SREE CHITRA TIRUNAL INSTITUTE OF MEDICAL SCIENCES AND TECHNOLOGY

PROJECT REPORT

CANDIDATE: DR. BALU VAIDYANATHAN

PROGRAMME: DM CARDIOLOGY

MONTH AND YEAR OF SUBMISSION: NOV 2003

CERTIFICATE

I, Dr. **Balu Vaidyanathan** , hereby declare that the projects included in this book were undertaken by me under the supervision of the faculty, Department of Cardiology, SCTIMST.

Trivandrum,

1-11-2003

Dr. Balu Vaidyanathan

Forwarded,

The candidate, **Dr. Balu Vaidyanathan**, has carried out the minimum required procedure.

Trivandrum,

1-11-2003

Prof. JaganMohan.A.Tharakan

Professor and Head

Department of Cardiology

SCTIMST

CONTENTS

COMPARISON OF LONG TERM OUTCOMES AFTER SURGERY AND BALLOON ANGIOPLASTY FOR NATIVE COARCTATION OF AORTA

INTRODUCTION

Coarctation of aorta is a discrete stenosis in the proximal descending aorta, presenting as a waist or concavity of the outer contour of the aorta usually opposite to the site of insertion of the duct. It may be associated with variable degree of hypoplasia of isthmus and transverse arch. Coarctation may present with severe congestive heart failure in infancy or it may present as an asymptomatic murmur or with systemic hypertension in adolescence or adulthood. Natural history of untreated coarctation is dismal with 90% of patients dying before 50 years of age due to heart failure, infective endocarditis, aortic rupture, intracranial hemorrhage, hypertension or associated valvular heart disease (1).

Three therapeutic options are available for management of patients with native Coarctation of Aorta – Surgery, Balloon Angioplasty and Endovascular Stenting(2).

Surgery remains the standard form of therapy ever since the first surgical repair reported by Crafoord in 1944. Several techniques of surgical repair have been introduced since then. These include Resection and end to end anastomosis, Patch aortoplasty, Subclavian Flap Aortoplasty, Jump Graft, Resection with interposition graft and Extended resection and end to end anastomosis(3,4). The initial mortality rates in most of the modern series in patients above age of 1 year are around 1%(4). In infants and neonates, the initial mortality rates are higher (1-10%). The other major immediate complications of surgery include hemorrhage, paradoxical hypertension and post coarctectomy syndrome (6%) and paraplegia(0.41%).

Long term results of surgery has been excellent with 2 large recent studies reporting survival of 95%, 89%, 82% and 79% at 10, 20, 30 and 40 years after repair (5, 6). The major causes of mortality on long-term follow-up in these studies were coronary artery disease (37%), Sudden death (13%), Heart Failure (9%), Cerebrovascular accident (7%)and Aortic Rupture (7%) (5). Restenosis occurred in 3-15% of patients on long-term follow-up. Re-operation was required in 3 – 9.5% cases for recurrent coarctation. Hypertension occurred in 25-40% of patients on long-term follow-up. Re-operations for other indications (aortic valve disease) were required in 5 – 7% of patients. Aneurysms are reported in 5 – 33% of long-term survivors with the highest incidence after patch aortplasty (3). Age at initial repair was the most important predictor of long-term survival

and prevalence of late hypertension in both studies. Younger age at repair (< 1 year) was the significant predictor of restenosis and re-operation for recoarctation.

Balloon Angioplasty was introduced as an alternative to surgery in the 1980s with the first report of Balloon angioplasty for Native Coarctation by Lababidi et al in 1984(7). Since then several reports of intermediate and long term follow-up of balloon angioplasty has been published (8-15). Immediate procedural success (defined as residual gradients less than 20 mmHg) was obtained in 78-91% of patients. Older age and higher pre-intervention gradients were identified as risk factors for sub optimal initial results (12). Restenosis (defined as pressure gradient > 20 mmHg) occurred in 13 – 35%(average 27%) cases, with rates as high as 83% in neonates, 39% in infants and 8% in older children (8). Young age (< 1 year), isthmal hypoplasia and small diameter of coarctation segment (< 3.5 mm before and < 6 mm after dilatation) were identified as risk factors for restenosis. Ray et al had reported higher incidence of late restenosis in patients in whom the balloon/isthmus ratio was less than 3 at time of angioplasty (13). Aneurysm formation has been reported in 5 – 20%(average 12%) cases after balloon angioplasty. Technical factors like larger balloons (13) and prolonged inflation times contribute to development of aneurysms.

Studies have attempted to compare results of Balloon Angioplasty and Surgery. Many of these have been hampered by varying definitions of restenosis and aneurysms and by the fact that they attempted to compare the 2 modalities of treatment from different time periods (20). In the only prospective randomized control trial of balloon angioplasty and surgery in children above 3 years of age, Shaddy et al reported similar initial results, but higher prevalence of restenosis (25% Versus 5%), and aneurysms (20% Vs 0%) in the angioplasty group (21). Johnson et al (22) in a meta-analysis reported much higher occurrence of restenosis in angioplasty in patients less than 1 year of age (57% vs. 14%). Rao et al have reported similar recoarctation rates (6% Vs 5.5%) and aneurysms (13% Vs 12%) for balloon angioplasty in patients above age of one year while the initial and late mortality was higher in the surgical group (23, 24). In neonates and infants, recoarctation rates are higher with balloon angioplasty. Rao et al opine that balloon angioplasty is an acceptable alternative to surgery in children above 1 year of age (24).

Endovascular stenting is the latest therapeutic armamentarium in the management of native coarctation. Stenting overcomes some of the problems associated with Balloon Angioplasty like high residual gradients, restenosis and late aneurysm formation. In the various published studies on stenting for Coarctation of aorta, the procedural success has been > 95% with a reported incidence of restenosis and aneurysms on follow-up being 0-10% and 4% respectively (25 – 29). Stenting for coarctation is however a evolving technology and currently it is advocated only in adolescents and adults. Long-term follow-up results of endovascular stenting for coarctation are not yet available.

AIMS OF STUDY

1. To compare long-term outcomes in adult life after Balloon angioplasty and surgery for Native Coarctation of Aorta.
2. To analyze the prevalence and predictors of long-term complications after intervention for native coarctation of aorta.

MATERIAL AND METHODS

Study design:

This study is a retrospective study. In –hospital records of all patients who had undergone either surgery or balloon angioplasty for coarctation of aorta at our center prior to 1997 was reviewed. From this, data of those patients who had completed 21 years of age at last follow-up were selected. These patients were called for follow-up and were evaluated for comparison of outcome variables. Those patients who did not respond to the initial request were sent a second communication for a follow-up visit along with a questionnaire. They were requested to fill in the questionnaire with the help of their local doctor in case they were unable to come for a follow-up visit. In case of patients who did not respond to both follow-up requests or to the questionnaire, hospital records of follow-up were analyzed and if there was no follow-up since 2001, the patient was considered to be lost to follow-up.

Inclusion criteria

1. All patients who had undergone intervention for Coarctation of Aorta (surgery or balloon dilation) and have completed at least 21 years of age at last follow-up.
2. Patients with complex coarctations (coarctation with associated cardiac anomalies) were included if the primary intervention was done for coarctation.

Exclusion Criteria

1. Patients with mild coarctation and having undergone intervention primarily for co-existing anomaly.
2. Patients who are less than 18 years of age at the time of last follow-up and patients with no follow-up visit after 2001.

Pre-intervention assessment

Clinical details like age at intervention, symptom status, Blood pressures in all 4 extremities and clinical coarctation gradient (difference in BP between Right upper limb and Right lower limb), evidence of CHF, details of antihypertensive medications were noted from hospital records. Echocardiographic parameters like location of Coarctation, gradient, dimensions of coarctation segment and arch presence of associated lesions were noted. Morphology of aortic valve was also noted (bicuspid or tricuspid) by trans thoracic echocardiogram, if morphology was discernible. From the pre-intervention catheterization data, pressures proximal and distal to coarctation and coarctation gradients were noted along with the presence of associated lesions.

Details of interventions

The indication for intervention was based on the symptoms of the patient. All patients with symptoms, hypertension or congestive failure not responding to medications and significant gradient across coarctation (> 20 mmHg) were considered for intervention.

In case of Balloon angioplasty, size of Balloon Used, balloon to isthmus ratio, residual gradient immediately after the procedure, proximal and distal pressures after procedure, complications during and immediately after the procedure (arterial occlusion, perforation, CVA, dissection), duration of hospital stay after the procedure and BP in right arm and arm-ankle BP index pre-discharge were noted.

In case of Surgery, type of surgical procedure employed, whether associated lesions were also repaired or not, residual gradient immediately after surgery, complications during or immediately after the procedure (Paradoxical hypertension, abdominal crises,

chylothorax, paraplegia, death), duration of hospital stay after surgery and BP in Right arm and Arm-ankle BP index at discharge were noted.

Initial successful result was defined as residual gradient of $\leq$ 20 mmHg and freedom from major complications associated with the procedure (7, 12).

Follow-up

All patients who came for follow-up were subjected to a detailed evaluation in similar lines of pre-intervention assessment. In case of patients who responded by questionnaire data as provided by the patient was included including details of echocardiogram (if provided) done at local center. Morphology of aortic valve was re-evaluated at follow-up also. Those patients with significant gradient across the coarctation site on echo along with medically refractory hypertension or suspected aneurysm were advised a repeat cardiac catheterization (in case of Balloon Angioplasty, a routine post intervention catheterization was done in several patients, especially those with initial sub-optimal results). Presence of other late complications like Coronary Artery disease, Neurological Complications (CVA, intra-cranial bleeds), Infective Endocarditis, Dissection of Aorta and late deaths were noted. Progress of associated lesions and interventions undertaken for associated lesions were also analyzed and compared between the 2 groups.

Restenosis was defined a presence of a gradient of > 20 mmHg between BP of right upper and lower limbs, > 20 mmHg at catheterization or > 25 mmHg on Doppler (30).

Aneurysm was defined as if the diameter of the affected segment was > 150% of descending thoracic aorta at level of diaphragm (30).

Re-intervention for restenosis was advised if the residual gradient was > 40 mmHg on catheterization or if there was medically refractory hypertension despite lower gradients (7).

Hypertension was defined as blood pressure more than 140/90 mmHg in adults or > 95th percentile for age and sex in children or requirement for antihypertensive medications.

Outcome Variables:

The results of surgery and balloon dilatation were compared at immediate post-intervention and then on last follow-up.

