SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY

THIRUVANANTHAPURAM, KERALA

PROJECT REPORT

submitted during the course

DM in Cardiology

Dr. HARIDASAN V.

DM Trainee

DEPARTMENT OF CARDIOLOGY

October 2008

DECLARATION

I, Dr. HARIDASAN V., hereby declare that the projects in this book were undertaken by me under the supervision of the faculty, Department of Cardiology, Sree Chitra Tirunal Institute of Medical Science and Technology.

Thiruvananthapuram
Date: 7/10/2008

Dr. HARIDASAN V.
DM Trainee

Forwarded

The candidate, Dr. HARIDASAN V., has carried out the minimum required procedure.

Thiruvananthapuram
Date: 7/10/2008

Prof. Dr. J. A. THARAKAN
Head of Department of Cardiology

GENERAL CONTENTS

CONTENTS

Report I

A STUDY ON CARDIAC GEOMETRIC REMODELLING AND RIGHT VENTRICULAR FUNCTION BEFORE AND AFTER TRANSCUTANEOUS DEVICE CLOSURE OF ATRIAL SEPTAL DEFECTS

Introduction

INTRODUCTION

Transcatheter 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 transcatheter closure of ASD in 1974. Since then several devices were introduced for this purpose. 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. Worldwide experience with the use of ASO has shown excellent results in both short term as well as intermediate term (up to 2 years) follow-up. The overall procedural success has been around 95 % in the various reported studies. Recently many new devices have come up which were proved to have similar efficacy in terms of technical success and complication rates to ASO devices. These include devices like HEART R (Manufactured by Lifetech Scientific Limited, Shenzhen, China) and BLOCKAID (Manufactured by Shanghai shape memory alloy limited, Shanghai, China). These devices are much cheaper than the ASO devices and are getting wider acceptance in developing countries like India. Many patients who were referred for surgery despite having a defect suitable for device closure due to the prohibitive cost of the device are now being considered for percutaneous closure with these cheaper devices. But unlike as in the case of ASO devices, long term safety and efficiency is not established with these devices. All of these devices can be successfully deployed in all patients with defect size of up to 40 mm on trans-thoracic echo (TTE) or trans-esophageal Echo (TEE) provided there are adequate margins (at least 5mm) from surrounding structures.[3] A deficient antero-superior (aortic) rim does not preclude use of the device.

Successful closure of the device results in abrupt cessation of the left to right shunt and volume overload of right sided chambers. At the same time, it also results in improved filling of the left ventricle. The extent of changes occurring in the geometry and function of the cardiac chamber after the closure of the ASD and its temporal course will depend on various parameters and will vary from patient to patient. There are numerous studies reported looking in to these aspects. These studies agree in that a significant left to right shunt across the atrial septum will result in considerable increase in the volumes and dimensions of right atrium and ventricle and they tend to normalize irrespective of the baseline change time course being slightly different in various studies. Some studies have shown that the normalization of dilatation of chambers is better and faster with percutaneous closure compared to surgical closure as it is felt that an intact pericardium is an important determinant of RV function and pericardiotomy during surgery leads to delayed recovery of RV function which can be avoided by percutaneous closure.

Studies have also reported on the ventricular function before and after percutaneous closures. Various modalities like 2D and Doppler echocardiography, tissue Doppler imaging, strain rate imaging, nuclear imaging and magnetic resonance imaging were used to estimate ventricular function in these studies. Right ventricular volumes and systolic function are difficult to estimate compared to left ventricular volumes due to the peculiar shape. Diastolic function assessment also at times difficult especially in faster heart rates due to fusion of early and late tricuspid inflow velocities. Myocardial performance index (MPI) which incorporates both systolic and diastolic time intervals is found to be useful in assessing combined right ventricular function in

various congenital heart diseases. For the estimation of MPI, systolic and diastolic time intervals are measured from the Doppler analysis of atrioventricular valve flows and the ventricular outflows. So the time intervals are not taken from the same cardiac cycle. Recently, studies have come up showing that these intervals can be measured in the same cardiac cycle using the tissue Doppler imaging of the tricuspid or mitral annular motion. The isovolumetric contraction time(ICT), isovolumetric relaxation time (IRT) , ejection time (ET) and the MPI obtained by this method were found to be well coordinating with corresponding values obtained by pulse Doppler imaging in normal people and in various disease states.

Different studies have reported differently on baseline RV MPI in ASD and its changes after device closure. While some studies reporting a normal MPI both pre and post closure, some studies have reported increased MPI which gets normalized after ASD closure.

Similar studies on cardiac dilation and function are lacking in Indian population. No such data available with the use of devices other than ASO devices.

Aim of the Study

AIM OF THE STUDY

1) To study the baseline right and left atrial volumes and changes occurring and the time course of changes after closure in patients undergoing percutaneous device closure of atrial septal defects.

2) To study the right and left ventricular diastolic dimensions at baseline and after closure and extent and time course of these changes.

3) To study the tissue Doppler derived myocardial performance index at baseline and on serial follow up evaluation in these patients.

Review of Literature

REVIEW OF LITERATURE

ASD and right heart enlargement

Atrial septal defect is the most common cause of chronic right heart volume overload. Over time, atrial shunts tend to increase due to a physiological ASD enlargement and an age dependant decline of left ventricular compliance. Natural history studies have shown that right heart volume overload caused by atrial shunt tend to increase progressively over time, thereby affecting cardiac performance even in asymptomatic patients.[12,13,14,28] Thus one of the targets of ASD closure is prevention of progressive cardiac enlargement in asymptomatic patients. The ideal ASD treatment should aim both to unload the right heart and also to normalize the right to left volumetric unbalance.

Impact of ASD closure

Surgical repair of ASD showed conflicting results in terms of cardiac geometric remodeling. In early series, it often failed to completely normalize the right chamber overload with a persistence of right ventricular enlargement in two-thirds of patients on mid term follow up.[15,16,17] These findings have been ascribed to either progressive myopathic change caused by long lasting volume overload or to functional anomalies related to cardio-pulmonary bypass or finally to cardiac geometric modifications resulting from pericardial opening. However the subsequent reports have not confirmed these early findings.[18]

Over the time, percutaneous closure emerged as a reliable, safe and more physiological alternative to surgery. Separating the hemodynamic consequences of

Almost all of the previous studies have shown significant increase in the RA volume at the time of ASD closure. Only patients with RA volume overload were planned for closure. In the studies by Pascotta et al.[6] and Santoro et al.,[8] all patients at baseline had significantly increased RA volume. When compared to standard value in general population. Both these studies did not have a control population.

In stead of the RA volume, some studies have looked in to 2D RA dimensions or RA areas. In a study by Veldtman et al.[10] mean RA superoinferior length was 52 ±7 mm while normal values are 34 to 39 mm. In the study by Kort et al.[7] patients with ASD had a mean basal RA area indexed to body surface area of 15.2 cm^2 (4.5) against 8.2 cm^2 (1.7) in the control group.

Both studies which analyzed the RA volume showed a significant regression in the volumes after the transcatheter closure. Maximum difference was noted in the immediate post 24 hr echo followed by changes occurred after one month. Beyond 6 months, there were no further changes. The study by Kort et al.[7] which had a control group to compare with showed that though the indexed RA area decreased considerably from pre closure value, it remained significantly elevated when compared to control value even at the end of 2 years. One other difference noted in this study was the maximum regression in the RA size was within 6 months unlike within 24 hours or one month in other studies. This study also looked in to the important aspect of the influence of the duration of volume overload as evidenced by the age at which device closure is done on the resolution of cardiac enlargement. By analysis by repeated measures ANOVA showed that change in RA area was strongly correlated to age at time of closure (p value 0.0013). In the study by Veldtman et al.,[10] the superoinferior dimension of right atrium showed a decreasing trend by 1 month and significantly came

down to the normal value by 6 months. Studies with head to head comparison of surgical and device closure have not specifically looked in to the RA volume or dimension changes.

Left atrial volume and changes

Data regarding the left atrial (LA) enlargement and its changes are really conflicting. When compared to RA volume, previous studies have shown, increase in the LA volume is significantly less (Santoro et al.,[8] Pascoto et al.[6]). This is probably because a significant amount of pulmonary venous return bypasses LA in to RA because of the proximity to the defect. Oliver et al. has shown an association between LA diameter and atrial fibrillation in ASD patients whether or not they have undergone surgical closure.

In the studies by Santoro et al.[8] and Pascoto et al.,[6] the LA volumes did not change from baseline over a period of 6 months. Both these studies did not have a control group to compare with. In the study by Salehian et al.[29] showed a statistically significant change after a variable period of follow up. But in the study, the actual percentage change observed in LA volume index was 15.6 % while the study had a very close inter observer variability of 13.2 % which might have contributed to the observed changes. In another study by Du et al.[37] which looked in to LA diameter, there was a significant change from pre closure value to value at 6 month follow up.

Ventricular dimensions and changes

Because of the crescent shape of the right ventricle, echocardiographic volume estimation is difficult. So only few echocardiographic studies have looked in to the RV

volume changes before and after ASD closure. Study by Kort et al.[7] which has taken the ellipsoid shell RV volume indexed to body surface area, the patient population had a significantly elevated baseline RV volume (81.9 ±20.4 ml/m^2 vs. 40.1 ±9 ml/m^2) which reduced significantly by 24 hours comparable to that of control population (45.3 ±16.3). There was no relationship between change in indexed RV volume and age at closure or baseline QP/QS. Magnetic resonance imaging studies also showed significant improvement in RV volume, mass and function 6 months after transcatheter closure of ASD.[38] Because of the difficulties in echocardiographic assessment of right ventricular volume, most of the studies have studied the right ventricular dimension before and after closure. Both M mode derived and 2 D derived parameters were used for this purpose.

M mode derived RV end diastolic dimension decreased progressively while LV end diastolic dimension increased similarly causing a progressive decrease in the RV LV ratio in the study by Wu et al.[11] The decrease in RV EDD/LV EDD ratio was not related to pre closure ratio, ASD size or QP/QS. In the study by Pascotto et al.,[6] both RV EDD derived by M mode and RV inlet derived by 2D were analyzed. Both these values progressively decreased over the study period of 6 months. This study also showed progressive increase in M mode and 2D derived LV dimensions. The changes in the LV dimensions were of lesser magnitude than those of RV dimensions. These changes resulted in a near 30 % decrease in RV to LV diameter ratio. In this study the significant changes occurred with in one month, thereafter the changes were in substantial. It was also noted that significant changes in RV inlet dimension occurred within 24 hours itself, while M mode dimensions showed maximum decrease by one

month. The study by Santoro et al.[8] which also analyzed both 2D and M mode RV and LV dimensions indexed to body surface area, showed exactly similar results with significant changes occurred within one month in all these parameters. This study did not show any influence of age at closure on these changes. The study by Veldtman et al.[10] analyzed the RV inlet dimension in the apical 4 chamber view at the tip of tricuspid annulus and RV outlet dimension in the parasternal long axis view. Both these dimensions were reduced significantly by one month. In this study, for 29 %, the dimensions were persisting above the reported normal range of 26 to 33 mm for RV inlet dimension and 18 to 33 mm for outlet dimension. All these patients were above 40 years at the time of device implantation suggesting an impaired ability of RV to remodel after prolonged volume loading or the aged state per se. But this study included 95 % patients above the age of 25 years and RV dimensions were fully normalized in most of them. A surgical cohort of 31 patients by Pearlman et al.[15] also had RV dimensions above the normal value in 23 % of patients; all of them were above 25 years of age at the time of device closure. In both these studies, there was no relation ship between the initial magnitude of shunting and the presence of residual shunt to the persistence of RV enlargement, suggesting the inability of RV to remodel due to prolonged volume loading as well as ageing.

Ventricular function

The previously mentioned studies have clearly shown the dramatic volumetric changes in both the atria and ventricles, both in adult as well as pediatric population with some minor differences on the timing of these changes and regarding the impact of age at closure on the speed and extent of the changes. These primarily reflect the

changes in pre load and changes occurring in right and left ventricular function both in the presence of ASD as well as after its closure by surgical or percutaneous to be analyzed independent of these volumetric changes.

