a flow rate computer (Sarns).

After initiation of CPB, body temperature was decreased and stabilised around 25°C, and the heart was arrested after aortic cross-clamping with a cold hyperkalemic cardioplegic solution. Systemic arterial blood pressure was kept between 50-70 mmHg by administration of sodium thiopental or ephedrine. The gas flow through the pump oxygenator consisted of 100 % oxygen at a flow rate equal to the blood flow rate.

Mitral valve replacement was performed for 7 patients as the valve leaflets and/or the subvalvular apparatus were severely disorganized and beyond repair. Aortic valve replacement was performed for 7 patients. St. Jude mechanical bileaflet valve (Model, 101) for mitral and for aortic replacement were inserted.

Post-bypass phase :

At the end of surgical correction, rewarming was started and the flow rate was increased. After optimization of temperature, blood gases and electrolytes, electric shock was used to defibrillate the fibrillated heart.At a beating heart, CPB weaning started after stabilization of hemodynamic state. Protamine was given to neutralize the heparin action. Anaesthesia was terminated, muscle relaxant used if needed, blood transfusion was given according to hemoglobin level and inotropes were given if needed. The patient was transported to the ICU mechanically ventilated until extubated.

Blood sampling and measurements :

Prebypass, arterial and venous blood samples were taken from the radial and pulmonary artery for blood gases analysis.

During bypass, the samples were withdrawn from the venous and arterial ports of the pump oxygenator every 20 minutes.

After weaning from CPB and stability of hemodynamics (postbypass), blood samples were withdrawn as in prebypass period and at interval of 1 hour for 2 hours, then every three hours in the ICU till extubation. Samples were analysed for hemoglobin conc., oxygen content, saturation and tension, pH, bicarbonate and base excess by blood gases analyser (Nova, Bio-Medical USA) at 37'C (uncorrected for temperature).

At the timing of blood samples, all of the following hemodynamic data were recorded from the monitors: Heart rate (HR), Systolic arterial blood pressure (SABP), diastolic arterial blood pressure (DABP), mean arterial blood pressure (MABP), central venous pressure (CV-P), cardiac output (CO), cardiac index (Cl), mean pulmonary artery pressure (NTAP) and pulmonary capillary wedge pressure (PCWP). The systemic vascular resistance (SVR) was also calculated, as $\frac{\text{MABP - CVP X 80}}{\text{CO}}$

The oxygen delivery values (D02) at different periods was computed as the product of arterial oxygen content multiplied by the perfusion flow.

D02 (ml/min/m2) = [(Hb x SaO2% X 1.36)m^2 + (PaO2 x 0.003)] X Cl x 10.

The oxygen consumption values (V02) were computed as the product of arterial-venous oxygen content difference multiplied by the perfusion flow.

V02 (ml/min/m^2) = [(SaO2% - SVO2%) X Hb x 1.361 + [(PaO2 - PVO2) X 0.0031 X Cl X 10.

Where Cl = perfusion flow index (L/min/m^2) = $\frac{\text{Co or pump flow L ; SaO2}}{\text{BSA } (M^2)}$

oxygen saturation; Hb = hemoglobin concentration (g/dL), 1.36 = Huffner factor. PaO2 uncorrected arterial oxygen tension (mmHg); PVO2 = uncorrected mixed venous oxygen tension (mmHg), 0.003 = saturability coefficient of oxygen at 37°C, BSA = body surface area.

Table I: Characteristics of the 14 patients shared in the study.

Age (years)	21.2 ± 3.3
Sex (M/F)	5/11
Body length (cm)	158.6 ± 6.5
Body weight (kg)	57 ± 0.6
Body surface area (M^2)	1.6 ± 0.1
Ischemic time (min)	55 ± 12
Total bypass time (min)	69 ± 23

Data are presented as mean ± SD.

The oxygen extraction ratio was computed as the ratio of oxygen consumption to oxygen delivery.

All data were recorded in a special chart for every patient. The mean values for readings in the three periods were calculated and presented as mean±SD. The paired t-test was used to compare the data in the different studied periods. $P<0.05$ was considered significant.

Results

Table 1 shows the demographic data of the patients shared in the study, the ischemic time (the time of clamping of the aorta), and the total bypass time, while Table II demonstrates the hemodynamic nature of the valve lesion and the type and size of the mechanical valve in the studied patients, all of them properly corrected with suitable sizes of the mechanical valve, and Table III shows some of their preoperative clinical data and cardiac conditions, as left ventricular end diastolic and end systolic dimensions and NYHA class for dyspnea, which indicate relatively healthy ventricles with chronic rheumatic valvular disease.

Table IV summarizes the changes in hemodynamic status of the 14 patients in the three studied periods. There was no significant difference between HR, SBP, DBP and MBP in the pre and postbypass periods. During the bypass period, MBP was maintained above 50 mmHg. CO (4.1±0.6) and CI (2.61±0.37) increased while the SVR (1134±195) decreased significantly in the postbypass period

Table II: Type of valve Lesion, and the Type and Size of the Mechanical Valve in 14 patients

Type of valve lesion	No. of patients	Surgical procedure	Type and size of mechanical valve		No. of procedures
- Mitral valve insufficiency	3	Replacement	St. Jude	31 mm 29 mm	2 1
- Double mitral valve lesion	4	Replacement	St. Jude	25 mm 27 mm	2 2
- Aortic valve insufficiency	4	Replacement	St. Jude	25 mm 23 mm	2 2
- Double aortic valve lesion	3	Replacement	St. Jude	23 mm 21 mm	2 1
Total	14				14

Table III: Preoperative Clinical Data and Cardiac Conditions of the Studied Patients

Item	Patients with mitral valve disease (N=7)	Patients with aortic valve disease (N=7)
NYHA	II & III	II & III
Cardiac Rhythm	Sinus Rhythm	Sinus Rhythm
LVEDD	Average (2.24 ± 0.68) Range (2.7 - 5.4)	Average (3.40 ± 0.64) Range (3.1 - 5.7)
LVESD	Average (2.66 ± 0.51) Range (1.7 - 3.7)	Average (2.70 ± 0.73) Range (2.3 - 3.8)
Valve lesion	3 cases of Mitral regurge 4 cases of double Mitral lesion	4 cases of Aortic regurge 3 cases of double Aortic lesion

NTHA = New York Heart Association Class of Dypsnea
LVEDD = Left Ventricular End Diastolic Dimension
LVESD = Left Ventrical End Systolic Dimention

compared with the prebypass period (3.2±0.5, 2.1±0.19 and 1302±300 respectively). The highest value for the SVR was recorded during the bypass period (1699±217). No significant changes in CVP, MPP and PCWP in the pre and postbypass periods.

Table IV: Hemodynamic Data of Patients in The Three Studied Periods.

Time	HR beats /min	SBP mmHg	DBP mmHg	MAP mmHg	CO L./min	CI L./min /m^2	SVR dyne/ sec/cm^{-5}	CVP ml /water	MPAP mmHg	PCWP mmHg
Prebypass	91.6±30	81.9±10	54±42	63.3±16.9	3.2±0.5	2.1±0.19	1302±300	8.8±1.9	28.6±5.7	24±2.8
Bypass	--	--	--	57±8.3 *P<0.05	--	--	1699±217 *P<0.01	--	--	--
Postbypass	95±22	87±12.1	56±7.7	66.1±9.7 **P<0.05	4.1±0.6 *P<0.05	2.61±0.37 *P<0.05	1134±195 *P<0.05 **P<0.01	8.09±1.8	27.6±5.3	22.7±3.1

HR, hear rate. SBP, systolic blood pressure; MAP, mean arterial pressure; Co. cardiac output; CI, cardiac index; SVR, systemic vascular resistance; CVP, central venous pressure; MPAP, mean pulmonary artery pressure, PCWP, pulmonary capillay wedge pressure.
*** t-test versus prebypass valve**
**** t-test versus bypass value.**

Table V: Arterial Blood Gases Analysis During the Three Studied Periods (uncorrected for body temperature).

Time	Temp.	PHa	PCO_2 mmHg	PO_2 mmHg	Sat. O_2 %	CTO_2 ml/dL
Prebypass	36.3 ± 0.4	7.37 ± 0.03	45.9 ± 5.19	233 ± 74	99.06 ± 0.9	16.9 ± 1.4
Bypass	25 ± 1	7.36 ± 0.05	36.8 ± 6.1 *P<0.05	349.9 ± 102 *P<0.05	99.8 ± 0.09	9.9 ± 1.05 *P<0.01
Postbypass	36 ± 0.1	7.36 ± 0.03	40.8 ± 4.6 **P<0.5	200 ± 57.6 **P<0.01	99.1 ± 0.9	14.6 ± 1.6 *P<0.05 **P<0.01

Pha, arterial PH; PCO2, carbon dioxide tension; PO2, oxygen tension; SatO2%, oxygen saturation; CTO_2, oxygen content.
*** t-test versus prebypass value.**
**** t-test versus bypass value.**

Table V shows changes in arterial blood gases analysis. Data measured uncorrected for body temperature. The pH was insignificantly different in the three studied periods. The PCO2 was lowest (36.8±6. 1) during bypass and the P02 was highest (349.9±102) due to increased solubility by cooling. The oxyhaemoglobin was fully saturated all over the studied periods.The arterial oxygen content was significantly low during bypass (9.9±1.05) due to hemodilution.

Table VI: Mixed Venous Blood Gases Analysis During the Three Studied Periods (uncorrected for body temperature).

Time	Temp.	PHv	PCO_2 mmHg	PO_2 mmHg	Sat. O_2 %	CTO_2 ml/dL	(A-V) CTO_2 ml/dL
Prebypass	36.3 ± 0.4	7.33 ± 0.03	46 ± 5.3	61.5 ± 11.7	77.7 ± 4	13.12 ± 0.9	3.65 ± 0.8
Bypass	25 ± 1	7.26 ± 0.6	41.9 ± 7 *P<0.05	66 ± 28.4 *P<0.05	90.8 ± 2 *P<0.01	9.22 ± 1.1 *P<0.01	1.26 ± 0.52 *P<0.01
Postbypass	36 ± 0.1	7.31 ± 0.05	45.9 ± 4	59 ± 10 **P<0.05	74 ± 5	10 ± 1.9 *P<0.05 **P<0.05	3.9 ± 1.4 **P<0.01

PHv, mixed venous PH; PCO_2, carbon dioxide tension; PO_2 oxygen tension; $SatO_2$, oxygen saturation; CT_2, oxygen content; (A-V) CTO_2 arterio-venous oxygen content differece. t-test versus prebypass value. **t-test versus bypass value.

Table VII: Oxygen Delivery, Consumption and Extraction Ratio.

	Pre-bypass (A)	Bypass (B)	Postbypass (C)	Paired t-test		
				Avs. B	Bvs. C	Avs. C
Oxygen delivery (DO_2) ml/min/m^2	350.9 ± 56	188 ± 19.1	543.2 ± 106	P<0.01	P<0.01	P<0.05
Oxygen consumption (VO_2) ml/min/m^2	74.6 ± 19.6	24.13 ± 4.4	96 ± 23	P<0.01	P<0.01	P<0.05
Oxygen extraction ratio	21.4 ± 4	12.82 ± 2.2	24.2 ± 5.2	P<0.01	P<0.01	N.S

Table VI shows the results of mixed venous blood gases analysis (measured uncorrected for body temperature). The pH was insignificantly changed in the three periods, the PC02 was slightly low during bypass period (41.9±7) of the three studied periods. The highest values for oxygen tension, saturation and content of mixed venous blood were obtained during the bypass period (66±28.4, 90.8±2 and 9.22+1.1 respectively). The arteriovenous oxygen content difference was lowest during the bypass period (1.26±0.52) compared with the prebypass (3.65+0.8) and postbypass (3.9±1.4) periods.

Table VII shows the values of oxygen delivery, consumption and extraction in the three studied periods.As regards the oxygen delivery and consumption, the lowest values were obtained during the bypass period

(188±19.1 and 24.13+4.4) with reduction of V02 by about 32% while the highest values were obtained in the postbypass period (543.2±106 and 96±23). Oxygen extraction decreased significantly during the bypass period (12.82±2.2) but it was insignificantly different in the postbypass period (24.2±5.2) compared with the prebypass value (21.4±4).

Discussion

Although CPB has significantly lowered morbidity and mortality rates from cardiac operations, it introduces several alterations of metabolic homeostasis such as sustained release of catecholamines with an associated rise in systemic vascular resistance (3), impaired insulin release and transport with a consequent defect of peripheral cell glucose use (4), decreased tissue oxygen-availability because of increased oxyhemoglobin affinity (5), and interference with the rate of cell enzymatic processes (6). Moreover, despite the improvement in CPB techniques over the past few decades, the use of pump oxygenator apparatus, as well as hypothermtia and hemodilution (which are intrinsic to the technique), may significantly alter the hemodynamic status, with possible adverse effects in the early postoperative period (7).

The results of the present study regarding the haemodynamic changes associated with CPB showed an increased in the cardiac output (4.1±0.6) and cardiac index (2.61±0.37) in the postbypass period compared with the prebypass period (3.2±5 and 2.1± 0.19).

The exact mechanism of how hemodilution increases CO are not totally clear. Changes in cardiac sympathetic tone and slow release of other humoral factors have been suggested as possible causes(8,9). It appears more likely that the mechanisms are associated with reduction of ventricular afterload resulting from decreased blood viscosity and peripheral vasodilution which allows for more complete ventricular emptying (I0,11). The latter mechanism is further proved by the present study since the systemic vascular resistance (SVR) was low (1134±195) in the postbypass period.Baraka in 1994(12) found also an increase in CO during rewarming after hypothermia associated with a decrease in SVR.

The results of this study regarding the effect of CPB on systemic oxygen uptake showed a significant reduction of oxygen consumption (V02) during CPB (Table VII) by about 32% of the normothermic value. This was associated with an increase in venous oxygen saturation and decreased arteriovenous oxygen content difference in mixed venous blood gases analysis (Table VI).

The reduction Of V02 during hypothermia was reported since 1983 by Robert et al (13) who assumed that for every change of IO'C, the V02 altered by two to three folds (QIO). Del-Canale et al (I4), found also a reduction Of V02 during CPB at 26'C by about 49% while in a study by Baraka in 1994 (12), the reduction was 45%. Factors attributed to reduction in V02 during CPB included arteriovenous shunting with consequent maldistribution of general or local circulation., hypothermic leftward shift of the oxyhemoglobin dissociation curve, thus limiting tissue

oxygen availability and the use of pulseless circulation which may contribute to worsen peripheral circulation and consequently decrease oxygen consumption(7,14). However, Baraka in 1993 (15) found that the decreased oxygen availability to the tissue during CPB was well matched by a proportional decrease in V02 and concluded that hypothermia with hemodilution during CPB does not adversely affect the whole body oxygen supply balance.

During the rewarming phase, the results showed an increase in V02 (96±23) by 29% more than the prebypass value (74.6±19.6) Table VII, this increase may be due to surgical stress, hormonal response or postoperative hypothermia (the after drop)(16). However, the increase in V02 was well matched by a proportional increase in CO as evident by a constant oxygen extraction ratio (Table VII).

In conclusion, after cardiac operations in patients with relatively healthy ventricles and properly corrected lesions who are normovolemic and adequately sedated, moderate hypothermia with hemodilution did not have a significant adverse effect on hemodynamic and oxygen supply demand balance of the whole body. Secondly, the first hours after CPB represent the period of highest risk for decompensation especially in patients with long standing cardiac lesion and low cardiac reserve since CO and V02 increase significantly. Adequate operative correction of the valve lesion and continuous monitoring to detect early postoperative changes is necessary.

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Comparison of Different Techniques of Reducing Blood Loss Following Open Heart Surgery

ABSTRACT

We have studied 120 patients who underwent open heart surgery for congenital or acquired heart diseases in cardiothoracic surgery unit, Tanta University Hospital. They were 62 males and 58 females ranging in age between 14-32 years and were divided into five equal groups each of 24 patients to evaluate and compare different methods of blood conservation during and after open heart surgery. In group I (control group) no active measures were done to save blood loss (only blood transfusion), group II were given a high dose aprotinin (trasylol group), group Ill were given tranexamic acid (cyklokapron group), group IV were given low initial dose heparin (200 IU /Kg) and group V were managed with 5 cm water positive end expiratory pressure (PEEP) in the ICU postoperatively. From this study there was a significant reduction in blood loss in the first 24 hours postoperatively in all groups and significant increase in the number of patients requiring no blood transfusion in the first 24 hours in group II by 25%. in group Ill by 16.6%, in group IV by 12.5% and in group V by 8.3%. We can conclude that high dose aprotinin (trasylol) has offered us excellent results in reducing blood loss followed by tranexamic acid (cyklokapron) then low initial dose heparin and PEEP are the second, third and fourth choice respectively and we recommend the use of one or more of the above techniques in patients where excessive blood loss is anticipated as in re-do surgery or patients with rare blood groups.

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INTRODUCTION

Patients undergoing open heart surgery with cardiopulmonary bypass (CPB) are at substantial risk of serious postoperative bleeding and often require blood or blood products transfusion (1)

The major known causes of bleeding after cardiac operations are inadequate surgical hemostasis, decrease in plasma coagulation factors, thrombocytopenia and platelet dysfunction, heparin overdose and inadequate heparin neutralization and hyperfibrinolysis (2) .

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Blood conservation has become a major area of concern for the cardiac surgeon as well as the anesthetist and many avenues have been explored to reduce the need for blood transfusion as a result of reducing blood loss. (3)

Aprotinin (trasylol) has an inhibitory activity against a variety of human serum proteases such as trypsin, chemotrypsin, plasmin and kallikreins, however the mechanism by which aprotinin reduces bleeding following open heart surgery is still uncertain. (4)

Tranexamic acid (cyklokapron) offers higher and more sustained antifibrinolytic

activity than other antifibrinolytic drugs and there are conflicting data about its efficacy as other antifibrinolytic agents. (5)

Excessive heparinization may result in abnormal bleeding, difficult reversal and the need for high dose of protamine that may induce thrombocytopenia and impairment of platelet aggregation. So, avoidance of heparin overdose have been tried with a small initial dose 200 IU/Kg with monitoring ACT to reach ACT just above 400 see. This may be explained by the presence of an individual sensitivity to the action of heparin that may vary threefolds. (6)

Positive end expiratoiy pressure (PEEP) as a mode of postoperative ventilation in the ICU have been tried by many authors, (7) however the mechanism of action in almost certainly mechanical by increasing the intrapulmonary pressure of mechanically inflated lung, the pleural and pericardial surfaces also are mechanically affected as a tamponade to the bleeding sites.

From the above techniques we tried to evaluate and compare the different lines of management of postoperative bleeding following open heart surgery.

Patients and Methods

The present study was carried out on 120 patients who underwent open heart surgery in Open Heart Surgery Unit of Tanta University Hospital. Operations performed either weres correction of congenital heart diseases or valve repair or replacement.

Patients with previous median sternotomy, bleeding disorders, or history of ingestion of platelet active drugs within 2 weeks prior to the operation were excluded from the study.

Patients were randomly classified into 5 equal groups each of 24 patients:

- Group I (control group) 24 patients: No active measures were taken to control postbypass bleeding, only blood transfusion as required.

Group II (Aprotinin group) 24 patients: Patients of this group received aprotinin in a dose of 80,000 KIU/Kg body weight. One third of the dose was given as infusion over 20 minutes beginning with skin incision. Another one third of the dose was added to the priming solution of the CPB and the last third was given as continuous infusion till the end of the operation.

-Group Ill (Tranexamic acid group) 24 patients: Patients of this group received tranexamic acid intravenously in a dose of 15 mg/Kg every 8 hours starting with anesthesia induction for 48 hours.

Group IV (Low initial dose heparin) 24 patients: Patients of this group were given an initial dose of heparin 200 IU/Kg followed by interrupted doses 25 IU/Kg, with measuring ACT until it becomes just above 400 sec permitting the surgeon to start cannulation of the great vessels.

Group V (PEEP) 24 patients: Patients of this group were ventilated with volume cycled ventilation (Bear 5) with positive end expiratory pressure (PEEP) of 5 cmH20. With exception of PEEP, all other aspects of ventilatory care were similar to other groups.

Table I: Shows the demographic data of patients of all groups (n = 24).

Group	Sex		Age (years)
	Male	Female	
I	11	13	23.2±4.2
II	15	9	24.4±6.1
III	12	12	20.8±3.4
IV	14	10	21.4±4.4
V	10	14	22.6±5.2

All patients were subjected to the following:

1- Preoperative studies including full clinical examination and coagulation studies (platelet count, bleeding time, clotting time, prothrombin time and hemoglobin concentration).

2- Cannulation was performed in the ICU under local anesthesia and anesthesia was induced and maintained with high dose fentanyl 50-80 ug/Kg and 100% O_2 for lung ventilation facilitated by pancuronium I- 12 mg/Kg.

3- Pump priming and perfusion were the same with no special prerequisites.

4- ACT was monitored by hemochron apparatus before heparin administration (baseline ACT), before cannulation, during bypass and after heparin reversal.

5- Postoperative studies:

a) Platelet count, bleeding time, clotting time, ACT and prothrombin time were done in the ICU 2 hours postbypass. Hemoglobin concentration was done at the next morning.

b) Mediastinal tube drainage was measured for the first 24 hours.

c) Blood transfusion requirements: Units of banked blood transfused during the first 24 hours were recorded.

Data were collected, tabulated and compared together using unpaired Student's "t" test.

Results

The operative procedures were correction of valvular heart disease either replacement or repair (96 patients) and correction of congenital heart diseases (24 patients) .

Table (II) shows the preoperative hematological profile of patients of all groups. There was no statistically significant difference between all groups .

Table II: Preoperative hematological studies (n = 24)

Group No.	I	II	III	IV	V
Platelet count (mm^3)	239000	230500	244000	233000	232000
	±3500	±4200	±9000	±3200	±4000
Bleeding time (sec)	175.5	176	173	175.1	171.5
	±5.6	±4.1	±4.8	±3.5	±3.1
Clotting time (sec)	329	320	324	327	318
	±5.2	±10.5	±6.8	±12.5	±9.5
Prothrombin time (sec)	14.2	14.5	13.8	14.6	14.1
	±0.8	±0.6	±0.7	±0.9	±1.1
Hemoglobin (gm%)	13.65	13.2	12.6	12.96	13.3
	±1.2	±0.5	±2.2	±2.0	±0.9

Table III: ACT values and protamin dose for reversal (n = 24)

Group No.	I	II	III	IV	V
Base line ACT	132	134	137	130	133
	±9	±6	±5	±11	±10
ACT before cannulation	602	690	788	422	722
	±34	±29	±26	±20*	±31
ACT during bypass	689	698	780	488	840
	±52	±32	±26	±18*	±42
ACT after reversal	148	149	144	138	150
	±8	±6	±11	±6*	±4
ACT 2 hrs after bypass	152	150	154	140	149
	±18	±12	±11	±6*	±16
Protamine dose (mg)	254	258	250	195	255
	±38	±30	±28	±42*	±32

Table IV: Postoperative hematological studies of all groups (n=24)

Group No.	I	II	III	IV	V
Platelet count (mm^3)	180000 ±4500	178500 ±3200	185500 ±2500	181500 ±1500	179000 ±3500
Bleeding time (sec)	540 ±52	320.5 ±13*	538.5 ±18	335 ±20*	585 ±24
Clotting time (sec)	465 ±12	358* ±8	348.5* ±18	358* ±10	467 ±21
Prothrombin time (sec)	15.6 ±2.1	15.9 ±1	15.7 ±1.9	15.6 ±0.8	15.8 ±1.5
Hemoglobin (gm%)	10.4 ±0.4	11.8 ±0.2	11.1 ±0.3	11.6 ±0.4	11.3 ±0.2

*** Denotes statiscally difference at $p<0.05$**

Table V: Shows blood loss and blood requirements in all groups (n=24)

Group No.	I	II	III	IV	V
Blood loss (ml)	850	450	600	500	750
Blood requirements (ml)	2500	1200	1800	1600	2000
No. of patients requiring no blood transfusion	1	6	4	3	2
% of patients requiring no blood	4.1	25	16.6	12.5	8.3

Table III shows the mean values of ACT before , during and after bypass, there was a statistically significant low ACT in group IV (low initial dose) heparin group than other groups before cannulation, during bypass and after reversal with significant lower protamine dose for reversal .