The following parameters were compared:

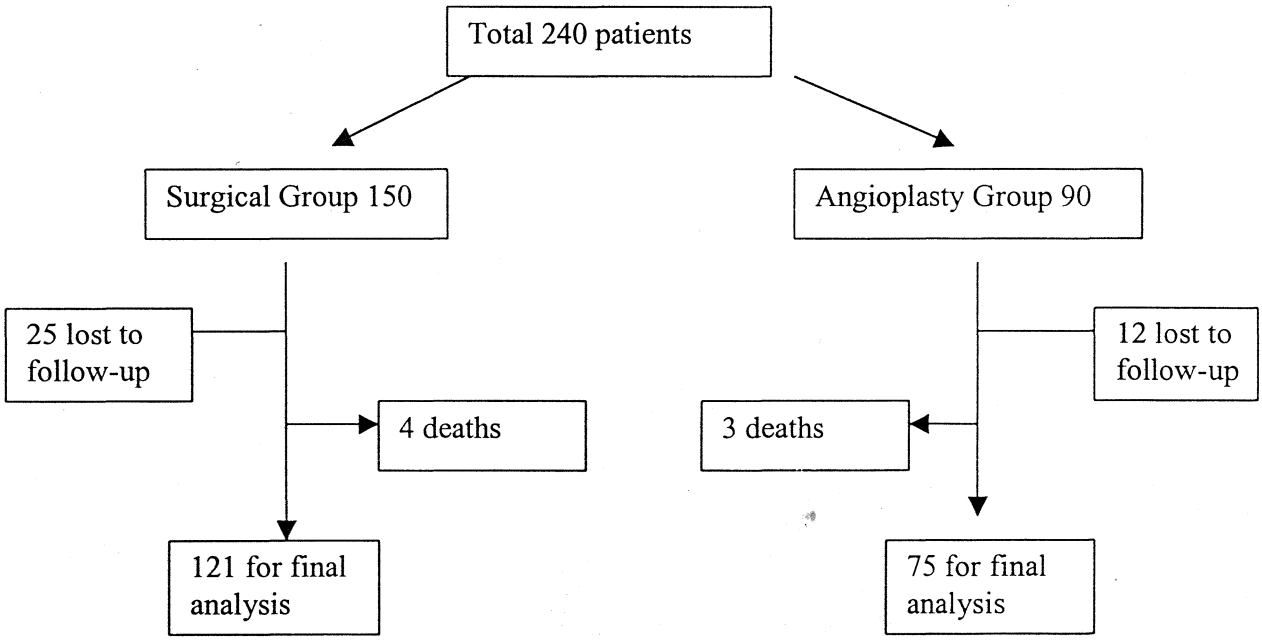
1. Immediate success and complications
2. Residual gradients after intervention.
3. Blood Pressure and arm-leg BP gradients on follow-up.
4. Gradient across Coarctation segment on Echocardiography and cardiac catheterization (if done) on follow-up.
5. Incidence of restenosis and need for re- intervention for restenosis
6. Incidence of aneurysm formation at the site of intervention.
7. Hypertension on long-term follow-up.
8. Late Complications and mortality
9. Progress of associated lesions and interventions for associated lesions.

Statistical Analysis:

Descriptive statistics were performed using the Excel software; results were expressed as mean $\pm$ standard deviation. Comparison of means between 2 groups was done using the Student's 2 tailed T test. Comparison of proportions was done using the Chi Square analysis. P values of < 0.05 were considered to be statistically significant. Multivariate analysis of predictors of restenosis, re-interventions and hypertension was done using SPSS 10 software.

RESULTS

A total of 150 patients satisfying the inclusion criteria had undergone surgical correction of coarctation at our center in the period 1981-1997(including 15 patients who had restenosis after previous balloon angioplasty). Of this, data of 125 patients were available for the present analysis. 90 patients had undergone Balloon Angioplasty during the period 1986-1997. 4 patients in the surgical group died (1 in immediate per-operative period and 3 on follow-up). 3 patients in the the balloon angioplasty group (all infants with complex associated lesions) died within 1 year of follow-up. Of the remaining patients, data of 121 patients in the surgical group and 75 in the balloon angioplasty group were analyzed for long-term results. The remaining 25 patients in surgical group and 12 patients in Balloon Angioplasty group were considered lost to follow-up.



Baseline Characteristics:

1. **Table 1: Clinical Data:**

	Surgery (125)	**Balloon Angioplasty (75)**	**P value**
Age at intervention (years)	16.7 ± 8	15.5 ± 10	NS
Age at follow-up (years)	28.4 ± 11	25.8 ± 12	NS
Sex	M 69.6%; F 30.4%	M: 82.6%; F 17.4%	NS
FC dyspnea			
Class 1	32 (25.6%)	16 (18.3%)	NS
Class 2	91 (72.8%)	58 (77.3%)	NS
Class 3	2 (1.6 %)	1 (1.4 %)	NS
Class 4	0	0	
FC claudication			
Class 1	27 (18.6%)	23 (30.7%)	0.05
Class 2	97 (77.6%)	50 (66.7%)	NS
Class 3	1 (0.8 %)	2 (2.6 %)	NS
Class 4	0	0	
H/O CHF	10 (8 %)	9 (12%)	NS
Blood Pressure (mmHg)			
RUL systolic	160 ± 24	152.9 ± 25	NS
RUL diastolic	93.3± 12	87.6 ± 16	0.004
LUL systolic	151.9 ± 25	148.4 ± 26	NS
LUL diastolic	91.8 ± 13	87.6 ± 16	NS
LL systolic	96 ± 17	91.5 ± 23	NS
Gradient (clinical) mmHg	64.6 ± 21	61.5 ± 25	NS
Antihypertensive Therapy			
No drugs	6 (4.8%)	21 (24%)	<0.001
1 drug	65 (52%)	45 (60%)	NS
2 drugs	47(37.6%)	8 (10.7%)	0.01
3 drugs	7 (5.6%)	1 (1.3%)	0.03

2. **Table 2: Echocardiography Data:**

	Surgery (125)	**Balloon Angioplasty (75)**	**P value**
Coarctation gradient (mmHg)	63.56 ± 17	58.4 ± 17	0.03
Location of Coarctation:			
Post-Subclavian	101 (80.8%)	72 (96%)	<0.01
Juxta-Subclavian	17 (13.6%)	3 (4%)	0.03
Pre-Subclavian	7 (5.6%)	0	
Aortic Valve:			
Bicuspid	99 (79.2%)	63 (84%)	NS
Tricuspid	26 (20.8%)	12 (16%)	NS

3. **Table 3: Catheterization Data:**

	Surgery (125)	**Balloon angioplasty (75)**	**P value**
Ascending Aorta:			
Systolic pressure (mmHg)	162.5 ± 27	154.5 ± 27	0.03
Diastolic Pressure (mmHg)	87.5 ± 16	83.6 ± 23	NS
Descending Aorta:			
Systolic Pressure (mmHg)	101.5 ± 21	98.2 ± 26	NS
Diastolic Pressure (mmHg)	74.3 ± 16	72.6 ± 22	NS
Coarctation gradient (mmHg)	61.6 ± 18	56.2 ± 26	0.06

As can be seen from the above data, baseline characteristics were more or less similar between the 2 groups. Patients in the surgical group had higher baseline diastolic BP which was significant. Though the systolic BP was also higher in the surgical group, it was not statistically significant. Requirement of anti-hypertensive medications were also higher in the surgical group. As expected, more patients in the angioplasty group had post-subclavian coarctation compared to surgical group (96% Vs 80.8%). The ascending aortic systolic pressure at catheterization was significantly higher in the surgical group (162.5 $\pm$ 27 Vs 154.5 $\pm$ 27 mmHg; p 0.03). Though the coarctation gradient at catheterization was higher in the surgical group, the difference was not statistically significant.

Table 4: Associated Lesions:

	Surgery (125)	**Balloon angioplasty (75)**
Total number of patients	47 (38%)	27 (36%)
Shunt lesions		
PDA	16	4
ASD	1	2
VSD	8	6
Aortic Valve Disease		
AS mild	13	5
AS moderate	1	3
AS severe	5	3
AR mild	3	2
AR moderate	1	2
AR severe	0	0
Sub aortic membrane	4	2
Mitral Valve disease		
Congenital MS	5	2
Congenital MR	5	3
Aneurysm	3	0
Peripheral PS	3	2

IMMEDIATE RESULTS

Table 5: Comparison of Immediate Results:

	Surgery (125)	**Balloon angioplasty (75)**	**P value**
Immediate Good Results	121(97%)	44(58.6%)	<0.001
Post- intervention Gradient (mmHg)	5.69 ± 0.7	22.4 ± 9	< 0.001
Mortality	1(0.8%)	0	NS
Non-fatal Complications	13(17.3%)	11(14.6%)	NS
Hospital stay (days)	9.27 ± 2.26	2.5 ± 1.0	<0.001

The comparison of immediate results after intervention overwhelmingly favored surgical group. The immediate good result after intervention (post-intervention gradient < 20 mmHg) as well as mean gradient after intervention was much better in the surgical group. There was a mortality due to post-operative bleeding in the surgical group. The incidence of non-fatal complication was not statistically different between the 2 groups. The mean hospital stay was significantly higher in the surgical group.

Balloon Angioplasty Group:

Of the 90 patients who underwent Balloon Angioplasty, 88 had native coarctation and 2 procedures were done on post surgical jump grafts. There were 10 infants. All patients had hypertension before procedure. The mean balloon diameter was 10.78 ± 3.2 mm. Initial procedural success was obtained in 58.6% of patients. There was no peri-procedural mortality. Post procedural complications were seen in 15 patients (14.6%) and these included femoral artery thrombosis (8), dissections (4), hypertensive crisis(1), transient visual defects(1) and femoral AV fistula(1). 3 patients(all infants) died during follow-up. 12 other patients were lost to follow-up. The data of the remaining 75 patients was available for analysis of long-term outcome.

Table 6: Analysis of predictors of immediate procedural success

	Optimal result	Sub optimal result	P value
Age at intervention (years)	12.06 ± 1.1	19.7 ± 1.4	0.002
SBP right upper limb	153.5 ± 26	153.9 ± 28	NS
DBP right upper limb	88.3 ± 21	86.6 ± 24	NS
Gradient (clinical) mmHg	61.6 ± 23	62.5 ± 24	NS
Gradient on Echo mmHg	57.4 ± 25	59.8 ± 22	NS
Gradient on Cath mmHg	50.4 ± 21	64.3 ± 24	0.003
Balloon size	11.0 ± 3	10.5 ± 2.9	NS
Post procedure gradient mmHg	11.46 ± 2.3	37.67 ± 9	<0.001

The only predictors of initial sub-optimal result were higher age at intervention and a higher gradient across the coarctation segment at catheterization prior to the procedure. Balloon size did not affect the initial results.

Surgical Group:

Of the total of 125 patients included in this analysis, 111 had native coarctation and 14 had undergone previous balloon angioplasty (mean 36 ± 9.8 months prior to surgery). 10 patients (8%) were infants.

The various surgical procedures performed were as follows:

1. Resection and end to end anastomosis (40).
2. Jump Graft (32)
3. Resection and Interposition Graft (30)
4. Patch aortoplasty (18)
5. Subclavian Flap Aortoplasty (5)

20 patients also underwent PDA ligation along with Coarctation repair. 2 patients had aneurysm excision. There was one mortality (0.8%). This was due to massive post-operative bleeding in a patient who had undergone Jump Graft. The other non-fatal complications included: Non-fatal bleeding (3), Paradoxical Hypertension (6), Pneumothorax(3), Wound Infection(1)and Stricture urethra(1).