The reported effects of ASD on left ventricular function are variable. In most echocardiographic studies, left ventricular systolic function was normal despite the RV volume overload.[20,21,22,35] However, a reduced ejection fraction has been found in patients with ASD and severe right ventricular volume overload[36] and cineangiographic studies suggest abnormalities of left ventricular function affecting the systole and diastole.[23,24,25] The effect of ASD on right ventricular function appears to be more consistent. Although delayed right ventricular contraction has been detected by radionuclide studies in the absence of conduction system defects,[26] echocardiographic assessment has shown that right ventricular function to be normal or exaggerated. Due to the abnormal shape of RV and due to the effects of surgery, echocardiographically assessed ejection fractions may not truly reflect the changes in right ventricular function comparing the pre and post scenarios as well as comparing the percutaneous and surgical modes of closure. So the investigators have resorted in to the analysis of Doppler velocities across the tricuspid and pulmonary valves, the analysis of atrioventricular plane movements and also in to the tissue Doppler imaging of the tricuspid annulus.

Atrioventricular plane movements

A study by Dhillon et al.[5] has analyzed the long axis movement of RV free wall, interventricular septum and left ventricular free wall pre closure and post closure in

both device closure and surgical closure patients. The study showed RV free wall total excursion and peak lengthening and shortening rates were higher than those in control patients in ASD patients indicating exaggerated systolic and diastolic performance. The septal and LV free wall values did not significantly deviate from normal. Post device closure, peak exertion of RV free wall and lengthening rate did not fall while peak shortening rate fell. All the three parameters fell in case of septum while none of the three parameters changed in case of LV free wall. But following surgical closure, all the three indices fell from pre closure value in both RV free wall and septum while LV free wall was spared by surgical closure also. The supra normal right ventricular function in ASD patients before intervention most probably reflects right ventricular volume loading. The reduction in the right ventricular peak shortening rate following ASD closure is likely to reflect volume unloading of the right ventricle as the measured values is not different from the control values. In surgical patients, the right ventricular peak excursion and peak lengthening rate also reduced suggesting an independent effect of cardiopulmonary bypass on right ventricular systolic and diastolic function. The right ventricle is particularly susceptible to the problems of cardiopulmonary bypass and intra operative ischemia and an intact pericardium is important for right ventricular function. The impairment of septal systolic and diastolic functions may reflect the imposition of a non–contractile element within the atrial septum affecting the excursion of ventricular septum beneath it. As these disturbances were shared equally by the two groups, they may represent a transitional stage for the septum, functioning as a part of right ventricle before the closure and as a part of LV afterwards. But the previous data by the same study group had shown that on a long term basis, the right ventricular dysfunction detected immediate post op period may not be translated in to

functional performance and the exercise performance is un affected by the age at closure.[27] A study by Hanseus KC et al.[4] analyzed the tissue Doppler velocities of lateral tricuspid annulus, septum and mitral annulus in patients for ASD closure. Study showed near normal systolic velocities before closure which were unaffected by device closure and reduced by surgical closure in the septum and tricuspid annulus. Diastolic velocities and E/A ratio were normal before closure and remained unaffected by device closure, but in surgical group, both diastolic velocities shortened without affecting the E/A ratio.

Myocardial performance index

The myocardial performance index (MPI) or Tei index is a Doppler derived time interval index, which combines both systolic and diastolic time intervals to generate a combined index of global ventricular function. This index is defined as the sum of isovolumetric contraction time and isovolumetric relaxation time divided by the ejection time. In previous studies, the index has been found to be easily obtainable and to correlate closely with invasive measures of both systolic and diastolic function being independent of heart rate and ventricular geometry.[30]

In previous studies, it has been shown that RV MPI is useful for quantitatively analyzing the right ventricular function in various congenital heart diseases. In congenital heart diseases with a definite right ventricular dysfunction evidenced by other echo parameters, like Ebstien's anomaly and corrected TGA with left AV valve regurgitation, the RV MPI is found to be significantly increased with a direct correlation with disease severity and shows some improvement after surgical.[34] The

results are not consistent in conditions with pure volume or pressure overload of RV with no manifest RV dysfunction. In isolated atrial septal defect with no significant pulmonary arterial hypertension, various studies on RV MPI before and after closure have reported different findings. Some studies report an RV MPI value similar to or insignificantly increased when compared to control population.[34,39,40,41] Some other studies showed a decrease in the RV Tei index after the device closure indicating an improvement in both RV systolic and diastolic function. One study actually showed an increase in the RV index from pre closure value later coming back to normal levels by 3 months.[11]

Assessment of RV MPI is accomplished by measuring the time intervals from Doppler interrogation of tricuspid and pulmonary flow velocities. Values are taken from several cardiac cycles and then averaging. One of the main disadvantages of this method of assessment is that systolic and diastolic intervals are taken note from the same cardiac cycle and hence may not truly reflect the cardiac function especially if there is significant variation in heart rate.

Recently, tissue Doppler imaging (TDI) of atrioventricular valve annulus has been used in estimating the systolic and diastolic time intervals and thereby estimating a tissue Doppler derived myocardial performance index. Studies have shown that TDI derived time intervals and hence the MPI correlates very well with ordinary Doppler derived values.[1,2,9] One study used this tissue Doppler derived RV MPI in ASD closure patients and found that RV MPI was increased in surgical patients when compared to control population and to patients undergoing device closure.[34]

Materials and Methods

MATERIALS AND METHODS

Patient population

The study was a prospective observational study conducted at Sree Chitra Tirunal Institute for medical sciences and technology, a tertiary care referral center for cardiovascular and neurological disorders. All patients who were planned to have an ASD device closure during the period of 6 months between December 2007 and May 2008 were included in the study. All these patients were selected based on initial clinical examination and transthoracic echocardiogram (TTE). All these patients had ostium secundum ASD with a significant right to left shunt with RA and RV volume overload and their defects appeared suitable for percutaneous device closure by TTE. Patients with any co existing congenital heart disease were excluded. Those patients who consented were included in the study.

Baseline evaluation

All patients were clinically assessed for the magnitude of shunt. Chest X-ray and ECG were performed in all. TTE was performed to assess the size and position of defect, number of defects, and adequacy of rim, septal motion, RA, RV size and RV systolic pressure (RVSP) by tricuspid regurgitation (TR) jet. Any associated cardiac defects were also looked for.

Echocardiographic data collection

Transthoracic echocardiography including tissue Doppler velocity imaging was performed with 3.5 Hz or 7 Hz probes (Vivid 7, General Electricals). Echocardiographic

measurements of flow velocities and time intervals were taken as an average of 3 consecutive cardiac cycles. Right and left atrial volumes were estimated from apical 4 chamber view in the end systolic frame of using single plane method of discs.[31] RV and LV M mode diastolic dimensions were taken from parasternal long axis view. In addition, RV 2D dimension was taken from apical 4 chamber view in long axis from the apex to the midpoint of tricuspid annulus. 2D dimensions were measured after timing with electrocardiogram (ECG) to the peak of the T wave.

TDI images were obtained by activating the TDI mode of the machine. The TDI program was set to pulse wave Doppler mode. Filters were set to exclude high velocity signals. Gains were minimized to allow a clear tissue signal with minimal background noise. A 2 mm sample volume was placed at the lateral corner of tricuspid annulus .The resulting velocities were recorded at a sweep speed of 100 mm/s. The intervals were determined by 2 carefully placed vertical cursors that were moved with a track ball. The time intervals from the peak of R wave to onset of diastolic velocity (a') and the duration between the onset and cessation of systolic velocity (b') were estimated. MPI was calculated using the formula a'—b'/b'. Interval from R wave to onset of diastolic velocity (c') and the interval from R wave to cessation of systolic velocity were (d') were also measured. IVRT was calculated using the formula c'—d' and the IVCT was calculated as IVCT = (a'—b') — IVRT. Values were taken as an average of 3 consecutive cardiac cycles.

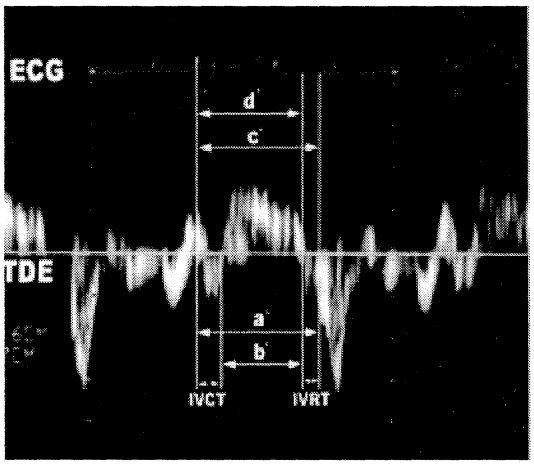


Fig. 1. Tissue Doppler imaging of tricuspid annulus and time intervals

Technique of device closure

The procedure was performed under general anesthesia in all patients. BSA was found out according to height, weight and sex from nomogram. A baseline oximetry study was performed initially. PA pressures were noted in all patients. Normal pulmonary vein drainage was ensured either by entering individual pulmonary veins or by demonstration by transesophageal echocardiography (TEE). Size of the ASD and the adequacy of rims were determined by a detailed intra procedural TEE. The device selected was either equal to size of the ASD or 2 mm larger as per the age of the patient and the total septal length. The device was later upsized if seemed necessary. Balloon sizing was not performed in any of the patients.

Standard techniques as previously described were used for implantation of the device. The selected ASD device was attached to the delivery wire by the screw mechanism and was withdrawn in to the loader by traction on the delivery wire. The collapsed ASD 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 were 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 ASD device was when then fully deployed by withdrawing the sheath over the delivery wire to extrude the right atrial disc.

The position and stability of the ASD device were confirmed by fluoroscopy and TTE and TEE. Its position was deemed optimal if the device was stable and did not obstruct the pulmonary veins, coronary sinus, caval veins or the mitral valve. Any residual shunt was documented by TEE. 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 and TEE 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 TTE was performed prior to discharge. Patients were discharged next day after the procedure if their clinical status was stable. Aspirin 5 mg/kg and clopidogrel were continued at discharge.

Follow up

The first follow up evaluation was done on the next day of the procedure before discharge. First follow up visit was scheduled at after one month when the device position is confirmed and any residual defects were looked for. All the 2 D volumes and dimensions were assessed and tissue Doppler imaging was performed. Second follow up visit was scheduled after 2 months that is 3 months from the time of procedure. Measurements of volumes and dimensions and tissue Doppler were repeated.

Observations and Results

OBSERVATIONS AND RESULTS

During the study period, a total number of 49 patients were planned to have ASD device closure in our institution. On baseline evaluation, 5 of these patients were found not to have an adequate echo window for all information and hence were excluded from the study. 44 patients underwent baseline evaluation. All of them were taken for device closure. Successful device closure could not be done in three patients. Two patents were found not to have an inadequate IVC rim after TEE and hence device closure was not attempted. One patient developed LA perforation and cardiac tamponade and underwent emergency repair and surgical closure. Hence a total of 41 patients were available for final analysis.

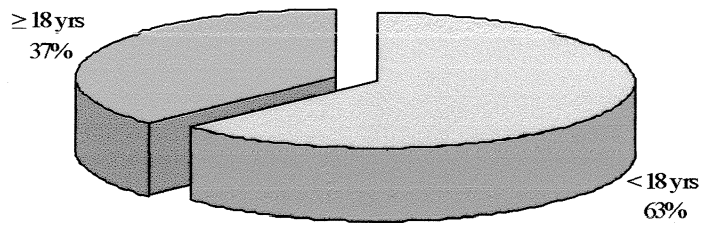
Baseline characteristics

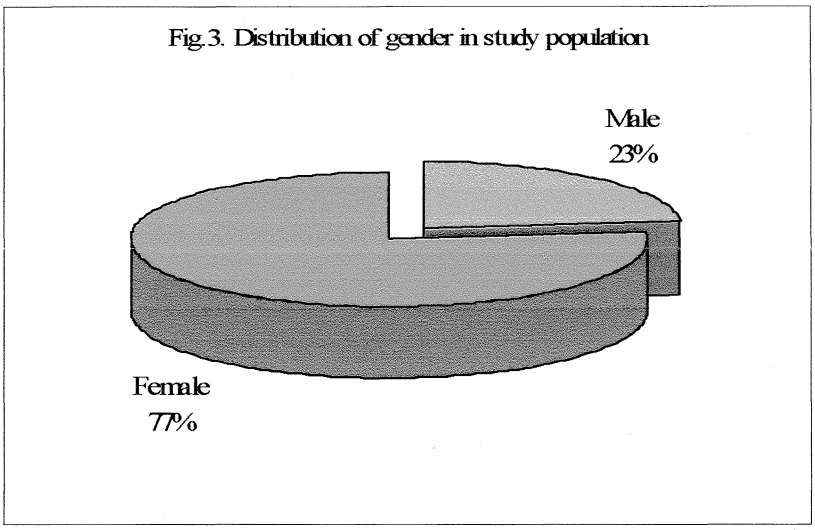
10 patients (23.3 %) were males and 33 patients (76.7 %) were females. 27 patients (62.8 %) were belonging to age group below 18 (group 1) and 16 patients (27.2%) were belonging to group above 18 (group 2). Mean age of the patients was 12.97 ±16.75 years. Mean body surface area was 1.11 ±0.4 cm^2 for 4 patients. Mean ratio of pulmonary to systemic blood flow (QP/QS) was 2.31:1 (0.57). The mean PA pressure was 20.23 mm Hg (3.7). Mean ASD size was 18.18 mm (5.62). The smallest ASD closed was 9 mm and the largest was 30 mm. Mean size of the device used was 20.17 mm (6.22). The smallest device used was 11 mm and the largest was 34 mm.