Table IV shows the postoperative hematological studies of all groups. There is

significant decrease in platelet count and hemoglobin concentration in postoperative period as compared to the preoperative values. Also there is significant prolongation of the bleeding time as compared to the preoperative values while the clotting time was insignificantly prolonged. There is no statistically significant difference between group I and the other four groups except for the prolongation of bleeding time in group II and IV, this prolongation of bleeding time in group II and IV is significantly less marked than group I,II and V.

Discussion

Despite improvements in the surgical and anesthetic techniques and evaluation of the equipments, patients undergoing cardiac operations with CPB are prone to serious hemorrhagic diathesis. (8) Several methods have been used to control this problem.

Group I (Control group):

The postoperative results of the hematological studies in group I is considered usual consequences of CPB which were reported by many authors. (1,3,9)

The significant reduction in platelet count may be due to hemodilution, interaction between platelets and foreign surfaces, formation of microaggregates and sequestration of some platelets by the reticuloendothelial system. This signifies the increase in bleeding time which reflects impairments of platelet function.(9,10) The slight insignificant increase in clotting time is due to the fact that the test is related to the heparinization of the patient and these results are due to adequate neutralization of heparin by protamine sulphate, a view which was supported by Bachmann et al. (11)

Group II (Aprotinin group):

The postoperative hematological studies of group II was similar to that of group I with no statistically significant difference except for the bleeding time which showed significant prolongation, however it was significantly less prolonged than the other groups. This result can be explained by the presence of platelet preservation action of aprotinin and prevention of hyperfibrinolysis or inhibiting the intrinsic pathway of coagulation through its antikallikrien action. So coagulation factors would not be activated or consumed and fibrinolysis would not be stimulated reactively.

Compared to group I, group II patients has significant reduction in blood loss by 47% and less blood requirements. In agreement with our results Vander Salm et al,(12) Royston et al. (13) Dietrich et al. (14) and Havel et al. (4) all reported significant reduction in blood loss and blood transfusion requirements after the use of aprotinin.

Group III (Tranexamic acid group):

The hematological studies done to patients in group Ill was similar to those in group I with no significant difference except the significant reduction in blood loss by 29.4%. This can be explained by the fact that tranexamic acid displays higher and

more sustained antifibrinolytic activity than other antifibrinolytic drugs.

Vander Salm et al. (12) reported significant reduction of blood loss by 22.1% using E-aminocaproic acid as an antifibrinolytic agent. Also, Horrow et al. (15) reported significant reduction in blood loss by 33.8% and insignificant blood requirements and they explained these results by inhibition of fibrinolysis by tranexamic acid. On the other hand, Garcia et al. (16) reported no significant reduction in blood loss by the use of E-aminocaproic acid.

Group IV (Low initial dose heparin group):

In this group, it is found that 200 IU/Kg initial dose heparin with small incremental doses, the total heparin dosing for safe anticoagulant was significantly lower than other groups. While postoperative blood loss and blood requirements was lower than group 1. Our explanation to these results in the presence of individual sensitivity that may vary threefolds, also other factors that may potentiate the action of heparin such as hypothermia, oliguria and type of heparin used. All these factors may prolong heparin action with excessive bleeding and difficult reversal.

Our results are in agreement with that of Gravlee et al (6) Who stated that the use of large doses of heparin increased the incidence of postoperative heparin rebound and excessive bleeding. Also, Dauchot et al(I7) stated that giving small initial dose of heparin to attain ACT just above 400 sec before cannulation of the great vessels and during CPB with proper titration of heparin dose is more safe for anticoagulation with less postoperative blood loss and easy reversal and proper monitoring of ACT.

Group V (PEEP group):

The postoperative hematological studies of group 4 did not show significant difference when compared to those of group 1. However, group 5 patients had significantly less blood loss by 41.1 %. These results are closely similar to the results of Hoffman et al (7) who reported significant reduction of blood loss by 17.64% and insignificant reduction of blood requirements by the use of 5 cm.H20 of PEEP.

Although Ilabaca et al (18) had successfully used PEEP to control the postoperative bleeding in patients requiring reoperation because of bleeding, their results cannot be compared with our results because of the difference in the indications of PEEP application and higher levels of PEEP they used.

On the other hand, Zurick et al (19) who used 10 cm.H2O of PEEP and found no significant difference in reducing blood loss or requirements and he did not recommend its routine use to control postbypass bleeding.

Mills (20) suggested that the results of Zurick et al (19) did not necessarily means that PEEP will not decrease excessive bleeding. He also suggested that since there is no clinical indication, PEEP cause damage and can be administered as long as the patients can tolerate it hemodynamically, PEEP may be used to control bleeding while coagulation studies are being obtained and the operating room is being prepared.

Conclusion

We can conclude that the use of aprotinin in cardiac surgery has the upper hand in reducing blood loss and blood transfusion requirements. tranexamic acid is the second choice. The use of low initial dose heparin (200 IU/Kg) followed by incremental titrated doses result in adequate anticoagulation, easy reversal and low postoperative blood loss. PEEP gives the lowest results but we still recommend its use if there is excessive bleeding. So, these measures can be combined if excessive bleeding is anticipated as in re-do surgery or in patients with rare blood groups.

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Lung Resections in School Age an Experimental and Applied Study on the use of Synchronous Clamping of the Hilum.

Abstract

This work aims at studying the pathophysiology of applying a synchronous clamp on the lung hilum during lung resections by studying this in 10 Mongrel dogs (Group I). It also aims at studing the indications, types and results of lung resections in 29 children in school age as an applied study utilizing such technique (Group II).

In Group I, all dogs tolerated well the synchronous clamping of the hilum for 15 minutes without previous heparinization. The changes in heart rate, aortic pressure and cardiac output were statistically insignificant. The pulmonary arterial pressure showed a significant rise. The pH, PaO2 and O_2 satuation showed a mild significant decrease. The PaCO2 showed a significant increase. All parameters returned to baseline values after releasing the clamp.

Group II included 7 patients with congenital, 19 patients with acquired and 3 patients with diffuse lung diseases. The operation was either in the form of wedge resection (6 patients), segmental resection (2 patients), lobectomy (16 patients), bilobectomy (one patient) or pneumonectomy (4 patients). No mortality was reported and morbidity occurred in 4 patients (13.79%). Early synchronous clamping of the hilum was applied during pneumonectomies. Intermittent clamping for 5-10 minutes during the difficult parts of dissection was used during lobectomies. The technique was found unnecessary for wedge resections and some lung cysts.

It was concluded that the technique of synchronous clamping of the hilum is well tolerated, easy to apply and effective in facilitating distal dissection in various forms of lung resections especially in this age group. It was also concluded that performing the lung resection in children is safer and easier than delaying it to an older age group. Another study is recommended to know how long the clamp could be safely left on the hilum without inducing venous thrombosis.

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INTRODUCTION

Pediatric patients had an important role in the development of the techniques of lung resections (1). The first successful staged pneumonectomy was done with mass ligature of the hilar structures in a 12-year-old girl with bronchiectasis (2). Pneumonectomy was then performed with individual ligation of the hilar structures in a 3-year-old girl with a benign tumour of the left bronchus (3). Since then, the standard technique of lung resection is by individual ligation of the hilar structures; classically starting by the artery, then the vein, then the bronchus (4). Vascular and Dr.

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bronchial stapling devices may be used to accomplish this (4) .

In malignant conditions, it is advisable to attack the vein first to minimize the risk of tumour dissemination during manipulation (5). In suppurative conditions, early attack of the bronchus will avoid the flooding of the bronchial tree with secretions during manipulations (5). In this concern, the standard methods of endobronchial separation as by double lumen tubes are inapplicable in children because of their small airways (6). To standardize a technique of lung resection suitable for the two indications; a single atraumatic clamp can be applied proximally to the lung hilum to simultaneously occlude the artery, vein and bronchus as a first step before proceeding with individual ligation of the structures distal to the clamp. Such early attack of the hilum is also of value in emergency lung resections for massive haemoptysis and trauma. In addition, it will allow distal dissection to be done in a bloodless clean field.

To study the pathophysiology of this technique, it was first tried experimentally. Then, it was applied on a group of school children requiring lung resection studying the indications, technique and results of the operation.

Material and Methods

This study included two groups:

Group I:

This included 10 Mongrel dogs, 6 males and 4 females, with a weight ranging from 9-14.5 Kg.

Each dog was anaesthetized using thiopentone sodium (15 mg/Kg.b.w). Additional doses were given when required. Endotracheal intubation using a cuffed tube was done. The dogs were then ventilated using 100% oxygen. A right posterolateral thoracotomy was done in the bed of the fifth rib. For each dog; the heart rate, aortic and main pulmonary systolic and diastolic pressures, cardiac output and arterial blood gases were recorded before and within 15 minutes after applying atraumatic synchronous clamp on the right lung hilum to include all its structures and then after releasing the clamp. The blood pressure was recorded using FC 137 strain gauge coupler, a pressure transducer and a two-channel direct writing oscillograph (Washington 400 MD2C). The cardiac output was measured using a quadruple Swan-Ganz catheter introduced via a cut done in the femoral vein and a thermodilution cardiac output catheter model TCCO-04.

Group II:

This group included 29 patients in school age requiring lung resection. They were admitted to Sporting Health Insurance Hospital or Alexandria Main University Hospital between January 1994 and February 1997. Their age ranged from 6-16 years and 17 were males and 12 were females.

For each patients, thorough history, clinical examination, necessary laboratory investigations and X-ray chest posteroanterior and lateral views were done. Pulmonary functions were done for most patients. Bronchoscopy, sputum studies and CT scan chest were done when required. Angiography for suspected pulmonary

arteriovenous fistulae was done. For diagnosis of bronchiectasis, CT scan replaced brochography; being less invasive, safer and easier to apply in this age group.

Preoperatively, proper antibiotics, mucolytics, expectorants and bronchodilators were used to control chest infection. Patients with bronchiectasis were only operated when they were almost dry. Tuberculous patients were only operated after being sputum negative by proper antituberclous therapy for sufficient time. Respiratory physiotherapy was encouraged pre and postoperatively.

For patients with suppurative lung diseases, before transferring the patients to the operating theater, the patient was placed in a lateral decubitus with the affected side up. Chest percussion and instructions to cough were done. Bronchoscopy was done at the induction of anaesthesia when required. A simple cuffed endotracheal tube was then placed and the patient was turned into the lateral decubitus position. The anaesthetist paid attention to proper prompt clearance of any secretions. All patients were monitored during operation using ECG, non-invasive blood pressure and pulse oxymetry. Any decrease in oxygen saturation was immediately managed.

A classical posterolateral thoracotomy was done through the bed of 6th rib, although higher or lower thoracotomies were done when required. Mobilization of the lung in the pleural space began medially in the mediastinum. Adhesions tend to be less dense in this location or may be absent when adhesions elsewhere are quite dense. (4) A suitable vascular atraumatic clamp was placed on the lung hilum before proceeding with further manipulations. (Fig 1) During lobectomies, clamping was done only intermittently for a maximum duration of 10 minutes each time. Then classical lung resection was completed. (4,5) The bronchial stump was closed by interrupted 2/0-3/0 absorbable Vicryl or Dexon sutures on atraumatic round needle to approximate the cartilaginous to the membranous bronchus. For patients requiring a wedge resection of the lung to obtain a biopsy as in patients with diffuse lung diseases and for straight forward congenital or hydatid cysts, the technique of proximal claming of the hilum was not necessary. The chest was finally closed with one or two intercostal tubes connected under water seal. After pneumonectomies, a tube was left for only 24 hs. to equalize the mediastinum and detect any serious bleeding.

Postoperatively, the patients were managed in an intermediate care unit for the first 24 hs. to monitor the patients' vital signs, ECG and oxygen saturation. Suction and breathing exercises were done to clear secretions and avoid atelectasis. Early mobilization was strongly encouraged. Presence of air leak was managed by low continuous suction till complete lung expansion. Rigid bronchoscopic suction and positive pressure inflation were done whenever there was evidence of mucus bluges interfering with lung expansion.

During follow up, based on clinical and radiological examination, the patients' conditions were divided into excellent, good, fair and poor (7). Excellent; when the patient had no respiratory symptoms, and physical and radiological examinations were essentially normal. Good; when the patient was markedly improved by the operation but still had minimal respiratory symptoms and less than normal examination and Xrays. Fair; when the

patient obtained little benefit. Poor; when the patient had persistent respiratory symptoms equal or greater than before operation.

Results

Group I:

All dogs tolerated well the synchronous clamping of the right hilar structures with a suitable vascular clamp for 15 minutes. The changes in the heart rate, aortic pressure and cardiac output were statistically insignificant as shown in table (1). However, there was a tendency for the heart rate to increase and for the aortic pressure and cardiac output to decrease. Pulmonary artery pressure showed a significant rise after clamping from a mean of 27.6/12 mm Hg to a mean of 41.1/15.4 mm Hg.

The results of blood gas analysis are shown in table (2). The pH, PaO2 and O2 saturation showed a mild significant decrease. The PaCO2 showed a significant increase.

All the parameters returned to baseline values after releasing the clamp.

Table (1): Haemodynamic parameters before and after clamping in group I.

		HR (Beats/min)	AoP (mm Hg)	PAP (mm Hg)	CO (L/min)
Basal	mean	136.6	135.5/86.5	27.6/12.1	1.366
	SD	± 17.233	±17.86±13.13	±3.75±2.23	±0.027
Clamping	mean	139.8	132/85.5	41.1/15.4	1.376
	SD	±14.94	±15.49±8.64	±6.4±2.46	±0.039
Significance		Insign	Insign	Sign	Insign

HR: Heart Rate, AoP: Aortic Pressure, PAP: Pulmonary Artery Artery Pressure, CO: Cardiac Output
SD: Standard Deviation. Sign: $p \leq 0.05$.

Table (2): Changes in blood gases before and after clamping in group I.

		pH	PaCO2	PaO2	O2Sat
Basal	mean	7.569	32.28	226	97.06
	SD	+0.170	+23.15	+176.86	+5.52
Clamping	mean	7.436	51.88	197.34	94.2
	SD	+0.22	+33.57	+203.76	+10.79
Significance		Sign	Sign	Sign	Sign

Sign: $p < 0.05$.

Table (3): Indications for lung resection.

Pathology	No. of cases
I. Congenital	
•Lung Cysts	5 (17.24%)
•Sequestrated lobe	1(3.45%)
•A-V Fistula	1(3.45%)
II. Acquired:	
Pulmonary Tuberculosis	4 (13.79%)
Chronic Non-specific infection	5 (17.24%)
Hydatid disease	3 (10.34%)
Bronchiectasis	5 (17.24%)
Trauma	1 (3.45%)
Tumour	1 (3.45%)
III. Diffuse Lung Disease:	3 (10.34%)
Total	**29 (100.00%)**

Group II:

The indications for lung resection performed for the 29 patients are illustrated in table (3). As shown in this table, 7 patients had congenital diseases, 19 patients had acquired diseases and 3 patients had diffuse lung diseases. Table (4) shows the various types of lung resections performed for each pathology. The resections varied from wedge resection to pneumonectomy.

The technique of early proximal clamping of the lung hilum was applied in all the cases requiring pneumonectomies and intermittently for those requiring lobectomies; for only 5-10 minutes each application.

It was found unnecessary during performance of lesser resections and some cases of lung cysts. Operatively, no undue difficulty was encountered in applying a proximal occluding clamp in the absence of pleural adhesions. In presence of such adhesions, they tend to be less dense at the mediastinum than elsewhere. This facilitates earlier dissection of the hilum and application of the clamp. During dissection, the site of the clamp especially during pneumonectomies could be modified. Two clamps might be applied simultaneously with their handles on the same side or one from above and the other from below. The clamp could also be momentarily released to check and identify bleeding sites and air leaks. This technique allowed dissection to be performed in a clean clear field, minimizing blood loss and aspiration of the contralateral lung and making the surgeon more courageous will dealing with the vascular structures.

Two of the five cases of congenital lung cysts presented with complications, one with tension cyst and the other with infected cyst. Two of them required segmental resection and three required lobectomy.(Fig 2)

Pulmonary sequestration was encountered in one patient and was managed by left lower lobectomy.

One patient presented with cyanosis with normal echocardiography. The chest Xray showed right lower lung shadow. Angiography confirmed the presence of an arteriovenous fistula in the right lower lobe. The condition was cured by right lower lobectomy.

Table (4): Type of resection.

	Congemtal	TB	Infecton	Hydatid	Bronchiectasm	Trauma	Tumour	Diffuse
wedge				2			1	3
Segmental	2							
Lobectomy	5	3	5	1	2			
Bilobectomv					1			
Pneumonectomy		1			2	1		
Associated:								
• Decortication					1			
• Reoperation			1					
• Rib resection							1	

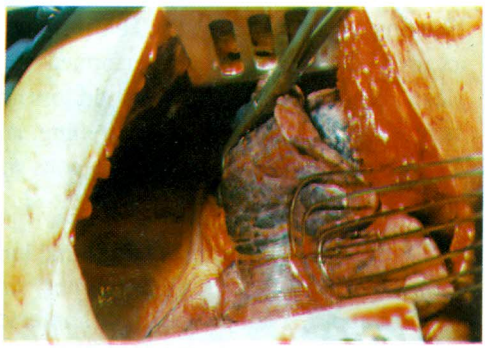

Fig. (1): Vaccular atraumatic clamp placced on lung hilum.

In the tuberculosis group, one was operated for middle lobe syndrome and two for persistent fibrocavitary lesion causing frequent attacks of haemoptysis and failing to respond to antituberculous drugs. The three patients required lobectomies. The fourth patient had a left tuberculosis destroyed lung and required pneumonectomy.

Lobectomy was performed for the five patients presenting with chromic non-specific infection in the form of chronic abscess (2 patients), septic granuloma (2 patients) or neglected foreign body (one patient).

Three patients with hydatid cysts of the lung were encountered in this study. Two patients required enucleation of the endocyst and trimming of the destroyed lung tissue. (Fig 3). One patient presented with infected cyst for which right lower lobectomy was done.

For bronchiectasis, two left lower lobectomies, one right lower bilobectomy, one right and one left pneumonectomies were performed. (Fig 4)

One patient had a car accident causing massive haemothorax and major bronchial laceration for whom left pneumonectomy was the only possible life-saving procedure.

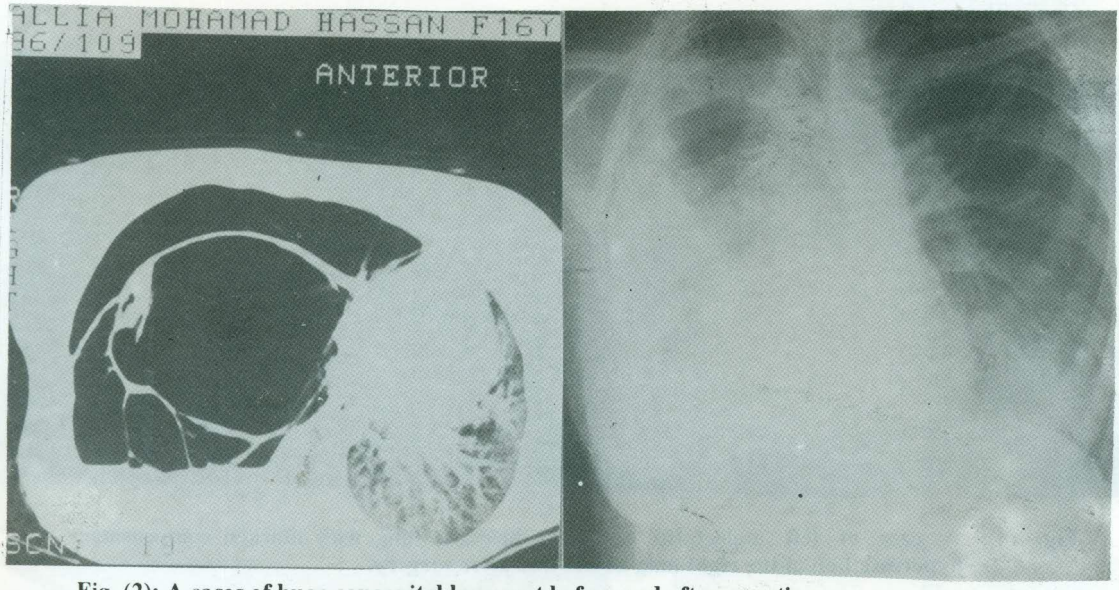

Fig. (2): A cases of huge congenital lung cyst before and after resection.

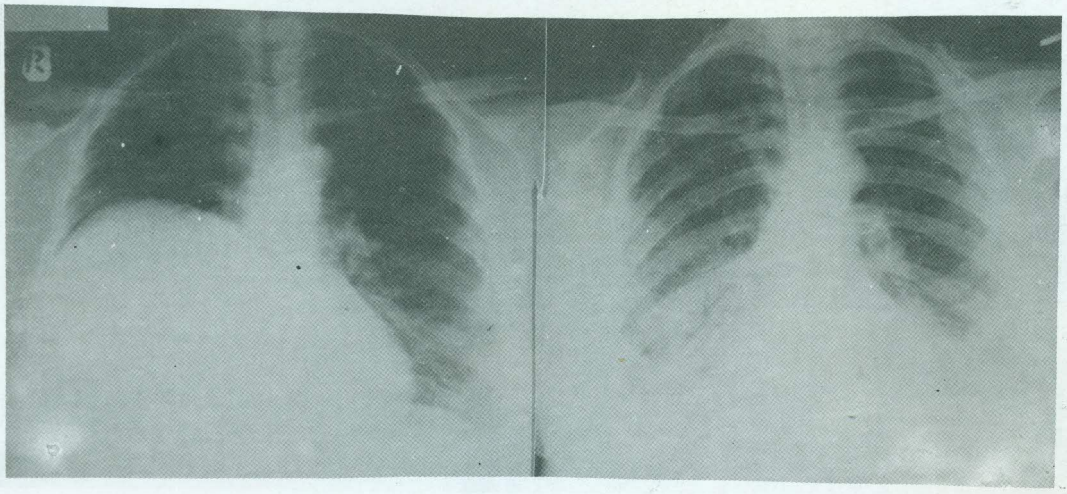

Fig. (3): A case of hydatid cyst before and after surgery.

In one patient, a neurosarcoma in the left upper paravertebral gutter was found infiltrating the left upper lobe and destroying the posterior parts of the left third and fourth ribs. At operation the tumour was resected together with chest wall resection and wedge resection of the infiltrated lung. (Fig 5).

For patients with diffuse lung diseases, the diagnosis of the diffuse

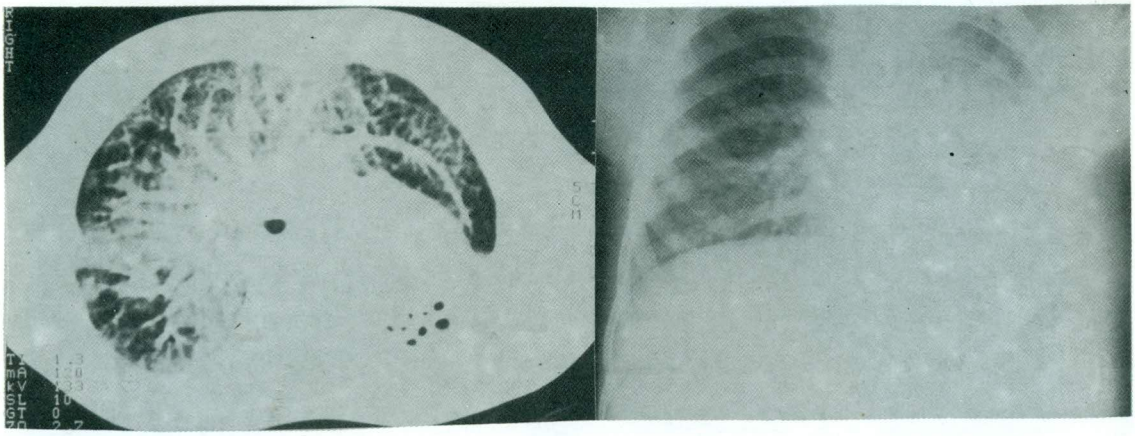

Fig. (4): A case of left atelectatic and bronchiectatic lung with marked compensatory hyperinflation of the right lung before and after surgery.