COMPARISON OF LONG TERM OUTCOME

A: Surgery Versus Balloon Angioplasty (Whole Group):

1. **Table 7: Clinical data**

	Surgery (121)	**Balloon Angioplasty (75)**	**P value**
Duration of follow-up (months)	122.04 ± 48	108 ± 50	0.05
Dyspnea FC 1 FC 2	 95 (78.5%) 26 (21.5%)	 61 (81.3%) 14 (18.7%)	 NS NS
Claudication: FC 1 FC 2	 106 (87.6%) 15 (12.4%)	 59 (79%) 16 (21%)	 NS NS
Blood Pressure (mmHg) SBP RUL DBP RUL SBP RLL	 136.2 ± 19 81.3 ± 13 120 ± 21	 142.8 ± 27 80.1 ± 16 111.7 ± 21	 0.03 NS 0.01
Gradient Clinical (mmHg)	17.2 ± 8	31 ± 7	< 0.001
Gradient (n/%) < 20 mmHg 20 – 40 mmHg > 40 mmHg	 91(75%) 19 (15.9%) 11 (9.1%)	 32 (42.6%) 30 (40%) 13 (17.4%)	 <0.001 0.05 0.05

2. **Table 8: Echocardiography Data**

	Surgery (110)	**Balloon Angioplasty (65)**	**P value**
Mean Gradient (mm Hg)	26.9 ± 8	37.5 ± 12	< 0.01
Echo Gradients: < 25 mmHg 25 – 40 mmHg > 40 mmHg	 72 (59.5%) 31 (25.6%) 18 (14.9%)	 24 (32%) 27 (36%) 24 (32%)	 <0.001 0.03 <0.001

3. Table 9: Re- Catheterization Data

	Surgery (26)	Balloon Angioplasty (45)	P value
Indication			
Routine	4(3.2%)	21 (28 %)	0.001
Recoarctation	12(9.6%)	15 (20%)	NS
Hypertension	3(2.4%)	4(5%)	NS
Aneurysm	1(0.8%)	3(4%)	NS
Associated Lesion	6 (4.8 %)	2(3%)	NS
Duration after intervention (months)	90.8 $\pm$ 15	22 $\pm$ 4	0.001
Gradient at recatheterization (mmHg)	29.9 $\pm$ 10	22.8 $\pm$ 8	NS
Aneurysms	1(4%)	5(11%)	0.03

As can be seen from these results, the overall outcome on long-term follow-up favored surgery over balloon angioplasty. The mean follow-up in both groups was similar (around 10 years). The surgical group had lower systolic BP in right arm as well as lower coarctation gradients on clinical and echocardiographic evaluation (statistically significant). Recatheterization was done in 45 patients in Angioplasty group (60%), while only 26 patients (21%) in surgical group had a recatheterization. Recatheterization was done in the surgical group mostly guided by clinical indication (recoarctation, hypertension, progress of associated lesion). In balloon angioplasty group, the commonest indication for recatheterization was for routine hemodyanamic evaluation to assess success of balloon dilation in the initial cases. This would probably have resulted in the overall higher residual gradients in the surgical group.

Comparison of Surgery with Initial Optimal Result Angioplasty:

a. Table 10: Baseline Characteristics

	Surgery (121)	**Balloon Angioplasty (44)**	**P value**
Age at intervention (years)	16.7 ± 4	12.03 ± 3	0.02
Age at follow-up	28.4 ± 8	22.8 ± 7	0.06
Systolic BP right upper limb (mmHg)	160 ± 24	153.5 ± 25	NS
Diastolic BP Right upper limb (mmHg)	93.3 ± 18	88 ± 17	0.03
Gradient (clinical)	64.6 ± 21	61.6 ± 25	NS
Gradient (echo)	63.56 ± 17	57.4 ± 17	0.03
Gradient (Cath)	61.6 ± 18	50.5 ± 24	0.007
Post-procedure gradient (mmHg)	5.69 ± 0.7	19.7 ± 8	<0.001

b. Table 11: Follow-up Data:

	Surgery (121)	**Balloon angioplasty (44)**	**P value**
Follow-up duration (months)	122 ± 48	123.8 ± 51	NS
Systolic BP Right upper limb (mmHg)	135.8 ± 19	138.3 ± 27	NS
Diastolic BP right upper limb (mmHg)	81.1 ± 13	78.2 ± 16	NS
Gradient Clinical	17.2 ± 7	25 ± 12	0.001
Gradient (echo)	26.9 ± 13	32.7 ± 12	0.02
Hypertension	68(56%)	18(44%)	NS
Re-stenosis Clinical Echo	 30(25%) 49(40.5%)	 20(45%) 26(59%)	 <0.001 0.01
Re-intervention for restenosis	5(4%)	3(6.8%)	NS

The age at intervention was lower in the angioplasty group (12 Vs 16.7 years). The Coarctation gradients by clinical, Echo and catheterization were higher in the surgical group. The immediate post-intervention gradient was lower in the surgical group (5.7 Vs 19.7 mmHg). Systolic blood pressures on follow-up were similar in both groups. The residual coarctation gradients (clinical and Echo)as well restenosis were lower in the surgical group. The re-intervention rates were lower in surgical group, though the result was not statistically significant.

Table 12: Comparison of Long-term outcomes of Initial Optimal Result Versus Sub optimal Result Balloon Angioplasty:

	Optimal result	**Sub optimal Result**	**P value**
Age at follow –up (years)	22.8 ± 10	29.1 ± 12	0.01
Follow-up duration (months)	138.3 ± 48	149 ± 50	0.001
SBP right upper limb (mmHg)	138.3 ± 23	149 ± 29	0.04
DBP right upper limb (mmHg)	78.1 ± 12	82.3 ± 15	NS
Coarctation Gradient mmHg	25 ± 8	39.1 ± 11	0.001
Echo Gradient mmHg	32.6 ± 10	42.9 ± 13	0.008
Recath done (n/%)	26(59%)	23(74%)	<0.001
Gradient Cath mmHg	20.4 ± 9	42.4 ± 12	0.001
Increase in gradient on follow-up mmHg	9.3 ± 2	3.5 ± 1.2	0.004
Reintervention (n/%)	3(6.8%)	15(48.3%)	<0.001
Hypertension n/%	18(41%)	22(71%)	<0.001
Number of anti-hypertensive drugs	0.6 ± 0.15	0.96 ± 0.2	0.05

Patients who had an initial sub-optimal result had higher systolic BP, higher coarctation gradients and greater need for re-interventions and anti-hypertensive medications. But, the increase in gradient from the immediate post-intervention value at recatheterization was greater in patients with initial optimal result.

LONG TERM COMPLICATIONS

Table 13: Complications On Follow-Up

	Surgery (124)	**Balloon angioplasty (75)**	**P value**
Late Deaths	3 (2.4%)	3(4%)	NS
Restenosis Clinical Echo	 30(25%) 49(40.5%)	 43(57.4%) 51(68%)	 <0.001 0.05
Re-intervention for restenosis	3.2%	22.7%	<0.001
Re-intervention for associated lesions	7.3%	8%	NS
Aneurysms	4%	11%	N S
Hypertension	56.2%	58.6%	NS
CAD symptoms	4 (3.2%)	0	NS
Neurological events	3 (2.4%)	4 (5.3%)	NS

1. Late Mortality:

Late mortality was similar in both the groups. There were 3 deaths in both groups on follow-up. In the balloon angioplasty group, all 3 deaths occurred in infants with complex associated lesions within 1 year of intervention. In the surgical group, I patient died of fungal endarteritis and sepsis, another patient died during redo surgery for SAM excision and the third patient had sudden cardiac death at home.

2. Restenosis and Re-interventions for Re- Coarctation:

Restenosis was higher in balloon angioplasty group compared to surgery (57.4% Vs 25%, $p < 0.001$). When a separate analysis comparing restenosis rate between initial good result angioplasty (defined as residual gradient < 20 mmHg) and surgery was done, the results still favored the surgical group.

Table 14: Re-Interventions For Coarctation

	Surgery (121)	Balloon Angioplasty (75)	P value
No: of re-interventions	4 (3.2%)	17 (22.7%)	<0.001
Type of re-intervention: Surgery PTBA	 1 (0.8%) 3 (2.4%)	 11 (14.7%) 6 (8%)	
Interval from primary procedure (months)	128 ± 90	29.1 ± 8.8	<0.001

Re-interventions of restenosis were also higher in balloon angioplasty group (22.7% Vs 3.2%; p <0.001). 3 of the 4 re-interventions in surgical groups were balloon angioplasties. In the balloon angioplasty group, 11 patients underwent surgery for re-stenosis while 6 were treated by repeat balloon angioplasty.

Predictors of restenosis and re-intervention:

Balloon Angioplasty Group:

Restenosis occurred in 43 out of 75 patients (57.4%) in the angioplasty group.

Predictors of restenosis:

On Univariate Analysis, predictors of restenosis included Balloon size (10.2 ± 1.6 in patients with restenosis Vs 11.6 ± 1.4 mm versus those without, p 0.04) and post intervention gradient(26.7 ± 5 Vs 16.3 ± 3 mmHg; p 0.006). Factors like age at intervention, sex, pre-intervention blood pressures, morphology of aortic valve (bicuspid or tricuspid) and pre-intervention gradients (clinical, Echo or catheterization) did not predict restenosis. Patients with restenosis had higher systolic and diastolic BP on follow-up and required re-intervention more often than those without restenosis (32.5% Vs 12.5% ; p <0.001). On multivariate analysis also, the same factors (balloon size and post-intervention gradient) remained as the only predictors of restenosis on follow-up.

Predictors of Re-intervention:

Re-intervention for restenosis was done in 17 patients (22.7%). 11 patients underwent surgery and 6 underwent repeat balloon angioplasty.

On univariate analysis, balloon size (9.7 ± 1.3 Vs 11.3 ± 2 mm ; p 0.02), post-intervention gradients(34 ± 6 Vs 16 ± 3 mmHg; p < 0.0001) and gradients on follow-up (40.9 ± 11 Vs 25.6 ± 9 mmHg; p 0.001) were significant predictors of need for re-intervention. Factors like age at intervention, sex, pre-intervention blood pressure, morphology of aortic valve and pre-intervention gradients (clinical, echo and Catheterization) were not associated with increased need for re-intervention. On multivariate analysis also, the same factors remained as significant predictors of re-intervention.

Surgical Group:

The only predictor of restenosis in the surgical group was higher residual gradient after surgery (8.9 ± 2.1 Vs 4.5 ± 1.2; p 0.008).