Table 1. Baseline characteristics

Parameters	Mean	± SD
Age	16.98	12.57
Body Surface Area	1.15	0.41
QPQS	2.31	0.58
PA Mean	20.23	3.70
ASD Size	18.19	5.62
Device	20.18	6.23
RA Volume	41.34	9.48
LA Volume	23.81	4.82
RV 2D Length	35.51	4.25
RV M Mode	24.90	4.70
LV M Mode	31.58	3.36
RV-LV Ratio	0.79	0.13
IVRT	57.58	9.88
IVCT	34.16	6.23
ET	284.81	21.54
MPI	0.32	0.05

Fig.2. Distribution of age in study population





Echocardiographic data

At baseline

Mean RA volume was 41.33 ml (9.37). Mean LA volume was 23.81 ml (4.81). Mean RV M mode end diastolic dimension was 24.89 mm (4.7). Mean LV M mode end diastolic dimension was 31.58 mm (3.35). At baseline, the mean RV to LV M mode ratio was 0.78 (0.13). Mean RV 2D long axis dimension was 35.51 (4.25) mm.

On tissue Doppler imaging, the mean IVRT was 57.58 millisec (9.88), mean IVCT was 34.16 millisec (6.22), and mean ET was 284.81 millisec (21.53). The mean myocardial performance index was 0.32 (0.05).

Follow up data

All the 41 patients underwent all the three follow up examinations.

RA volume

From baseline value of 41.33 (9.34) ml, RA volume fell on successive evaluation in to 29.67 (9.65) at post 24 hrs to 25.07 (5.85) at post one month to 23.54

(4.5) ml at post 3 months. The difference from the baseline to the volume at end of follow up was statistically significant (p value <0.001). The most significant change occurred within the first 24 hours (p value <0.001). The RA volume continued to fall beyond that also, the change being statistically significant within one month of repeat echocardiography (p value <0.001). From this, the post 3 months echo also showed a minor but statistically significant decline (p value 0.03).

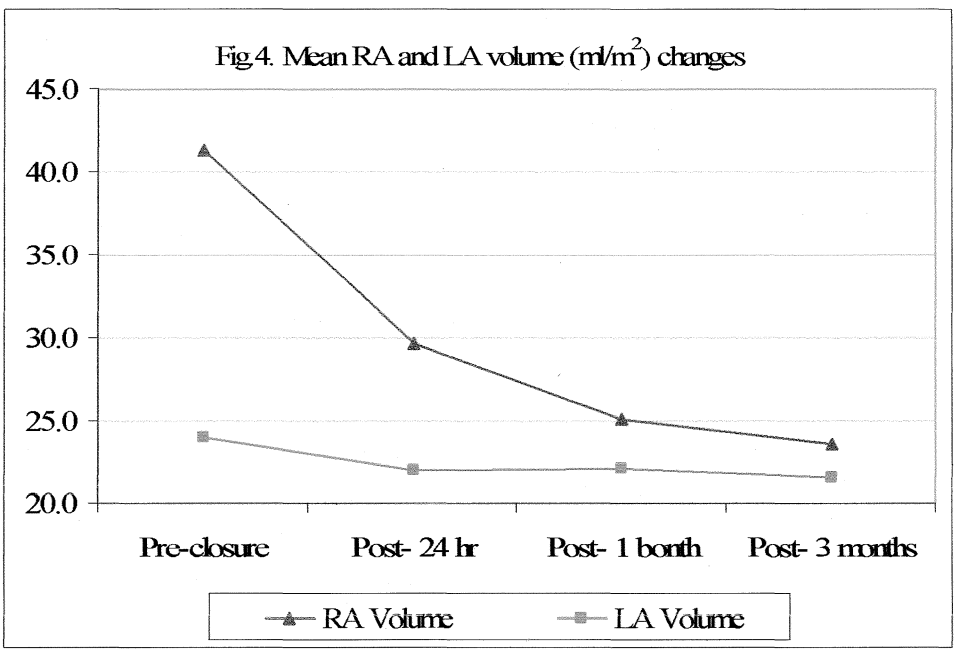
The mean change in RA volume in group I was 17.55 (7.911) and in group II, it was 18.23 (7.17). The difference was not statistically significant (p value 0.13). The change in RA volume from baseline to post 3 months value was correlated with age, ASD size, mean PA pressure and the QP/QS ratio. There was no correlation between the extend of RA volume change from baseline to post 3 months with the age at closure (p value 0.923) or with the mean ASD size (p value 0.678) or with mean PA pressure (p value 0.769) or with the QP/QS ratio.

LA volume

From the baseline value of 23.81 (4.81) ml, on serial evaluation, LA volume changed to 21.93 (5.270) at post 24 hrs to 22.04 (4.07) at post one month and then to 21.51 (4.07) ml at post 3 months. The significant change was between the baseline value and first evaluation within 24 hours (p value 0.001). Rest of the changes was not significant. The change in LA volume was similar in both groups and the change has no correlation with age, mean PA pressure and the QP/QS ratio.

Table 2. Changes in the atrial volume

Parameters	Observations	Mean	± SD	t value	P value
RA Volume	Pre-closure	41.34	9.83	10.228	< 0.001
	Post- 24 hr	29.68	9.46		
	Post- 24 hr	29.68	9.46	4.411	< 0.001
	Post- 1 month	25.08	5.86		
	Post- 1 month	25.08	5.86	2.212	< 0.05
	Post- 3 months	23.54	4.51		
	Pre-closure	41.34	9.83	14.857	< 0.001
	Post- 3 months	23.54	4.51		
LA Volume	Pre-closure	23.91	4.92	3.733	< 0.01
	Post- 24 hr	21.93	5.27		
	Post- 24 hr	21.93	5.27	- 0.218	> 0.05
	Post- 1 month	22.04	4.07		
	Post- 1 month	22.04	4.07	1.543	> 0.05
	Post- 3 months	21.52	4.08		
	Pre-closure	23.91	4.92	3.225	< 0.01
	Post- 3 months	21.52	4.08		



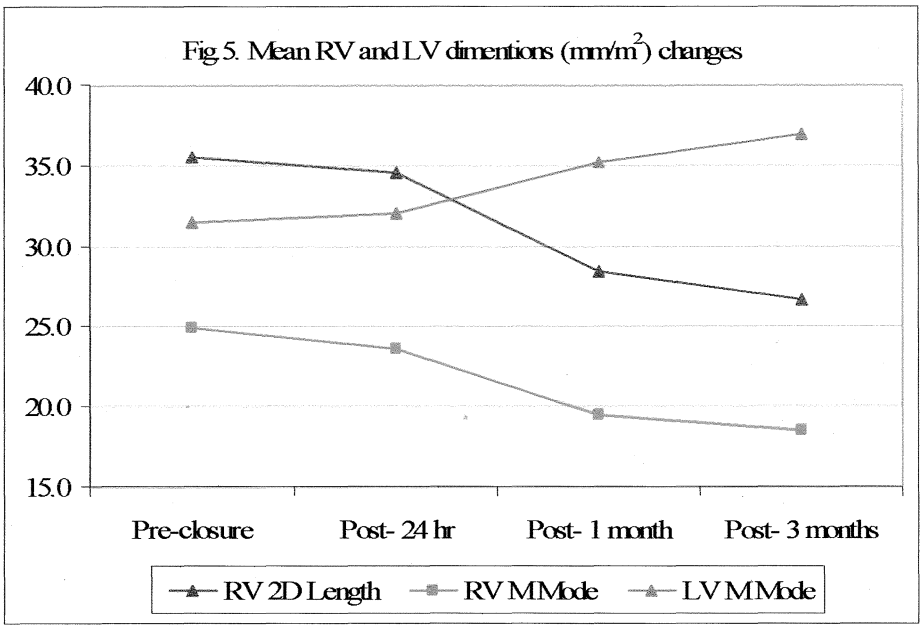
Ventricular dimensions

RV M mode dimension fell serially from 24.89 (4.70) at baseline to 23.54 (4.61) at post 24 hr to 19.65 (4.61) at post one month and finally to 18.37 (3.09) mm at post 3 months. At the same time, the LVEDD increased serially from 31.58 (3.35) to 31.99 (3.99) to 35.29 (3.69) and finally to 36.95 (2.71) mm. This resulted a serial change in LV to RV ratio of 0.78 (0.13) to 0.73 (0.12) to 0.53 (0.12) to 0.49 (0.07). The change in RV EDD was statistically significant (p value <0.001). The change from pre closure value to post 24 hour value and the change from this value to post 1 month were significant (p values 0.001 and <0.001 respectively. The change from post 1 month value to post 3 months value was also significant (p value 0.001).The change in the LV dimension also was significant at all the three serial echocardiographic evaluation. Maximum change was at one month follow up (< 0.001). The change in RV to LV ratio was also significant at all stages (p value <0.001).

The 2D RV inlet dimension from apical four chamber view also fell serially from 35.5 (4.25) at baseline to 34.57 (3.95) post 24 hour, to 28.38 (3.93) post one month and finally to 26.67 (1.83) post three months. These changes were significant at all the three stages.

Table 3. Changes in ventricular dimensions

Parameters	Observations	Mean	± SD	t value	P value
RV 2D Length	Pre-closure	35.55	4.28	2.443	< 0.05
	Post- 24 hr	34.58	3.96		
	Post- 24 hr	34.58	3.96	10.381	< 0.001
	Post- 1 month	28.39	3.93		
	Post- 1 month	28.46	3.96	3.411	< 0.01
	Post- 3 months	26.67	1.84		
	Pre-closure	35.57	4.34	13.551	< 0.001
	Post- 3 months	26.67	1.84		
RV M Mode	Pre-closure	24.92	4.77	3.588	< 0.01
	Post- 24 hr	23.61	4.59		
	Post- 24 hr	23.48	4.58	7.021	< 0.001
	Post- 1 month	19.46	4.62		
	Post- 1 month	19.46	4.62	2.785	< 0.01
	Post- 3 months	18.32	3.11		
	Pre-closure	24.92	4.77	10.874	< 0.001
	Post- 3 months	18.53	2.99		
LV M Mode	Pre-closure	31.50	3.38	- 2.071	< 0.05
	Post- 24 hr	32.00	3.39		
	Post- 24 hr	32.00	3.39	- 8.078	< 0.001
	Post- 1 month	35.22	3.39		
	Post- 1 month	35.22	3.39	- 4.342	< 0.001
	Post- 3 months	36.95	2.72		
	Pre-closure	31.50	3.38	- 13.185	< 0.001
	Post- 3 months	36.95	2.72		
RV-LV Ratio	Pre-closure	0.79	0.13	4.342	< 0.001
	Post- 24 hr	0.74	0.13		
	Post- 24 hr	0.74	0.13	10.611	< 0.001
	Post- 1 month	0.56	0.13		
	Post- 1 month	0.56	0.13	4.885	< 0.001
	Post- 3 months	0.50	0.08		
	Pre-closure	0.79	0.13	17.161	< 0.001
	Post- 3 months	0.50	0.08		



Tissue Doppler imaging

The IVRT increased from the baseline value of 57.58 (9.88) to the post three month value of 59.62 (7.25). The change was not statistically significant (p value 0.113). IVCT decreased from baseline 34.16 (6.23) to final 30.07 (2.59). This change was statistically significant (p value <0.001). Over this three month period, the change in ejection time was from 284.81 (21.53) to 282.92 (17.3) within 24 hours to 291.67 (14.17) post one month and finally to 291.9 (13.73). The change from post one month to post three month was significant (p value <0.001). The mean RV MPI of the total study population was 0.32 (0.05). It was 0.32 (0.04) in group I and 0.31 (0.06) in group II. The difference was not statistically significant. On serial evaluation, the mean MPI came down to 0.3 (0.03) at the end of 3 months. The change was significant within first month. The change was similar in both the groups. The change in MPI was correlated with age, ASD size, and QP/QS but found no association.