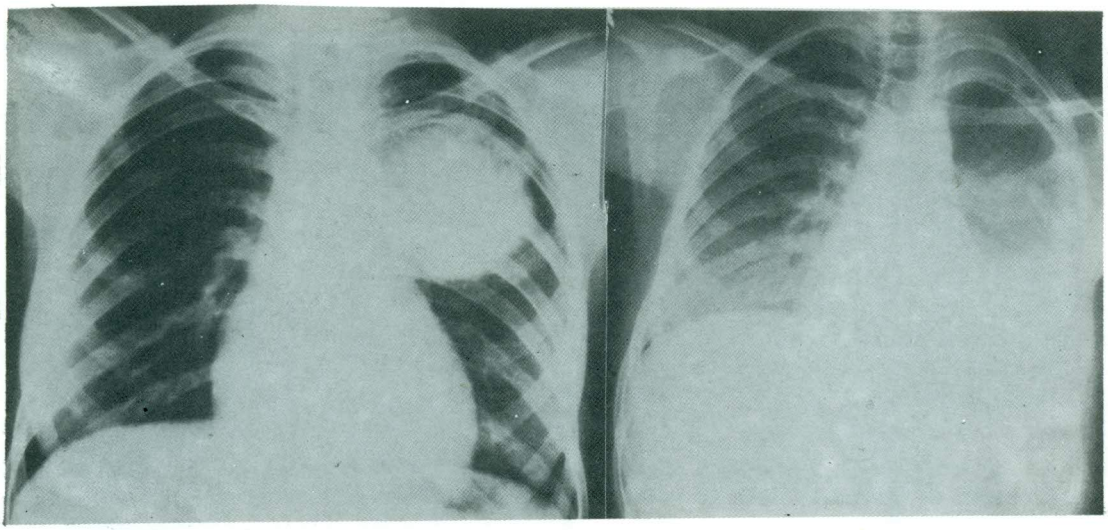

Fig. (5): A case of left neurosarcoma with chest wall and lung infiltration before and after surgery.

infiltrate was uncertain by conventional methods and open lung biopsy was recommended. The biopsy was performed through a limited thoracotomy on the right in one patient or the left in two. Excision of a part of the lingula was the preferred

procedure on the left side. The pathology demonstrated tuberculous infiltrate in two patients and non-Hodgkin lymphoma in one.

One of the patients with bronchiectasis required decortication together with lobectomy because of associated localized empyema. Reoperation, five days postoperatively, was done to evacuate a haemothorax complicating a lobectomy for chronic lung abscess. Chest wall resection and wedge resection of the lung were done during removal of a posterior mediastinal neurofibroma. (Fig 5)

Apart from the case of pneumonectomy for trauma, three pneumonectomies were performed for three children between 7 and 11 years; one for tuberculosis destroyed lung and two for bronchiectatic lungs. Preoperatively, their contralateral lungs showed compensatory hyperinflation. The operations were conducted with relative ease compared with pneumonectomies of older age groups, with minimal pleural adhesions and little blood loss. Their postoperative course was also quite smooth.

No mortality was encountered in the present study. Postoperative complications occurred in 4 patients (13.79%). One patient required reoperation five days postoperatively to evacuate a clotted haemothorax. After right lower lobectomy for a huge congenital lung cyst, the residual lung was hypo-plastic failing to expand to fill the right hemithorax. (Fig 2) The intercostal tube was left under water seal for three weeks, then converted into open drainage for about 2.5 months till complete obliteration of the residual space. Two patients showed postoperative atelectasis and required bronchoscopic suction with repositioning of the tube in one of them.

During follow up, the three patients with diffuse lung diseases were given their definitive medical treatment after obtaining their biopsy reports. For the remaining 26 patients who were subjected to curative lung resection, 21 patients (80.8%) had excellent results and 5 patients (19.2%) had good results. The female patient who was subjected to resection of a neurosarcoma was transferred to the oncology department for radio-chemotherapy. In the tuberculosis group, antituberculous therapy was continued for at least six months postoperatively.

Discussion

It is an already established surgical technique that a tourniquet placed proximally on a limb, a finger or a toe will allow distal dissection to be done in a bloodless and clear field (8). The same technique had been tried in this study by applying a proximal atraumatic clamp on the lung hilum to facilitate distal dissection allowing it to be performed in a bloodless field without frothing from air leaks and without fighting an inflated lung by the retractors. Furthermore, this technique has the theoretical advantage of simultaneously occluding; 1) the bronchus; avoiding over flooding the other lung with secretions in suppurative indications, 2) the pulmonary and bronchial arteries; minimizing bleeding in trauma and massive haemoptysis, 3) the veins; minimizing the risk of tumour embolization in malignant indications (5) . Proximal control of the pulmonary artery alone before dissecting an adherent lymph node or tumour using a Rumel tourniquet is a previously described technique (4).

Kaiser (4), in describing the technique of lobectomy, stated that there is no particular importance to the order in which

the hilar structures are divided, the easiest should be taken on first. He also stated that classically, the arteries are divided first, followed by the veins and finally the bronchus. Yet, what is more physiological to the patient; to start first by the arteries, the veins, the bronchus or to simultaneously occlude all. Starting first by dividing the bronchus will theoretically result in shunting as a result of perfusion of non-ventilated alveoli causing transient hypoxia, increase in arterial carbon dioxide pressure (PaCO2) and decrease in end-tidal carbon dioxide pressure (PETCO2) (9). This effect is transient because the non-ventilated lung gradually becomes more hypoxic, resulting in hypoxic pulmonary vasoconstriction which reduces blood flow to the non-ventilated lung thereby decreasing the intrapulmonary shunting (10). Shifting of blood from the non-ventilated to the ventilated lung will improve the hypoxia provided that later pulmonary functions are normal, otherwise serious life-threatening hypoxia may occur. However, simultaneous bronchial and pulmonary artery occlusion prevented any changes in PETCO2 (9). It can be concluded from the forgoing that simultaneous clamping of the hilum could be more physiological than starting first by occluding the bronchus by avoiding shunting.

When the lobar venous outflow was experimentally occluded in dogs, the lobar venous pressure rose suddenly to a level somewhere below the arterial pressure, and then the arterial and venous pressures began to rise more slowly (11). As a result of such elevated venous pressure and venous congestion, the veins will bleed more profusely when injured during dissection. In one study, where lung resection started by ligating the veins first, the cardiac output was found to decrease significantly after resection (12). In studies where lung resection was done by simultaneous clamping of the hilum, as this study and others, the changes in cardiac output were insignificant (13).

Progressive inflation of a balloon inside the main pulmonary artery in conscious dogs resulted in the initial phases of inflation in increase in right ventricular systolic pressure, heart rate and cardiac output, a decrease in peripheral resistance and no change in blood pressure and right ventricular end diastolic pressure (14). This is probably due to stimulation of stretch receptors in the pulmonary artery and/or right ventricle causing reflex increase in heart rate and decrease in total peripheral resistance, resulting in an increase in cardiac output and no change in blood pressure (14). In anaesthetized open-chested dogs, pulmonary hypertension created by a balloon in a branch of the pulmonary artery was accompanied by systemic hypotension (15). The hypotension is probably due to exaggerated vasodilatation reflex from anaesthesia.

In this study and in others, synchronous clamping of the hilar structures resulted in insignificant changes in heart rate, aortic pressure and cardiac output and significant increase in pulmonary arterial pressure(12). Other studies had demonstrated also an increase in pulmonary vascular resistance and in the oscillatory work of the right heart with increase in right intraventricular pressured 3,16)

The atraumatic vascular clamp was left safely in this study on the hilum for 15 minutes in dogs and 5-10 minutes in children without prior heparinization. During pneumonectomies the clamp was left for longer durations because the lung was going to be removed. Another study is needed to see for how long the clamp could be left without inducing thrombosis or pulmonary infarction.

About the timing of lung resection, is it preferable to operate early or to delay interference to adolescent or adult age? Those preferring delaying the operation may argue that adults are more cooperative in respiratory physiotherapy postoperatively and that pneumonectomy in young age may result in chest wall deformity on the same side during development. However, interfering as early as indicated has physiological, developmental and pathological advantages. Physiologically, when the hemodynanamics were studied after pneumonectomy in puppies and adult dogs, puppies were found to have marked facilitory adaptation. Whereas the cardiac output decrease, pulmonary vascular resistance increase and pulmonary impedance increase were statistically significant in adults, they were insignificant in puppies (14). Five years postpneumonectomy, dogs operated upon as puppies were also found to be more reactive to hypoxia than dogs operated upon as adults indicating more facilitory adaptation of the right ventricular pump characteristics (17). Developmentally, the studies had demonstrated that the residual lobes in the young increase in volume by compensatory emphysema and alveolar enlargement (18-20), and in tissue mass and collagen content (21). Early resection facilitates also compensatory growth of the remaining lung by increasing the alveolar multiplication rate beyond the normal rate which produces a twelvefold increase in alveoli between birth and early adolescence, (18,22-24). Pulmonary vessels that accompany the airways and alveoli would presumably hypertrophy and proliferate at a similarly augmented rate (25,26). Pathologically, the pulmonary functions of the contralateral lung may start to deteriorate as a result of chronic infection from the diseased lung. In addition, dense vascular adhesions will develop with time between the diseased lung and the surroundings that will make dissection more bloody and difficult. The thin-walled neovascularization is effected by systemic arterial connections between the bronchial arterial system and the adjacent intercostal arteries, branches of the subclavian, axillary, pericardial, diaphragmatic and esophageal arteries (6,27). The findings in the cases of pneumonectomies performed for destroyed lungs in this study strongly support this view. There were no troublesome intrapleural adhesions, no undue bleeding, the lung size was small and the other lung compensated well intra and postoperatively.

The incidence of morbidity and mortality of lung resections in children is quite low as detected in this study and others (7). A mortality of 0-1.7% in this age group is compared with that of 2.4-15% for adult lung resections in modern series, (6,28). The forgoing discussion may offer the necessary explanation. The proper preoperative evaluation and preparation, the meticulous intraoperative surgical techniques and precise anaesthetic measures are additive factors in improving the results. Any active infection, especially tuberculosis, should be controlled before operation. Associated empyema is

preferably managed by closed or open drainage before operation is done (6) .

The problem of flooding of the other lung with secretions during anaesthesia can be prevented by proper preoperative preparation, various methods of endobronchial separation, prone posture for operation or the present technique of early application of a proximal clamp on the hilum. Endobronchial separation could be done by double lumen tube, single tube-single lung ventilation and bronchial blockers (6). In children, because of their small airways these methods are inapplicable (6). In addition these measures are not available in all centers and require proper training for their accurate placement otherwise they will be hazardous (9) . Operating in a prone position is found by some authors to be a suitable alternative in this age group (6) . On the other hand, other authors find that the prone position precludes access to the pulmonary vessels from the front, making the operation unnecessarily difficult and makes early ligation of the superior pulmonary vein in carcinoma resections impossible (5). In this study, the technique of early proximal control of the hilum adds another alternative which is easier to apply without forcing the anaesthetist and the surgeon to work in a position they are not used to it.

In peumonectomies for carcinoma, early attack of the vein is recommended to minimizes the theoretical risk of tumour cell dissemination. (5,29) Yet, this has the disadvantage that venous infarction will occur in the event that the lung proves to be nonresectable. Also venous congestion will increase bleeding during dissection (29). The technique of synchronous clamping of the hilum is accordingly more advantageous in this indication because the clamp can be simply removed if the case proved to be nonresectable. The veins and arteries are also simultaneously occluded with less liability of venous congestion.

Comparing the indications for lung resection in this study and a similar study done in the50's, the infective indications including tuberculosis become less frequent with relative increase, in congenital indications (7). This reflects the development of new generations of antibiotics and antituberculous therapy treating the infection before producing surgical complications. However, surgery continues to have both diagnostic and therapeutic indications for the management of pulmonary tuberculosis (30). Surgery was required in this study to obtain lung biopsy in patients with undiagnosed diffuse lung infiltrations and to resect resistant pulmonary fibrocavitary lesions and destroyed lungs.

In operating patients with lung cysts whether congenital or hydatid, a trial was made to conserve lung tissue as much as possible. Yet, lobectomies were performed in this group for complicated cysts with evident destruction of the affected lobe (31).

80.8% of patients in this study got excellent results of their resection, a comparable figure to a previous study of 72.7% (7). This strengthens the conclusion that lung resection in school age in a properly prepared patient having a properly selected indication and extend of resection will give the best results and should not be delayed to an older age group.

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Present Status of Thoracoplasty

Abstract

Sixty five consequative thoracoplasty operations were done in the Cardiothoracic Surgery Department, Mansoura University between 1972 and 1996. In this prospective and retrospective study two types of thoracoplasty were done.

Standard thoracoplasty described by Alexander was done in 50 operations (76.9%). It was indicated for apical cavities, postresection or postdecortication pleural pouches, chronic empyema pouches, and bronchopleural fistulae. It was successful in collapse of cavitary lesions, obliteration of postresection or postdecortication pleural pouches, closure of empyema pouches and closure of bronchopleural fistulae. The first rib was excised in the first 24 cases of this type. The incidence of standard thoracoplasty to major thoracic operations is decreasing from 4.4% to 3.3%.

Reconstructive thoracoplasty operations were done in 15 operations (23.1%). It was indicated for excision of primary benign and malignant and metastatic chest wall tumors. It was successful in excision of chest wall tumors as well as chest wall reconstruction. Different techniques of chest wall reconstruction were used including simple closure, with or without repair of the diaphragm and costal margin, reconstruction using prolene mesh, stainless steel mesh and bone cement. The incidence of reconstructive thoracoplasty to major thoracic operations is increasing from 3.3% to 5%. The overall mortality in our study was 5.2%.

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INTRODUCTION

The idea of collapse therapy developed many years ago before the advent of chemotherapy by putting the affected part of the lung at rest allowing the lung to collapse or relax. The term thoracoplasty was first used by Estlander in 1879 to describe removal of ribs to collapse the chest wall down to the lung which would not expand after drainage of an empyema. In 1885, De Cerenville first applied this operation to collapse the cavity in a tuberculous lung. Friedrich, in 1907 resected from the second to the ninth ribs in the begining of his series. He resected the periosteum, the intercostal muscles, the nerves, in addition to the ribs. Brauer suggested subperiosteal resection of the ribs so that they might regenerate and stabilize the chest wall (Langston and Barker, 1978). The very radical operation suggested by Brayer and Friedrich was modified by Gourdet and Sauerbruch. They pointed out that resection of the posterior or paravertebral segments of the ribs would bring about a greater collapse of, the underlying lung than if the Longer, more anterior segments were resected (Alexander, 1925).

Alexander refined the modern operation of standard thoracoplasty. He staged the operation and recognized the importance of the transverse process in increasing the amount of collapse obtained (Alexander,

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1925). An important variant of standard thoracoplasty was plombage thoracoplasty introduced by Tuffier in 1891. An extraperiosteal pocket was made by denuding the ribs overlying the diseased area to be collapsed and this pocket was filled by a "plomb" such as polyethylene spheres enclosed in a polyethylene bag. The plombs were filled by air, fat, oil, or paraffin. The operation has the advantage of selective collapse with less effect on pulmonary function, it is done in one stage, and it has less deformity as it needs no removal of the first rib. Infection is the main limitation of this procedure (Brantigan, and Rigdon, 1950).

Material and Methods

This prospective and retrospective study was done in the Cardiothoracic Surgical Department, Faculty of Medicine, Mansoura University between 1972-1996.

It included 59 patients to whom 65 thoracoplasty operations were done. Standard thoracoplasty as described by Alexander was done in 44 patients, 39 males and 5 females. The minimal, maximal, and mean ages in this group were 16, 65, and 33.7 years respectively.

Reconstructive thoracoplasty was done in 15 patients, 9 males and 6 females. The minimal, maximal, and mean ages in this group were 4 months, 66, and 39.9 years respectively.

Full history taking and clinical examination were done for all patients. Routine hematologic study, sputum examination for specific and non specific organisms, Tuberclin test, and bronchoscopy were also done. The radiologic study included plain chest x-rays (PA, and lateral views), bronchography, tomography and chest CT.

In the first group of standard thoracoplasty, all operations were done under general anaesthesia except 1 (2.3%) in which local infiltration anaesthesia was used. The operation was used to produce concetric retaxtion of the diseased lobe by subperiosteal resection of the ribs overlying the diseased area, in addition to apicolysis, by division through Sibson's fascia and its three bands of Sibelau. First stage thoracoplasty was used in all except 6 patients (13.6%) in which second stage thoracoplasty was needed two weeks after the first stage.

In the second group of reconstructive thoracoplasty, all operations were done under general anaesthesia with excision of the benign or malignant chest wall tumor with a sufficient safety margin. Reconstruction of the chest wall was done either by simple closure or by different types of autogenous grafts, artificial meshes or bone cement.

Results

Our Study included 59 patients to whom 65 thoracoplasty operations were done. The patients were divided into two groups. The first group included 44 patients to whom standard thoracoplasty was done. The second group included 15 patients to whom reconstructive thoracoplasty was done. Table I illustrates the type and no. of operations in our 59 patients.

Hemoptysis was the main symptom in the first group while a painless chest wall swelling was the main symptom in the

Table I: Type and no. of operations in 59 patients.

Group	Type and no. of operations	No. of patients	%
A	Standard thoracoplasty (First stage 44 second stage 6)	44 (M39 F5)	74.6%
B	Reconstructive 15 thoracoplasty	15 (M9 F6)	25.4%
Total	65 operations	59	100%

Table II: Symptoms in the standard thoracoplasty group.

Symptom	No. of patients	%
Hemoptysis	30	70
Excessive expectoration	20	45
Shortness of breath	14	31.3
Continuous air leakage through thoracostomy tube drainage due to bronchopleural fistula	5	13.3
Chronic sinus in the chest wall discharging pus	1	2.3

Table III: Symptoms in the reconstructive thoracoplasty group.

Symptom	No. of patients	%
Painless chest wall swelling	7	47.2
Painful chest wall swelling	6	39.6
Chest pain (totally intrathoracic swelling)	1	6.6
Asymptomatic	1	6.6
Total	15	100

second group. More than one symptom were present. Tables II and III illustrate the symptoms in both groups respectively.

In the first group, all patients were receiving regular antituberculous treatment for 3 months before surgery except 3 (6.8%) to whom non specific treatment was given. Sputum examination (for acid fast bacilli were negative before surgery in all those patients except 2 (5.5%). One of these patients converted to negative after operation while the other is still sputum

Table IV: Radiological findings in the standard thoracoplasty group.

Radiological findings	*Site*	*No. of patients*	*%*
Apical cavitary lesion	10Rt.-4Lt.	14	31.8
Post-resection pleural pouch	9Rt.-4Lt.	13	29.1
Post-decortication pleural pouch	4Rt.-1Lt.	5	11.5
Chronic empyema pouch	4Rt.-1Lt.	5	11.5
Bronchopleural fistula (BPF)	4Rt.-1Lt.	5	11.5
Pleural pouch following resection and decortication	1Rt.-1Lt.	2	4.6
Total	32Rt.-12Lt.	44	100

Table V: Radiological findings in the reconstructive thoracoplasty group.

Radiological findings	Site	No. of patients	%
Bone tumors in relation to the ribs	3Rt.-4Lt.	7	46.7
Soft tissue tumor in relation to the ribs	1Rt.-5Lt.	6	39.9
Bone tumor in the sternum		1	6.7
Chronic osteomyelits of sternum		1	6.7
Total	4Rt.-9Lt.	15	100

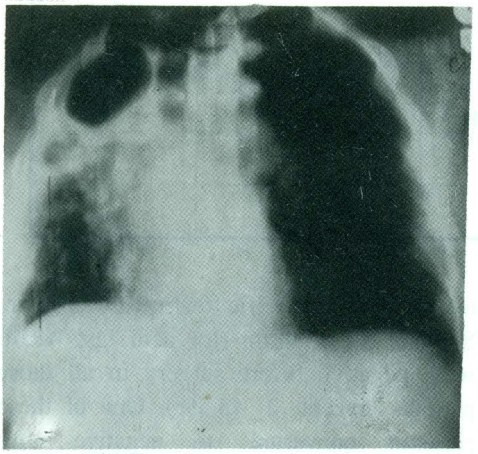

Fig.1: Tomogram of TB right upper lobe cavity.

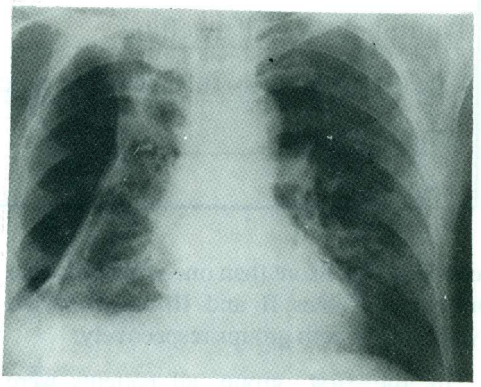

Fig.2: Chronic TB empyema pouch.

Table VI: Pathological lesions in the standard thoracoplasty group.

Pathological lesion	No. of patients	%
Tuberculous upper lobe cavities	14	31.8
Tuberculous post resection pleural pouch (after RUL7-LUL2-LLL+L1)	10	22.5
Tuberculous post decortication pleural pouch	5	11.5
Chronic tuberculous empyema pouch	5	11.5
Tuberculous bronchopleural fistulae (after RU & ML 2- RUL 2 - RN 1)	5	11.5
Non specific post resection pleural pouch (after LUL2-RUL1)	3	6.6
Tuberculous pleural pouches following resection and decortication (after RUL1-LLL1)	2	4.6
Total	44	100

NB: RUL: Right upper lobectomy.
LUL: Left upper lobectomy.
LLL+L: Left lower lobectomy.
RU&ML: Right upper and middle lobectomy.
RN: Right pneumonectomy.

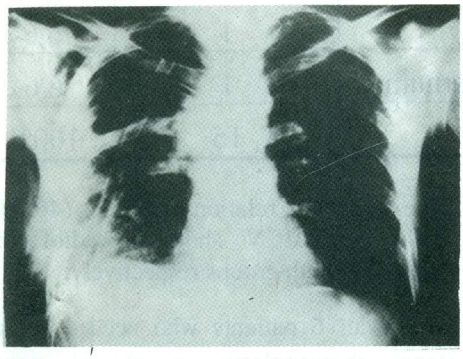

Fig.3: A large pleural pouch following right upper lobectomy.

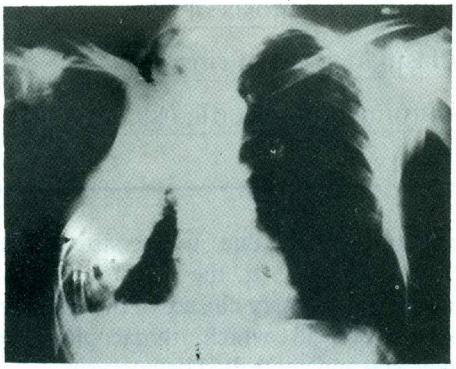

Fig.4: Successful right thoracoplasty for the same patient with preservation of the first rib.

Table VII: Pathological lesions in the reconstructive thoracoplasty group.

Pathological lesions	*No. of patients*	*%*
Chondrosarcoma:	4	27.4
Chondrosarcoma of ribs	1	
Dedifferentiated chondrosarcoma of ribs	1	
Recurrent chondrosarcoma of ribs	1	
Recurrent chondrosarcoma of sternum	1	
Desmoid tumor of ribs	1	6.6
Lymphosarcoma of ribs	1	6.6
Ewing's sarcoma of ribs	1	6.6
Embryonal rhabdomyosarcoma of ribs	1	6.6
Fibrous dysplasia of ribs	1	6.6
Chondroplastoma of ribs	1	6.6
Osteochondroma of ribs	1	6.6
Hemangioendothelioma of ribs	1	6.6
Lipoblastomatosis of ribs	1	6.6
Plasmacytoma of ribs	1	6.6
Chronic non-specific osteomyelitis of sternum	1	6.6
Total	15	100%

positive (2.3%) due to persistent small cavitary lesion in the right lower lobe inspite of cavitary closure in the ipsilateral upper lobe to which thoracoplasty was indicated and controlled hemoptysis.