3. Re-Interventions For Other Indications (Table 15)

	Surgery (121)	**Balloon angioplasty (75)**	**P**
Aneurysm	1 (0.8%)	0	NS
Associated Cardiac anomalies:			
Done already	8 (6.5%)	6 (8%)	NS
Advised, but not done	3 (2.4%)	4 (5.3%)	NS
Non-cardiac reasons	0	2 (2.7%)	NS

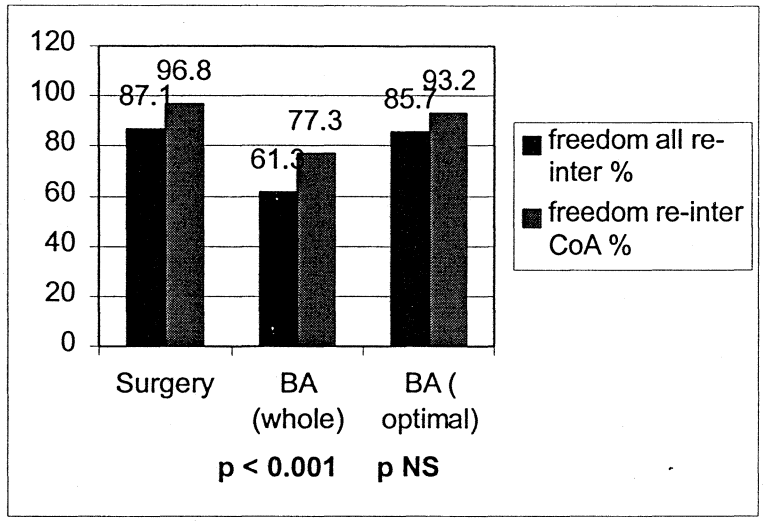
Details of Interventions for associated lesions were as follows:

Surgical Group: AVR 5 patients (all for severe AS), AVR + SAM excision 1 patient, SAM excision 1 and ASD closure 1. 3 patients were advised AVR which has not yet been done.

Angioplasty group: AVR 3 patients, AVR + SAM excision 1, ASD closure 1 and VSD closure 1. 2 patients underwent neurosurgical procedures (aneurysm clipping). 4 other patients were advised surgery (DVR 1, Bentall procedure + MVR 1, AVR + Coarctation repair 1 and ASD closure 1).

Freedom from Re-intervention

The overall freedom from re-intervention at 10 years is presented in **Figure 1.**



Surgical group had lower incidence of re-interventions at 10 years primarily because of lower incidence of re-interventions for re-coarctations. Comparison of surgery and initial optimal result angioplasty showed no statistically significant difference in incidence of re-interventions at 10 years.

4. HYPERTENSION ON FOLLOW-UP

Hypertension was observed in 56.2% of surgical patients and 58.6% of balloon angioplasty patients on long-term follow-up (no statistically significant difference). The mean systolic BP was higher in the angioplasty group (142.8 $\pm$ 26 Vs 135.8 $\pm$ 19 mmHg; p 0.03). Diastolic BP or the requirement of number of anti-hypertensive drugs was not significantly different between the 2 groups. In all groups there was a significant reduction in number of anti-hypertensive medications on follow-up compared to before intervention.

Analysis of predictors of hypertension on follow-up are summarized below.

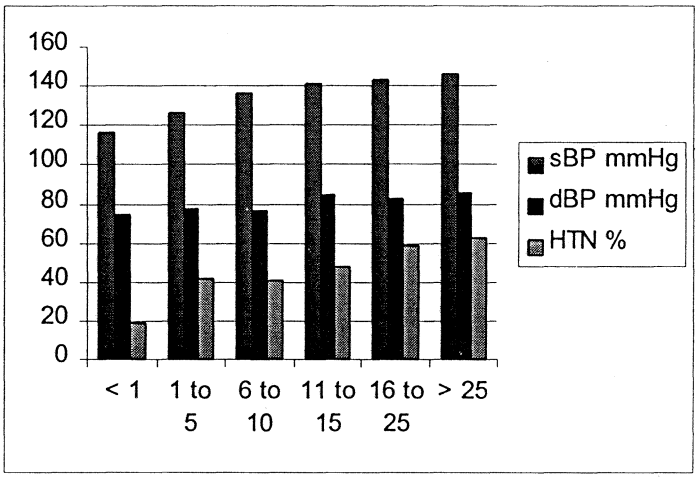
A: Whole group:

Table 16: Univariate Predictors of hypertension

	No hypertension	**Hypertension**	**P**
Age at intervention (years)	13.3 ± 6	18.5 ± 10	0.001
Age at follow-up (years)	24.5 ± 12	29.8 ± 14	0.001
SBP pre-intervention (mmHg)	150.6 ± 26	163.6 ± 18	0.001
DBP pre-intervention (mmHg)	90 ± 14	91.8 ± 13	NS
Gradient clinical pre (mmHg)	61.4 ± 23	64.9 ± 18	NS
Gradient echo Pre (mmHg)	58.9 ± 15	64.2 ± 16	0.005
Gradient cath pre (mmHg)	55.7 ± 22	62.3 ± 18	0.02
Post intervention gradient mmHg	10.8 ± 5	13 ± 6	NS
Follow-up duration (months)	108.2 ± 46	124.5 ±51	0.02
SBP follow-up (mmHg)	124 ± 17	151.9 ± 17	<0.001
DBP follow-up (mmHg)	75.3 ± 11	85.8 ± 15	<0.001
Follow-up Gradient clinical mmHg	17.4 ± 8	27.3 ± 12	<0.001
Follow-up Gradient Echo mmHg	25.4 ± 12	36.2 ± 17	<0.001

On multivariate analysis, only age at intervention, pre-procedure Echo gradient and residual gradient on follow-up (both clinical and Echo) remained as significant predictors of hypertension. Age at intervention of ≤ 10 years was significantly associated with lower systolic (129.5 ± 20 Vs 143.5 ± 35 mmHg; p <0.0001) and diastolic blood pressures (76 ± 19 Vs 83.4 ± 22 mmHg; p 0.0002) compared with age > 10 years. The overall prevalence of hypertension was 37% in patients intervened ≤ 10 years compared to 57% in those whose age at intervention was > 10 years (p < 0.0001).

Figure 2: Effect of Age at intervention on Blood Pressures and Hypertension on follow-up.



B: **Surgical Group:**

On univariate analysis, post-intervention gradient (6.6 ± 2 Vs 3.8 ±1.9 mmHg, p 0.05), duration of follow-up (148.6 ± 51 Vs 110.5 ± 74 months, p 0.03) and residual gradients on follow-up (clinical 22.2 ± 17 Vs 11 ± 6 mmHg, p<0.001; Echo 32.8 ± 19 Vs 19.7 ± 12 mmHg, p<0.001) were significant predictors of hypertension. On multivariate analysis, only follow-up residual gradient remained as significant predictors.

C : **Balloon angioplasty group:**

On univariate analysis, pre-intervention Echo gradients (61.2 ± 18 Vs 54.5 ± 18 mmHg, p 0.03), post-dilatation gradient (26.8 ± 15 Vs 16 ± 8 mmHg, p 0.003) and residual gradient on follow-up(clinical 38.4 ± 12 Vs 18 ± 10 mmHg, p < 0.001; Echo 43.2 ± 18 Vs 29.8 ± 10 mmHg, p <0.001) were significantly associated with hypertension. On multivariate analysis, the only predictor of hypertension was residual gradient on follow-up (clinical and echo).

6.Aneurysms

The incidence of aneurysm was lower in surgical group, though not statistically significant. (4 % Vs 11%). One reason could be under detection of aneurysms in the surgical group since only 21% of surgical patients had undergone re-catheterization compared to 60% of angioplasty patients. No predictors of late aneurysms could be identified in this study.

7.Coronary artery Disease

Anginal symptoms were noted in 4 patients (3.5%) in the surgical group. 3 patients had a positive ischemic response during TMT. Of these, 2 had angiographically documented CAD (one proximal LAD lesion and another 3 vessel disease). These patients were advised CABG. The 3rd patient with positive TMT has been advised CAG. No patient in the balloon angioplasty had anginal symptoms or positive TMT.

7. Neurological Complications

Neurological complications occurred in 3 patients in surgical group (1 intra-cranial bleed, one CVA and one case of cerebral palsy) and 6 patients in the angioplasty group(3 SAH, 1 seizure and 1 case of CVA).

DISCUSSION

Surgery and Balloon Angioplasty are the 2 major forms of interventional treatment for Native Coarctation of Aorta. Several studies reported in the past have attempted to compare the outcomes of these 2 forms of treatment for coarctation (20 –24). Limitations of these comparisons included relatively short duration of follow-up (21) and comparison of surgical series in the 1960s and 1970s with angioplasty series of the 1980s (22,23). The results of these comparisons are conflicting with Shaddy et al (21) and Johnson et al (22) emphasizing superiority of surgery, while Rao et al (23, 24) reporting equivalent results in patients above 1 year of age. In this study, we have attempted to compare long term results with a 10 year follow-up of the 2 modalities of treatment done at the same center during similar time periods (Surgery 1981-1997; Angioplasty 1986 – 1997).

Baseline Characteristics and Associated Lesions:

The baseline characteristics were evenly matched the 2 groups. The patients in the surgical group had Blood Pressures and Coarctation gradients slightly higher than those in angioplasty group. Associated anomalies (excluding bicuspid aortic valve) were seen in about 38% in surgical group and 36% in angioplasty group, commonest being PDA. The prevalence of bicuspid aortic valve was very high in this study (around 80% in the whole group). The prevalence of bicuspid aortic valve in association with coarctation is 25 – 60% in most of the published studies (31, 32). The only other study which has reported a similar high association of Bicuspid Aortic Valve with coarctation was the one by Edwards et al (33), who reported a prevalence of 85%.

Immediate Results:

Immediate results (as defined by post-procedure gradient $\leq$ 20 mmHg) were considerably superior with surgery compared to balloon angioplasty. Initial optimal results were obtained in 97% of surgery patients compared to 58.6% of angioplasty patients. The initial successful result with angioplasty is much lower in this study compared to most of

the published studies, which have reported initial procedural success in 78 – 91%(7, 8, 12). Shaddy et al had reported similar initial results in their randomized control trial (21).

There was only one immediate mortality in the whole group (in surgical group). There was no significant difference in the incidence of nonfatal complications (17.3% in surgery vs. 14.6% in angioplasty). In the angioplasty group, the significant predictors of initial successful result included younger age at intervention and lower pre-intervention gradients. Balloon size did not affect the immediate outcome. These results are similar to those reported previously (McCrindle et al 1996 – VACA Registry)(12).

Long Term Outcomes:

Long-term follow-up in this study was primarily by assessment of clinical parameters. Majority of patients underwent Echocardiography for assessment of residual gradients and evaluation of associated lesions. Cardiac catheterization was performed only in 20% of surgical patients on follow-up while 60% of patients in angioplasty group had follow-up catheterizations. This was because repeat catheterization in surgical patients was primarily due to clinical indications while in majority of angioplasty patients it was done for routine hemodynamic evaluation, especially in the early cases of balloon dilation. The overall long-term results favored surgery in comparison to balloon angioplasty as has been shown Shaddy et al (21) and Johnson et al (22). Our findings contradict the results of Rao et al (23,24) who reported equivalent results in patients above age of one year.

Residual Gradients , Restenosis and Re-interventions:

Residual gradients in this study was assessed primarily by clinical (arm-leg BP difference) and by Echocardiography. Cardiac Catheterization was performed only in a minority of surgical patients. Residual gradients were significantly higher by clinical and Echocardiography in angioplasty patients compared to surgery. Comparison of residual gradients between initial optimal angioplasty and surgery still favored surgery. In contrast, there was no significant difference between residual gradients on cardiac catheterization between the 2 groups. This is probably because of the fact that repeat

cardiac catheterization in surgical patients was primarily done when indicated clinically (restenosis, hypertension).