Table 4. Changes in time intervals

Parameters	Observations	Mean	± SD	t value	P value
IVRT	Pre-closure	58.00	10.08	- 1.542	> 0.05
	Post- 3 months	59.63	7.26		
IVCT	Pre-closure	34.25	6.34	4.706	< 0.001
	Post- 3 months	30.08	3.59		
ET	Pre-closure	285.83	20.61	- 2.441	< 0.05
	Post- 3 months	291.90	13.73		

Table 5. Changes in RV MPI

Parameters	Observations	Mean	± SD	t value	P value
MPI	Pre-closure	0.32	0.05	- 0.075	> 0.05
	Post- 24 hrs	0.33	0.05		
	Post- 24 hrs	0.33	0.05	3.291	< 0.01
	Post- 1 month	0.31	0.03		
	Post- 1 month	0.31	0.03	- 0.231	> 0.0.5
	Post- 3 months	0.31	0.03		
	Pre-closure	0.32	0.05	2.557	< 0.05
	Post- 3 months	0.31	0.03		

Discussion

Table 6. Cardiac remodeling comparing age groups

Parameters	Age Group	Mean	± SD	t value	P value
Body Surface Area	< 18 yrs	0.90	0.33	- 6.016	< 0.001
	≥ 18 yrs	1.46	0.22		
QPQS	< 18 yrs	2.33	0.61	0.194	> 0.05
	≥ 18 yrs	2.29	0.53		
PA Mean	< 18 yrs	19.87	3.70	- 0.726	> 0.05
	≥ 18 yrs	20.75	3.77		
ASD Size	< 18 yrs	15.11	3.45	- 6.617	< 0.001
	≥ 18 yrs	23.38	4.72		
RA Change	< 18 yrs	17.56	7.91	- 0.267	> 0.05
	≥ 18 yrs	18.24	7.17		
LA Change	< 18 yrs	3.59	3.79	0.066	> 0.05
	≥ 18 yrs	3.51	4.11		
RV 2D Length Change	< 18 yrs	10.31	6.90	1.139	> 0.05
	≥ 18 yrs	8.13	2.25		
RV M Mode Change	< 18 yrs	7.22	3.84	1.896	> 0.05
	≥ 18 yrs	5.00	2.80		
LV M Mode Change	< 18 yrs	5.26	2.86	- 0.661	> 0.05
	≥ 18 yrs	5.83	2.15		
MPI Change	< 18 yrs	0.03	0.03	0.541	> 0.05
	≥ 18 yrs	0.03	0.03		

DISCUSSION

Of the 44 patients who underwent baseline evaluation, the device closure could be accomplished in 41 patients. IVC rim is the most difficult rim to assess by TTE, as it is best evaluated by sub costal view. However a good sub costal window is not always found. Again some time the elongated Eustachian valve is mistaken as the IVC rim. The IVC rim is evaluated better by TEE. That is the reason for backing out in two patients. As per the current practice in our institute the device size is determine based only on the TEE and balloon sizing is not performed. This helps to save considerable time and hardware. The results are comparable to centers which routinely perform the balloon sizing.

Only a single patient developed complication during the procedure (LA perforation with cardiac tamponade). There was no mortality in the series. The female preponderance in the study population is reflective of the female preponderance of the ASD.

The study population was heterogenous with respect to age and ASD size. The youngest patient being of 4 years old, while the oldest being 50 years. In contrast to many other studies, the present study population consisted of significant number of older adults with 15 % of patients being above 30 years of age. The study population was heterogeneous with respect to the ASD size also with smallest defect closed being 9 mm and the largest being 30 mm.

RA volume changes

The mean RA volume indexed to body surface area of the present study population was 41.33 (9.34) ml/m^2. This appears significantly higher when compared to

the value obtained in the previous studies. In the study by Pascotto et al.[16] which predominantly included children and young adults (mean age 22 ±18 years) had a mean BSA of 1.43 ±0.39 cm^2, the mean RA volume was 45 ±24 ml which was not indexed to BSA. The study by Santoro et al.[8] had mean RA volume 31 ml/m^2 indexed to body surface area. Both of these studies did not have a cohort of normal control population to compare. The normal RA and LA volume in healthy population indexed to body surface area from previous studies is 22 ml/m^2 BSA.[32,33] The mean ASD diameter in our study population was 18.18 mm and mean QP/QS ratio was 2.31:1 (0.57). These values are similar to those of the above mentioned studies. ASD diameter and QP/QS ratio were 17 ±6 and 2.2 ±0.9 in study by Pascotto et al. and were 23 ±7 and 2.2 ±0.9 in the study by Santoro et al. Both these studies were conducted in the same centre and had overlapping population. Though our patients were younger than patients in those two studies, our patients had significantly higher RA volume despite having almost similar ASD size and shunts.

Though the RA volume was high to begin with in the present study population, it rapidly decreased to almost normal values by the end of study period of 3 months. This is in accordance with the previous two studies. In both of these studies the significant change was within one month and thereafter the change was not very significant. The study by Santoro et al.[8] had a post 24 hr echo value also which showed the maximum change. These studies did not have a post 3 month's value. In the present study the RA volume continued to decline beyond one month and reached the normal value by 3 months. In the present study also the maximum change was between the pre closure value and post 24 hr value followed by the change between post 24 hr and post one month value.

The extent and time course of regression of RA volume overload was similar in both the groups of patients. This is in accordance with the study by Santoro et al.,[8] which compared the changes in patients above 16 and below 16 years of age. The RA volume regression had no correlation with age at closure, ASD size, mean PA pressure or QP/QS ratio. This is in agreement with the data in the Santoro and the Pascoto study groups.

Only the study by Kort et al.[7] showed that change in RA area was strongly correlated to age at time of closure (p value 0.0013). The present study did not correlate the change in the RA size to the baseline RA size. Previous studies have shown that change in RA size correlates with baseline RA size causing a similar final RA size despite the pre closure differences in RA volume overload. In the present study population also, though started with a higher RA volume at baseline, finally reached an RA volume similar to the final values obtained in the other two studies.

Left atrial volumes and changes

Present study population has a mean pre closure LA volume of 23.81 (4.81) which is mildly increased when compared to the normal value of 22 ml/m^2. This is similar to the values obtained in the previous two studies (18 ±6 ml/m^2 in study by Santoro et al.[8] 26 ±13 ml by Pascoto et al.[6]) but slightly lower when compared to study by Salehian et al.[29] ((25.7 ±8 ml/m^2).

From the baseline value of 23.81 (4.81) ml, on serial evaluation, LA volume changed to 21.93 (5.270) to 22.04 (4.07) and then to 21.51(4.07) ml. The significant change was between the baseline value and first evaluation within 24 hours (p value

0.001). Rest of the changes was not significant. This is similar to the studies by Pascoto et al.[6] and Santoro et al.[8]and different from study by Salehian et al.[10]which showed a significant fall in LA volume. The change in LA volume was similar in both groups I and II and there was no correlation between the age or ASD size and degree of shunting.

Ventricular dimensions

RV M mode dimension fell serially from 24.89 (4.7) to 23.54 (4.61) to 19.65 (4.61) and finally to 18.37 (3.09) mm/mm^2 BSA. The study by Satoro et al.[8] also got similar values (26.3 ± pre closure to 19.1 ±4.3 mm/m^2 after 6 months). LVEDD increased serially from 31.58 (3.35) to 31.99 (3.99) to 35.29 (3.69) and finally to 36.95 (2.71) mm. This resulted a serial change in LV to RV ratio of 0.78 (0.13) to 0.73 (0.12) to 0.53 (0.12) to 0.49 (0.07). These changes are also are similar to the previous study (LV to RV M mode ratio changed from 0.8 at baseline to 0.5 at 6 months post closure). These changes continued to occur up to 3 months ad the changes were significant at all three stages. The maximum change in the LV and RV dimensions and the RV to LV ratio occurred within one month follow up.

The 2D RV inlet dimension from apical four chamber view also fell serially from 35.5 (4.25) at baseline to 34.57 (3.95) post 24 hour, to 28.38 (3.93) post one month and finally to 26.67 (1.83) post three months. The values are very much similar to those obtained by Santoro et al.[8] (34.2 ±9.4 mm/m^2 pre closure to 25.7 ±6 mm /m^2 at 6 months). The extent and time course was same in both inlet (2D) and outflow regions (M mode). An earlier study reported that the outflow portion lagged behind the inflow portion in remodeling.

The final change in the RV and LV M mode dimensions and the RV 2D dimensions were similar in both groups. The changes were correlated with age at closure. ASD size, mean PA pressure or QP/QS and there was no association.

Myocardial performance index

The IVRT increased from the baseline value of 57.58 (9.88) to the post three month value of 59.62 (7.25). This change was not significant. The mean IVRT in patients with ASD in the study by Baysal et al. was 34.71 (26.95) while in control group it was 39.58 (16.28). In the study by Eiden et al.[34] the mean IVRT of the control population was 49 (9) while that of ASD patients was 65 (23) milliseconds. In the study by Cheung et al.[41] which used the tissue Doppler imaging, the IVRT was similar in both the controls and ASD patients after closure. Pre closure values were not available in the study. It was suggested earlier that an increased pre load may cause a shortened IVRT and ASD closure may result in lengthening of IVRT. But as seen in the Baysal study,[39] the IVRT was not significantly shorter than controls and in Eidem et al.[34] study, it was higher than controls. In the Eidem study,[34] IVRT actually shortened after the closure in the adult patients but did not change significantly in pediatric patients..

In the present study, IVCT decreased from baseline 34.16 (6.23) to final 30.07 (2.59). This change was statistically significant (p value <0.001). Baseline value is similar to the value obtained in the control population as well as ASD patients in the study by Eiden et al.[34] But in the study by Baysal et al.[39] which had only children in the study population had lower values for ICT in controls (10.83 ±15.86) as well as in ASD patients (20.59 ±25.85). But the study by Cheung et al.[41]which used the TDI derived

time intervals, the IVCT was much higher in controls (52 ±16) as well as ASD patients after closure. This study did not have pre closure values. In the Eiden et al.[34] study, the IVCT shortened significantly in both pediatric and adult patients which they attributed to an increase in heart rate.

The baseline ejection time was 284.81 (21.3) millisec. This is similar to the value obtained in control population as well as patients with ASD in the study by Eiden et al.[34] On follow up evaluation, this changed to 282.92 (17.3) within 24 hours to 291.67 (14.17) post one month and finally to 291.9 (13.73). The change from post one month to post three month was significant (p value <0.001). The study by Cheung et al. also got a similar value in normal patients and patients with ASD after device closure or surgical closure.

The mean tissue Doppler derived RV myocardial performance index of the total population was 0.32 (0.05). There was no difference between the two groups (0.32 ±0.04 vs. 0.31 ±0.06). The value obtained in the normal population and in ASD patients before closure varied significantly between various studies. In the study by Baysal et al.[39] the control population had an RV MPI of 0.2 ±0.08 and the ASD patients had an MPI of 0.24 ±0.15. In the study by Eidem et al. the normal children had an RV MPI of 0.32 and adult had a value of 0.28. In this study, the children and adults with ASD had a mean MPI value of 0.35 (0.09) and 0.38 (0.04). The differences between the control group and ASD as well as the difference between children and adults were not statistically significant. In the study by Ishii et al. had RV MPI of 0.24 (0.04) and 0.25 (0.13) in normal subjects and patients with ASD respectively. In the study by Salehian et al.,[10] the mean MPI before ASD closure was 0.35 ±0.14. The study by Cheung et al.

which used the tissue Doppler derived MPI had a value of 0.4 (0.03) in the control group and 0.4 (0.01) in the ASD patients who underwent device closure. The present study population had a higher baseline RV MPI similar to that in study by Eiden et al.[34] This is due to a higher IVRT and IVCT .High values are probably due to the use of tissue Doppler instead of the ordinary Doppler but the value is lower when compared to that obtained in the study which also used the TDI. In the previous studies, the time intervals and MPI derived by TDI were found not to be significantly different from those obtained by pulse Doppler in normal subjects but no such direct comparison studies available specifically in ASD patients.