The commonest radiological finding in the first group was an apical cavitary lesion (31.8%) while in the second group it was a bone tumor in relation to the ribs (46.7%). Table IV and V show the radiological findings in both groups respectively.

For all 6 patients who needed second stage thoracoplasty, a pleural pouch following the first stage thoracoplasty was found.

Table VIII: Operative details in the standard thoracoplasty group.

Operative details	*No. of patients*	*%*
First stage:		
Subperiosteal resection of ribs from 1st-5th	13	29.5
subperiosteal resection of ribs from 1st-6th	8	18.5
Subperiosteal resection of ribs from 1st-4 th	3	6.8
The first rib was resected in (total)	24	54.8
Subperiosteal resection of ribs from 2nd-7th	8	18
Subperiosteal resection of ribs from 2 nd -5th	7	15.9
Subperiosteal resection of ribs from 2 nd -6th	5	11.3
The first rib was preserved in (total)	20	45.2
Total	44	100
Second stage		
Subperiosteal resection of ribs from 6th to 7th	4	66.7
Subperiosteal resection of ribs from 5th to 7th	2	33.3
Total	6	100

The commonest pathological lesion in the first group was a tuberculous upper lobe cavitary lesion (31.8%) while in the second group it was chondrosarcoma (27.4%). Tables VI and VII show the pathological lesions in both groups respectively.

The commonest operation in the first group was done in 13 patients (29%) in the form of subperiosteal resection of the first 5 ribs including the first rib together with apicolysis. The first rib was resected in the first 24 operations (54.8%) and preserved in the last 20 operations (45.2%). In the second group, the commonest operation was done in 8 patients (52.8%) in the form of excision of chest wall tumor from multiple ribs with a safety margin and chest wall reconstruction using autogenous graft. Tables VIII and IX illustrate the operative details in both groups respectively.

The commonest minor complication in the standard thoracoplasty group was accidental pleural injury which was managed by thoracostomy tube drainage. Tables X and XI represent the complications and mortality in both groups respectively.

Table IX: Operative details in the reconstructive thoracoplasty group.Table

Operative details	No. of patients	%
A- Autogenous grafts :		
- Multiple rib resection and fascia lata graft	3	19.8
- Multiple rib resection with repair of the diaphragm, costal margin and bone graft.	3	19.8
- Multiple rib resection and myocutaneous graft (pectoralis major) repair	2	13.2
Total autogenous grafts	8	52.8
B- Artificial grafts :		
- Multiple rib resection and prolene mesh	4	27.4
- Multiple rib resection and bone cement	1	6.6
- Sternal resection and stainless steel mesh	1	6.6
- Sternal resection and bone cement repair	1	6.6
- Total artificial grafts.	7	47.2
Total autogenous and artificial grafts	15	100

Table X: Conplications and mortality in the standard thoracoplasty group.

Complications	No. of patients	%
Minor:		
Accidental pleural injury	9	20.4
Chest wall sinus	1	2.3
Major:	1	2.3
Persistant pleural pouch corrected by pectoralis major muscle flap	1	2.3
Significant scoliosis	1	2.3
Mortality :		
Early mortality	1	2.3
Late mortality	2	4.6
Total	3	6.9

Table XI: Complications and mortality in the reconstructive thoracoplasty group.

Complications	No. of patients	%
Minor complications:		
Wound infection	1	6.6.
Minimal chest deformity	1	6.6
Major complications:		
None	-	-
Mortality		
Early mortality	-	-
Late mortality	-	-

Table XII: Operative results in both groups.

Groups included	*Total No. of patients*	*No. of succeeded operations*	*% success*
A- Standard thoracoplasty group :			
Control of hemoptysis	30	29	96.3
Obliteration of pleural post resection and post decortication pouches (1st stage) (2 patients died).	20	18	90
Cavitary closure (one patient died)	14	13	92
Obliteration of pleural pouch (2nd stage)	6	6	100
Obliteration of chronic empyema pouch	5	4	80
Closure of bronchopleural fistulae	5	5	100
B- Reconstructive thoracoplasty group :			
Excision of chest wall tumor with chest wall reconstruction	15	15	100

Discussion

Alexander in 1925 refined the standard thoracoplasty which was used initially for the management of advanced fibrocavernous tuberculosis (Alexander, 1925). Althought the frequency of standard thoracoplasty is decreasing all over the world due to better control of tuberculosis,

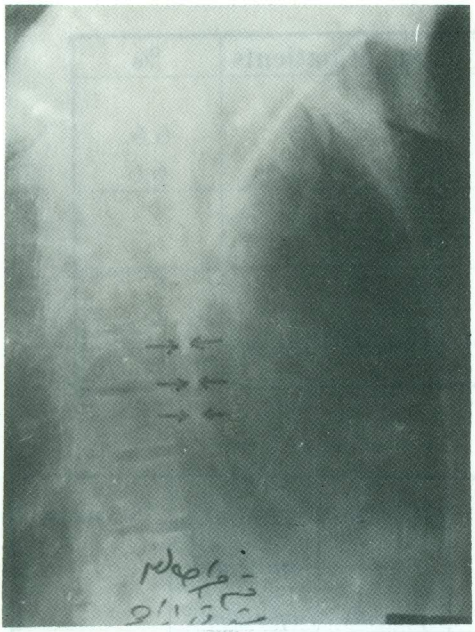

Fig. 5: Right bronchography confirming bronchopleural.

Fig. 6: CT of right recurrent chondrosarcoma of ribs.

and advances in anaesthesia and surgical techniques the term thoracoplasty has been expanded and the frequency of

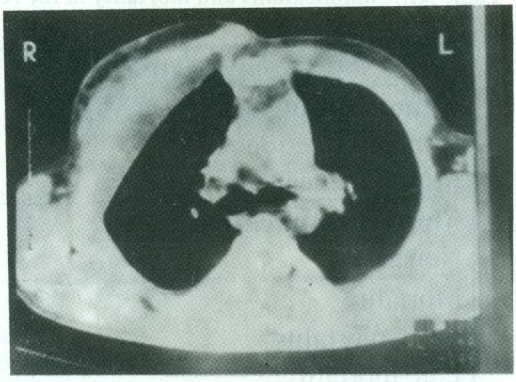

Fig.7: Postoperative CT of the same patient after reconstructive thoracoplasty using bone cement.

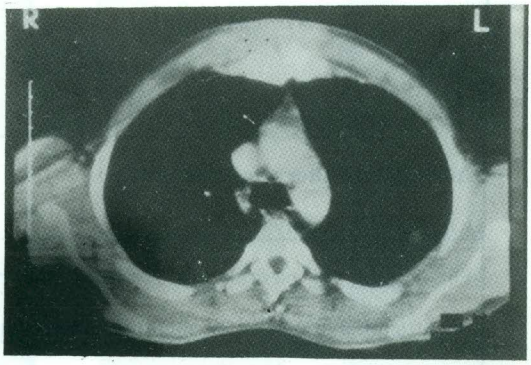

Fig.8: CT of chronic osteomyelitis of sternum.

reconstructive thoracoplasty is increasing to control primary and metastatic chest wall tumors as well as chest wall deformities.

The present status of thoracoplasty represent marked change regarding the frequency, indications, results, operative technique, complications, mortality and success rates.

As regards the frequency of thoracoplasty, it is decreasing in most

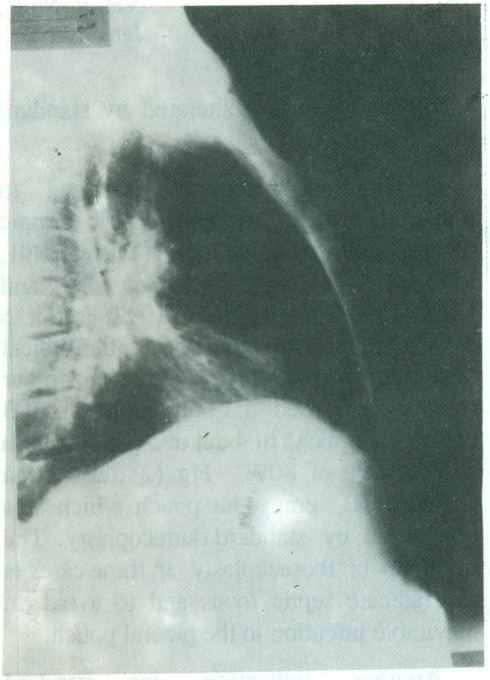

Fig.9: Lateral X-ray chest of the same patient.

Fig.10: lateral x-ray chest after sternectomy and reconstruction using bone cement.

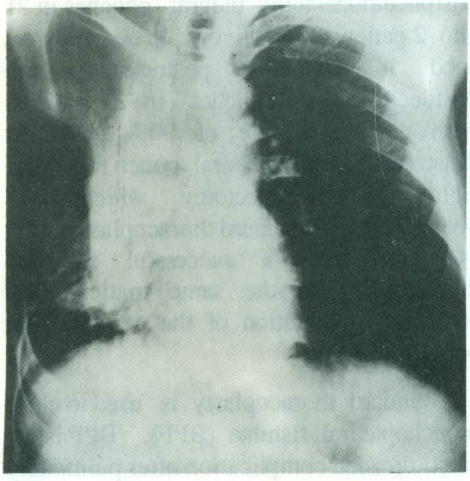

Fig.11: Standard thoracoplasty with resection of the first rib.

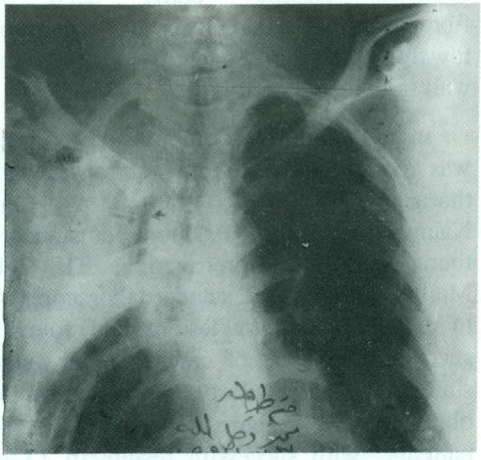

Fig. 12: Standard thoracoplasty with presecrvation of the first rib and a small pleural pouch.

recent publications. Peppas et al., (1993) studied 37 retrospective cases and concluded that thoracoplasty has become a rarity. Dai, (1992) and Stamatis et al., (1992) collected 108, and 21 cases in 14 and 30 years respectively. Also Massard et al., (1992) and Otsuka et al., (1992) collected 77 and 26 cases of thoracoplasty in 17 and 10 years respectively which all confirm that this operation became a rarity.

The rarity of thoracoplasty is also reflected in the number of patients studied in recent publications, 17 patients Balogh and Brigovacz, (1993), 16 patients Ohuchi et al.,(1993),12 patients Maddern et al., (1993), 3 patients Utley, (1993) and 1 patient Uchida et al. (1992). Our study included 59 patients collected in 24 years which also confirms the rarity of thoracoplasty.

There is marked change in the indications of thoracoplasty with tapering towards disease entity such as fibrocavernous tuberculosis and expansion towards other disease entity such as chest wall tumors and deformities.

In the past, fibrocavernous tuberculosis was the commonest indication for standard thoracoplasty. El Mallah, (1974), and Naumav et al., (1991) used standard thoracoplasty for fibrocavernous TB. El-Mallah, (1974) used standard thoracoplasty to close TB cavitary lesions and found it successful in 80% of cases. In our study, standard thoracoplasty was used to obliterate TB upper lobe cavities in 14 patients with successful results In 13 of them (92%). The success rate to control hemoptysis in our study was 96.3%. Fig. (I) shows a tomogram of TB right upper lobe cavity which was obliterated by standard thoracoplasty.

Standard thoracoplasty is used to obliterate specific and non specific chronic pleural empyema pouches (Yuste, 1991, Massard et al., 1992, Otsuka, 1992, and Utley, 1993). Narita et al., (1992) used it to close chronic empyema pouch after radical operations for oesophageal cancer. In our study it was used to obliterate chronic TB empyema pouch in 4 out of 5 patients with success rate of 80%. Fig. (2) illustrates a chronic TB empyema pouch which was obliterated by standard thoracoplasty. The rationale of thoracoplasty in these cases is to eradicate septic focus and to avoid an inevitable infection in the pleural pouch.

Another indication for standard thoracoplasty is to obliterate a postresection or postdecortication pleural pouch. Smolle Juttner et al., (1992) and Stamatis et al., (1992) used standard thoracoplasty to close postpneumonectomy pleural pouches in 21 and 2 patients respectively. In our study we used it to close postresection and postdecortication pouches in 20 patients with a success rate of 90%. Fig. (3) illustrates a large pleural pouch following right upper lobectomy which was obliterated by standard thoracoplasty . Fig. (4) represents a successful standard thoracoplasty to the same patient with complete obliteration of the postresection pouch.

Standard thoracoplasty is used to close bronchopleural fistulae (BPF). BPF is the most dreaded complication after pulmonary resection (El-Saeid et al., 1995). Utley, (1993) used it in 3 cases with BPF secondary to pneumonectomy, and Narita et

al., (1992), used it to close BPF but with the help of pectoralis major muscle flap. In our study we used it for 5 cases with a success rate of 100%, and pectoralis major mucle flap was used in only one patient (2.3%). Fig. (4) represents right bronchography with confirmation of BPF. The success rate of standard thoracoplasty is judged by obliteration of cavitary lesions, obliteration of postresection or postdecortication or chronic empyema pouches, closure of BPF, sputum conversion, control of hemoptysis and other symptoms and absence of postoperative deformity. Our results for both groups are summerized in table XII.

The indications for reconstructive thoracoplasty are expanding. Vasil et at., (1991) used it for correction of funnel chest deformity in 186 patients and Dai et al., (1992) used it for correction of scoliosis in 108 cases. Ultey, (1993) used it for a case of metastatic squamous cell carcinoma in the ribs originating from the left lung with good result.

In our study we used it for malignant rib tumors in 7 out of 15 cases (46.2%). Fig. no. (6) shows CT of recurrent chondrosarcoma of the ribs and fig. no. (7) shows CT of the same patient after radical excision of the ribs with reconstruction using bone cement.

Hamabuchi and Shimizu in 1991 used it for one patient after total sternectomy for chondrosarcoma with good result. In our study we used it for one patient for recurrent chondrosarcoma of the sternum using stainless steel mesh with good result.

Reconstructive thoracoplasty is used for control of acute mediastinitis and sternal infection (Maddern et al., 1993). In our study we used it for control of chronic non specific mediastinitis in one case. Fig. no. (8) is a CT of chronic mediastinitis, fig, no. (9) is a lateral chest x-ray for the same patient and fig. no. (10) is a lateral chest x-ray after resection and reconstruction using bone cement.

Reconstructive thoracoplasty is used for defects following excision of local recurrence following breast cancer (Tschantz et al., 1991, and Ohuchi et al., 1993).

Bender and Lucas, (1990), used it to close a shotgun chest wall defect by detaching the diaphragm peripherally and suturing it above the chest wall defect resulting in an intact chest cavity and an abdominal wall defect. The success rate of reconstructive thoracoplasty is judged by excision of chest wall tumor with safety margin, correction of chest wall deformity, adequate chest wall reconstruction and absence of chest wall deformity.

As regards the operative technique, little change has developed on the standard thoracoplasty such as preservation of the first rib which is preferred by some but not all surgeons as it decreases the postoperative deformity. Preservation of the first rib, subperiosteal resection of as few ribs as possible, epidural control of pain, and perioperative physiotherapy especially gymnastics, all decrease the postoperative deformity (Balogh and Brigovacz, 1993). In our study the first rib was removed in the first 24 cases (54.8%) and was preserved in the last 20 cases (45.2%). Fig. no. (11) shows right thoracoplasty with resection of the first rib.

Larger segments of the resected ribs are left anteriorly to minimize deformity while larger segments are resected posteriorly to increase, the achieved collapse.

For reconstructive thoracoplasty, the benign tumors were resected with a 2 cm safety margin while the malignant lesions were resected with a 4 cm safety margin. Different autogenous and synthetic materials were used for closure of the resultant defects.

The autogenous materials used for reconstructive thoracoplasty are many. Autogenous bone was used in internal thoracoplasty and obviated the need for artificial graft (Shufflebarger, 1994).

Myocutaneous flaps are commonly used to close large chest wall defects. They have the advantage of resisting infection. lattismus dorsi, serratus anterior, and pectoralis major either alone or in combination were used in 30 cases of chronic pleural empyema (Yuste et al., 1991). Nomori et al., (1992) used pectoral myoplasty for single stage closure of post pneumonectomy empyema with good results. For closure of chest wall defects after local recurrrence of breast cancer, 1-2 rectus abdomini, pectoralis major, greater omentum, or breast flap were used when the defects were too large with 79% 3 year survival (Tschantz et al., 1991, and Ohuchi et al., 1993). Maddern et al., (1993) used omental and muscle flap for closure of the defect after sternotomy for mediastinitis in 19 patients with good results. In our study, we used autogenous grafts in 8 patients (52.8%). These grafts included fascia lata graft in 3 patients (19.8%), bone graft in 3 patients (19.8%), and myocutaneous graft in 2 patients (13.2%).

Polyethylene hard mesh (heavy marlex mesh) was used after excision of the whole sternum for malignant chondrosarcoma (Hamabuchi and Shimizu 1991). Metal plate and nitinol clips were used for internal thoracoplasty for stabilization of complicated cases of infundibular chest deformity (Vasil et al., 1991). Mersilene mesh was used for big chest wall defects as it is strong, stable , flexible, inert and integrated in the body's own tissues (Largiader, 1991). Artificial rib was used to close the defect following excision of metastatic squamous cell carcinoma. This rib was formed of two layers of Dacron fabric which were laid together, stitched to the rib with nylon thread, and the resulting cavity was packed with a filler made of combination hydroxyapatite (Uchida et al., 1992).

In our study we used synthetic material in 7 patients (47%). These included prolene mesh in 4 patients (27.2%), bone cement in 2 patients (13.2%), and stainless steel mesh in 1 patient (6.6%).

As regards the complications of standard thoracoplasty, Strelis and Lenskaia in 1994 examined 42 thoracoplasty patients and found that the viscosity-induced resistance to respiration resulted basically from inflammation of the tracheobronchial tree and bronchospasm. Brander et al., 1993 found a scoliotic angle of 4-53 degrees and found the median values of pulmonary functions as, 49% for FEVI (forced expiratory volume in the first second), 54% for VC (Vital capacity), and 62% for TLC (total lung capacity). In our study the major, complications were a significant scoliosis in one patient (2.3%), and persistant pleural pouch in one patient (2.3%) corrected by pectoral major muscle flap. Fig. no. (12) illustrates a small pleural pouch after right thoracoplasty, which

closes spontaneously and is not considered as a complication.

For the reconstructive group, Samsygin et al., 1990, found in 136 children that suppurative complications of thoracoplasty in heriditary syndromes of systemic connective tissue dyshistogenesis such as Marfan syndrome were 33.3% as compared to 15% in isolated developmental chest wall defects due to serious immunological deviations. Reconstructive thoracoplasty was done to correct scoliosis in 108 patients with no effect on the pulmonary function (Dai, 1992). Maddern et al., (1993), and Shufflebarger et al., (1994), in their series for correction of chest wall defects and deformities respectively found no complication. In our study we have minor complications of wound infection, and minimal chest wall deformity in one patient for each (6.6 %).

The mortality rates were different in both groups of thoracoplasty. For the standard thoracoplasty group, the mortality rate was 56% in 7 patients done by Friedrich in 1907 and 1 1% in 119 patients done by Alexander (Alexander, 1925), 66% in 3 patients with BPF (Eckersberger, 1990), 11.1% in 27 patients with chronic pleural empyema (Stamatis et al., 1992), 15% in 10 patients (Massard et al., 1992), and 10.8 % 37 patients for complications of lung cancer resection (Peppas et al., 1993). The mortality rate in our series was 6.9% in 44 patients with different etiologies which is lower than those of other authors.

In the reconstrutive group there was no mortality in Yuste series, 1991 (30 patients), Smolle-Juttner series, 1992 (7 patients), and Shufflebarger series, (1994) (7 patients). Also we have no mortality in this group in our series.

Conclusion

1-Although thoracoplasty became a rare operation, it still has strong indications.

2-Standard thoracoplasty decreased markedly due to better medical treatment of tuberculosis and improved anaesthetic and surgical techniques.

3-Reconstructive thoracoplasty is increasing with use of a large variety of synthetic and autogenous grafts.

4-The complications, and operative mortality are higher in the standard group and the success rate is better in the reconstructive group.

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Tracheobronchial Injuries : Presentation and Management of 52 Patients

Abstract

Tracheobronchial injury is one of the less common injuries in chest trauma. This report concerns 52 patients with injuries of the tracheobronchial tree. There were 29 males (55.8%) and 23 were females (44.2%). The majority of injuries were due to blunt chest trauma; forty nine (94.2%) and only three (5.8%) were due to penetrating trauma. Thirty seven (71.2%) patients presented early, within hours after trauma and fifteen (28.8%) patients presented late after trauma. The clinical findings in 37 patients presented early were ; severe respiratory distress in 31 patients, massive subcutaneous emphysema in 31, cervical emphysema in 3, pneumothorax in 26, cyanosis in 8, hemoptysis in 6 and massive air leak form the intercostal tube in 26 patients. Patients presented late had signs and symptoms of recurrent chest infections and lung collapse. Radiological findings included; pneumothorax in 26, pneumomediastinum in 31 and subcutaneous emphysema in 31 patients. Bronchoscopy was the important diagnostic tool. Tracheobronchial injury is a potentially lethal entity in chest trauma. Once it is suspected it should be managed immediately and in a proper way. Meticulous co-ordination between the surgeon and the anasthiologist is of utmost importance. The surgical management is tailored to every patient depending on the site , the length of the tear and in late cases, the condition of the related lung. Excellent results could be achieved with early detection and proper reconstruction of the airway. Failure to diagnose this injury early results in delayed presentation with lung suppuration and surgical resection of the affected lobe or lung.

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INTRODUCTION

The possibility of tracheobronchial rupture following blunt trauma to the chest has been recognized for many years. Griffith, in 1949, reported the first successful correction of traumatic bronchial stenosis eight months following blunt chest trauma (1).

The true incidence of tracheobronchial injuries is unknown, or more precisely, is difficult to establish because many patients sustaining trauma severe enough to cause such injuries die before reaching the hospital(2). In a review of 1178 postmortem reports of patients dying of trauma, Bertebsen and Howitz reported that only 33 (2.8%) had tracheobronchial injuries (3). Although rare, this injury appears to be on the increase , associated with the increasing number of high speed traffic accidents and improved ambulance services (4).

The estimated mortality of patients with such injuries is 30%, but 90% of patients reaching the hospital alive can anticipate full recovery (5). Successful outcome depends on timely, accurate assessment of the injury and immediate appropriate surgical intervention.

We present our experience in the diagnosis and management of 52 patients with tracheobronchial injuries in the Cardiothoracic Surgery Department; Faculty of Medicine, Mansoura University.

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Aim of the Work

The purpose of this study is to review our experience with tracheobronchial injuries , to elucidate the diagnostic and therapeutic problems and to emphasize the importance of early diagnosis and management to avoid the possible sequelae of late presentation.

Patients and Methods

This study includes 52 patients; 29 were males (55.8%) and 23 were females (44.2%). There age ranged from 2.5 years to 48 years, with a mean of 12±1.4 years (SEM). Fourty nine (94.2%) of the injuries were due to blunt chest trauma and only three (5.8%) were due to penetrating trauma (Figure 1). Thirty seven (71.2%) patients presented early, within hours after trauma, and fifteen (28.8%) patients presented late after trauma. The time elapsed between the history of chest trauma and presentation in late cases was known in 14 out of 15 patients. It ranged from one month to 12 years, with a mean of 25.5 ±9.4 months (SEM).