Restenosis in this study was defined as clinical gradients > 20 mmHg (7) and Echo gradients > 25 mmHg (30). Rao etal (34) and Marx et al (35) in previous studies have pointed out fallacies associated with Echocardiographic assessment of restenosis. The prevalence of restenosis was higher in angioplasty group (57.4% vs. 25%; p <0.001). Restenosis was also higher in the optimal result angioplasty compared with the surgical group (45% vs. 25%; p <0.001).

Re-interventions for restenosis were also much higher in angioplasty group (22.7% vs.3.2%; p<0.001). Comparison between initial optimal balloon angioplasty and surgery showed no significant difference in re-intervention rates between the 2 groups. Comparison of long-term outcomes after initial optimal and sub-optimal angioplasty groups overwhelmingly favored the optimal result group with respect to residual gradients, restenosis and re-interventions.

These results agree with those reported by Shaddy et al (21) and Johnson et al (22) in that surgery in superior to angioplasty for native coarctation of aorta. Compared to other studies, restenosis rates are higher for both surgery (3-6) as well as balloon angioplasty (7-19). Re-intervention rates are similar to both forms of treatment as compared to previous studies, perhaps because of higher thresholds followed for re-interventions (residual gradients > 40 mmHg or severe medically refractory hypertension with lower gradients).

Analysis of predictors of restenosis and re-interventions in the angioplasty group identified balloon size and immediate post-angioplasty gradients as the significant factors. These results are similar to those previously reported (7, 8, 13). We did not analyze the effect of arch hypoplasia and isthmus size on restenosis in angioplasty group. There was no influence of morphology of aortic valve on restenosis. In the surgical group, the only predictor of restenosis was higher post-operative residual gradient.

Shaddy et al (21) had reported residual gradient of $\geq$ 12 mmHg as a predictor of restenosis on follow-up. The overall superior results in the surgical group in the present study was primarily because of much lower immediate post-intervention residual gradients in the surgical group compared to angioplasty (5.69 mmHg vs 22.4 mmHg). There was no association between age at repair and restenosis in both groups. These results contradict previous reports which report higher restenosis rates in younger patients (5, 6, 7, 8). This may be because of the fact that there were very few infants in the present study.

Aneurysms:

Most of the published studies (7-19, 21) have reported higher frequency of aneurysms after balloon angioplasty compared to surgery. The only form of surgery which has a high prevalence of aneurysms on follow-up is Patch Aortoplasty (up to 33% in some series). In this study also, the prevalence of aneurysms were higher in angioplasty group, though not statistically significant (11% vs. 4%). However, there is a distinct possibility that aneurysms were under-detected in the surgical group because of fewer recatheterizations. MRI or CT was not employed in this study. Therrien et al (30) had reported that the most sensitive and specific modality to detect aneurysms was MRI. In their study, the sensitivity and specificity of clinical evaluation combined with Echocardiography (the method followed in our study) for detection of aneurysms was 83% and 34% respectively.

Hypertension:

Hypertension is a very common complication in survivors of Coarctation repair, with reported incidence of 20 – 70% (average 35%) in various studies (5, 6, 16, 36 -40). In the present study, Hypertension was observed in 56% of surgical and 58.6% of angioplasty patients on long term follow-up (no statistically significant difference between the 2 groups). The systolic blood pressures were significantly higher in the angioplasty group. The prevalence of hypertension on follow-up is much higher in our study compared to previous studies reporting long-term follow-up (4, 5,6). Analysis of predictors of hypertension showed that age at repair was the most important predictor of long-term

hypertension. Prevalence of hypertension as well as systolic and diastolic Blood Pressures were significantly lower in patients intervened before 10 years of age compared to those intervened later. This is similar to the findings of Cohen et al (5) who reported lowest prevalence of hypertension in patients operated before 9 years of age. The possible reason for the high prevalence of hypertension in our series may be because of the relatively higher age at initial intervention compared to other reported studies.

The only other factor which predicted hypertension on follow-up was the residual coarctation gradient. This contradicts the findings of Toro-Salazar et al who reported no association between residual gradients and long-term hypertension (6).

The findings of our study indicates that intervening at a younger age (< 10 years) and ensuring a optimal relief of coarctation at initial intervention are the required strategies to reduce the incidence of long-term hypertension.

Interventions for Associated Lesions:

Interventions for associated lesions were required in 10% of surgical patients and 16% in angioplasty group. The commonest indication for intervention was progression of aortic valve disease necessitating Aortic Valve replacement (75% of all interventions for associated lesions in surgical group and 60% in angioplasty group). Most of these (> 90%) occurred in the setting of bicuspid aortic valve. Roos-Hesslink et al (32) had recently reported that 22% of patients surviving coarctation repair require AVR for progression of aortic valve disease. Aortic Valve Replacement was required in 7% of late survivors of Coarctation repair in the series reported by Cohen et al (5) and 5.9% in the study by Toro-Salazar et al (6) respectively.

Late mortality and other complications:

Late mortality was similar in both groups and was relatively low (2.4% in surgery vs. 4% in angioplasty). The causes of death in surgical group included death during re-intervention, infective endarteritis and sudden death. All deaths in angioplasty group occurred in infants with complex coarctation primarily due to the other associated conditions. There were no deaths directly attributed to Coronary artery Death (cause of one sudden death was unknown). In both the large surgical series from Mayo Clinic (5)

and Michigan University (6), the commonest cause of late death was Coronary artery disease. In our series, documented CAD (positive stress test or coronary angiogram) was found only in 3.5% of surgical patients and none in the angioplasty patients. This low incidence of coronary artery disease on follow-up is perhaps due to the relatively young age of patient on follow-up (mean age at follow-up < 30 years in both groups). The average age for development of CAD was 38 years in the Mayo Series (5) and 34.4 years in Michigan series(6).

LIMITATIONS OF THE STUDY

1. This being a retrospective analysis has inherent limitations in analysis of pre-intervention data and clinical assessment.
2. Analysis of arch dimensions with respect to results of balloon angioplasty was not attempted in this study (though patients with unfavorable arch anatomy were not considered of angioplasty).
3. Follow-up of most of the patients were based on clinical assessment and Echocardiography. Cardiac catheterization was sparingly employed in the surgery group on follow-up.
4. Aneurysms on follow-up may have been under-detected in surgical group since catheterization was performed only in 20% of these patients on follow-up. Also, MRI / CT scans were not employed in this study. Also, the fate of these aneurysms has not been addressed to in this study.
5. Around 16% of patients in both groups were lost to follow-up. This may have interfered with analysis of long-term survival and re-intervention rates.

CONCLUSIONS

1. Long-term follow-up results are superior with Surgery compared to Balloon Angioplasty for native Coarctation of Aorta. The prevalence of restenosis and re-interventions are lower with surgery compared to angioplasty.
2. One major factor which determines the long-term outcome is the completeness of relief of coarctation at the time of initial intervention. Patients with significant residual gradients after intervention have higher prevalence of restenosis and hypertension on long-term follow-up compared to those with initial optimal results.
3. Hypertension is very common in long term survivors of coarctation repair. The most important predictor of hypertension on follow-up was age at intervention. Intervention before the age of 10 years is recommended to reduce the prevalence of long-term hypertension.
4. About 20% of survivors require interventions for progression of associated lesions, especially aortic valve disease.
5. The present study underlines the hypothesis that "survivors of coarctation repair are only fixed, not cured" and emphasizes the importance of continuous monitoring of these patients into adult life to detect long-term complications.

REFERENCES

1. Campbell M. Natural History of Coarctation of Aorta . British Heart journal 1970;32:633-640

2. Gibbs J. Treatment options for Coarctation of Aorta. Heart 2000; 84: 11-13

3. Backer CL, Mavroudis C. Coarctation of Aorta and Interurupted Aortic Arch. In Glenn's Thoracic and Cardiovascular Surgery Editors: Baue AE, Geha AS, Laks H, Hammond GL, Naunheim KS 1996 (6th edition) Vol II: pp 1243-69. Appleton and Lange Publications.

4. Kirklin JW, Barrat-Boyes BG. Coarctation of Aorta and Interrupted Aortic Arch. In: Cardiac Surgery. 1993 (2nd edition) pp 1263-1326. Churchill Livingstone Publications.

5. Cohen M, Fuster V, Steele PM, Driscoll D, McGoon DC . Coarctation of Aorta : Long term follow-up and prediction of outcome after surgical correction. Circulation 1989; 80 : 840 – 845

6. Toro-Salazar OH, Steinberger J, Thomas W, Rocchini AP, Carpenter B, Moller JH. Long-Term Follow-up of patients after Coarctation of Aorta repair. American Journal of Cardiology. 2002; 89: 541-547

7. Ovaert C, Benson LN, Nykanen D, Freedom RM. Transcatheter treatment of Coarctation of Aorta: A review. Pediatric Cardiology 1998; 19: 27-44

8. Rao PS, Galal O, Smith PA, Wilson AD. Five to Nine year follow-up results of Balloon Angioplasty of Native Aortic Coarctation in infants and children. Journal of American College of Cardiology 1996;27: 462-70

9. Ovaert C, McCrindle BW, Nykanen D, Macdonald C, Freedom RM, Benson LN. Balloon Angioplasty of Native Coarctation : Clinical outcomes and predictors of success. Journal of American College of Cardiology 2000;35:988-996

10. Tynan M, Finley JP, Fontes V, Hess J, Kan J. Balloon Angioplasty for the treatment of native coarctation: results of Valvuloplasty and angioplasty of Congenital Anomalies Registry. American Journal of Cardiology 1990;65:790-792

11. Koerlselmann J, deVreies H, Jaarsma W, Muyldermans L, Ernst JMPG, Plokker HWM. Balloon Angioplasty of Coarctation of Aorta: a safe alternative for surgery in adults. Immediate and Mid term results. Catheterization and Cardiovascular Interventions.2000; 50: 28-33

12. McCrindle BW, Jones TK, Morrow WM, Hagler DJ, Lloyd TR, Nouri S, Latson LA. Acute results of Balloon angioplasty of native coarctation versus recurrent aortic obstruction are equivalent.(VACA Registry). JACC 1996;28: 1810-7

13. Ray DG, Subramanyam R, Titus T, Tharakan JM, Joy J, Venkitachalam CG, Balakrishnan KG. Balloon angioplasty for native coarctation of aorta in children and adults: factors determining outcome. Int Journal of Cardiology 1992;36:273-81

14. Kaine SF, Smith EO, Mott AR, Mullins CE, Geva T. Quantitative echocardiographic analysis of the aortic arch predicts outcome of balloon angioplasty of native coarctation of aorta. Circulation 1997; 96:1057-9

15. Tyagi S, Arora R, Kaul UA, Sethi KK, Gambhir DS, Khalilillah M. Balloon angioplasty of native coarctation of aorta in adolescents and young adults. Am Heart journal 1992; 123: 674-80

16. Fawzy ME, Sivanandam V, Pieters F, Stefadouros MA, Galal O, Dunn B et al . Long term effects of balloon angioplasty on systemic hypertension in adolescent and adult patients with coarctation of aorta. Eur Heart Journal 1999;20: 827-32