On serial evaluation, the RV MPI came down to 0.3 (0.03) the difference was statistically significant. This is in contrast to the study by Wu et al.[11] which actually showed a progressive increase in RV Tei index up to one month. Subsequently the index started to fall but remained significantly elevated compared to pre closure value even after 3 months. The study by Salehian et al.[10] also reported a decrease in the RV MPI after ASD device closure similar to the present study. In the study by Edeim et al., the RV MPI showed a mild but statistically in significant increase in RV MPI. The improvement in the MPI was due to the decrease in the IVCT and the increase in the ET. In the study by Eiden et al.,[34] the patient who underwent surgical closure of ASD had a significantly higher RV MPI than those who underwent device closure. Direct comparison studies with large sample size are needed to really say the surgical closure will result in development of RV dysfunction compared to device closure. Long term follow up is needed to find whether this RV dysfunction improve later in surgical patients.

Conclusions

CONCLUSIONS

Percutaneous transcatheter closure of atrial septal defect results in significant and rapid resolution of right atrial and right ventricular dilatation by a period of 3 months. Majority of this remodeling takes place within first 24 hours or within first month.

Left atrial enlargement is minimal in these patients at baseline and does not change much after the closure.

The speed and extent of remodeling is independent of age at device closure, ASD size or degree of shunt indicating the ability of cardiac chambers to re model despite the chronicity and magnitude of the hemodynamic insult.

The right ventricular function as assessed by tissue Doppler derived myocardial performance index has improved little but significantly after the device closure.

LIMITATIONS

The study did not have a control population. For most of the parameters there were standard normal values and the study basically intended to compare the parameters before and after the closure.

Though few studies have compared the Doppler and tissue velocity derived MPI and found out excellent correlation in normal subjects, such data is not there for pathological conditions like ASD. The study did not take the simultaneous Doppler derived values and compare with tissue Doppler derived values.

All the echocardiographic measurements were taken online real time and were not recorded and analyzed offline. Hence the intra observer variability was not estimated and not accounted for.

Bibliography

BIBLIOGRAPHY

1) Kenji Harada, Masamichi Tamura, Manatono Toiono and Kenji Yasuoka: Comparison of the right ventricular Tei index by tissue Doppler imaging to that obtained by pulsed Doppler in children without heart disease. *The American Journal of Cardiology.* 2002; Vol 90: 566—69.

2) Yuqing Duan, Kenji Harada, Veiling Wu, Haruka Ishii, Goro Takada: Correlation between right ventricular Tei index by tissue Doppler imaging and pulsed Doppler imaging in fetuses. *Pediatric Cardiology.* 2008; 29: 739—743.

3) Abd El Rahman MY, Hui W, Timme J, Ewert P, Berger F, Dsebissowa F, Hetzer R, Lange PE and Abdul–Khaliq H: Analysis of atrial and ventricular performance by tissue Doppler imaging in patients with atrial septal defects before and after surgical and catheter closure. *Echocardiography.* 2005; 22(7): 579—85.

4) Hanseus KC, Bjorkhen GE, Brodin LA, Pesonen E: Analysis of atrioventricular plane movements by Doppler tissue imaging and M mode in children with atrial septal defects before and after surgical and device closure. *Pediatric Cardiology.* 2002; 23: 152-159.

5) Dhillon R, Josen M, Henein M, Reddington A: Transcatheter closure of atrial septal defect preserves right ventricular function. *Heart.* 2002; 87: 461 – 465.

6) Marco Pascoto, Giuseppe Santoro, Fabiana Cerrato, Salvatori Capupo, Naurizio Cappelli Bigazzi, Carola Iacano, Marianna Carrozza, Maria Giovanna Russo, Guiseppe Caianiello Raffaele Calabro: Time course of cardiac remodeling following transcatheter closure of atrial septal defect. *International Journal of Cardiology.* 2006; 112: 348—352.

7) Henry W Kort, David T Banzer, Mark C Johnson: Resolution of right heart enlargement after closure of secundum atrial septal defect with transcatheter technique. *JACC.* 2001; 38(5): 1547—9.

8) Santoro G, Pascoto M, Cerrato F, Cappelli Bigazzi M, Palladino MT, Lacono C, Carroozza M, Russo MG, Calabro R: Similar cardiac remodeling after transcatheter atrial septal defect closure in children and young adults. *Heart.* 2006; 92: 958—62.

9) Tarkan Terkten, Alper O Onbasili, Ceyhun Ceyhan, Selim Unal, Pinar Agaoglu. Tissue Doppler myocardial performance index. *Journal of Turkish Society of Cardiology.* 2003; 31: 262—9.

10) Gruschen R Veldtman, Vanessa Razak, Samuel Siu, Hassan El Hajj, Fiona Walker, Garry D Webb, Leland N Benson, Peter R McLaughlin: Right ventricular form and function after percutaneous atrial septal defect closure. *Journal of American Society of Cardiology.* 2001; 37(8): 2108—13.

11) En Ting Wu, Teiji Akagi, Manabu Taniguchi, Satoru Sakuragi, Shinichi Otsuki, Yoshio Okomoto, Shunji Sano: Differences in right and left ventricular remodeling after transcatheter closure of atrial septal defect among adults. *Catheterization and Cardiovascular Interventions.* 2007; 69: 866—71.

12) Campbell M: Natural history of atrial septal. *British Heart Journal;* 1970; 32: 820—6.

13) Ascah KJ, King ME, Gillan LD: The effects of right ventricular hemodynamics on left ventricular configuration. *Canadian Journal of Cardiology;* 1990; 6(3): 99—106.

14) Walker RE, Moran AM, Gavreau K: Evidence of adverse ventricular inter dependence in patients with atrial septal defects. *American Journal of Cardiology*; 2004; 93:1374—7.

15) Pearlman AS, Borer JS, Clark CE: Abnormal right ventricular size and ventricular septal motion after atrial septal defect closure: etiology and functional significance. *American Journal of Cardiology.* 1978; 41: 295—301.

16) Meyer RA , Korfhageh JC, Covitz: Long term follow up study after closure of secundum atrial septal defect in children: An echocardiographic study. *American Journal of Cardiology.* 1982; 50: 143—8.

17) Ning SB, Fazal H, Cook D: Right ventricular size and ventricular septal motion after repair of atrial septal defect in children. *Canadian Journal of Surgery.* 1984; 27:395—8.

18) Attenhofer Jost CH, Oechslin E, Seifert: Remodeling after surgical repair of atrial septal defects within the oval fossa. *Cardiology in Young.* 2002; 12(6): 506—12.

19) McMohan CJ, Feltes TF, Fraley JK: Natural history of growth of secundum atrial septal defects and implications of transcatheter closure. *Heart.* 2002; 87: 256—9.

20) Vincent RN, Saurette RH, Pelech AN: Interventricular septal motion and left ventricular function in patients with atrial septal defect. *Pediatric Cardiology.* 1988; 9:143—8.

21) Kim WH, Otsuji Y, Sewart JB: Estimation of left ventricular function in right ventricular pressure and volume overload. Detection of early left ventricular dysfunction by Tei index. *Japan Heart Journal.* 1999; 40: 145—54.

22) Sutton MGStJ, Tajik AJ, Mercier LA: Assessment of left ventricular function in atrial septal defect by computer analysis of M mode echocardiogram. *Circulation.* 1979; 60:1082—90.

23) Altieri PI, Martinez TJ, Del Valle L. Left ventricular function in adults with atrial septal defect. *Proc R Health Sci J.* 1987; 6: 17—21.

24) Papio KA, Gorlin R, Teicholz LE: Abnormalities of left ventricular function and geometry in adults with an atrial septal defect. Ventricular, hemodynamic and echocardiographic studies. *American Journal of Cardiology.* 1975; 36: 302—8.

25) Satoh A, Katayama K, Hiro T: Effect of right ventricular volume overload on left ventricular diastolic function in patients with atrial septal defect. *Jpn Circ J.* 1996; 60: 758—66.

26) Baker EJ, Shubao C, Clarke SE, et al.: Radionuclide measurement of right ventricular function in atrial septal defect, ventricular septal defect and complete transposition of great arteries. *American Journal of Cardiology.* 1986; 57:1142—6.

27) Rosenthal M, Redington A, Bush A: Cardiopulmonary physiology after surgical closure after asymptomatic atrial septal defects in childhood. Exercise performance unaffected by age at closure. *European Heart Journal.* 1997; 18: 1816—22.

28) Giardini A, Donti A, Formogari R, et al.: Determinants of cardiopulmonary function improvement after transcatheter atrial septal defect percutaneous closure. *Journal of American College of Cardiology.* 2004; 43:1886—91.

29) Salehian O, Horlik E, et al.: Improvement in cardiac form and function after transcatheter closure of secundum atrial septal defect. *Journal of American College of Cardiology.* 2005; 45: 499-504.

30) Tei C, Ling LH, Hodge Do, Bailey KR, Oh JK, Tajik JK, Seward JB: New index of combined systolic and diastolic myocardial performance: a simple and reproducible measure of cardiac function: a study in normal and dilated cardiomyopathy. *Journal of Cardiology.* 1995; 26: 357—66.

31) Kaplan JD, Evans T, Foster C, et al.: Evaluation of electrocardiographic criteria for right atrial enlargement by quantitative two dimensional echocardiography. *J Am Coll of Cardiology.* 1994; 24: 747—52.

32) Pritchett AM, Jacobsen SJ, Mahoney DW et al.: Left atrial volume as an index of atrial size: a population based study. *J Am Coll Cardiology.* 2003; 41(6): 1036.

33) Wang Y, Gutman JM, Heilbron D, Wahr D, Schiller NB et al.: Atrial volume in a normal adult population by two dimensional echocardiography. *Chest.* 1984; 86: 596—601.

34) Eidem BW, O'Leary PW, Tei C, Seward JB: Usefulness of the myocardial performance index for assessing the right ventricular function in congenital heart diseases. *American Journal of Cardiology.* 2000; 86: 654—658.

35) Bjorkhem G, Lunstorm, NR: Echocardiographic studies of children operated on for congenital heart disease: Evaluation during first post operative year. *Eur J Cardiology.* 1980; 11: 33—50.

36) Louie EK, Linn SS, Reyertson SL, et al. : Pressure and volume loading of right ventricle have opposite effects on left ventricular ejection fraction. *Circulation.* 1995; 92(8): 819—24.

37) Du ZD, Hijazi ZM, Cao QL, Koenig P, Heitschimidt M: Speed of normalization of right ventricular volume overload after transcutaneous closure of atrial septal defect in children and adults. *American Journal of Cardiology.* 2001; 88:1450—53.

38) Schoen SP, Kittner T, Bohl S, et al.: Transcatheter closure of atrial septal defect improves right ventricular volume, mass, function, pulmonary pressure and functional class: a magnetic resonance imaging study. *Heart.* 2006; 92: 821—26.

39) Tamer Baysal, Bulin T Oran, Mustafa Dogen, et al.: Myocardial performance index in children with isolated left to right shunt lesions. *Turkish Medical Journal.* 2005; 5: 108-11.

40) Ishii M, Geto C Tei, Tsutsumi T, et al.: Quantitation of global right ventricular function in children with normal heart and congenital heart disease: A right ventricular myocardial performance index. *Pediatric Cardiology.* 2000; 21:416—421.

41) Yiu-fai Cheung, Kinshing Lun, et al. : Doppler tissue imaging analysis of ventricular function after surgical and transcatheter closure of atrial septal defect. *American Journal of Cardiology.* 2004; 93: 375—378.