Clinical findings : Figure 2 shows the clinical findings in 37 patients presented early after trauma. Associated injuries were present in 10 patients; rib fracture in 6, fracture humorous in one, scalp hematoma and skull fissure fracture in 2 patients and one patient with longitudinal esophageal tear. Patients presented late showed signs and symptoms of recurrent chest infections, lung collapse and/or bronchiectasis. One patient presented with hemopneumothorax. Although history of blunt trauma in the past was retrieved in all delayed cases, only two patients had symptoms to seek medical attention, and treated by intercostal tube for right pneumothorax.

Patient management : All patients, who presented early were managed on an emergency basis. Erect plain x-ray chest films were done for all cases. One or two intercostal tubes were inserted to drain air and blood from the pleural space and to relieve respiratory distress. Continuous and massive air leak from chest tube were highly suspicious signs of tracheobronchial injuries. Immediate resuscitative measures went hand in hand, and the patients were then taken to the operating room. Rigid and /or flexible bronchoscopy were done to visualize the tracheobronchial tree and to assess the site and the extent of the tear. Rigid bronchoscope failed to diagnose upper lobar bronchial injuries. Three patients presented early with right pneumotharax and surgical emphysema. After intercostal tube insertion, the lung fully expanded and air leak stopped. Plain x-ray showed residual right apical shadow. Bronchogram showed amputated right upper lobe bronchus.

In patients who presented late (15 patients), there was enpugh time to investigate them radiologically. This showed radiological manifestation of consolidation collapse of one lobe or the whole lung. Rigid and flexible bronchoscopic examination showed the site of bronchial stenosis or obstruction. Bronchogram was done in 11 out of 15 late patients and showed amputated main or lobar bronchus. CT scan of the chest was done in 4 patients. Figure 3, 4, 5, 6, 7 show plain x-rays and bronchograms of some patients.

Operative strategy : once the patient with chest trauma was received in the emergency room and major airway injury was suspected, immediate intercostal tube was inserted when needed and the patient was transferred to the operating room, and bronchoscopy was done; usually rigid in children and flexible in adults, under general anesthesia. When the tear was around one third of the circumference of the airway,it was considered small and managed conservatively. Tracheostomy was performed when the surgical emphysema was extensive and progressive with no pneumothorax.When the tear was long or one main stem bronchus was avulsed, immediate thoracotomy was done. Right posterolateral thoracotomy was used for tracheal tear, right main stem bronchus injuries, complex injuries, and for left main stem bronchial injury less than 2 cm distal to the carina (two patients in our series). Left posterolateral thoracotomy was done for left main bronchial injuries more than 2 cm distal to the carina. Anesthetic management of these cases was very difficult. A double lumen endotracheal tube was inserted in adult patient. In children, a simple endotracheal tube was used. After thoracotomy the surgeon handled it in a sterile way and guided to the healthy bronchus, and the tear is controlled digitally to prevent anesthetic gas leak. In complex injuries, we used shunt ventilation using a sterile endotracheal tube passed through the surgical field and guided to ventilate the separated lung through its avulsed bronchus, while the endotracheal tube was guided to the contralateral lung. After simple debridement of the airway with attention to remove denuded cartilage, the defect was repaired with 3/0 or 4/0 interrupted sutures. Figure 8 shows the operative management of the 37 cases presented immediately after trauma.

In patients who presented late, a thorough preoperative workup was conducted to assess the condition of the collapsed lung. Rigid and flexible bronchoscopic examination, bronchogram and CT scan of the chest were done. When the collapsed lobe or lung was found bronchiectatic or fibrotic. resection was done. When the lobe or the lung was found, intraoperatively, healthy and the bronchus was not malichic, the stenosed part was resected and the bronchus was reanastomosed. One patient presented late with traumatic tracheoesophageal fistula and this case was repaired through right posterolateral thoracotomy using pleural flap interposed between the trachea and esophagus, but this patient died two weeks postoperatively because of failure of the suture line and severe mediastinitis. Figure 9 shows the operative procedures in the 15 cases who presented late after trauma.

Results

Figure 10 shows the radiological findings in 37 patients who presented immediately after trauma. Table 1 shows the description of the tracheobronchial injuries in the 37 patients who presented immediately following trauma, based on preoperative bronchoscopic and intraoperative findings. Table 2 shows the description of tracheobronchial injuries in the 15 patients who presented late after trauma, also based on preoperative bronchoscopic, bronchographic and intraoperative findings .

Mortality : The overall mortality rate was 15.4% (8 in 52 patients). The cause of death was:

Table (1): Description of the tracheobronchial injuries in 37 patients presented immediately after trauma, based on preoperative bronchoscopy and intraoperative findings.

Injury	Number of patients
Tracheal injuries	
* Longitudinal tear in membranous part of the trachea	5
* Small transverse tear in membranous part of the trachea	3
* Complete transection of the cervical tracheal	3
Main stem bronchial injuries	
* Longitudinal tear of the R.M.S.B.	5
* Avulsed R.M.S.B.	3
* Avulsed L.M.S.B.	6
Lobar bronchial injuries	
* Avulsed R.U.L.B.	4
Complex injuries	
* Y-shaped tear involving the lower trachea and extending to R.M.S.B. & L.M.S.B.	2
* Longitudinal tear involving the lower trachea and extending to R.M.S.B.	4
* Longitudinal tear involving the lower trachea and extending to L.M.S.B.	1
* Longitudinal tear involving trachea and avulsion of R.M.S.B.	1
Total	37

Legend: R.M.S.B. = Right main stem bronchus.
L.M.S.B. = Left main stem bronchus.
R.U.L.B. = Right upper lobe bronchus.

Table (2): Description of the tracheobronchial injuries in 15 patients presented late after trauma, based on preoperative and intraoperative findings.

Injury	Number of patients
Longitudinal tear in the trachea	1
Amputated stenosed right main stem bronchus	6
Amputated stenosed left main stem bronchus	7
Amputated stenosed left lower lobe bronchus	1
Total	15

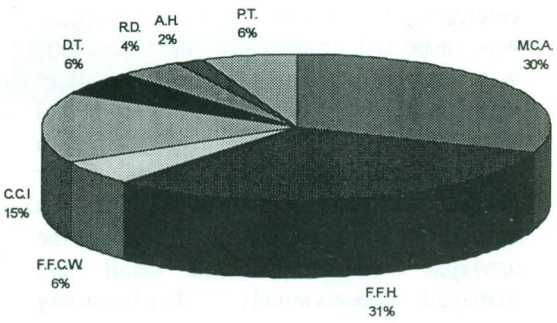

Figure 1:Etiology of Tracheobronchial Injuries in 52 Patients.

Legend: M.C.A. (N=16) = Motor car accident; F.F.H. (N =16) Fall from height; F.F.C.W. (N=3) = Fall from a cart whell; C.C.I. (N=8) = Cruching chest injury; D.T. (N=3) = Diect trauma to the neck; R.D. (N=2) = Rolling down over a stair; A.H. (N=1) = Accidental hanging; P.T. (N=3) = Penetrating trauma.

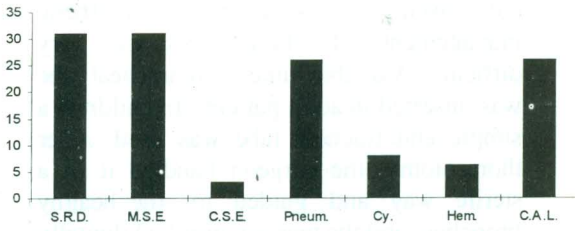

Figure 2:Clinical Manifestations in 37 Patients Presented Immediately After Trauma

Legend: S.R.D. (N=31) = Severe respiratory distress; M.S.E. (N =31) Massive subcutaneous emphysema; C.S.E. (N=3) = Cervical subcutaneous emphysema; Pneum. (N=26) = Pneumothorax; Cy. (N=8) Cyanosis; Hem. (N=6) = Hemoptysis; C.A.L. (N=26) = Continuous and massive air leak fom the intercostal tube.

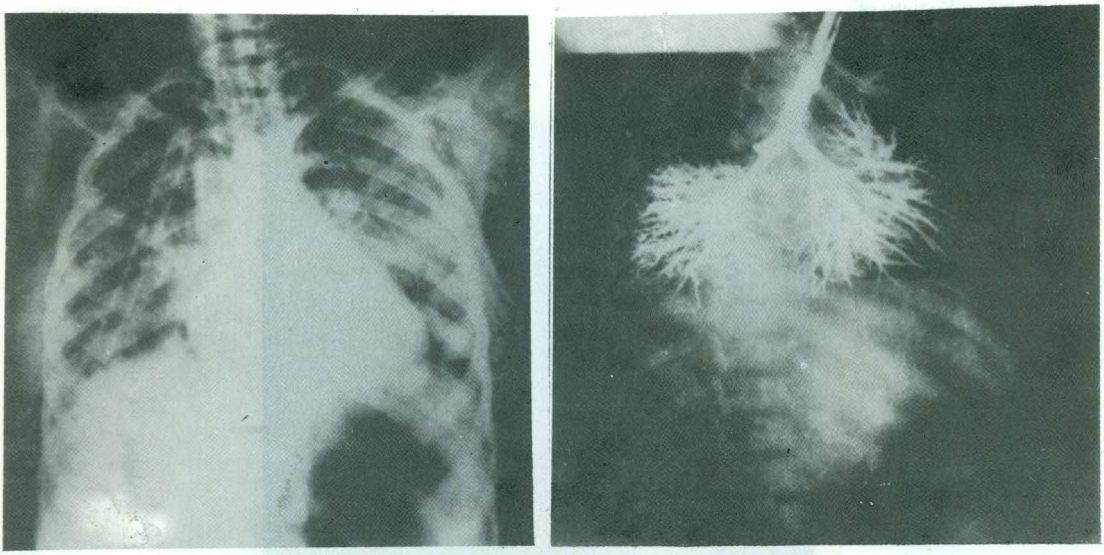

Figure 3: Bilateral pneumothorax from crushing chest injury. Rigid bronchoscopy was free. Bronchography showed amputation of right upper lobe bronchus.

Figure 4: Fallen lung sign on the left side. Note the superior margin of the collapsed left lung falls below the level of the hilum.

2 from hemorrhagic shock.

1 from blockage of the endotracheal tube left for suction by inspissated blood clot.

1 from failure of suture line and severe mediastinitis.

4 from perioperative cardiac arrest and cerebral hypoxia.

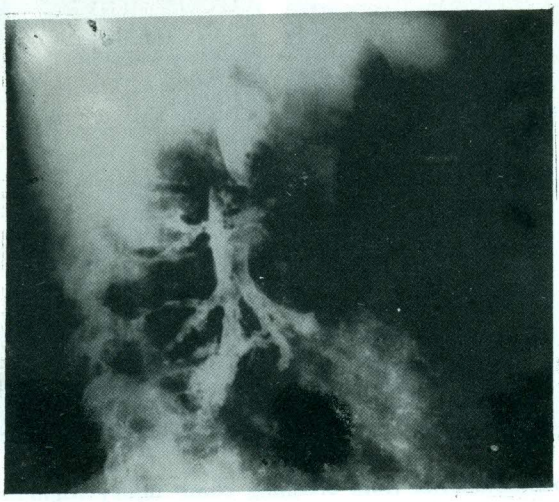

Figure 5: Stenosis of right main bronchus and bronchiectasis of right lung with history of motor car accident since 12 years.

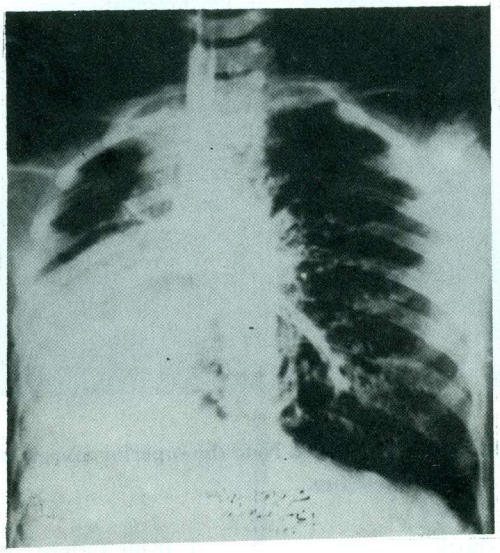

Figure 6: Complete obstruction of the main bronchus. History of motor car accident since 3 years. Fibrosis of the three lobar bronchi with shift of the mediatinum to the right.

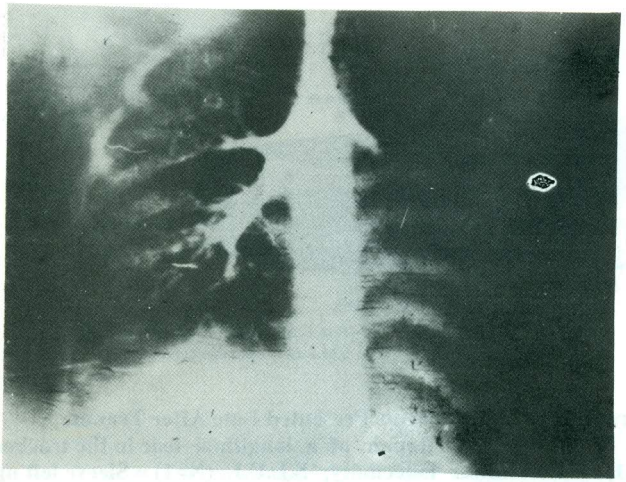

Figure 7: Stenosis of left main bronchus with excessive granulation fllowing sture of complete rupture by 2-0 slik suture. Failure of repeated dilatation. Left penumonctomy.

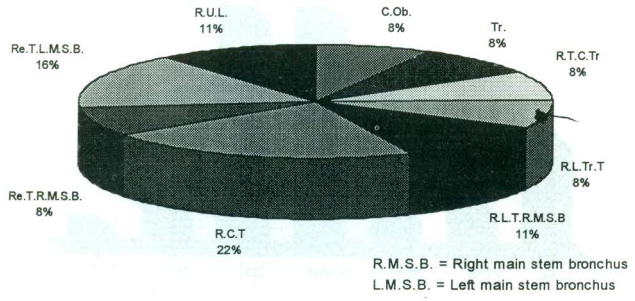

Figure 8: Surgical Management in 37 Patients Presented Immediately After Trauma
Legend:C.Ob (N=3) = Conservative observation; Tr. (N=3) = Tracheostomy; R.T.C. Tr. (N=3) = Repair of transected cervical trachea; R.L.Tr.T. (N=3) = Repair of a longitudinal tracheal tear; R.L.T.R.M.S.B. (N=4) = Repair of a longitudinal tear in the R.M.S.B.; R.C.T. (N=8) = Repair of a complex tear; Re. T.R.M.S.B. (N=3) = Reanastomosis of transected R.M.S.B.; Re.T.L.M.S.B. (N=6) = Reanastomosis of transected L.M.S.B.; R.U.L. (N=4) = Right upper lobectomy for amputated right upper lobe bronchus.

Complications :

1- Bronchial suture line stenosis. This complication occurred in 8 patients. The surgical repair in these 8 patients was done with braided absorbable suture or silk suture. All patients responded to repeated bronchoscopic excision of the granulation tissue and bronchial dilatation, except one patient, in whom silk suture was used for repair, pneumonectomy was done.

2- Post-pneumectomy space empyema in one patient.

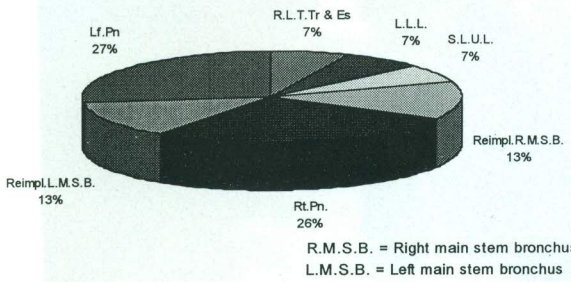

Figure 9: Surgical Procedures in 15 Patients Presented Late After Trauma
Legend: R.L.T. Tr. & Es. (N=1) = Repair of a longitinal tear in the trachea and esphagus; L.L.L. (N=1) = Left lower lobectomy; S.L.U.L. (N=1) = Sleeve left upper lobectomy; Reimpl. R.M.S.B. (N=2) = Reimplantation of R.M.S.B.: Rt. Pn. (N=4) = Right pnumonectomy: Reimpl. L.M.S.B. (N=2) Reimplantation of L.M.S.B.; Lf Pn. (N=4) Left pnumopnectomy.

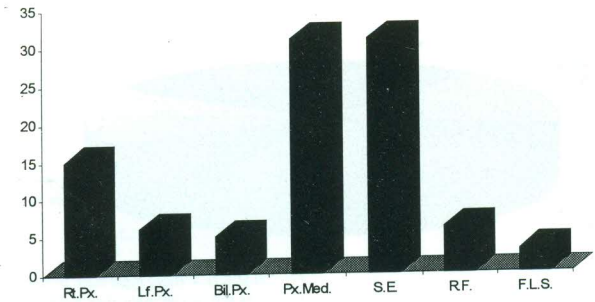

Figure 10: Radiological Findings in 37 Cases Presented Immediately After Trauma
Legend:RT. Px. (N=15) = Right pneumothorax; Lt. Px (N=6) Left pneumothorax; Bil. Px. (N=5) = Bilateral pneumothorax; Px. Med. (N=31) = Pneumomediastinum; S.E. (N=31) = Subectaneous emphysema; R.F. (N=6) = Rib fracture; F.L.S. (N=3) Fallen lung sign.

Discussion

Rupture of the major airways is a relatively rare injury. Bertelsen and Howitz (3) found in a review of 1178 autopsy reports of blunt trauma victims only 33 cases of rupture of major airway. As a result of the increased mechanization and speed of travel, there has been a corresponding increase in the volume and severity of blunt trauma. The increased reporting of this injury is attributable both to improvements in the care of trauma victims (Pre-hospital and in hospital) and an increased use of bronchoscopy in patients with blunt chest trauma (6). Nevertheless, the true incidence of such injuries is difficult to be determined precisely as an appreciable number either die before reaching a hospital or pass the acute stage with minimal clinical manifestation or missed diagnosis by inexperienced surgeon (7) .

Tracheobronchial injuries is one of the most serious intrathoracic injuries resulting from closed chest trauma. It is usually a consequence of deceleration, it could also be caused by crushing or twisting injuries (8). In our series, motor car accident and fall from a height were the commonest causes (32 patients), followed by crushing chest injuries (8 patients). Of particular interest is that we have three patient with fall from a cart wheel (only 15 meter height) with tracheobronchial rupture. Penetrating injuries are usually located in the neck (9). In this series, we have only three cases caused by penetrating injuries and all were limited to the cervical trachea, and there is no single case of penetrating trauma to the intrathoracic trachea or to bronchi.

The pathogenesis of tracherbronchial rupture in blunt trauma can be divided into three mechanisms which may act singly or in combination. First, a decrease in the anteroposterior diameter of the thorax occurs, with widening of the transverse diameter. The lungs remain in contact with the chest wall and thus are pulled apart, creating traction at the carina, if this traction exceeds the elasticity of the tracheobronchial tree, rupture will occur. Second, when the trachea and major bronchi are crushed between the sternum and vertebral column with the glottis closed, the sudden increase in intrabronchial pressure produced is greatest in the larger bronchi and rupture may occur Third, rapid deceleration may result in shearing forces at the area of fixation, mainly the carina (2).

Most of these injuries occur within 2.5 cm from the carina either in the trachea or the main bronchi (10). This is true in our series, we had 41 patients out of 52 (78.8%) with tracheobronchial injuries around the area of the carina. Rupture of lobar bronchi is rare, we have only 5 cases (9.6%). The rare incidence of lobar and segmental bronchial injuries had been reported by several authors (11,12). The rupture may be transverse between the cartilaginous rings, longitudinal along the membranous part of the airways, or complex with a combination of both transverse rupture and longitudinal or multiple ruptures. Symbas et al.(13) reviewed a total of 189 in the literature found that transverse rupture was the most common (74%), followed by longitudinal rupture (18%) and lastly complex rupture (8%). We have 49 patients with blunt tracheobronchial rupture, 30 (61.2%) had transverse rupture, 11 (22.4%) had longitudinal rupture, and 8 (16.3%) had complex rupture. Of particular importance is to mention that we had no isolated longitudinal tear of left main bronchus,it is usually an extension to a longitudinal tracheal tear.

There is some controversy about the relative incidence of bronchial rupture in right and left main bronchi. Review of the old literature shows bronchial injuries equally divided between right and left (11) . However, Battersby and kilman (11) and other recent reports (14) showed the right-sided predominance. In our experience, we have 27 patients with bronchial rupture, 14 right and 13 left main bronchial rupture. All cases of left bronchial rupture were transverse (avulsion) while on the right side there were 9 avulsions and 5 longitudinal tears.

Signs and symptoms of penetrating injuries of the cervical trachea are clearly evident with cervical cut and air with blood are seen frothing from the cut trachea.

Signs and symptoms of tracheobronchial rupture from blunt chest trauma include respiratory distress, subcutaneous emphysema, pneumothorax and mild hemoptysis. Continuous and massive air leak through an inserted intercostal tube with failure of the lung to expand are the major diagnostic clues (12,15). There is often increased respiratory distress when suction is applied to the chest tube, since most of inspired air will be sucked from the tube. Pneumomediastium and cervical emphysema are the most sensitive radiological findings in major airway rupture. A very pathognomonic radiological sign from bronchial avulsion is the "fallen lung" sign, the superior margin of the collapsed lung fall below the level of the hilum (16). This "fallen lung sign was found in three patients in our series. Figure 4 shows an x-ray with left fallen lung sign. Inspite of this dramatic presentation of patients with blunt tracheobronchial rupture, some patients pass the initial stage with very minimal symptoms. Hood and Sloan in 1959 reported that 41% of bronchial ruptures were diagnosed more than 30 days after injury i.e. delayed presentation (11). Fifteen patients (28.8%) in our series presented late after trauma. All of them reported a definite history of blunt chest trauma, but only two patients stated that they had had intercostal tube drainage for pneumothorax. The late presentation occurs when the bronchial rupture does not communicate with the pleural space, and the bronchial continuity is preserved by peribronchial tissue. The peribronchial tissue and the pretracheal fascia may be stout enough to maintain an airway and the patient may be only minimally symptomatizing. Later on the ruptured bronchus heals by granulation tissue resulting in bronchial stenosis.

The patients presented with lung collapse, recurrent chest infections and bronchiectasis (7). Although, there are some studies reporting associated injuries in 50% of patients with blunt tracheobronchial rupture, we had only 10 patients (15.4%). The reported associated injuries in the literature include, rib fracture, aortic, great vessels, pulmonary artery damage, diaphragmatic rupture, hepatic injury and skeletal fracture (15,16,17,18). Bronchoscopy remains the most important and the gold standard technique for diagnosis of tracheobronchial rupture. It should be done in every patient with suspected rupture of the airways to prevent the mortality and morbidity associated with missing these injuries. The bronchoscopy should be done in a fully equipped operating theater to carry out the repair of the injury, if needed (13). Bronchoscopic examination, apart from confirming the injury, it helps to identify the site and the extent of it which is essential in deciding the treatment. It was done in all patients in this series, rigid bronchoscope was used in children, while rigid and flexible fiberoptic bronchoscope were done in adults. The only disadvantage of rigid bronchoscope is that it could miss the diagnosis of upper lobes bronchial injuries. This occurred in three pediatric patients with right upper lobe bronchial rupture, bronchoscopic examination were free and the lung expanded, air leak ceased by intercostal tube. Two to three weeks later, clinical and radiological evidence of right upper lobe

collapse was present, bronchography was done and the diagnosis was established. Flexible fiberoptic bronchoscopy had 100% diagnostic accuracy in our patients, bronchocopies were done by a cardiothoracic surgeon. Baumgartner et al.(14) addressed the issue of the bronchoscopist in diagnosis of airway injuries in nine patients and concluded that the cardiothoracic surgeon is the most accurate in detecting airway injuries during bronchoscopy in comparison with the trauma surgeon, pulmonologist and the surgical residents. The bronchoscopic findings of tracheobronchial injuries include abrupt ending of the bronchial mucosa, heaped up mucosa, curled fragment of cartilage and bleeding (14,19) .