17. Mendelsohn AM, Lloyd TR, Crowley DC, sandhu SK, Kocis KC, Beekman RH. Late follow-up of balloon angioplasty in children with native coarctation of aorta. Am Journal of cardiology 1994; 74: 696-700

18. Fawzy ME, Sivanandam V, Galal O, Dunn B, Patel A, Rifai A et al. One to Ten year follow-up results of balloon angioplasty of native coarctation of aorta in adolescents and adults. JACC 1997: 30: 1542-6

19. Fletcher SE, Nihill MR, Grifka RG, O'Laughlin MP, Mullins CE. Balloon angioplasty of native coarctation of aorta: mid term follow-up and prognostic factors. JACC 1995;25:730-4

20. Hanley FL. The various therapeutic approaches to aortic coarctation: is it fair to compare? JACC 1996;27:471-2

21. Shaddy RE, Boucek MM, Sturtevant JE, Ruttenburg HD, Jaffe RB, Tani LY et al. Comparison of angioplasty and surgery for unoperated coarctation of aorta. Circulation 1993;87:793-799

22. Johnson MC, Canter CE, Strauss AW, Spray TL. Reapir of coarctation of aorta in infancy: comparison of surgical and balloon angioplasty. Am Heart Journal 1993;125:464-468

23. Rao PS, Chopra PS. Role of balloon angioplasty in treatment of coarctation of aorta. Annals of thoracic surgery 1991;52: 621-31

24. Rao PS. Should balloon angioplasty be used instead of surgery for native coarctation? British Heart journal 1995;74:578-579

25. Rosenthal E. Stent Implantation for aortic coarctation: the treatment of choice in adults? JACC 2001;38:1524-27

26. Cheatham JP. Stenting of Coarctation of aorta. Catheterization and cardiovascular interventions 2001;54:112-125

27. Hamdan MA, Maheswari S, Fahey JT, Hellenbrand WE. Endovascular stents for coarctation of aorta. Initial results and intermediate term follow-up.JACC 2001;38:1518-23

28. Ledesma M, Alva C, Gomez D, Sannchez-Soberanis A, Diaz ED, Benitez-Perez C et al . results of stenting for aortic coarctation Am Journal of Cardiology 2001;88:460-2

29. Mullen MJ. Coarctation of aorta in adults: do we need surgeons? Heart 2003;89: 3-5

30. Therrien J, Thorne SA, Wright A, Kilner PJ, Somerville J. Repaired coarctation: A cost effective approach to identify complications in adults. JACC 2000; 35: 997-1002

31. Tawes RL, Berry CL, Aberdeen E. Congenital bicuspid aortic valve associated with coarctation of aorta in children. British Heart journal 1969; 31:127-8

32. Roos-Hesslink JW, Scholzel BE, Heijdra RJ, Spitaels SEC, Meijboom FJ, Boersma E et al. Aortic Valve and arch pathology after coarctation repair. Heart 2003; 89: 1074-77

33. Edwards JE. The congenitally bicuspid aortic valve. Circulation 1961;23:485-8

34. Rao PS, Carey P. Doppler ultrasound in prediction of pressure gradients across Coarctation of the aorta. Am Heart J 1989;118:299

35. Marx GR, Hugh DA. Accuracy and pitfalls of Doppler evaluation of pressure gradient in aortic coarctation. JACC 1986;7: 1379-85

36. Bhat MA, Neelakandhan KS, Unnikrishnan M, Rathore RS, Mohan Singh MP, Lone GN. Fate of hypertension after repair of coarctation of aorta in adults. British journal of Surgery. 2001;88: 536-538.

37. de Divitiis M, Pilla C, Kattenhorn M, Donald A, Zadinello M, Wallace S et al. Ambulatory Blood pressure, left ventricular mass and conduit artery function late after successful repair of coarctation of aorta. JACC 2003; 41: 2259-65

38. O'Sullivan JJ, Derrick G, Darnell R. Prevalence of hypertension in children after early repair of coarctation of aorta: a cohort study using casual and 24 hour blood pressure measurement. Heart 2002;88:163-66.

39. Schrader R, Bussmann WD, Jacobi V, Kadel C. Long term effects of balloon coarctation angioplasty on arterial blood pressure in adolescent and adult patients. Catheterization and Cardiovascular Diagnosis 1995;36:220-5

40. Celermajer DS, Greaves K. Survivors of coarctation repair: fixed not cured. Heart 2002;88:113-4.

INTERMEDIATE TERM (2 YEAR) FOLLOW-UP OF TRANSCATHETER CLOSURE OF SECUNDUM TYPE OF ATRIAL SEPTAL DEFECTS WITH AMPLATZER SEPTAL OCCLUDER WITHOUT THE AID OF PERI-PROCEDURAL TRANS-ESOPHAGEAL ECHOCARDIOGARPHY

INTRODUCTION

Trans-catheter closure has emerged as an effective alternative to surgery in patients with secundum type of Atrial Septal defects (ASD). King and Mills first successfully performed trans-catheter closure of ASD in 1974. Since then several devices were introduced for this purpose like the Rashkind ASD Occluder, Clamshell Device, Angelwing Device, ASDOS device, Sideris Buttoned device and the CardioSeal device (1). These devices did not find wide spread clinical application in view of problems like need for large delivery sheaths, complex implantation procedures, inability in repositioning, high degree of residual shunts, arm fractures and embolisation (1).

The Amplatzer Septal Occluder (ASO) has become the most widely used device for trans-catheter closure of secundum ASD , overcoming the disadvantages of its predecessors (2). The main advantages of the ASO device are the relatively simple technique of implantation, ability to be successfully retrieved and repositioned even after opening and the very low incidence of residual shunts on follow-up. This is particularly the case in patients with large defects with deficient rims.

A recent study by Podnar et al had shown that 80% of secundum ASDs can be successfully closed using the ASO(3). This device can be successfully deployed in all patients with defect size of upto 30 mm on trans-thoracic or trans-esophageal Echo (TEE) provided there are adequate margins (at least 5 mm) from surrounding structures(3). A deficient antero-superior(aortic) rim does not preclude use of the ASO device. Worldwide experience with the use of ASO has shown excellent results in both short term as well as intermediate term(upto 2 years) follow-up (4 – 18). The overall procedural success has been around 95% in the various reported studies . Recent studies have shown that with modifications of techniques of deployment , the ASO device can be successfully used to close larger defects of upto 35 mm (19).

Most of the studies of ASD closure using the ASO have reported that intra-procedural use of TEE greatly facilitates the successful implantation of the device and significantly lowers failure rates. (20 - 27). Peri-procedural TEE is recommended by many authors as an essential pre-requisite for trans-catheter closure of ASD, especially large defects

(2).There has been very few reports of ASD device closure using the ASO device without the use of intra-procedure TEE.

Procedural complications have been described in 3-10% of cases(17, 28). The most common of these include device embolisation(3.5%), arrhythmias(2.6%), pericardial effusion, transient ST segment elevation in inferior leads(air embolism), groin complications and rupture of sizing balloon (20). There has been no reported mortality during the procedure(17).

Most of the studies reporting follow-up have shown excellent results on long term follow-up(4-18). Complete occlusion without residual shunts have been reported in 85%, 92% and 98.7% of patients at 24 hours, 1 month and 3 months after procedure(5). A meta-analysis by Omeish et al on the world wide experience with ASO device (3535 patients; 3580 implants) had shown 97% total occlusion rate at 1 month which became nearly 100% at 6 months (17). Most of the studies have analyzed residual shunts on follow-up using transthoracic echocardiography. Cao et al reported use of TEE for assessing residual shunt on follow-up and reported complete closure of the defect in 91.4% of patients at 6 months after implantation (29).

Studies have shown that after ASO implantation there is significant resolution of right heart enlargement(RA, RV volumes.), particularly in the first 3-6 months after the procedure(30). After 6 months, significant regression of RA, RV size does not occur. The resolution of right heart enlargement in significantly more in younger patients

The incidence of long term complications after ASD closure using the ASO device has been relatively few in most of the studies. Late device embolisation, thromboembolic complications, atrial tachyarrythmias, stroke, nickel toxicity, RA-Aorta Fistula and sudden cardiac death(1 report) are among the various long term complications reported in various studies(4-19, 28). Studies reporting on 24 hour Holter monitoring after ASO implantation have shown higher prevalence of Atrial Premature Complexes, supraventricular tachycardias and occasional instances of AV conduction blocks(31, 32). Higher incidence of conduction abnormalities are more common in patients with older age at device implantation and a larger Qp/Qs ratio before procedure(31).

AIMS OF THE STUDY

1. To assess the feasibility of trans-catheter closure of secundum ASD using the Amplatzer Septal Occluder(ASO) device without the aid of peri-procedural TEE.
2. To analyze the long term results and prevalence of residual shunts after trans-catheter closure of secundum ASD using the ASO device.

MATERIAL AND METHODS

Patient Population:

The present study was conducted in a tertiary care referral center in South India between Nov 1998 and December 2002. All patients with clinically significant secundum ASDs which required correction were considered for device closure with ASO. These patients were then evaluated for suitability for trans-catheter closure using ASO by trans-thoracic and subsequently trans-esophageal echocardiogram. All patients with a defect size of less than 30 mm on TEE and a septal rim of at least 5 mm from the right pulmonary vein, coronary sinus, superior and inferior venae cavae and mitral valve were considered potentially suitable for device closure (1). Patients with only deficient aortic rim were also considered for device closure. Patients with multiple defects, inadequate rims other than aortic rim, defects in primum or sinus venosus location and those with significant associated cardiac defects which merited surgery were excluded

Pre-implantation assessment

All patients were clinically assessed for the magnitude of the shunt. Chest X-ray and ECG were performed in all. Trans-thoracic Echocardiogram (TTE) was performed to assess the size and position of defect, number of defects, adequacy of rims, septal motion, RA, RV size and RV systolic pressure (RVSP) by tricuspid regurgitation jet. Any associated cardiac defects were also looked for. Subsequently, a trans-esophageal echocardiogram was performed in transverse and longitudinal planes to confirm the findings of TTE and also to check the adequacy of septal rims. The maximum measured diameter of the ASD in any given plane was taken as the size of the defect.

The device

The Amplatzer Septal Occluder (ASO; AGA Medical Corporation; Golden Valley, Minnesota,USA) was used for transcatheter closure of the ASD in all patients. A prototype of the device has been described previously (4).

Technique of implantation:

The procedure was performed under local anesthesia in adults. Children were done under sedation or ketamine without need for intubation. A complete oximetry and hemodyanamic study was performed initially. The shunt ratio (Qp/Qs ratio), PA pressures and PVR were noted in all patients. Normal pulmonary vein drainage was ensured either by entering individual pulmonary veins or by using levophase of pulmonary artery angiography. After that balloon sizing of the defect was performed using the Meditech sizing balloon catheter by standard methods. The stretched diameter of the ASD was defined as the diameter of a balloon that can be withdrawn across the ASD with mild resistance and slight deformity. The selected ASO device was either the same size as the stretched diameter or upto 2 mm larger. (In the last few patients, we have switched over to the use of the Amplatzer/ Numed balloon for sizing of the defect, where the waist is measured as the size of the defect).