Report II

A STUDY ON PACEMAKER FOLLOW UP, END OF LIFE BEHAVIOUR AND PULSE GENERATOR REPLACEMENT OF CARDIAC PACEMAKERS

CONTENTS

Introduction

INTRODUCTION

Cardiac pacemakers are life saving devices initially developed to give periodic electrical stimulation to the heart which captures the myocardium, which if gave rise to an effective mechanical contraction will help to maintain an adequate cardiac output in situations with bradycardia. Later many other functions were added on to it including delivering an effective therapy to tachyarrhythmias as well as providing cardiac resynchronisation in conditions with dyssynchrony. The most important components of the pacemaker are the pulse generator which stations the electronic circuitry required for the sensing and pacing as well as the battery as the power source and the lead which delivers the electrical energy in to the tissue interface.

Like in the case of any other devices implanted in to a patient's body, the physician's responsibility does not end with simply putting the device. This is especially true in the case of devices like pacemakers which can be evaluated and whose functions can be influenced non-invasively by the use of telemetry. A methodical follow up which involves regular visits to the physician's office, meticulous record keeping and interrogation and programming is essential part of any pacing therapy programme. Pacemaker clinics are established for this purpose.

Detection and management of any pacemaker malfunction or impending pacemaker malfunction is essential part of any pacemaker follow up programme. There will be continuous energy depletion from the battery of pulse generator and it will ultimately reach a level at which an energy output sufficient to stimulate the cardiac tissue is not possible. This stage can be considered as the end of life of the pulse

generator. Before reaching this level, the pacemaker try to conserve the available energy by loosing many of its special functions and limiting the function to maintaining the pacing output alone. This can make a patient symptomatic and in some cases like loss of rate responsiveness or mode switch producing sudden bradycardia in the middle of a physical activity can produce syncope with dare consequences. On approaching the end of life some pacemakers behaviour may become very much erratic which includes a 'run away pacemaker' giving pacing stimulation at un physiologically high rates which if result in capture, is often fatal. To avoid these consequences, the battery depletion is to be recognised before reaching the end of life and the pulse generator is to be replaced. For this purpose, the pacemakers are provided with indicators for an elective replacement time.

In developed countries with well functioning pacemaker clinics, the battery depletion is promptly recognised and pulse generators are replaced. In developing countries, such a methodical follow up is not being taken place both due to logistic reasons as well as due to patient related factors. Patient's visits are scheduled at longer intervals, timely intensification of visits is not advised and a detailed telemetric evaluation is not performed. As a result, many pulse generators are reaching their ends of life with or without consequences. Magnitude of the problem is not perceived properly because many patients remain free of events despite losing the pacing support till the malfunction is eventually detected in a routine visit.

Aim of the Study

AIM OF THE STUDY

1) To evaluate adequacy of the post implantation follow up in terms of frequency of visits, tests performed and the patient compliance.

2) To analyse the efficiency of follow up for timely detection of the battery depletion and the need for battery replacement.

3) To study the behaviour of the pacemakers at or near the end of life and its clinical impacts.

4) To study the impact of threshold and impedance at implantation on the longevity of the pulse generator.

Review of Literature

REVIEW OF LITERATURE

At the time of the follow up visit to a pacemaker clinic, all the components of a pacing system are to be evaluated. This includes:

1) Patient
2) Pulse generator
3) Programmable settings of the pulse generator
4) Leads

The objectives of a complete follow up programme include:

1) Ensuring optimal functioning of the device and exploiting the full capabilities of the device to improve the patients well being.
2) To detect, diagnose and correct any abnormalities that arise in the pacing system
3) To improve longevity of the device by appropriate programming.
4) To assess and predict the elective replacement time of the pulse generator.
5) To appropriately manage various situations arising in patient's lifetime that may interfere with functioning of the pacing system.
6) To educate and reassure the patient and the family
7) To generate database of pacing systems and to train medical personnel.

Transtelephonic monitoring

An integral part of many pacing system follow up program is Tran telephonic monitoring. This can be initiated by the physician and support staff out of an individual office or provided by a commercial service based on the prescription by the physician

Reports of each periodic evaluation are sent to the patients physician. This provides a cost effective mean for a frequent monitoring as the device is getting older and there is concern about approaching RRT. The system usually comprises of a special transmitter that is acoustically coupled to the telephone when the mouthpiece of the telephone is placed over the transmitter. The transmitter is connected to the patient via two electrode cables. The transmitter converts the electrical signal in to an auditory signal, which is the decoded by the receiver in physician's office. This is particularly good at identifying markers of battery depletion by measurement of magnet rate. For an otherwise stable system, TTM may be needed on a frequent basis while the detailed evaluations are performed much less frequently or on an as needed basis should symptoms or other concerns arise.

Frequency of follow up evaluations

The frequency of follow up and whether this be a detailed in office evaluation or a much simpler trans telephonic evaluation should be dictated by the clinical needs of the patient. One schedule, which is provided by the Health care financing administration of United States, is given below. It is slightly different for single chamber and dual chamber devices and whether the pulse generator has a known track record or not.

Group I: Devices for which there is not an established track record.

Single chamber pacemakers

1st month - every two weeks

2nd through 36th month - every 8 weeks

37th moth until RRT - every 4 weeks

Dual chamber pacemakers

1st month - every two weeks

2nd through 6th month - every 4 weeks

7th through 36th month - every 8 weeks

37th month until RRT - every 4 weeks

Group II: Devices for which there is an established track record of good performance.

Single chamber pacemakers

1st month - every 2 weeks

2nd through 48th month - every 12 weeks

49th month through 72nd month - every 8 weeks

73rd month until RRT - every 4 weeks

Dual chamber pacemakers

1st month - every 2 weeks

2nd through 30th month - every 12 weeks

31st through 48th month - every 8 weeks

From 49th month to until RRT - every 4 weeks

Such methodical and exhaustive follow up may not be applicable to the Indian circumstances due to the logistic reasons. An article published in JAPI suggest an yearly follow up visit for single chamber pacemakers and 6 monthly visits for dual chamber pacemakers after the initial post implantation evaluation.[17]

A complete pacemaker follow up program should include the following:

1 Assessment of the patient status

a) Symptoms - Palpitations, syncope, CCF

b) Examination of pacemaker pocket site

c) Assessment for venous sufficiency.

2) Status of the intrinsic rhythm

Pacemaker dependency

3) Appropriateness of the current pacemaker prescription

1) Capture thresholds and safety margin
2) Sensing thresholds and safety margin
3) Rate modulation
4) Special algorithms
5) Assessment of the Battery status.

Replacement of the pulse generator

At some time in the life of any patient who has a pacemaker, replacement of the device pulse generator may be required. Although this need is most often the result of finite lifespan of the battery, replacement of the devices may be precipitated by such diverse causes as infection, erosion, trauma, device malfunction or migration and the need for system upgrade. Lead replacement or revision may also result secondarily in generator change especially if the generator is already near the end of its service. Lead malfunction particularly the low lead impedance may secondarily require premature battery replacement owing to high current drain.

Most bradycardia pacemaker pulse generators provide direct or indirect indicators of battery depletion, documenting the need for enhanced follow-up, elective generator replacement or incipient battery failure.

Indicators for PG replacement

Primary Indicators	Generator end of service: Elective replacement indication Complete failure due to end of service Loss of output Sensing malfunction Generator upgrade - Unipolar to bipolar - Single to dual chamber - Need for high energy ICD Pocket twitch - Due to generator insulation break - Due to lead insulation break - Due to Unipolar system Unanticipated generator failure Device recall
Secondary Indicators	Pocket issues Generator migration Persistent pain Pronounced pocket effusion or hematoma Erosion Infection of pacing system Trauma Lead issues Need for lead revision High thresholds (pacing or sensing) High de fibrillation threshold Lead conductor fracture Lead insulation break Loose lead generator connection Myopotential sensing Diaphragmatic pacing or sensing Twiddlers syndrome Change bifurcated bipolar to Unipolar due to malfunction of one conductor

Indicators of pacemaker battery depletion

Primary indicators	Abrupt decrease in magnet rate
	Gradual decrease in magnet rate
	Mode switch (DDD to VVI)
	Abrupt loss of sensing or pacing
	Interrogated marker of battery depletion
Secondary indicators	Rise in internal battery impedance
	Drop in battery voltage
	Pulse width stretch
	Battery depletion curve

A change in magnet activated paced rate remains the most common indicator of reduced battery output voltage for pace makers.[2,10,13] Some pacemaker pulse generator models respond to declining voltage through a gradual reduction in magnet activated pacing rate. Other models demonstrate abrupt shifts in the magnet activated paced rate at the enhanced follow-up period or at the time of elective replacement.

A demand mode switch from DDD to VVI may occur at the elective replacement time or as an obligatory replacement indicator for dual chamber systems before complete battery failure. Inability to reprogram the device, inaccurate measurement of lead impedances, and loss of data collections may also occur as a generator approaches obligate replacement.

In the office, other secondary parameters suggest gradual battery depletion. As lithium iodide batteries are depleted the internal battery impedance increases, providing a secondary indicator.[4,14] With high internal battery impedances some devices compensate for reduced current output by increasing the pulse width to maintain an adequate energy delivering to the lead tip. The extent of pulse width stretching is measurable and may be precipitated by high output pacing; it serves as another secondary indicator of battery depletion. The rate of battery depletion may accelerate as the device reach send of service making timely replacement in dependent patients very important.

General magnet responses of pulse generators

Pacemaker	Battery depletion indicators: Mode switch (DOO to VOO) Rate change – gradual or abrupt Noise reversion modes: DOO – usual asynchronous operation in dual chamber system AAT, VVT - usual asynchronous operation in single chamber system P R synchronous pacing Magnet rate: Fixed Variable First few complexes faster Last few complexes faster Output Fixed Variable Voltage or PW decreased in first few complexes Voltage or PW decreased in last few complexes Duration: Continuous as long as magnet is apply Fixed number paced complexes

Since the magnet rate and its changes with battery depletion are pre fixed by the manufacturers, different pacemakers will have different behavior of their magnet rate. All the pacemakers will have a specific magnet rate at the beginning of the life (BOL). Subsequently, some manufactures provide three pre specified magnet rate:

1) Indicating the need for enhanced follow up (EFI): After reaching this value, the frequency of follow up visits or Trans telephonic monitoring is to be increased.
2) Indicating the elective replacement time (ERT): After reaching this value, the pulse generator has a definite expected longevity of a variable period of 3 to 6 months. So the pulse generator is to be electively replaced by 3 months.
3) Indicating the end of life of the pulse generator (EOL): After reaching this value, the behavior of the pulse generator cannot be predicted and it is to be replaced on an urgent basis.

Materials and Methods

MATERIALS AND METHODS

Patient population

This was a retrospective observational study conducted at Sree Chitra Tirunal institute for medical sciences and technology, a tertiary care referral centre for cardiovascular and neurological diseases. The study population consisted of patients on a permanent pacemaker and underwent replacement of their pulse generator (PG) during the period of 7 years between 2000 and 2006.

Data collection

Data were collected by review of medical records. These patients were retrospectively followed up from the day of pacemaker implantation to the day of PG change. Data were collected regarding the initial diagnosis which required implantation of the pacemaker, lead parameters like threshold and impedance at the time of implantation, number of follow up visits to the out patient department and duration of interval between follow up visits and the evaluation during follow up including the telemetry. Any pacemaker malfunction occurred during the follow up visits were noted down. Data were collected regarding the mode of detection of the need for PG replacement and the function of pacemaker, clinical condition of the patient at the time of detection of PG replacement time. Data were collected about the condition of the pacemaker and the patient at the time of admission for PG change if there was a delay in PG replacement after the recommendation. Data were also collected regarding the parameters like lead impedance and threshold at the time of implantation as well at the time of replacement.

Patients follow up status were determined based on the number of follow up visits. Those patients who were seen with an inter follow up interval less than 6 months for a minimum duration of 25 % of the total life of PG were grouped as having good follow up. Among the others, those who had an inter follow up interval of 6 months for a minimum duration of 25 % of the life of PG were grouped as having fair follow up. Among the others, who were seen at least yearly once were grouped as poor follow up and those who had an inter follow up interval more than an year during any time of follow up were considered to have very poor follow up. Patients who had their last follow up visit more than 2 years before the time of detection were taken as those who were lost to follow up.