Bronchography was used to diagnose patients presented late after the accident. It showed bronchial amputation with or without distal bronchiectatic changes.

After diagnosis of a tracheobronchial rupture early following trauma, thoracotomy is required except in two situations. One, if the injury is in the cervical trachea which could be repaired by a cervical approach. We have three patients in this series with completely transected cervical trachea have been repaired through a transverse cervical incision. Second, in those cases in which less than one third of the circumference of the airway is disrupted and there is no pneumothorax or the lung fully expanded with chest tube. In this series we have 6 patients in this category, 5 small tracheal and 1 small right main bronchial tears. All of these patients had pneumomediastinum and subcutaneous emphysema, none had pneumothorax.Three of the small tracheal tears had been managed conservatively and the other two, together with the small right bronchial tear had been managed by tracheostomy to eleminate the effect of glottic closure and thus decrease the intraluminal pressure in the trachea and consequently reduce the escape of air to the peritracheal tissue. We did not use tracheostomy routinely.The routine use of tracheostomy in the management of these injuries is controversal. It has been recommended routinely by Ursche (20) .

On the other hand, Lawhome consider it an unnecessary procedure (21).

Surgical repair, of the majority of tracheobronchial injuries could be made using conventional surgical techniques in the majority of cases. We used right posterolateral thoracotomy in the fourth intercostal space for tracheal injuries, right main stem bronchial injuries and left main stem bronchial injuries within 2 cm distal to the carina. The mediastinal pleura was opened and the azygos arch was doubly ligated and cut to improve the exposure. Injuries of left main stem bronchus more than 2 cm distal to the carina were approached via left fourth space posterolateral thoracotomy. We avoid the use of braided absorbable and silk sutures because it had a high incidence of suture granuloma and stenosis, in early cases of this series. We have been using 3/0 or 4/0 polypropylene suture with no single case of suture line complication. Our view of using monofilament nonabsorbable suture for repair of airway injuries is strongly supported by many reports (7,13,22,23,24). Only few reports favour the use of absorbable materials (16,25) .

Throughout the procedure it is of utmost importance to have expert cooperation between the anesthetist and the surgeon as

regards both to the positioning of the tube and the use of small tidal volumes at higher rates to minimize the air leak from the site of injury. The use of jet ventilation is optimal for these patients as reported recently (27). Shunt ventilation through a sterile side tube to the amputated lung passed through the operative field was used in our eight patients with complex injuries. The endotracheal tube is passed to the other lung guided by the surgeon. By that way the two lungs are ventilated and the patient's oxygen saturation was kept around 95% as measured by pulse oxymetery.

Symbas et al. (13) reported a series of 6 patients with complex tracheobronchial injuries with the use of cardiopulmonary bypass during repair in one case, and cardiopulmonary bypass standby in another one case. In our series we have 8 patients with such injuries, we felt we should have used the cardiopulmonary bypass in one patient. This patient died intraoperatively from hypoxia.

In cases presented and diagnosed late after trauma (15 in our series), we have studied the affected lung to determine the degree of damage. Bronchoscopy and bronchography were used. In the last few cases CT was used as an alternative to bronchography because of the unavailability of the dye. Very recently, MRI with its multiplanar capabilities, has been used for defining the location and extent of the injury (26). However, those investigations may be misleading and the final decision on treatment was made only at operation. The surgical treatment ranged from resection of the stenosed bronchial segment and reimplantation of the lung to sleeve lobar resection to pneumonectomy in cases with bronchiectasis of the lung.

Regarding our results, we have 37 patients presented immediately after the trauma, 7 died postoperatively, 18.9% mortality. The estimated mortality of that type of injury is 30%, and expected mortality in patients reaching the hospital alive is about 15%. In patients with delayed presentation we have only one mortality in 15 patients (6.7%). Thus the overall mortality rate in this series was 15.4% (8 deaths in 52 patients).

The most frequent complication is suture line granuloma and bronchial stenosis. In our experience, this complication occurred with the use of braided absorbable suture or Silk suture. All cases responded to repeated bronchoscopic excision and dilation except one patient for whom pneumectomy was done.

In conclusion, tracheobronchial injuries is a rare entity of trauma that has increased in frequency largely because of modern life style trends and marked improvement of ambulance transport and emergency hospital care of trauma patients. Early diagnosis presents an opportunity for prompt and definitive life-saving treatment. Bronchoscopy, which is the golden standard of the diagnosis, should be done immediately in any patient with blunt chest trauma presented with dyspnea, subcutaneous emphysema, pneumomediastinum and pneumothorax. Bronchoscopic examination should be done by an experienced cardiothoracic surgeon in a well-equipped theature under general

anesthesia. Depending on the nature of the airway injury, surgical management is tailored to every case. Meticulous coordination with anesthesia is mandatory to ensure a successful outcome. We favor the use of synthetic nonabsorbable monofilament suture material, particularly polypropylene. Small tears could be managed conservatively with or without tracheostomy. Excellent results could be achieved with early detection and proper reconstruction of tracheobronchial injuries even in cases with complex tears. It should be kept in mind that some cases surprisingly enough, could have too few signs and symptoms to be diagnosed early. So, the clinical presentation could be deceptive, diagnosis therefore may be delayed manifestations of the cicatricial stricture occur. In these cases with late presentation the diagnosis is made by recalling the history of chest trauma, clinical finding, bronchoscopy and bronchography. Depending on the degree of damage of the lung, treatment ranges from resection of the stenosed bronchus, lobecotomy or pneumonectomy.

Penetrating injuries are usually located in the cervical trachea. The diagnosis is easily made and it should be managed by exploration and primary repair through a transverse cervical incision.

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Revival of Malignant Mesothelioma.

Abstract

Thirty nine patients (pts) with malignant mesothelloma (MM.) of the pleura have been diagnosed and managed between 1980 and 1996 at Ain Shams University hospitals.We have recorded an increasing incidence of MM in recent years. Thirty eight pts were men all of them had diffuse malignant mesothelioma (DMM) and only one woman who had localised mesothelloma. Age ranged between 21 to 77 years mean 52 ys. Three pts (7%) had a history' of exposure to asbestos. The lesions were in the right hemithorax in 15 (38%)) cases and in the left hemithorax in 24 pts (62%). Fifteen cases (35%) were diagnosed by thoracocentesis and cytology,six cases (14%) were diagnosed by pleural biopsy using Abram's needle. Two cases (4%) were diagnosed by minithoracotomy while 16 cases (37%) were diagnosed by open surgical biopsy. Five pts (12%) received chemotherapy, and three pts (7%) had radiotherapy.Eleven pts (28%) appeared to have early disease,and therefore underwent thoracotomy; six pts (15%) had complete resection of all gross disease by pleuropneumonectomy, three pts, whose pulmonary functions did not permit lung resection had pleurectomy, one pt had tumour resection and lobectomy for localised mesothelioma and two cases deemed unresectable. Following surgery, six pts (54%) had syptomatic benifit that lasted no more than 3 months. Two pts (18%) developed bronchopleural fistula, four pts (36%) had recurrent effusion, and one pt (9%) had recurrence after 28 days. Early surgical mortality was 18% (two pts). Nine pts (23%) had palliative procedures like intercostal tubes and pleurodesis. Twelve pts (30%) had no interference. Chemo and radiotherapy had no correlation with the course of the disease and all cases treated by them showed no or little improvement. In conclusion, while localised mesothelloma is a surgically curable disease, diffuse malignant mesothelloma is a multicentric process and should be considered as unresectable disease. We should apply the most simple surgical procedure for diagnosis and palliation.

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INTRODUCTION

Malignant mesothelioma (MM is a relatively rare tumor that arises most commonly from the pleura. It has assumed increasing importance in recent years, mainly because of its rising incidence and its etiologic association with asbestos exposure (1). Pleural mesotheliomas occur in two forms, the diffuse type, which is always malignant, microscopically it exhibits epithelial-like as well as sarcomatous components.

This type often kills the patient within 12 months whatever the treatment is (2). The other form is a localised or solitary tumor which is microscopically, usually made up of fibrous tissue of variable cellularity, it may be benign or malignant.

Our report describes thirty nine patients with MM of the pleura.

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Aim of the work

Assessment of the best strategy for the management of MM. We compared different treatment strategies.

Patients and Methods

The records of all patients with DMM who have been diagnosed and treated at the department of cardiothoracic surgery of Ain Shams University from January 1980 through December 1996 were reviewed. Only the cases with adequate clinical and histopathologic documentation were included in this study. All cases have been subjected to clinical and occupational histories, physical and radiological findings and the course of the disease in all patients was reviewed.

Fifteen cases (35%) were diagnosed by thoracentesis and cytology, six cases (14%) were diagnosed by pleural biopsy using Abram's needle. Two cases (4%) were diagnosed by minithoracotomy, while 16 cases (37%) were diagnosed by open surgical biopsy, two of them had thoracotomy on the assumption of treating chronic empyema that were diagnosed later as DMM

Five patients (12%) received chemotherapy, and three patients (7%) received radiotherapy. Eleven patients (28%) appeared to have early disease and therefore underwent thoracotomy. Six patients had complete resection of all gross disease by pleuropneumonectomy, three patients whose pulmonary functions did not permit lung resection had pleurectomy. One patient had tumor resection and lobectomy for localised mesothelloma, and two cases deemed unresectable. Nine patients (23%) had palliative procedures like intercostal tubes and pleurodesis. Twelve patients (30%) had no interference.

Results

Thirty eight patients were men, all of them had DMM. We had only one woman who had a localised mesothelioma. Ages ranged from 21 to 77 years with mean age of 52 years.

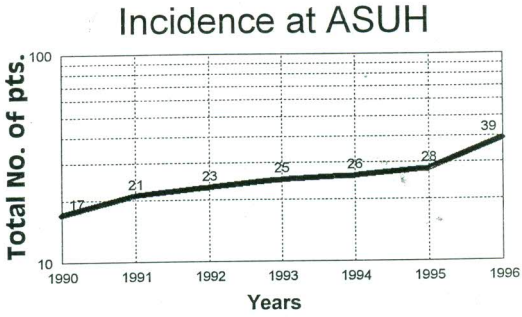

Fig.1: The rising incidence of mesothelioma in recent years

Occupational exposure: Of the 39 patients, three patients (7%) had a definite history of exposure to asbestos for more than 25 years; a security man and 2 workers in asbestos pipe factory. All the other 36 patients had no history of exposure to asbestos, they were from rural or non industrial urban areas.We have noted a rising incidence of MM in recent years (Fig 1).

Signs and symptoms: the presenting symptom in 30 cases (70%) was chest pain, while 25 patients (62%) complained of

dyspnea. Less frequent complains were cough in 6 cases (14%),loss of weight in 5 patients (12%),abdominal symptoms in 2 cases (4%). None of the cases was asymptomatic and none had arthralgia or hypoglycemia.

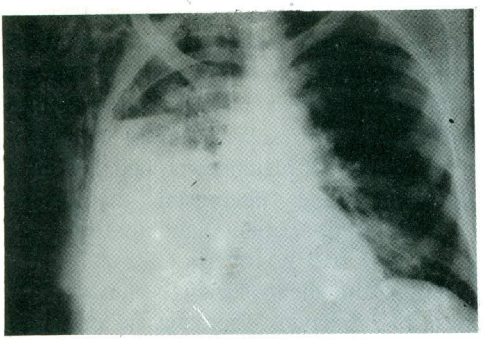

Fig.2: P.A. view showing obliteration of Rt. costophrenic angle and pleural thickening

Fig.3: C.T. of the chest showing irregular circumferential pleural thickening on the Rt. side

On initial physical examination, signs of pleural effusion were present in all cases and it was the only notable finding in most of the cases. Neither clubbing nor osteoarthropathy was noted in any of the patients.

Roentgenologic examination revealed pleural effusion or irregular pleural thickening with homogenous pattern or both in all patients (Fig., 2,3). Localised fluid or pleural thickening in the costophrenic angle in all patients. Compression collapse of the underlying lung was evident in all cases.

Evident localised thickening of the pericardium opposite the affected mediastinal pleura in 3 cases (7%). Bony erosion of the chest wall was noted in 4 cases (8%) and lymphnode enlargement in 6 cases (14%) as evidenced by the CT scans. .

Pathologic Features:

The total pleural involvement in the series was 15 in right pleura and 24 in the left pleura. Cytologic study of pleural fluid was done in 15 patients (35%). Pleural biopsy by Abram's needle in 6 cases (14%) and open surgical biopsy in 16 cases (37%). Two cases had minithoracotomy. All biopsies and cytology specimens proved to be positive.

All examinations of sputum and bronchial washings were negative for malignant cells, as were all bronchial biopsy specimens.

The gross pathologic appearance in all cases consisted of thickened visceral or parietal pleura or both with dense, fibrous-like, firm, pink-white or yellow-white nodules or plaques with hemorrhagic and purulent areas. The pleural thickening ranged from 5 to 20 - mm. In all cases, there was direct extension of the tumor to one or more of the following: underlying lung, chest wall, mediastinum, pericardium, peritoneum and regional nodes. Metastasis to the liver was recorded in one case,

however, no bilateral involvement was noted. Histopathologically, all the cases were of the mixed type of malignant mesothelioma. The histopathological findings in all of our cases were similar to those of Lewes et al (3) .

Prognosis:

Surgery produced symptomatic benefit, (improvement of pain and dyspnea) that was transient in 5 patients (45%).It ranged from 2 weeks to 3 months (mean, 46 days) in patients with DMM. There was one woman who had Rt. lower lobectomy and tumor resection for a big localized mesothelioma, she arrived to our department again 12 months later with multiple bilateral secondaries and she is receiving radio and chemotherapy. Recurrent pleural effusion occurred in 4 cases (36%).Little or no palliation was achieved in the other patients. Pleuritic pain persisted from outset to treatment despite the effusion. In the 11 Patients who underwent surgery, early surgical mortality was 17% (two deaths). One patient died from hemorrhage after pleurectomy and two patients (17%) developed bronchopleural fistula after pleuropneumonectomy. Recurrence after total decortication occurred in one case 28 days postoperatively. This patient died of burst chest (due to fungation of the tumor from the wound and deep obstructive jaundice). Postoperative chemotherapy and/or radiotherapy was completed in 3 cases (27%). One patients is alive for 14 months at the time of review March, 1997, she is the lady with localized mesothelioma. Seven other patients of the surgical group died in a period ranging from 3 to 8 months postopertively (mean survival time, 167 days). There was no follow-up available on one patient. In the patients who had advanced disease (11 cases), and who were treated by radiotherapy or chemotherapy, there was no correlation between therapy and course of the disease, all these cases showed little or no improvement. All died within 4 months from the onset of symptoms (mean survival time, 98 days). In the group of patients who had palliative procedures like intercostal tubes and pleurodesis (9 patients),and in the other group who had no interference at all (12 patients), the mean survival time was 159 days (80-205 days). There was no statistical significance in survival between the surgical and the palliation groups.

Discussion

The diagnosis of DMM is sometimes suggested by the constellation of clinical and radiographic findings. The diagnosis, however, is made by microscopic exammation of the tissue. However, clinical and radiographic findings useful in the workup are discussed.

Clinical considerations:

As regards the age and sex distribution, Thirty eight patients were men and only one woman. median age was 52 years. This goes hand in hand with all the reports of DMM of the pleura. (4), (5), (6). Adams and his colleagues (7) found that the tumor was right-sided in 55 %, left-sided in 4 1 % and bilateral in 4%. On the other hand Huncharek and Muscat (8) reported a reversed incidence i.e., 40% in the left pleura, 55% in the right pleura and 5% had bilateral tumor. Our group of patients

showed right side involvement in 44% and left side in 56% with no bilateral involvement.

Mesotheliomas induced in rats by intrapleural injection of asbestos often showed an epithelial or sarcomatous pattern only in early tumors (9), suggesting a degree of histological mutuality in mixed cases (10). It has been found that exposure to asbestos was documented in 80% of epithelial, 77% of mixed and 88% of sarcomatous type (10). Particles of asbestos, carried home on the colthings of the workers, have also been implicated as a cause of the disease in family members who have never been engaged in these occupations (6). More recent studies showed also that tremolite is widespread in domestic and enviromnental dust as well as agricultural soil samples, so mines are not the major source of the disease, as exposure to tremolite is equally if not more important as a cause of this tumor (11),(25). A mean time of exposure to asbestos has been reported to be 20.9 years with a range between one month and 46 years (8). It has been settled that. in a person exposed to asbestos who had unilateral pleural thickening and effusion, the differential diagnosis lies between mesothelioma and benign asbestos effusion after the usual causes of effusion have been excluded. However, benign asbestos effusion is a self limiting disease (12). Only 3 of our cases gave history of exposure to asbestos for about 25 years. MM of the pleura can also arise in scars from old tuberculosis especially after therapeutic pneumothorax and in chronic empyema and fistulas (25). Histologically these tumors differ somewhat from other mesotheliomas being mainly of the squamous cell carcinoma. Whether these tumors developed from metaplastic mesothelium or implanted cells from skin, is not clear (13). No history of old scars was documented in our cases.

Radiographic Considerations:

Law and his colleagues (10) reported that over 70% of both epithelial and mixed tumors were associated with large effusion whereas 84% of sarcomatous type had small or no effusion and this difference is highly significant as we have reported pleural effusion in all our cases. pleural pain persisted from the beginning despite the effusion. This is in contradiction to pleuritic pain experienced in other malignant or inflammatory disease, in which chest pain **is** present at the outset but promptly subsides as the effusion develops. This observation is specific to DMM associated with effusion and may be due to invasion of chest wall structures other than the pleura (6), (25).

Diffuse pleural metastasis from carcinoma can occasionally produce diffuse nodular pleural thickenmg, but it usually manifests as bilateral discrete pleural masses. More importantly, metastasis rarely causes irregular thickening of a fissure or decreased volume of a lung due to encasement of the lung by metastatic neoplasm. However, unilateral involvement of the pleura is a clinical finding that indicates DMM rather than metastatic carcinoma (25). The distinction between pleural extension of an occult primary lung tumor and pleural mesothelioma must be made microscopically (7). Pleural mesothelioma involving the lung parenchyma bilaterally in a diffuse nodular fashion has been reported by Uri and his colleagues (14). Unilateral involvement of the underlying lung was reported in all of our 39 cases.

Computed tomography can detect tumors from 1-8 months before the onset of signs or symptoms (15). It was of great help in the diagnosis of most of our cases. Despite its limitations, it is probably the most accurate way to provide follow up and detection of recurrence for patients during treatment (25).

Histopathologic Considerations :

DMM is a relentless process, which is multicentric in origin and develops in metachronous fashion (3). Three histologic subtypes have been described purely epithelial, mixed and sarcomatous (including desmoplastic). The mixed type was described as the most typical kind of DMM (I3). All our cases were of this type.

Blobel and his colleagues (16) in their immunohistochemical studies demonstrated the epithelial nature of all types of malignant mesotheliomas and this justify their classification as carcinomas. So terms as sarcomatoid and fibrous malignant mesotheliomas are purely descriptive (25). Desomplastic mesothelioma is an unusual variant of DMM in which the tumor is fibrous and which on this account may be difficult to distinguish from fibrous pleurisy except on clinical basis (17). However, desmoplastic component was described in all three types of malignant mesotheliomas (4). The cellular variability of mesotheliomas has been explained by the concept of embryological identity of mesothelium to mesoderm, which can differentiate to several histological patterns (18), (25).

In small needle biopsy specimens, the fibrous reaction to metastatic carcinoma can easily be confused with DMM. In inflammatory pleurisy, however, the mesothelium is usually replaced by a superficial inflammatory exudate, the intermediate layer is composed of vascular granulation tissue and there are underlying bands of connective tissue oriented parallel to the pleural surface. In contrast, the collagen and fibroblasts in malignant mesothelioma are haphazardly arranged and granulation tissue is usually absent. It was also reported that mesothelial hyperplasia is common in biopsies preceding the diagnosis of DMM. Meanwhile, some multilayering of the parietal mesothelium was occasionally seen in chronic pleurisy and around fibrosis, while papillary mesothelial proliferation and sheets of atypical mesothelial cells occur in DMM (19), (25) .

Prognostic Considerations:

Ginsberg (12) reported that survival in DMM is dependent on the stage of the disease. Within the stage 1 category i.e.; very early tumor with pleural effusion as well as a very diffuse process provided, no matter what the treatment, very long term survival can occur. Simultaneously, longer survival in women than in men has been reported (7). Also microscopic lymphatic invasion and spread to the regional lymph node groups and underlying lung is well described (20). Bilateral malignant lymphangitis complicating DMM was reported (21). However ; other authors found no statistical significant associations between the histological types and presence

of metastasis, or between the histological types and age at diagnosis and that distant metastasis is generally a common feature of DMM (8).

When we review DMM by thoracoscope (we have it recently at our department), it usually appears as multicentric in origin. DMM involves large areas of parietal and visceral pleura and diaphragm. Most frequently the mediastinal pleura is as well infiltrated by the tumor. It usually invades the chest wall, and diaphragm, thus, eliminating any chance of free plane of dissection (3).

One might question whether the pleura presents a barrier to the tumor therefore, pleurectomy might permit more rapid spread of the tumor (23). This might explain the rapid recurrence with fungation of the tumor from thoracotomy incision after decorication in one of our patients. We had no statistically significant difference in survival between surgical and palliation groups.

Chemotherapy was without objective benefit while, radiotherapy abolished pain and dyspnea and terminated recurrent pleural effusion in few cases, but it was of no value in other patients (3). The visual evidence of regression of the superficial extension of tumor and the long disease free survival after fast neutron therapy is encouraging (24).

Current investigations involve the multimodality approach using various combinations of surgery, chemotherapy, and radiotherapy in hopes of obtaining better results with this deadly disease (26,27), reported a survival rate of 70% at 1 year and 48% at 2ys using extrapleural pneumonectomy with postoperative cyclophosphamide, doxorubicin, and cis-platinum chemotherapy with or without radiotherapy.

In conclusion, until further prospective controlled studies prove otherwise, while localized mesothelioma is potentially a surgically curable disease, DMM is a multicentric process. Patients with DMM should have the most simple surgical procedure necessary to establish a diagnosis and palliation. Accurate diagnosis and differential diagnosis specially from other pleural disease is necessary to avoid the hazards of unnecessary procedures.

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Cefobid* (cefoperazone sodium)

No Dosage Adjustment In Renal or Hepatic Impairment [3]

Cefobid* (cefoperazone sodium)

Just Twice Daily [2]

Cefobid* (cefoperazone sodium)

Good Manufacturing Procedures Ensure PFIZER'S High Quality Standards

Pfizer

Quality ★★★★★★★ Products

Cefobid* IM/IV q12h

(cefoperazone sodium)

IN TREATING SERIOUS INFECTIONS

NO TIME FOR SECOND THOUGHTS OR SECOND BEST...

References:

1- Gibbs, D.L Cefoperazone a mircobiological, pharmacological, and clinical review . Internal Medicine ; 2 (3), 1983: 1-6

2- Physician's Desk Reference, ed. 40, 1986

3- GreenField, RA et al: Pharmacokinetics of cefoperazone in patients with normal and impaired hepatic and renal function. Reviews of infectious diseases ; 5, (suppl), 1983: S 127- 136

Prescribing Information

INDICATIONS

CEFOBID is indicated for the treatment of the following infections when caused by susceptible organisms:

Respiratory Tract Infections (Upper and Lower)
Urinary Tract Infections (Upper and Lower)
Peritonitis, Cholecystitis, Cholangitis, and Other Intra-Abdominal Infections.
Septicemia
Meningitis
Skin and Soft Tissue Infections
Infections of Bones and Joints
Pelvic Inflammatory Disease, Endometritis, Gonorrhea, and Other Infections of the Genital Tract
Prophylaxis

(Cefoperazone sodium may be indicated in the prophylaxis of post-operative infection in patients undergoing abdominal and gynaecological surgery, cardiovascular and orthopedic surgery.)