Standard techniques as previously described were used for implantation of the device (2, 5). The implantation was carried out under fluoroscopy and TTE guidance under local anesthesia. The selected ASO device was attached to the delivery wire by the screw mechanism and was withdrawn into the loader by traction on the delivery wire. The collapsed ASO device was then advanced through the long sheath that had been previously placed in the left atrium. Under fluoroscopic control, the left atrial disc and the waist was extruded either by advancing the delivery wire or withdrawing the sheath. The sheath and the delivery wire were withdrawn in unison until the extruded left atrial disc was apposed to the atrial septum. The ASO device was then fully deployed by withdrawing the sheath over the delivery wire to extrude the right atrial disc.

The position and stability of the ASO device were confirmed by fluoroscopy and TTE. Its position was deemed optimal if the device was stable and did not obstruct the right

pulmonary veins, coronary sinus, caval veins or the mitral valve. Any residual shunt was documented by TTE .A Right atrial angiogram was done through the sheath to confirm the position of the Right Atrial disc. Once the position and stability of the device was confirmed, it was released by anticlockwise rotation of the delivery wire. A final assessment of the position of the device was performed by TTE after its release.

Post-procedure management:

The patients were observed in ICU overnight and then transferred to the general ward the next day. A repeat trans-thoracic echo was performed prior to discharge. Patients were discharged 2 days after the procedure if their clinical status was stable. Aspirin (5 mg/kg) was continued for 6 months after the procedure while Clopidogrel/Ticlopedine was given for 8 weeks.

Follow-Up:

All patients were followed up at 1, 3, 6 and 12 months after the procedure and then yearly afterwards. During the follow-up visits, a trans-thoracic echocardiogram was performed to assess any residual shunt, position and stability of the device and obstruction to surrounding structures. The septal motion, RA, RV size and RVSP by TR jet were also noticed.

In adult patients who had undergone a pre-procedure TEE, a follow-up TEE was performed 6 months after the implantation. In the follow-up TEE, residual shunt, obstruction to surrounding structures and profile of the device (length of RA and LA disc and thickness of the discs) were noted. The device was visualized in 0, 45 and 90 degrees with all measurements taken in 45 degree view. All TEE procedures were done under infective endocarditis prophylaxis.

A Holter monitoring was performed in all patients who complained of symptoms suggestive of arrhythmias (palpitation, giddiness etc).

Outcome Measures:

Safety and efficacy were defined as follows (5):

Safety: The avoidance of death or major complications (cerebral embolism, cardiac perforation, device embolisation, endocarditis)

Efficacy: The successful closure of the ASD without residual shunt or only trivial shunt.

Residual shunts were classified as follows (5):

Trivial: < 1 mm in diameter

Small: 1-2 mm in diameter

Moderate: 3-4 mm in diameter

Large: > 4 mm in diameter

Statistical analysis:

Descriptive Statistics was performed using Microsoft Excel Statistical Package. All results were expressed as mean + standard deviation. Comparison of RV size before and after procedure was done using student T test(2 tailed). P values of < 0.05 was considered to be significant .

RESULTS

All patients who were diagnosed to have secundum ASDs that merited closure (Clinically significant shunt, RA, RV volume overload on Echo) were evaluated for feasibility for trans-catheter closure. After evaluation with TTE and TEE using the selection criteria mentioned previously, a total of 55 consecutive patients were taken up for ASD device closure using the Amplatzer Septal Occluder.

Baseline Clinical Characteristics:

The mean age of the patients was 23.3 ± 16.6 years (range 4.5 – 72 years). 32 patients were females and the rest male. 5 patients were below 5 years of age, 17 were between 5-15 years and the remaining were above 15 years of age. Most of the patients were in either FC 1 or FC 2. All but one patient was in sinus rhythm. One 72 year old lady with a 30 mm ASD was in Atrial Fibrillation. Another patient had Sick Sinus Syndrome with significant sinus pauses on Holter.

Baseline Echocardiography:

All patients had isolated secundum atrial septal defects. There was evidence of RA, RV volume overload in all patients. The RV internal dimension was 31.5 ± 1.14 mm (median 32; 14 – 47 mm). The septal motion was paradoxic in all patients. The average size of the defect by TTE was 15.5 ± 4.66 mm (median 14.5; range 8 – 30 mm); 30 patients (all > 15 years) underwent TEE pre-procedure and average size of defect by TEE 16.7 ± 4.85 mm (median 16; range 9 – 28 mm) . The mean RV systolic pressure assessed by TR jet was 41.8 ± 3.2 mm Hg (median 41; 20 – 75 mmHg) . One patient had PAPVC of Left upper PV to RA.

Baseline Cardiac Catheterization findings:

The average size of the defect by balloon sizing 22.5 ± 4.7 mm (median 22; range 10 –34 mm). The mean Qp/QS was 2.15 ± 0.77 (range 1.4 – 5.9). The mean PA pressure was 19.8 ± 5.6 mmHg (range 10 – 50) and the mean PVR was 1.2 ± 0.37 Wood units (range 0.33 – 9.71). One patient had isolated PAPVC of LUPV to RA. One patient had severe

PAH which was sub-optimally responding to oxygen. (Possibility of primary pulmonary hypertension co-existing with ASD was considered.)

4 patients were excluded since the balloon stretched diameter of the defect was more than 32 mm and they were subsequently referred for surgery. Device closure was attempted in the remaining 51 patients.

Device Implantation:

The average size of the ASO deployed was 23 ± 4.68 mm (range 11 – 32 mm). In 18 patients, the size of the device deployed was more than 25 mm. The ASO device size employed was 1.5 ± 1 mm (median 0; range 0 – 3 mm) above the balloon stretched diameter of the defect. The device could be successfully implanted in 49 patients under TTE and fluoroscopy guidance. One patient with a 30 mm defect required TEE guidance for device deployment. The average fluoroscopy time was 23.7 ± 12 minutes and the mean procedure time was 120.7 ± 18 minutes. In one patient with a 32 mm defect, the defect could not be implanted, as adequate position could not be achieved. The procedure was then attempted under TEE guidance unsuccessfully. This patient also was subsequently referred for surgery. Post procedure the device position was found optimal by TTE and fluoroscopy in all 50 patients.

Peri-procedural complications:

Peri- procedural complications were observed in 2 patients. One patient had a transient ST segment elevation in inferior leads due to suspected air embolism. Another patient had a transient PSVT which reverted to sinus rhythm spontaneously. There were no deaths or instances of device embolisation.

Post-procedure Management and Complications:

The average hospital stay was 4.3 ± 1.5 days (3 – 10 days). 4 patients had minor complications during hospital stay. 2 had transient supraventricular tachycardias which responded to medications (one had SVT and the other atrial fibrillation). One patient had Ticlopedine induced neutropenia, thrombocytopenia and rectus sheath hematoma, which led to discontinuation of the drug. The fourth patient had a groin hematoma that resolved

later. All patients were discharged on anti-platelet doses of Aspirin for 6 months. 32 patients were discharged on additional Ticlopedine/ Clopidogrel for a period of 8 weeks. The single patient with Atrial Fibrillation was continued on oral anticoagulants.

Pre-discharge TTE (at 24 hours) revealed no residual shunts in 46 patients (92%). 3 patients (6 %) had trivial shunts had 1 patient (2 %) had a small shunt. In all patients the device position was optimal and there was no obstruction to pulmonary veins, venae cavae or the mitral valve.

FOLLOW-UP

The average duration of follow-up was 22.7 + 1.54 months(median 24; 6 – 48 months). All patients had a 6 month follow-up. 45 patients(90%) had a 1 year follow-up. 34, 10 and 3 patients had completed a 2 year, 3 year and 4 year follow-up at the time of writing this report.

Clinical Events on Follow-up:

All patients were free of symptoms on follow-up. One patient who was in Atrial Fibrillation continued to be AF on follow-up. She was continued on oral anti-coagulants. The patient with Sick Sinus Syndrome prior to device implantation was advised a permanent pacemaker implantation in view of significant sinus pauses on Holter. She was lost to follow-up after 6 months. There were no instances of late deaths, endocarditis, cerebrovascular events, device embolisation or any other major cardiac events on follow-up.

Residual shunts on follow-up (Table 3)

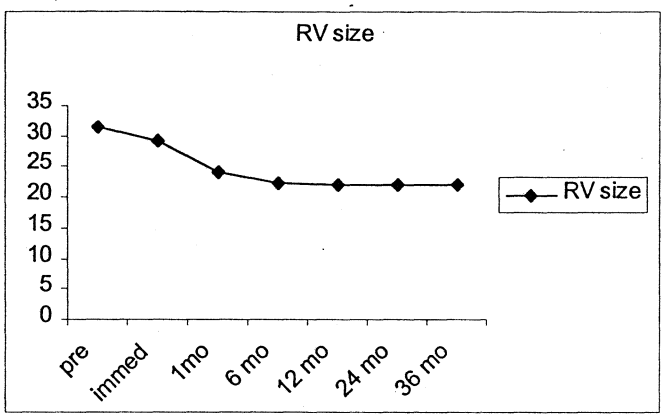
Follow-up (No: of Patients)	No residual Shunt	Trivial 1+	Mild 2+	Small 2+	Moderate-large 3-4+
24 hrs(50)	43	4	2	1	0
1 month(50)	47	1	1	1	0
6 months(50)	48	1	0	1	0
1 year (45)	44	0	0	1	0
2 years (34)	33	0	0	1	0
3 years (10)	10	0	0	0	0
4 years (3)	3	0	0	0	0

Septal Motion and RV size:

Septal motion normalized within 24 hours in 44 patients(88%). By one month, all but 2 patients had normal septal motion. Only one patient (the elderly patient with persistent AF with dilated RA) continued to have abnormal septal motion at 6 months.

The changes in RV internal dimensions are depicted in the figure below:

Figure 1: RV dimensions on follow-up:



The significant change in RV dimension occurred in the 1st month after device implantation (31.5 $\pm$ 6.8 mm pre-device Vs 24 $\pm$ 5.9 mm at one month; $p < 0.001$). After that there was no significant change in RV dimensions.

RV systolic Pressures:

The RV systolic pressure assessed by TR jet reduced from 41.8 $\pm$ 3.2 mmHg pre-procedure to 30 $\pm$ 3.9 mmHg 6 months after procedure(P =0.03). Only one patient continued to have persistent PAH (probably primary pulmonary hypertension co-existing with ASD). This patient continues to have FC 2 symptoms without evidence of Congestive heart failure.

TEE on follow-up:

A post-procedure TEE was done in 21 of the 30 patients(70%) who had TEE before device implantation. TEE was done 28.8 + 2.5 months(median 28.5; 7 –51 months) after the device implantation. None of the 21 patients had any residual shunts on TEE. All these patients had no residual shunts on TTE as well. The device position was optimal without any obstruction to AV valves, IVC, SVC or pulmonary veins. The one patient who continued to have small shunt on TTE declined to undergo a TEE on follow-up.