Statistical analysis

Continuous variables were expressed as mean and standard deviation. Discrete variables were expressed as proportions. Chi-squire test was used to compare the proportions and paired t- test was used to compare the means. A p value < 0.05 was considered significant. The analysis was done with SPSS-14 statistical software.

Observations and Results

OBSERVATIONS AND RESULTS

Baseline characteristics

155 patients underwent PG replacement during the specified period. Mean age of patients at the time of PG replacement was 54.36 ±14.78 years (Range 21- 84). 72 (47.1 %) were males and 83 (52.9 %) were females. 97 patients (62.6 %) had AV nodal disease at the time of implantation of the pacemaker while 58 patients (37.4 %) had sick sinus syndrome as the primary diagnosis. For 132 patients (85.2 %), the procedure was their first PG replacement, 20 patients (12.9 %) had one PG replacement earlier while 3 patients (1.9 %) had 2 replacements before. Average duration of interval from PPI to PG replacement was 10.01(±2.93) years (Range 4 to 17 years). 153 patients had VVI pacing. One patient with sick sinus syndrome had AAI pacing while one patient with complete heart block had DDD pacing. 3 patients had rate responsive property for their pacemaker. 116 patients (74.8%) had right cephalic vein access for their lead placement, 27 patients (17.4 %) had right subclavian vein access, 2 patients (1.3 %) had left cephalic vein access and 6 (3.9 %) patient had left subclavian vein access, 3 patients (1.9 %) had right EJV access and in one patient (0.6 %), lead was epicardially placed.

Table 1. Baseline characteristics

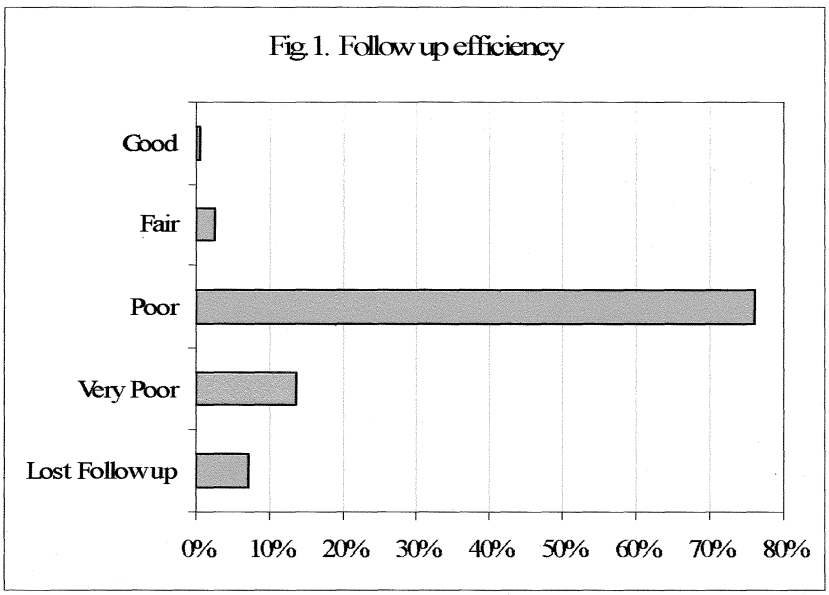
Parameter	Value
Age at PPI (Mean ±SD)	44.35 ±14.75
Age at PG change (Mean ±SD)	54.36 ±13.68
Sex	
Male	72 (47.9 %)
Female	83 (52.1 %)
Diagnosis	
Sinus node disease	58 (37.4 %)
AV node disease	97 (62.6 %)
Mode	
VVI	153
DDD	1
AAI	1
Previous PG change	
Nil	132
One	2
Two	3
Access site	
R. Cephalic	116 (74.8 %)
R. SCV	27 (17.4 %)
L. Cephalic	2 (1.6 %)
L. SCV	6 (3.9 %)
R. EJV	3 (1.9 %)
Epicardial	1 (0.6 %)
Duration of life of PG (Mean ±SD)	10.01 ±2.94

Follow up efficiency

11 patients (7.1 %) of the cohort belonged to the category of lost to follow up. Among others who had regular follow up visits, only one patient (0.6 %) satisfied the criteria for good follow up. 4 patients (2.6 %) belonged to the group with fair follow up. A majority of 118 patients (76.1 %) belonged to the group with poor follow up and 21 patients (13.5 %) had very poor follow up.

Table 2. Follow up Efficiency

Follow up Efficiency	Frequency	Percent
Lost Follow up	11	7.1
Very Poor	21	13.5
Poor	118	76.1
Fair	4	2.6
Good	1	0.6

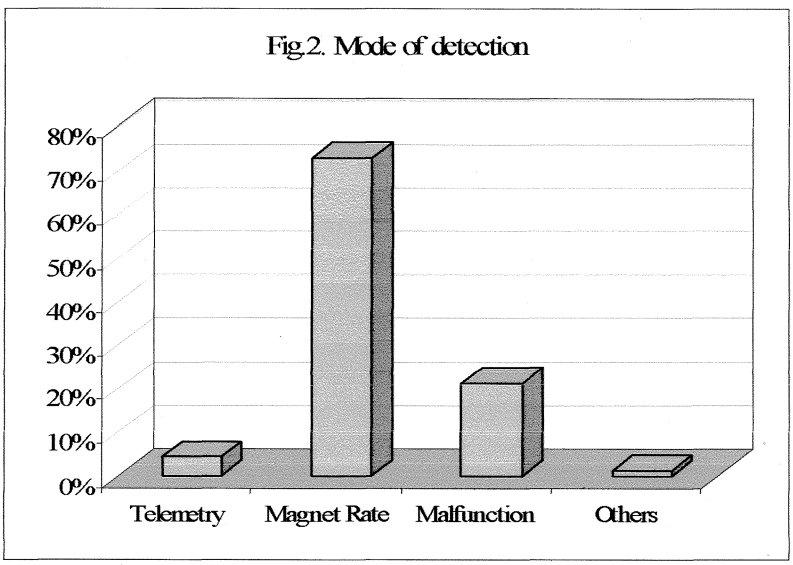


Mode of detection

Detection by an ECG with magnet was the predominant mode of detection of replacement time. Magnet rate suggested the PG replacement in 113 patients (72.9 %). Telemetry suggested PG replacement in 7 patients (4.5 %) before magnet rate attained the RRT. 33 patients (21.3 %) presented with pacemaker malfunction as the manifestation of end of life (20.6 %). Two patients were primarily taken for a lead change due to lead malfunction and hence the magnet rate could not be assessed at the time of presentation. One PG has implanted 13 years back, so decided to replace even though the RRT was not reached by analysing after the lead change. In the other patient end of life was detected by battery voltage by telemetry.

Table 3. Mode of detection

Mode of Detection	Frequency	Percent
Telemetry	7	4.5
Magnet Rate	113	72.9
Malfunction	33	21.3
Others	2	1.3

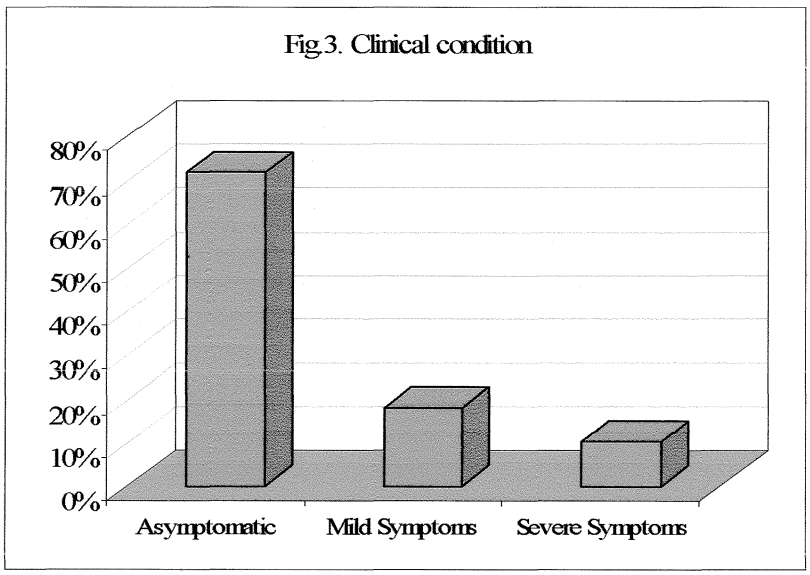


Clinical presentation

111 patients (71.6 %) were asymptomatic at the time of detection of need for PG change. 28 patients had mild symptoms like fatigue and giddiness. 16 patients (10.3%) bad history of recurrent syncope at the time of presentation. Five of these patients had hemodynamic instability necessitating an urgent temporary pacemaker implantation. One patient had Stoke-Adams attack at the presentation.

Table 4. Clinical status at PG change

Clinical condition	Frequency	Percent
Asymptomatic	111	71.6
Mild Symptoms	28	18.1
Severe Symptoms	16	10.3



Magnet rates

Of the 141 patients, who were coming on scheduled follow up visits, the change of magnet rate on serial visits was analysed. 88 patients (62.41 %) had a gradual decline from the BOL value before reaching the ERT or EOL value or before the loss of pacing. 55 patients (27 %) had an abrupt change in magnet rate. For 3 patients data of serial magnet rates were not available. The distinction between the magnet rate at ERT and EOL was not made due to heterogeneity of pacemakers and absence of the data.

Telemetry

Of the 144 patients who were on follow up, 84 patients (58 %) did not have their pacemakers interrogated once after the initial post implantation programming till the PG change. 36 patients (25 %) had their pacemakers interrogated once, 16 patients had two interrogations, 6 patients had three interrogations and 2 patients had 4 interrogations.

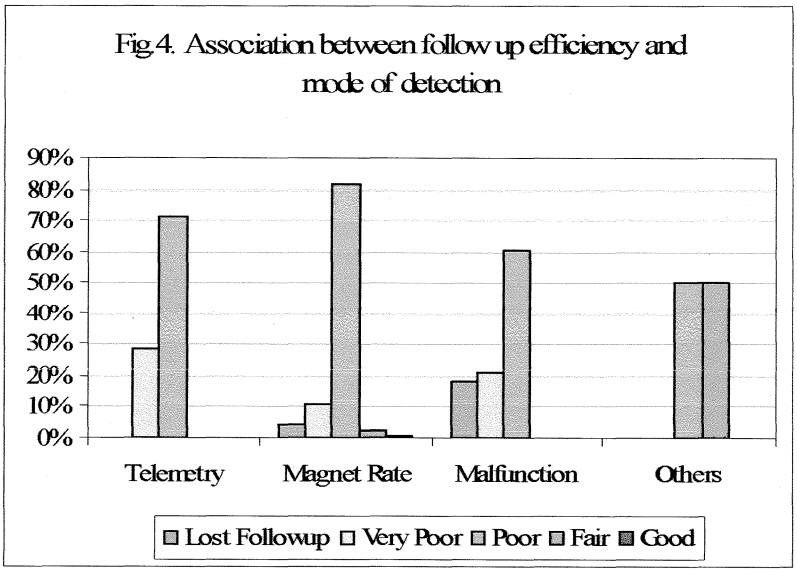
Failed detection and follow up efficiency

Of patients who were lost to follow up, 54.5 % presented with loss of pacing. Among patients with very poor follow up, 33.3 % had pacemaker malfunction. 16.9 % of the patients who were on poor follow up had pacemaker malfunction. None of the patients belonging to the group of fair or good follow up had pacemaker malfunction at the time of presentation. Since none of the patients had a minimum yearly interrogation, a relationship between the frequency of interrogation and development of

pacemaker malfunction at end of life was not analysed. The difference in the incidence of loss of pacing at presentation was not statistically significant between the groups with two groups of poor follow up and very poor follow up.

Table 5. Follow up efficiency and mode of detection

Follow up efficiency	**Mode of detection**			
	Telemetry	**Magnet rate**	**Malfunction**	**Others**
Lost Follow up	-	5 4.40%	6 18.20%	-
Very Poor	2 28.60%	12 10.60%	7 21.20%	-
Poor	5 71.40%	92 81.40%	20 60.60%	1 50.00%
Fair	-	3 2.70%	-	1 50.00%
Good	-	1 0.90%	-	-



Failed detection and basic diagnosis

25.8 % of patients with AV nodal disease (25/97) developed loss of pacing on follow up while 13.8 % of patients with sinus nodal disease (8/58) developed loss of pacing on follow up. This difference was not statistically significant.