Combination Therapy

Because of the broad spectrum of activity of CEFOBID, most infections can be treated adequately with this antibiotic alone. However, CEFOBID may be used concomitantly with other antibiotics if such combinations are indicated. If an aminoglycoside is used, renal function should be monitored during the course of therapy. (See DOSAGE AND ADMINISTRATION Section)

CONTRAINDICATIONS

CEFOBID is contraindicated in patients with known allergy to the cephalosporin class of antibiotics.

WARNINGS

Before therapy with CEFOBID is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins or other drugs. This product should be given cautiously to penicillin-sensitive patients. Antibiotics should be administered with caution to any patient who has demonstrated some form of allergy, particularly to drugs.

If an allergic reaction occurs, the drug should be discontinued and the appropriate therapy instituted. Serious anaphylactoid reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids, and airway management, including intubation, should be administed as indicated.

PRECAUTIONS

General

CEFOBID is extensively excreted in bile. The serum half-life of CEFOBID is usually prolonged and urinary excretion of the drug increased in patients with hepatic diseases and/or biliary obstruction. Even with severe hepatic dysfunction, therapeutic concentrations of cefoperazone are obtained in bile and only a 2 to 4 fold increase in half-life is seen.

Dose modification may be necessary in cases of severe biliary obstruction, severe hepatic disease or coexistent renal dysfunction.

In patients with both hepatic dysfunction and concomitant renal impairment, CEFOBID serum concentrations should be monitored and dosage adjusted as necessary. In these cases dosage should not exceed 2 g/day without close monitoring of serum concentrations.

The serum half-life of CEFOBID is reduced slightly during hemodialysis. Thus dosing should be scheduled to follow a dialysis period.

As with other antibiotics, Vitamin K deficiency has occurred in a few patients treated with CEFOBID. The mechanism is most probably related to the suppression of gut flora which normally synthesize this vitamin. Those at risk include patients with poor diet, malabsorption states (e.g. cystic fibrosis) and patients on prolonged intravenous alimentation regimens. Prothrombin time should be monitored in these patients and exogenous vitamin K administered as indicated.

A reaction characterized by flushing, sweating, headache, and tachycardia has been reported when alcohol was ingested during and as late as the fifth day after administration of CEFOBID. A similar reaction has been reported with certain other cephalosporins and patients should be cautioned concerning ingestion of alcoholic beverages in conjunction with administration of CEFOBID. For patients requiring artificial feeding orally or parenterally, solutions containing ethanol should be avoided.

As with other antibiotics, overgrowth of nonsusceptible organisms may occur during prolonged use of CEFOBID. Patients should be observed carefully during treatment.

Drug Laboratory Test Interactions

A false-positive reaction for glucose in the urine may occur with Benedict's or Fehling's solution.

Usage During Pregnancy

Reproduction studies have been performed in mice, rats and monkeys at doses up to 10 times the human dose and have revealed no evidence of impaired fertility and did not show any teratological findings. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Usage in Nursing Mothers

Only small quantities of CEFOBID are excreted in human milk. Although cefoperazone passes poorly into breast milk of nursing mothers, caution should be exercised when CEFOBID is administered to a nursing mother.

Usage in Paediatrics

CEFOBID had adverse effects on the testes of prepubertal rats at all doses tested. Subcutaneous administration of 1000 mg. per kg. per day (approximately 16 times the average adult human dose) resulted in reduced testicular weight, arrested spermatogenesis, reduced germinal cell population and vacuolation of Sertoli cell cytoplasm. The severity of lesions was dose dependent in the 100 to 1000 mg/kg per day range, the low dose caused a minor decrease in spermatocytes. This effect has not been observed in adult rats. Histologically the lesions were reversible at all but the highest dosage levels. However, these studies did not evaluate subsequent development of reproductive function in the rats. The relationship of these findings to humans is unknown.

Usage in Infancy:

CEFOBID has been effective', used in infants. It has not been extensively studied in premature infants and neonates. Therefore in treating premature infants and neonates potential benefits and possible risks involved should be considered before instituting therapy (See Usage in Paediatrics).

CEFOBID does not displaced bilirubin from plasma protein binding sites.

ADVERSE REACTIONS

Hypersensitivity: As with all cephalosporins, hypersensitivity manifested by maculopapular rash, urticaria, eosinophilia and drug fever has been reported. These reactions are more likely to occur in patients with a history of allergies, particularly to penicillin.

Hematology: Slight decreases in neutrophils have been reported. As with other beta-lactam antibiotics, reversible neutropenia may occur with prolonged administration. Some individuals have developed a positive direct Coombs test during treatment with cephalosporin antibiotics. Decreased hemoglobins or hematocrits have been reported, which is consistent with published literature on other cephalosporins. Transient eosinophilia has occured, and hypoprothrombinemia has been reported (See Precautions section on vitamin K deficiency).

Liver: Transient elevation of SGOT, SGPT and alkaline phosphatase levels have been noted.

Gastrointestinal: Altered bowel habits (loose stools or diarrhea) have been reported. Most of these events have been mild or moderate in severity. In all cases, these symptoms responded to symptomatic therapy when therapy was stopped.

Local reactions: CEFOBID is well tolerated following intramuscular administration. Occasionally, transient pain may follow administration by this route. As with other cephalosporins, when CEFOBID is administred by an intravenous catheter some patients develop phlebitis at the infusion site.

DOSAGE AND ADMINISTRATION

The usual adult daily dosage of CEFOBID is 2 to 4 grams per day administered in equally divided doses every 12 hours. In severe infections the dosage may be increased to a total of 8 grams per day in equally divided doses every 12 hours. Twelve grams per day have been administered in equally divided doses every 8 hours and usage of up to 16 grams per day in divided doses has been reported without complications. Treatment may be started before results of susceptibility testing are available.

The recommended dosage for uncomplicated gonococcal urethritis is 500 mg intramuscularly as a single dose.

Because renal excretion is not the main route of elimination of CEFOBID, patients with renal failure require no adjustment in dosing when usual dosages (2-4 g daily) are administered. For patients whose glomerular filtration rate is less than 18 ml/min or whose serum creatinine level is greater than 3.5 mg/dl, the maximum dosage of CEFOBID should be 4 grams per day.

Solutions of CEFOBID and aminoglycoside should not be directly mixed, since there is a physical incompatibility between them. If combination therapy with CEFOBID and an aminoglycoside is contemplated (See INDICATIONS section) this can be accomplished by sequential intermittent intravenous infusion provided that separate secondary intravenous tubing is used, and that the primary intravenous tubing is adequately irrigated with an approved diluent between doses. It is also suggested that CEFOBID be administered prior to the aminoglycoside.

In infants and children a 50 to 200 mg/kg/day dosage of CEFOBID should be given in two administrations (every 12 hours) or more if necessary. For neonates aged less than 8 days, the drug should be given every 12 hours. A dosage of up to 300 mg/kg/day has been used to treat some infants and children with severe infections, including several with bacterial meningitis, without complication.

Intravenous Administration:

Vials of CEFOBID sterile powder may be initially reconstituted with a minimum of 2.8 ml per gram of cefoperazone of any compatible reconstituting solution appropriate for intravenous administration. For ease of reconstitution the use of 5 ml of compatible solution per gram of CEFOBID is recommended.

For intermittent intravenous infusion each one-or two-gram vial of CEFOBID should be dissolved in 20 to 100 ml of a compatible sterile intravenous solution and infused over a period of 15 minutes to one hour. If sterile water for injection is the preferred diluent, no more than 20 ml should be added to the vial.

For continuous intravenous infusion, each gram of CEFOBID should be dissolved in either 5 ml of Sterile Water for Injection or Bacteriostatic Water for Injection and the solution added to an appropriate intravenous diluent.

For direct intravenous injection, the maximum dose of CEFOBID should be two grams per administration for adults and 50 mg/kg per administration for children. The drug should be dissolved in an appropriate diluent to give a final concentration of 100 mg/ml and administered over a period of no less than three minutes to five minutes.

Intramuscular Administration

Sterile Water for Injection of Bacteriostatic Water for Injection may be used to prepare CEFOBID for intramuscular injection. When concentrations of 250 mg/ml or more are to be administered, a lidocaine solution should be used. These solutions should be prepared using a combination of Sterile Water for Injection and 2% Lidocaine Hydrochloride Injection that approximates a 0.5% Lidocaine Hydrochloride Solution. A two-step dilution process as follows is recommended: First, add the required amount of Sterile Water for Injection and agitate until CEFOBID powder is completely dissolved. Second, add the required amount of 2% lidocaine and mix.

The drug should be given by deep intramuscular injection into the large muscle mass of the gluteus maximum or anterior thigh.

Reconstituted CEFOBID solutions may be stored in plastic syringes, or in flexible plastic parenteral solution containers.

Frozen samples should be thawed at room temperature before use. After thawing, unused portions should be discarded. Do not refreeze.

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NEW UNASYN*

sultamicillin TABLETS & SUSPENSION

The oral antibiotic that says it all

- *Expanded spectrum for community infections*
- *Overpowers β-lactamase-related resistance*
- *Rapid, dependable delivery*
- *Effective in infections you treat every day—upper and lower respiratory tracts, skin and soft tissue, genitourinary tract, pediatric*
- *Maximum convenience with BID dosing in two oral forms*
- *Penicillin-class safety profile*

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NEW UNASYN*

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The oral antibiotic that says it all

Prescribing Information

DESCRIPTION

Sultamicillin is a double ester in which ampicillin and the beta-lactamase inhibitor sulbactam are linked via a methylene group. Chemically sultamicillin is the oxymethylpenicillinate sulphone ester of ampicillin and has a molecular weight of 594.7.

UNASYN ORAL is available as:

tablets containing the tosylate salt equivalent to 375 mg sultamicillin which is a mutual prodrug of sulbactam and ampicillin yielding the equivalent of 147 mg sulbactam and 220 mg ampicillin.

UNASYN ORAL is also available as a powder for oral suspension containing sultamicillin base that after reconstitution with water provides 250 mg sultamicillin per 5 ml.

ACTIONS

Following oral administration in humans, sultamicillin is hydrolysed during absorption to provide sulbactam and ampicillin in a 1:1 molar ratio in the systemic circulation. The bioavailability of an oral dose is 80% of an equal intravenous dose of sulbactam and ampicillin. Administration following food does not affect the systemic bioavailability of sultamicillin. Peak serum levels of ampicillin following sultamicillin are approximately twice those of an equal dose of oral ampicillin. Elimination half-lives are approximately 0.75 and 1 hour for sulbactam and ampicillin respectively in healthy volunteers, with 50-75% of each agent being excreted in the urine unchanged. Elimination half-lives are increased in the elderly and in patients with renal dysfunction. Probenecid decreases the renal tubular secretion of both ampicillin and sulbactam. Concurrent use of probenecid with sultamicillin results in increased and prolonged blood levels of ampicillin and sulbactam.

Biochemical studies with cell-free bacterial systems have shown sulbactam to be an irreversible inhibitor of most important beta-lactamases that occur in penicillin-resistant organisms. It possesses singificant antibacterial activity only against **Neisseriaceae, Acinetobacter calcoaceticus, Bacteroides** sp., **Branhamella catarrhalis,** and **Pseudomonas cepacia.** The potential for sulbactam sodium's preventing the destruction of penicillins and cephalosporins by resistant organisms was confirmed in whole organism studies using resistant strains, in which sulbactam sodium exhibited marked synergistic effects with penicillins and cephalosporins. Since sulbactam also binds to some penicillin-binding proteins, some sensitive strains are rendered more susceptible to the combination than to the beta-lactam antibiotic alone.

The bactericidal component of this product is ampicillin which, like benzyl penicillin, acts against sensitive organisms during the stage of active multiplication by the inhibition of biosynthesis of cell wall mucopeptide.

UNASYN ORAL is effective against a wide range of gram-positive and gram-negative bacteria including: **staphylococcus aureus** and **epidermidis** (including penicillin-resistant and some methicillin resistant strains); **streptococcus pneumoniae, streptococcus faecalis** and other **streptococcus** species; **Haemophilus influenzae** and **parainfluenzae** (both beta-lactamase positive and negative strains); **Branhamella catarrhalis;** anaerobes including **Bacteroides fragilis** and related species; **Escherichia coli; klebsiella** species; **Proteus** species (both indole-positive and indole-negative); **Enterobacter** species; **Morganella morganii; Citrobacter** species; **Neisseria meningitidis** and **Neisseria gonorrhoeae.**

INDICATIONS

UNASYN ORAL is indicated for infections caused by susceptible micro-organisms. Typical indications are upper respiratory tract infections including sinusitis, otitis media and tonsillitis; lower respiratory tract infections including bacterial pneumonias and bronchitis; urinary tract infections and pyelonephritis; skin and soft tissue infections and gonococcal infections.

Sultamicillin may also be indicated in patients requiring sulbactam/ampicillin therapy following initial treatment with UNASYN IM/IV.

CONTRAINDICATIONS

The use of this product is contraindicated in individuals with a history of and allergic reaction to any of the penicillins.

WARNINGS

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. These reactions are more apt to occur in individuals with a history of penicillin hypersensitivity and / or hypersensitivity reactions to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe reactions when treated with cephalosporins. Before therapy with a penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, and other allergens. If an allergic reaction occures, the drug should be discontinued and the appropriate therapy instituted.

Serious anaphylactic reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids, and airway management, including intubation, should be administered as indicated.

PRECAUTIONS

As with any antibiotic prepartion, constant observation for signs of overgrowth of nonsusceptible organisms, including fungi, is essential. Should superinfection occur, the drug should be discontinued and/or appropriate therapy instituted.

It is advisable to check periodically for organ system dysfunction during prolonged therapy; this includes renal, hepatic and hematopietic systems.

Use During Pregnancy

Animal reproduction studies have revealed no evidence of impaired fertility or harm to the fetus due to sultamicilin. However, safety for use in human pregnancy has not been established.

Use During Lactation

Low concentrations of ampicillin and sulbactam are excreted in the milk; therefore, caution should be exercised when sultamicillin is administered to a nursing woman.

Use in Children

The principal route of excretion of sulbactam and ampicillin following oral administration of sultamicillin is via the urine. Because renal function is not fully developed in neonates, this should be considered when using sultamcillin in neonates.

Drug Interactions

The concurrent administration of allopurinol and ampicillin increases substantially the incidence of rashes in patients receiving both drugs as compared to patients receiving ampicillin alone. There are no data concerning concurrent administration of sultamicillin and allopurinol.

ADVERSE REACTIONS

Sultamicillin is generally well tolerated. The majority of side effects observed were of mild or moderate severity and were normally tolerated with continued treatment.

Gastrointestinal- the most frequently observed side effect was diarrhea/loose stool. Nausea, vomiting, epigastric distress, and abdominal pain/cramps have been observed. As with other ampicillin-class antibiotics, enterocolitis and pseudomembranous colitis rarely may occur.

Skin/Skin structures- rash and itching were infrequently observed.

Miscellaneous- drowsiness/ sedation, fatigue/malaise and headache have been rarely observed.

Since infectious mononucleosis is viral in origin, ampicillin should not be used in the treatment. A high percentage of patients with mononucleosis who receive ampicillin develop a skin rash.

It is expected that the adverse reactions associated with use of ampicillin will be occasionally observed.

DOSAGE AND ADMINISTRATION

The recommended dose of sultamicillin in adults (including elderly patients) is 375 mg-750 mg twice daily.

The dosage for most infections in children weighing less than 30kg is sultamicillin 25-50mg/Kg/day in 2 divided doses depending on the severity of the infection and the physician's judgement. For children weighing 30 kg or more the usual adult dose should be given.

In both adults and children treatment is usually continued until 48 hours after pyrexia and other abnormal signs have resolved. Treatment is normally given for 5-14 days, but the treatment period may be extended if necessary.

In the treatment of uncomplicated gonorrhoea, sultamicillin can be given as a single oral dose of 2.25 grams (six 375 mg tablets). Concomitant probenecid 1.0 gram should be administered in order to prolong plasma concentrations of sulbactam and ampicillin.

Cases of gonorrhoea with a suspected lesion of syphilis should have dark field examinations before receiving sultamicillin and monthly serological tests for a minimum of four months.

It is recommended that there be at least 10 days treatment for any infection caused by hemolytic streptococci to prevent the occurrence of acute rheumatic fever or glomerulonephritis.

In patients with severe impairment of renal function (creatinine clearance 30 ml/min), the elimination kinetics of sulbactam and ampicillin are similarly affected and hence the plasma ratio of one to the other will remain constant. The dose of sultamicillin in such patients should be administered less frequently in accordance with usual practice for ampicillin.

The reconstituted oral suspension must be stored under refrigeration and discarded arter 14 days.

HOW SUPPLIED

☐Unasyn oral (Sultamicillin) tablets 375mg. Pack of 12tablets.

☐Bottles contitution, each 5ml (one teaspoonful) contains 250mg Unasyn (Sultamicillin).

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Further information is available on request
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Sulperazon*

DESCRIPTION

Sulbactam sodium is a derivative of the basic penicillin nucleus. Chemically it is sodium penicillinate sulfone and is an off-white crystalline powder highly soluble in water. The molecular weight is 255.22.

Cefoperazone sodium is a semisynthetic broad-spectrum cephalosporin antibiotic for parenteral use only. It is the sodium salt of 7-D (-) - (4 - ethyl - 2,3 - dioxo - 1 - piperazinecarboxamido) - (4 - hydroxyphenyl) acetamido - 3 - (1 - methyl - 1H - tetrazol - 5 - yl) thiomethyl - 3 - cephem - 4 - carboxylic acid. It contains 34 mg sodium (1.5 mEq) per gram . Cefoperazone is a white crystalline powder which is freely soluble in water . The molecular weight is 667.65 .

SULPERAZON brand of sulbactam sodium/ cefoperazone sodium combination is available as a dry powder for reconstitution in a 1: 2 ratio in terms of free sulbactam and cefoperazone. Vial contains 500 mg + 1000 mg of sulbactam and cefoperazone, respectively .

ACTIONS

Human Pharmacokinetics

Approximately 84% of the sulbactam dose and 25% of the cefoperazone dose administered with SULPERAZON is excreted by the kidney. Most of the remaining dose of cefoperazone is excreted in the bile. After SULPERAZON administration the mean half-life for sulbactam is about one hour while that for cefoperazone is 1.7 hours . Serum concentrations have been shown to be proportional to the dose administered .These values are consistent with previously published values for the agents when given alone. Mean peak sulbactam and cefoperazone concentrations after the administration of 3 grams of SULPERAZON (1g sulbactam, 2 g of cefoperazone) intravenously over 5 - 15 minutes have ranged between 76.8 and 128.7 mcg/ml for sulbactam and 245.7 and 254.4 mcg/ml for cefoperazone. This reflects the larger volume of distribution for sulbactam (Vd = 18.0 - 27.6L) compared to cefoperazone (Vd = 10.2-11.3L). After intramuscular administration of 1.5 g SULPERAZON (0.5 g sulbactam, 1 g cefoperazone) peak serum concentrations of sulbactam and cefoperazone are seen from 15 minutes to two hours after administration. Mean peak serum concentrations were 19.0 and 64.2 mcg/ml for sulbactam and cefoperazone, respectively.

After multiple dosing no significant changes in the pharmacokinetics of either component of SULPERAZON have been reported and no accumulation has been observed when administered every eight to 12 hours.

The pharmacokinetics of SULPERAZON have been studied in elderly individuals with renal insufficiency and compromised hepatic function. Both sulbactam and cefoperazone exhibited longer half-life, lower clearance, and larger volumes of distribution when compared to data from normal volunteers. The pharmacokinetics of sulbactam correlated well with the degree of renal dysfunction while for cefoperazone there was a good correlation with the degree of hepatic dysfunction.

In patients with different degrees of renal function administered SULPERAZON, the total body clearance of sulbactam was highly correlated with estimated creatinine clearance. Patients who are functionally anephric show a significantly longer half-life of sulbactam (mean 6.9 and 9.7 hours in separate studies). Hemodialysis significantly altered the total body clearance, and volume of distribution of sulbactam. No significant differences have been observed in the pharmacokinetics of cefoperazone in renal failure patients. Studies conducted in pediatrics have shown no significant changes in the pharmacokinetics of the components of SULPERAZON compared to adult values. The mean half-life in children has ranged from 0.91 to 1.42 hours for sulbactam and from 1.44 to 1.88 hours for cefoperazone.

Both sulbactam and cefoperazone distribute well into a variety of tissues and fluids including bile, gall bladder, skin, appendix fallopian tubes, ovary, uterus, and others.

There is no evidence of any pharmacokinetic drug interaction between sulbactam and cefoperazone when administered together in the form of SULPERAZON.

Microbiology (in vitro **Susceptibility** Data):

The anti-bacterial component of SULPERAZON is cefoperazone, a third generation cephalosporin, which acts against sensitive organisms during the stage of active gruttiplication by inhibiting biosynthesis of cell wall mucopeptide. Cefoperazone does not possess any useful antibacterial activity, however, against **Neisseriacase and Acinetobacter.** However, biochemical studies with cell-free bacterial systems have shown it to be an irreversible inhibitor of most important beta-lactamases produced by beta-lactam antibiotic-resistant organisms.

The potential for sulbactam's preventing the destruction of penicillins and cephalosporins by resistant organisms is confirmed in whole organism studies using resistant strains in which sulbactam exhibits marked synergistic effects when given together with penicillins and cephalosporins. As sulbactam also binds with some penicillin binding proteins, sensitive strains are also often rendered more susceptible to SULPERAZON than to cefoperazone alone.

The combination of sulbactam and cefoperazone is active against all organisms sensitive to cefoperazone but in addition demonstrates synergistic activity (up to fourfold reduction in minimum inhibitory concentration values with the combination versus those for each component) in a variety of organisms, most markedly the following:

- Haemophilus influenzae	- Bacteroides species	- Staphylococcus species
- Acinetobacter calcoaceticus	- Enterobacter aerogenes	- Escherichia coli
- Proteus mirabilis	- Klebsiella pneumoniae	- Morganella morganii
- Citrobacter freundii	- Enterobacter cloacae	- Citrobacter diversus

SULPERAZON is active in vitro against a wide variety of clinically significant organisms:

Gram-Positive Organisms:

Staphylococcus aureus, penicillinase and non-penicillinase-producing strains

Staphylococcus epidermidis

Streptococcus pneumoniae (formerly **Diplococcus pneumoniae).**

Streptococcus pyogenes (Group A beta-hemolytic streptococci)

Streptococcus agalactiae (Group B beta-hemolytic streptococci).

Most other strains of beta-hemolytic streptococci.

Many strains of **Streptococcus faecalis** (enterococcus)

Gram-Negative Organisms:

- **Escherichia coli**
- **Klebsiella** species
- **Enterobacter species**
- **Citrobacter species**
- **Haemophilus influenzae**
- **Proteus mirabilis**
- **Proteus vulgaris**
- **Morganella morganii (formerly Proteus morganii)**
- **Providencia rettgeri (formerly Proteus rettgeri)**
- **Providencia species.**
- **Serratia species (including S. marcescens).**
- **Salmonella and shigella species**
- **Pseudomonas aeruginosa and some other pseudomonas species.**
- **Acinetobacter calcoaceticus**
- **Neisseria gonorrhoeae**
- **Neisseria meningitidis**
- **Bordetella pertussis**
- **Yersinia enterocolitica**

Anaerobic Organisms:

Gram - negative bacilli (including Bacteroides fragilis, other Bacteroides species, and Fusobacterium species).

Gram-positive and gram-negative cocci (including Peptococcus, Peptostreptococcus and Veillonella species).

Gram -positive bacilli (including Clostridium, Eubacterium and Lactobacillus species).

The following susceptibility ranges (according to guidelines of the U.S. National committee for Clinical Laboratory Standards) have been established for SULPERAZON:

	Minimal inhibitory concentration (MIC), mcg / ml (expressed as cefoperazone concentration)
Susceptible	16
Resistant	64

	Susceptibility Disc Zone Size, mm (Kirby - Bauer)
Susceptible	21
Intermediate	16 - 20
Resistant	15

For MIC determinations, serial dilutions of SULPERAZON may be used with a broth or agar dilution method. Use of a susceptibility test disc containing 30 mcg of sulbactam and 75 mcg of cefoperazone is recommended. A report from the laboratory of "susceptible" indicates that the infecting organism is likely to respond to SULPERAZON therapy; and a report of "Resistant" indicates that the organism is not likely to respond. A report of "Intermediate" suggests that the organism would be susceptible to SULPERAZON if a higher dosage is used or if the infection is confined to tissues or fluids where high antibiotic levels are attained.