Holter Evaluation on follow-up:

Holter evaluation was done in 10 patients who had symptoms of occasional palpitation or giddiness. None had any clinical documented arrhythmias. 6 patients had APCs on Holter while 4 had occasional VPCs. There were no instances of persistent supraventricular or ventricular arrhythmias on Holter. The one patient who had Sick sinus Syndrome prior to device implantation continued to have significant sinus pauses in post procedure Holter.

DISCUSSION

Trans-catheter closure of secundum ASD using the Amplatzer Septal Occluder has become a standard practice for closure of these defects in modern pediatric cardiology practice. A large number of studies reported in literature have confirmed the efficacy and safety of this device in the closure of secundum ASD. The results of our study confirms the observations of the previous reports.

In a series of 55 consecutive patients, procedural success was obtained in 91% cases(4 backouts, 1 failure). No major peri-procedural complications were observed. There were no deaths or instances of device embolisation. There were 4 patients who had transient arrhythmias in the immediate post-deployment period. None required any long term medications.

One of the notable aspects of this study is that the implantation of the ASO device was carried out in the majority of patients(98%) without the aid of peri-procedure TEE. In most of the published reports, device implantation has been done under TEE guidance. The use of peri-procedure TEE entails the need for general anesthesia and all problems associated with it. All the implantations in this study were performed under local anesthesia(or ketamine anesthesia in case of children.)

The prevalence of residual shunts in our study is similar to those reported in the literature, despite the fact that implantation of the device was done without TEE guidance. Complete occlusion of the defect was obtained in 86%, 94%, 96% and 98% of patients at 24 hours, 1 , 6 and 12 months after procedure respectively. 70% of the patients who had a TEE prior to procedure underwent a TEE evaluation on follow-up. All these patients had no residual shunts. Cao et al (29) had reported 1.4%, 5.7% and 1.4% of trivial, small and large residual shunts on follow-up TEE done 6 months after the implantation.

There was significant reduction in RV internal dimension and RV systolic pressures on follow-up. The RV size reduced from 31.5 $\pm$ 1.1 mm to 24 $\pm$ 0.95 mm within 1 month of device closure($p<0.001$). After that there was no significant change in the RV size over the next 24 months. The septal motion(indicator of RV volume overload) normalized within 24 hours of procedure in 88% patients and 96% within 1 month. These results agree with the observations of Kort et al (29). There was a significant reduction in RV

systolic pressures within 6 months of the procedure(41.8 $\pm$ 3.2 mmHg Vs 30 $\pm$ 3.9 mmHg ; p0.03).

There were no major long term complications during the follow-up period which averaged 22.7 $\pm$ 1.5 months. There were no instances of new clinical arrhythmias(2 patients with pre-procedural arrhythmias continued to have those on follow-up). Holter evaluation done in 10 patients was essentially normal except for an increased frequency of atrial premature contractions.

Limitations of the Study:

1. Patients with defect size of more than 30 mm on TEE were not considered for device closure in this study. We cannot draw conclusions from this study whether peri-procedural use of TEE will be superior to TTE in aiding device implantation in patients with defect size of more than 30 mm on TEE.
2. Comparison with surgical closure of ASD as regards to long term results was not attempted in this study.

CONCLUSIONS:

1. Trans-catheter closure of secundum ASD can be accomplished using the Amplatzer Septal Occluder without peri-procedure TEE guidance in vast majority of patients with a defect size of less than 30 mm and with adequate margins .
2. The long term results of trans-catheter closure of ASD using the ASO device are excellent with very low incidence of residual shunts or other long term complications.

REFERENCES

1. Latson L.A Per-catheter ASD Closure. Pediatric Cardiology 1998; 19: 86 – 93.

2. Harper RW, Mottram PM, McGaw DJ. Closure of Secundum Atrial Septal Defects with the Amplatzer Septal Occluder Device: Techniques and Problems. Catheterization and Cardiovascular Interventions 2002; 57: 508-524

3. Podnar T, Martanovic P, Gavora P, Masura J Morphological variations of secundum type atrial septal defects: feasibility for percutaneous closure using amplatzer septal occluders . Catheterization and Cardiovascular Interventions 2001; 53: 386-391.

4. Masura J, Gavora P, Formanek A, Hijazi Z M Transcatheter closure of secundum atrial defects using the new self centering Amplatzer septal occluder: Initial Human experience .Catheterization and cardiovascular diagnosis 1997 42: 388-393

5. Chan KC, Godman MJ, Walsh K, Wilson N, Redington A, Gibbs JL Transcatheter Closure of atrial septal defect and interatrial communications with a new self expanding nitinol double disc device(Amplatzer septal occluder): multicentre UK experience Heart 1999;82:300-306.

6. Arora R, Kalra GS, Singh S, Passey R, Sinha S, Nigam M. Transcatheter closure of atrial septal defects using self expandable septal occluder Indian Heart Journal 1999; 51: 289-293

7. Taeed R, Shim D, Kimball T, Michelfelder EC, Salaymeh KJ, Koons LM, Beekman RH III One year follow-up of the amplatzer device to close atrial septal defects American Journal of cardiology 2001; 87: 116-118

8. Demkow M, Ruzyllo W, Konka M, Kepka C, Kowalski M, Wilczynski J, Rydlewska-Sadowska W Transvenous closure of moderate and large secundum atrial septal defects in adults using the Amplatzer septal occluder Catheter Cardiovasc Interv 2001; 52:188-93

9. Berger F, Ewert P, Bjornstad PG, Dahnert I, Krings G, Brilla-Austenat I, Vogel M, Lange PE Transcatheter closure as standard treatment for most interatrial defects: experience in 200 patients treated with the Amplatzer Septal Occluder. Cardiol Young 1999; 9:468-73

10. Dhillon R, Thanopoulos B, Tsaousis G, Triposkiadis F, Kyriakidis M, Redington A.Transcatheter closure of atrial septal defects in adults with the Amplatzer septal occluder. Heart 1999; 82(5):559-62

11. Fischer G, Kramer HH, Stieh J, Harding P, Jung O.. Transcatheter closure of secundum atrial septal defects with the new self-centering Amplatzer Septal Occluder. Eur Heart J 1999;20(7):541-9

12. Chan KY, Yip WC, Godman MJ. Transcatheter occlusion of atrial septal defects: an initial experience with the Amplatzer septal occluder. J Paediatr Child Health 1998 ;34(4):369-73

13. Thanopoulos BD, Laskari CV, Tsaousis GS, Zarayelyan A, Vekiou A, Papadopoulos GS. Closure of atrial septal defects with the Amplatzer occlusion device: preliminary results. J Am Coll Cardiol 1998; 31(5):1110-6

14. Vogel M, Berger F, Dahnert I, Ewert P, Lange PE. Treatment of atrial septal defects in symptomatic children aged less than 2 years of age using the Amplatzer septal occluder. Cardiol Young 2000;10(5):534-7

15. Lee CH, Kwok OH, Fan K, Chau E, Yip A, Chow WH. Transcatheter closure of atrial septal defect using Amplatzer septal occluder in Chinese adults. Catheter Cardiovasc Interv 2001;53(3):373-7

16. Losay J, Petit J, Lambert V, Esna G, Berthaux X, Brenot P, Angel C. Percutaneous closure with Amplatzer device is a safe and efficient alternative to surgery in adults with large atrial septal defects. Am Heart J 2001 Sep;142(3):544-8

17. Omeish A, Hijazi ZM. Transcatheter closure of atrial septal defects in children and adults using the Amplatzer Septal Occluder. J Interv Cardiol 2001 ;14(1):37-44

18. Radhakrishnan S, Marwah A, Shrivastava S. Non surgical closure of atrial septal defect using the Amplatzer septal occluder in children--feasibility and early results. Indian Pediatr 2000 Nov;37(11):1181-7

19. Kannan BRJ, Francis E, Sivakumar K, Anil SR, Kumar RK. Trans-catheter Closure of Very Large (> 25 mm) Atrial septal Defects Using the Amplatzer Septal Occluder. Catheterization and Cardiovascular Interventions 2003; 59: 522 –527.

20. Mazic U, Gavora P, Masura J. The role of transesophageal echocardiography in Transcatheter closure of secundum atrial septal defects by the Amplatzer septal occluder. Am Heart J 2001;142(3):482-8

21. Salaymeh KJ, Taeed R, Michelfelder EC, Beekman RH III , Shim D, Kimball TR Unique echocardiographic features associated with deployment of the amplatzer atrial septal defect device Journal of the American Society of Echocardiography 2001; 14: 128-137

22. Cooke JC, Gelman JS, Harper RW Echocardiologists' role in the deployment of the Amplatzer Atrial Septal Occluder device in adults .J Am Soc Echocardiogr 2001;14:588-94.

23. Figueroa MI, Balaguru D, McClure C, Kline CH, Radtke WA, Shirali GS Experience with use of multiplane transesophageal echocardiography to guide closure of atrial septal defects using the amplatzer device. Pediatr Cardiol 2002 Jul-Aug;23(4):430-6

24. Van Der Velde ME, Perry SB Transesophageal Echocardiography During Interventional Catheterization in Congenital Heart Disease. Echocardiography 1997 Sep;14(5):513-528

25. Tseng HC, Hsiao PN, Lin YH, Wang JK, Tsai SK. Transesophageal echocardiographic monitoring for transcatheter closure of atrial septal defect. J Formos Med Assoc 2000 Sep;99(9):684-8

26. Cheung YF, Leung MP, Lee J, Yung TC. An evolving role of transesophageal echocardiography for the monitoring of interventional catheterization in children. Clin Cardiol 1999 Dec;22(12):804-10

27. Pedra SR, Pedra CA, Assef JE, Cassar Rde S, Esteves CA, Braga SN, Pontes Junior S, Fontes VF. Percutaneous closure of atrial septal defects. The role of transesophageal echocardiography. Arq Bras Cardiol 1999 Jan;72(1):59-69

28. Chessa M, Carminati M, Butera G, Bini RG, Drago M, Rosti L et al . Early and late complications associated with Transcatheter occlusion of secundum atrial septal defect. Journal of American college of Cardiology 2002;39: 1061-1065.

29. Cao QL, Du ZD, Joseph A, Koeing P, Heitschimdt M, Rhodes J, Hijazi ZM. Immediate and Six-month Results of the Profile of the Amplatzer Septal Occluder as assessed by Transoesophageal Echocardiography. American Journal of Cardiology 2001;88: 754-759.

30. Kort HW, Balzer DT, Johnson MC. Resolution of Right Heart Enlargement After Closure of Secundum Atrial septal Defect with Transcatheter Technique. Journal of American college of Cardiology 2001;38: 1528-1532.

31. Hill SL, Berul CI, Patel HAT. Early ECG abnormalities associated with transcathter closure of atrial septal defects using the Amplatzer septal Occluder. J Interv Card Electrophysiology 2000; 4: 469-474.

32. Hessling G, Hyca S, Brockmeir K, Ulmer HE. Cardiac Dysarrhythmias in pediatric patients before and 1 year after transcatheter closure of atrial septal defects using the Amplatzer Septal Occluder. Pediatric Cardiology 2003; 24: 259-262