The following quality control limits are recommended for 30 mcg/75 mcg Sulbactam/ cefoperazone susceptibility discs.

CONTROL STRAIN	ZONE SIZE MM
Acinetobacter Spp, ATCC 43498	26 - 32
Pseudomonas aeruginosa ATCC 27853	22 - 28
Escherichia Coli, ATCC 25922	27 - 33
Staphylococcus aureus, ATCC 25923	23 - 30

INDICATIONS

SULPERAZON is indicated for the treatment of the following infections when caused by susceptible organisms:

Respiratory Tract Infections (Upper and Lower)
- Urinary Tract Infections (Upper and Lower)
- Peritonitis, Cholecystitis, Cholangitis, and Other Intra-Abdominal Infections
- Septicemia
- Meningitis
- Skin and Soft Tissue Infections
- Bone and Joint Infections
- Pelvic Inflammatory Disease, Endometritis, Gonorrhea, and Other Infections of the Genital Tract.
Combination Therapy

Because of the broad spectrum of activity of SULPERAZON, most infections can be treated adequately with this antibiotic alone. However, SULPERAZON may be used concomitantly with other antibiotics if such combinations are indicated. If an aminoglycoside is used, renal function should be monitored during the course of therapy. (See DOSAGE AND ADMINISTRATION SECTION).

CONTRAINDICATIONS

SULPERAZON is contraindicated in patients with known allergy to penicillins or any of the cephalosporins.

WARNINGS

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving beta-Lactam therapy. These reactions are more apt to occur in individuals with a history of hypersensitivity reactions to multiple allergens. If an allergic reaction occurs, the drug should be discontinued and the appropriate therapy instituted.

Serious anaphylactic reactions require immediate emergency treatment with epinephrine. Oxygen, intravenous steroids, and airway management, including intubation, should be administered as indicated.

PRECAUTIONS

General

Those precautions that pertain to sulbactam and cefoperazone will also pertain to the combination as discussed below.

Cefoperazone is extensively excreted in bile. The serum half-life of cefoperazone is usually prolonged and urinary excretion of the drug increased in patients with hepatic diseases and/or biliary obstruction. Even with severe hepatic dysfunction, therapeutic concentrations of cefoperazone are obtained in bile and only a 2 to 4 fold increase in half-life is seen.

Dose modification may be necessary in cases of severe biliary obstruction, severe hepatic disease or in cases of renal dysfunction coexistent with either of those conditions.

In patients with hepatic dysfunction and concomitant renal impairment, cefoperazone serum concentrations should be monitored and dosage adjusted as necessary. In these cases dosage should not exceed 2g/day of cefoperazone without close monitoring of serum concentrations.

The serum half-life of cefoperazone is reduced slightly during hemodialysis. Thus, dosing should be scheduled to follow a dialysis period.

As with other antibiotics, Vitamin K deficiency has occurred in a few patients treated with cefoperazone The mechanism of this deficiency related to the suppression of gut flora which normally synthesize this vitamin. Those at risk include patients with poor diet, malabsorption states (e.g. cystic fibrosis) and patients on prolonged intravenous alimentation regimens. Prothrombin time should be monitored in these patients and exogenous vitamin K administered as indicated.

A reaction characterized by flushing, sweating, headache, and tachycardia has been reported when alcohol was ingested during and as late as the fifth day after cefoperazone administration. A similar reaction has been reported with certain other cephalosporins and patients should be cautioned concerning ingestion of alcoholic beverages in conjunction with administration of SULPERAZON. For patients requiring artificial feeding orally or parenterally, solutions containing ethanol should be avoided.

As with other antibiotics, overgrowth of nonsusceptible organisms may occur during prolonged use of SULPERAZON .Patients should be observed carefully during treatment. As with any potent systemic agent, it is advisable to check periodically for organ system dysfunction during extended therapy; this includes renal, hepatic, and hematopoietic systems. This is particularly important in neonates, especially when premature, and other infants.

Drug Laboratory Test Interactions

A false-positive reaction for glucose in the urine may occur with Benedict's or Fehling's solution.

Usage During Pregnancy

Reproduction studies have been performed in rats at doses up to 10 times the human dose and have revealed no evidence of impaired fertility and no teratological findings. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Usage in Nursing Mothers

Only small quantities of sulbactam and cefoperazone are excreted in human milk. Although both drugs pass poorly into breast milk of nursing mothers, caution should be exercised when SULPERAZON is administered to a nursing mother.

Usage In Infancy

SULPERAZON has been effectively used in infants. It has not been extensively studied in premature infants and neonates. Therefore, in treating premature infants and neonates potential benefits and possible risks involved should be considered before instituting therapy.

Cefoperazone does not displace bilirubin from plasma protein binding sites.

Adverse reactions

SULPERAZON is generally well tolerated. The majority of adverse events are of mild or moderate severity and are tolerated with continued treatment.

Gastrointestinal - As with other antibiotics, the most frequent side effects observed with SULPERAZON have been gastrointestinal.

Diarrhea/loose stools have been reported most frequently followed by nausea and vomiting. The frequency of these reported reactions has ranged from 3.6 to 10.8%.

Dermatologic Reactions - As with all penicillins and cephalosporins, hypersensitivity manifested by Maculopapular rash, urticaria, eosinophilia and drug fever has been reported. These reactions which have been reported in 0.8 to 1.3% of the cases, are more likely to occur in patients with a history of allergies, particularly to penicillin.

Hematology: Slight decreases in neutrophils have been reported. As with other beta-lactam antibiotics, reversible neutropenia may occur with prolonged administration. Some individuals have developed a positive direct Coombs test during treatment with cephalosporin antibiotics. Decreased hemoglobin or hematocrit have been reported, which is consistent with published literature on cephalosporins. Transient eosinophilia and thrombocytopenia have occurred, and hypo-prothrombinemia has been reported.

Miscellaneous adverse events (headache, fever, injection pain, chills) occurred in less than1% of patients.

Laboratory Abnormalities: Transient elevations of SGOT, SGPT, alkaline phosphatase and bilirubin levels have been noted in 6.3 to 10.0% of the reported cases.

Local Reactions: SULPERAZON is well tolerated following intramuscular administration. Occasionally, transient pain may follow administration by this route. As with other cephalosporins and penicillins, when SULPERAZON is administered by an intravenous catheter some patients may develop phlebitis at the infusion site.

DOSAGE AND ADMINISTRATION

SULPERAZON is available in 1.5 g strength vial.

Total Dosage (g)	Equivalent Dosage of sulb. + cefoperazone (g)	Total Volume of Reconstituted Solution (ml)	Maximum Final Conc. (mg/ml)
1.5	0.5 + 1.0	4.0	125 + 250

The usual adult dose of SULPERAZON is 1.5 to 3 g per day (i.e., 1 to 2 g cefoperazone activity) given intravenously or intramuscularly in equally divided doses every 12 hours.

In severe or refractory infections the daily dosage may be increased up to 12 g of SULPERAZON (8 g cefoperazone activity) given intravenously in equally divided doses every 12 hours. The recommended maximum daily dosage of sulbactam is 4 g (8 g SULPERAZON).

Dosage regimens of SULPERAZON should be adjusted in patients with marked decrease in renal function (creatinine clearance of less than 30 ml/min) to compensate for the reduced clearance of sulbactam. Patients with creatinine clearances between 15 and 30 ml/min should receive a maximum of 1 g of sulbactam administered every 12 hours (maximum daily dosage of 2 g sulbactam), while patients with creatinine clearances of less than 14 ml/min should receive a maximum of 500 mg of sulbactam every 12 hours (maximum daily dosage of 1 g sulbactam). In severe infections it may be necessary to administer additional cefoperazone.

The usual dosage of SULPERAZON in children is 30 to 60 mg/kg/day (i.e., 20 - 40 mg/kg/day cefoperazone activity) in 2 to 4 equally divided doses. In serious or refractory infections, these dosages may be increased up to 240 mg/kg/day SULPERAZON (i.e. 160 mg/kg/day cefoperazone activity) in 2 to 4 equally divided doses. For neonates in the first week of life, the drug should be given every 12 hours. The maximum daily dosage of sulbactam in pediatrics should not exceed 80 mg/kg/day.

Intravenous Administration

For intermittent infusion, each vial of SULPERAZON should be reconstituted with the appropriate amount (shown in table) of 5% dextrose in water, 0.9% Sodium Chloride Injection or Sterile for water Injection and then diluted to 20 ml with the same solution followed by administration over 15 to 60 minutes. For intravenous injection, each vial should be reconstituted as above and administered over a minimum of three minutes.

Intramuscular Administration

Sterile water for Injection should be used for reconstitution. For a concentration of cefoperazone of 250 mg/ml or larger, a two step dilution is required using Sterile water followed by 2% lidocaine to approximate a 0.5% lidocaine solution (see below).

Incompatibilities

SULPERAZON has been shown to be compatible with water for injection, 5% dextrose, normal saline, 5% dextrose in 0.225% saline, and 5% dextrose in normal saline at concentrations of 10 mg per cefoperazone and 5 mg sulbactam per ml and up to 250 mg cefoperazone and 125 mg sulbactam per ml. Initial reconstitution with Lactated Ringer's Solution or with 2% lidocaine HCl solution should be avoided since these mixtures have been shown to be incompatible. However, a two step dilution process involving initial reconstitution in water for injection will result in a compatible mixture when further diluted with Lactated Ringer's Solution at a sulbactam concentration of 5 mg/ml. Similarly, after appropriate initial reconstitution with water for injection SULPERAZON could be further diluted with 2% lidocaine hydrochloride to yield solutions containing up to 250 mg cefoperazone and 125 mg sulbactam per ml in 0.5% lidocaine HCl solution. Solutions of SULPERAZON and aminoglycosides should not be directly mixed, since there is a physical incompatibility between them. If combination therapy with SULPERAZON and an aminoglycoside is contemplated (SEE INDICATIONS section) this can be accomplished by sequential intermittent intravenous infusion provided that separate secondary intravenous tubing is used, and that the primary intravenous tubing is adequately irrigated with an approved diluent between doses. It is also suggested that doses of SULPERAZON be administered throughout the day at times as far removed from administration of the aminoglycoside as possible.

How Supplied

One vial containing 1.5 gm Sulperazon (500 mg sulbactam + 1000 mg cefoperazone) + distilled water ampoule for injection.

Manufactured by PFIZER EGYPT, S.A.E. CAIRO, A.R.E.
Under authority of PFIZER INC., U.S.A.

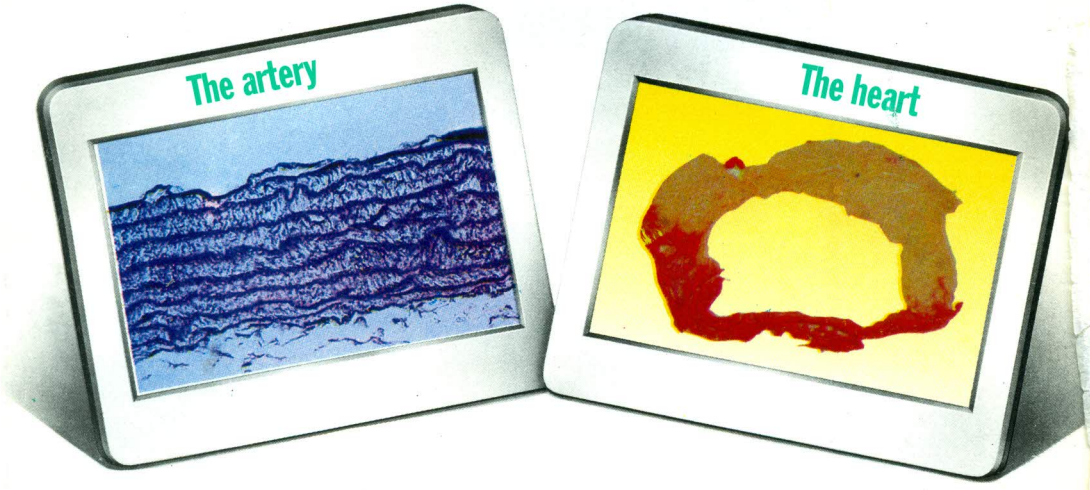
LPD No 179 B
Date January 29,1988

Further information is available on request
Pfizer Egypt SAE 47 Ramses Street
CAIRO - EGYPT

PF - Egy - LB - SULP - 1/97

Pfizer

Scoring an ACE in cardiovascular remodeling



1 tablet daily

COVERSYL® 4 mg

PERINDOPRIL

in hypertension and heart failure...

...cardiovascular remodeling is a key pathogenic feature. Coversyl 4 mg actively combats cardiovascular remodeling by correcting the structural and functional alterations of the heart and artery.[1-4]

Coversyl 4 mg is a true once daily ACE inhibitor with guaranteed antihypertensive efficacy right up to 24 hours post dose.[5]

In heart failure, Coversyl 4 mg (half-a-tablet) offers a safer start to treatment thanks to an absence of significant hypotensive first-dose response.[6]

With its original properties, Coversyl 4 mg is a high-performance ACE inhibitor in both its indications.

1. SIHM I et al. *Eur Heart J.* 1993; 14(suppl) : 63 - 2. LEVY BI et al. *Circ Res.* 1988; 63 : 227-239 - 3. ASMAR RG et al. *J Hypertens.* 1988; (suppl 3) : S33-S39 - 4. MICHEL JB et al. *Circ Res.* 1988; 62 : 641-650
5. MORGAN TO et al. *Am J Hypertens.* 1993; 6 : 116 A - 6. MAC FADYEN RJ et al. *Br Heart J.* 1991; 66 : 206-211.

Coversyl is a long-acting ACE inhibitor. **International nonproprietary name** : Perindopril. **Indications :** Essential hypertension. Congestive heart failure (adjunctive therapy). **Dosage and administration :** *Hypertension :* 4 mg once a day in the morning. If necessary, the dose may be increased to 8 mg after one month of treatment. Coversyl should be taken before food. *Congestive heart failure :* Coversyl should be started under close medical supervision at a starting dose of 2 mg in the morning. This may be increased to 4 mg once blood pressure acceptability has been demonstrated. *Elderly patients :* start treatment at 2 mg daily. **Contraindications :** Children. Pregnancy. Lactation. Patients with a history of hypersensitivity to Coversyl. **Precautions :** Assess renal function before and during treatment where appropriate. Renovascular hypertension. Surgery/Anesthesia. Renal insufficiency : the dose should be cautiously adjusted in accordance with the creatinine clearance *(refer to complete data sheet).* Symptomatic hypotension is rarely seen, but is more likely in volume-depleted patients, those receiving diuretics, or with the first two doses. In diuretic-treated patients, stop the diuretic 3 days before starting Coversyl. A diuretic may later be given in combination if necessary; potassium-sparing diuretics are not recommended. Combination with neuroleptics or imipramine-type drugs may increase the hypotensive effect. Serum lithium concentrations may rise during lithium therapy. **Side effects :** Rare and mild, usually at the start of treatment. Cough, fatigue, asthenia, headache, disturbances of mood and/or sleep have been reported. Less often, taste impairment, epigastric discomfort, nausea, abdominal pain, and rash. Reversible increases in blood urea and creatinine may be observed. Proteinuria has occurred in some patients. Rarely, angioneurotic edema and decreases in hemoglobin, red cells, and platelets have been reported. **Composition :** Each tablet contains 4 mg of the tert-butylamine salt of perindopril. **Presentation :** Packs of 30 tablets of Coversyl 4 mg (scored). *Refer to data sheet for complete prescribing information.*

Les Laboratoires Servier, 45520 Gidy - France. Correspondent : **Servier International,** 6, place des Pléiades, 92415 Courbevoie Cedex - France.

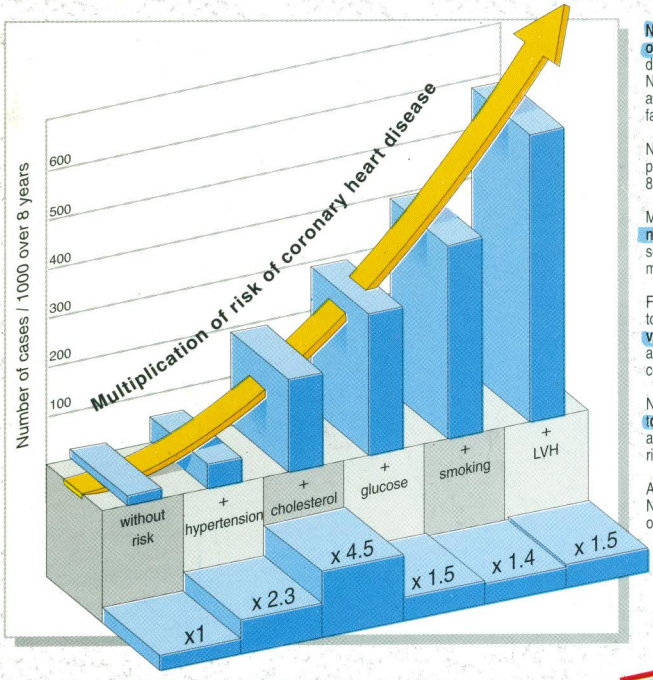
SERVIER

NATRILIX®

INDAPAMIDE 2.5 mg

1 tablet daily

THE REFERENCE DIURETIC FOR OPTIMAL CARDIOPROTECTION



As shown in a reference epidemiological trial,[6] when other risk factors coexist with hypertension, the risk of coronary heart disease increases dramatically.

Natrilix is the reference diuretic for optimal cardioprotection: specifically designed for treating hypertension, Natrilix is the only diuretic that addresses all the cardiovascular risk factors of the hypertensive patient.

Natrilix is **highly effective** on blood pressure readings,[1] normalizing up to 80% of hypertensive patients.

Moreover, Natrilix is **metabolically neutral:** Natrilix does not compromise serum cholesterol[2] or glucose metabolism[3].

Furthermore, Natrilix has been proven to **consistently reduce left ventricular hypertrophy,**[4] a recognized critical and independent coronary risk factor.

Natrilix has also been demonstrated **to reduce microalbuminuria,**[5] another independent cardiovascular risk factor in the diabetic hypertensive.

All these major advantages make Natrilix the reference diuretic in terms of cardioprotection.

HYPERTENSION

Treats hypertension without replacing one risk factor by another

1. Abbou CB et al. *Curr Med Res Opin.* 1985; 9 (7): 494-499.
2. Leonetti G et al. *Am J Cardiol.* 1990; 65 (17): 67-71.
3. Raggi U et al. *Hypertension.* 1985; 7 (6) (Part II): 157-160.
4. Raftery EB et al. *J Cardiovasc Pharmacol,* 1993; 22 (suppl 6): 106-110.
5. Flack JR et al. *J Cardiovasc Pharmacol.* 1993; 22 (suppl 6): 75-77
6. Kannel WB. *Am J Hypertens.* 1991; 4: 283-287

Composition: Each coated tablet contains 2.5 mg of 1-(4-chloro-3-sulfamyl-benzamidol)-2-methylindoline (or indapamide hemihydrate). **Indication:** Essential hypertension. **Contraindications:** Severe hepatic insufficiency, recent cerebrovascular accidents. Drug combinations to be avoided: tienilic acid, lithium, fenoxedil, lidoflazine, prenylamine, vincamine. **Combination treatments:** Natrilix may be combined with all nonthiazide antihypertensive agents, with beta-blockers, calcium channel blockers, and ACE inhibitors. **Precautions:** Pregnancy. Lactation. Monitoring of potassium and uric acid serum levels is recommended, especially in subjects with a predisposition or a sensitivity to hypokalemia and in patients with gout. Although no allergic manifestations have been reported during clinical trials, patients with a history of allergy to sulfonamide derivatives should be closely monitored. **Adverse effects:** Hypokalemia, fatigue, orthostatic hypotension, allergic manifestations. **Dosage and administration:** One tablet daily. **Overdosage:** Symptoms of overdosage would be those associated with a diuretic effect; electrolyte disturbances, hypotension, and muscular weakness. Treatment should be symptomatic, directed at correcting the electrolyte abnormalities. Refer to data sheet for complete prescribing information.

Les Laboratoires Servier - 45520 Gidy - France. Correspondent: **Servier International** - 6, place des Pléiades, 92415 Courbevoie Cedex - France

SERVIER

ADTEM - 06 NV 275 IA

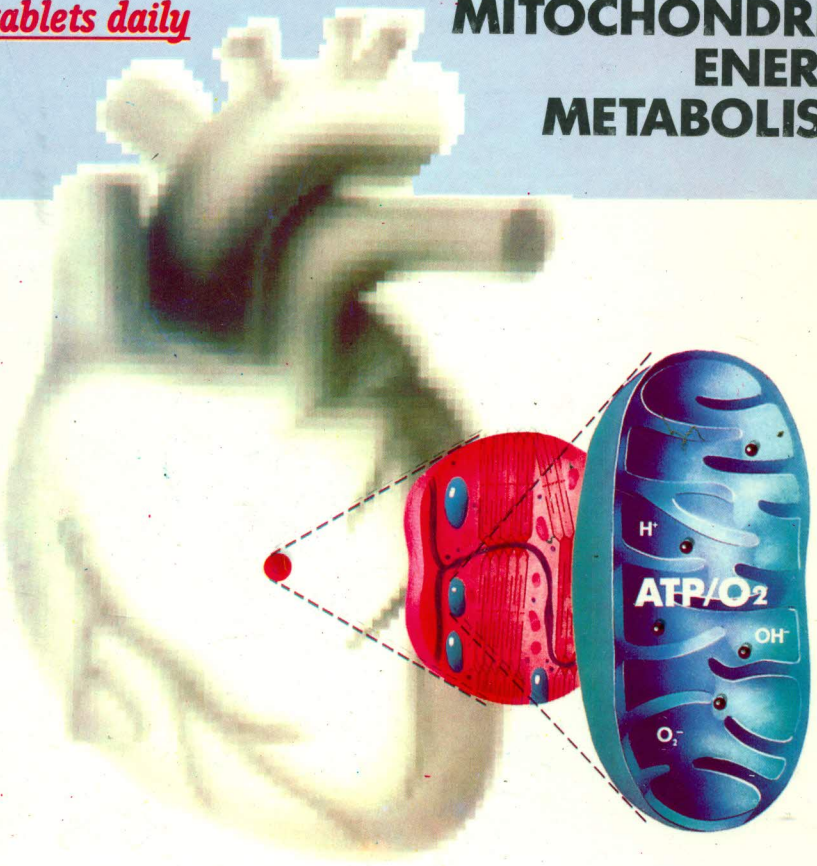
AT THE HEART OF THE ISCHEMIC CELL

VASTAREL® 20

Trimetazidine

3 tablets daily

OPTIMIZES MITOCHONDRIAL ENERGY METABOLISM[1-3]



providing all coronary patients with

- **permanent myocardial cytoprotection**[4]
- **major antianginal efficacy**[4-6]

Indications: Ischemic heart disease (angina pectoris, sequelae of infarction).
How supplied: Box of 60 tablets, each containing 0.02 g trimetazidine dihydrochloride.
Dosage: 3 tablets per day in three divided doses, with meals.
Les Laboratoires **Servier** · 45520 Gidy · France.
Correspondent **Servier International**
6, place des Pléiades · 92415 Courbevoie Cedex · France.

SERVIER

1. Guarnieri C et al. *Biochem Pharmacol.* 1988; 21: 128-135.
2. Aussedat J et al. *J Cardiovasc Pharmacol.* 1993; 21: 128-135.
3. Fantini E, Grynberg A. *J Mol Cell Cardiol.* 1994; 26: 949-958.
4. Detry JM et al. *Br J Clin Pharmacol.* 1994; 37: 279-288.
5. Dalla Volta S et al. *Cardiovasc Drugs Ther.* 1990; vol 4 (suppl 4): 814-825.
6. Monpère C et al. *Cardiovasc Drugs Ther.* 1990: 4 (suppl 4): 824-826.

VASTAREL® 20

Trimetazidine

3 tablets daily