Failed detection and magnet rate behaviour

Of the patients with abrupt fall in magnet rate, 14 patients had (25.5 %) had developed loss of pacing on follow up. In the group with a gradual fall in magnet rate, 12 patients (13.3 %) had developed loss of pacing. This difference was not statistically significant.

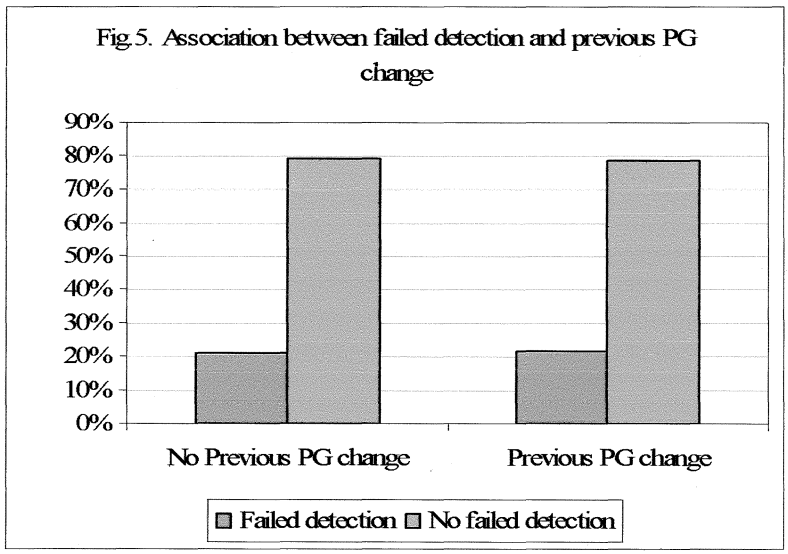
Previous PG change and follow up

Of 23 patients who had previous PG change , only one patient (4.34 %) was lost to follow up while 10 out of 132 (13.2 %) in the group with no previous PG change were lost to follow up. The change was significant.

28 patients of the patients with no previous change had failed detection of battery depletion and developed pacemaker malfunction while 5 patients out of 23 patients who had previous PG change developed pacemaker malfunction. Difference was not statistically significant.

Table 6. Failed detection and previous PG change

Previous PG change	Failed detection		Total	Percent
	Present	Absent		
Nil	28	104	132	21.21
Present	5	18	23	21.73



Behaviour of pacemaker after ERT

Of the 118 patients who were suggested PG change on the basis of telemetry or magnet rate, 90 patients (76.27 %) got their PG replaced within the recommended time of 3 months. All of them were asymptomatic with normally functioning pacemakers at the time of admission for PG change. 28 patients (23.76 %) patients got their PG replaced after 3 months with a mean delay of 5 months (range 4 to 60 months, mean 11.93 ±13.78) months. Of these 28 patients, 15 patients (53.57 %) were having normal pacemaker function with the programmed pacing rate and were asymptomatic at the time of PG change. 13 patients (46.42 %) were having pacemaker dysfunction. All of them were symptomatic. 6 patients (21.42 %) had total loss of pacing while 7 patients had (25 %) significant reduction in the pacing rate from programmed rate.

Lead change along with PG change

138 patients (89 %) had retained their old leads at the time of PG replacement while 17 patients (11 %) got their leads changed due to various reasons. 8 patients had high thresholds mandating lead change while 5 patients had a size mismatch between their lead and new pulse generators for which an appropriate adaptor was not available, for one patient, lead could not be disconnected from the old PG, one had a lead fracture necessitating replacement and one had a lead insulation break and one patient got her epicardial lead converted to endocardial lead.

Table 7. Lead change along with PG change

Reason for Lead Change	Frequency	Percent
Lead Not Changed	138	89
High Thresholds	8	5.2
Pocket Change	1	0.6
Size Mismatch	5	3.2
Others	3	1.9

Threshold and impedance changes

The mean threshold at the time of implantation was 0.68 (0.47) volts. At the time of PG change the mean threshold was 1.21 (0.59) volts. The change was statistically significant. The duration of PG change was found to be negatively correlating with the threshold at implantation. The mean impedance at the time of implantation was 733.98 (222.6) Ohms. The mean impedance at the time of PG change was 672.08 (177.6) Ohms. This difference also was statistically significant though to a lesser extent than the change in threshold (p value < 0.05). The impedance at the time of implantation was found to be positively correlating with duration of the PG change.

Table 8. Threshold and impedance changes

	Mean	**± SD**	**t value**	**p value**
Impedance at PPI	733.98	221.60	2.633	< 0.05
Impedance at PG Change	672.08	177.26		
Threshold at PPI	0.68	0.47	-8.166	< 0.001
Threshold at PG Change	1.21	0.59		

Table 9. Threshold and impedance: Correlation with PG change

	Duration of Life of PG	Impedance at PPI	Threshold at PPI
Duration of Life of PG	1		
Impedance at PPI	0.255**	1	
Threshold at PPI	-0.235**	-0.002	1

** P < 0.01

LV function

152 patients (98.1 %) had normal LV function at the time of pacemaker implantation. 3 patients (1.3 %) had mild LV dysfunction while 1 patient (0.6 %) had moderate LV dysfunction. None of the patients had severe LV dysfunction. At the time of PG change 149 patients continued to have normal LV function while 6 patients had LV dysfunction. 5 of them had mild LV dysfunction and one had moderate LV dysfunction. None had severe LV dysfunction. 3 patients who had mild LV dysfunction to begin with continued to have mild LV dysfunction and the patient who had moderate LV dysfunction continued to have moderate LV dysfunction. Two new patients developed mild LV dysfunction on follow up.

Own rhythm at follow up and LV function

Of the 144 patients who had follow up visits, 19 patients had own rhythm reported at some point during follow up visits. In 125 patients, only paced rhythm was reported on all follow up visits. 5.2 % of patients with own rhythm and 4 % patients without own rhythm were having normal LV function at the time of PG change. The difference was not statistically significant.

Table 10. Presence of own rhythm and LV function

	LV dysfunction	**No LV dysfunction**	**Total**	**Percent**
Own rhythm	1	18	19	5.2
No own rhythm	5	120	125	4.0

Discussion

DISCUSSION

A total of 155 patients underwent pacemaker pulse generator replacement during the specified time period in the institution. The average duration of the life of pulse generator was around 10 years. This is in agreement with the standard expected longevity of single chamber pacemakers with no special functions. Longest duration of service of PG reported was 17 years in a patient with sick sinus syndrome with own rhythm on follow up. Shortest duration was 4 years. This patient had a lead insulation break which caused the accelerated battery drain. So most of these patients had their pacemakers implanted or pulse generators last changed in late eighties and early nineties. Despite the fact that most of these patients were middle aged and active, almost all of them have received a single chamber pacemaker. Only a single patient has relieved a dual chamber pacemaker and only 3 pacemakers had rate responsive properties. This probably reflects the poor socio-economic status of the study cohort.

For most of the patients in the study group (85 %), the follow up, the PG replacement done during the study period was the first replacement. But around 15 % had their PG replaced earlier. Male and female population were almost same. A larger number of patients had AV nodal disease as the diagnosis compared to those with sinus node dysfunction as the diagnosis

Detection of the need for PG change

Like in the case of previous reports, battery depletion as indicated by a fall in magnet rate to the manufacture specified rate was the commonest indication for the PG

replacement in the present study.[2,10,13] The study population was very much heterogeneous with respect to the manufacturers and models with respect to the pulse generators. Many of the pulse generators were provided with two separate magnet rates one indicating a relative replacement time and other one indicating end of life. But a significant number of manufacturers gave only a single magnet rate value indicating replacement. None of the pacemakers had a magnet rate value indicating enhanced follow up. Because of this heterogeneity of magnet rate, this study did not discriminate the detection at ERT or at EOL and have taken both as detection of battery depletion by magnet rate.

Nearly 5 % of patients were detected by battery voltage measured by telemetry before the magnet rate has reached the ERT value. In two patients, lead change was the primarily planned procedure and PG was detected to be depleted along with it. In contrast to the previous series, in 21.3 % of the patients, the detection of battery depletion was failed and they presented with pacemaker malfunction.

Loss of pacing before PG change

The finding that in 21.3 % patients, the timely detection of battery depletion was not done and that they went on to develop loss of pacing reflects very poorly on the follow up. Even if we exclude the 11 patients who did not turn up for follow up till their PG failed, still 18.75 % patients who were on a scheduled follow up programme developed loss of pacing after a failed detection of battery depletion. All these patients were reported to have a normal pacemaker function in the previous visit and an elective follow up date was given. All these patients could have had a significant event during this interval and could even have mortality.

The classification of follow up based on frequency of follow up visits was arbitrary. The frequency of follow up examination required at various stages as suggested in the review of literature may not be feasible in our patients due to lack of infrastructure required for the same. Trans telephonic monitoring is not well established in our scenario. Towards the end of life of pulse generator, frequent examinations at 3 monthly or shorter intervals evaluation is necessary to pick up ERT correctly. Because of this, the patients who had short interval visits for a minimum period amounting to 25% of total life span of PG were considered to have good follow up. Instead of shot interval visits, if the patient had 6 monthly visits during same period were considered fair follow up. Rest of all were considered poor follow up.

High incidence of loss of pacing on follow up is basically due to insufficient follow up visits as evidenced by the fact that among the patients who had a good or fair follow up though the number is small, none developed a loss of pacing. The high incidence of loss of pacing in poor follow up not being different from those with still lesser number of follow up visits implicates the patient should be in a 6 monthly or lesser interval for a significant time of the follow up for timely detection of end of life.

Another important factor accounting for high incidence of failed detection of battery depletion is inadequate number of interrogations done on follow up. Telemetry will give clues to the impending battery depletion by analysis of stretch of pulse width, measurement of battery impedance, the measured battery voltage left and will also report on a projected longevity left in the battery. When the battery is reaching towards the end of life the pacemaker will try to conserve the energy by loosing the specialised functions like rate responsiveness and may have a mode switch to VVI mode. Since the

number of interrogations done was very small in the total follow up with a majority of patients having no interrogations after the initial programming, a meaningful analysis of the relationship between the frequency of interrogations and the incidence of failed detection could not be made.

The incidence of failed detection and loss of pacing was similar whether the diagnosis is SA nodal or AV nodal disease. Theoretically, the chance of a failed detection would be higher if the magnet rate changed abruptly at various stages rather than a gradual reduction. But the study did not show a significant difference between the two groups.

Follow up pattern in patients with previous PG change

The study analysed whether the fact that patient had already undergone one PG change will improve on the follow up and detection of battery depletion. After the one PG change only one out of 23 patients lost to follow up while 10 out of 132 patients in the other group was lost to follow up. This change was statistically significant. Probably the awareness for future battery depletion might have helped the patient to be remained in the follow up. But the incidence of the development of loss of pacing on follow up remained the same (around 21 %) in both groups. This is because the frequency of follow up visits and interrogations were similar in both groups.

Behaviour of the pacemaker after the detection of battery depletion

After the detection of battery depletion either by telemetry or by magnet rate at ERT or EOL, the replacement of the pulse generator was suggested. Usually the manufacturers provide a lifetime warranty of the pulse generator and replacement is

done without much financial burden to the patient. But patients have to be ready with finances for a lead change if needed. But sometimes in some of the old models, the lifetime warranty is not available due to various reasons. So the patient has to arrange finances for a PG change as well. Because of these and due to various other personal reasons, the PG replacement is delayed for a variable period of time after the suggestion of replacement in some patients.

In the study cohort, 76 % of patients who were picked up in time for PG replacement got the actual PG change done within the recommended time delay of 3 months and remained asymptomatic with normal pacemaker function. Around a quarter of the patients who were suggested an elective replacement got the actual PG change done after 3 months. Though the PG change was done with a median duration of 5 months, nearly half of them developed symptomatic pacemaker malfunction with a half of them having total pacing failure. Since the number of patients was not very large, an analysis of duration after the recommended time at which more patients develop malfunction could not be performed. The cut off of 3 months is validated in the study as none of the patients developed malfunction if replaced within 3 months.

Pacing induced LV dysfunction

Prolonged right ventricular pacing with the LBBB like dysynchronous activation of ventricular on long run can induce myocardial dysfunction and a reduced left ventricular dysfunction fraction. But the present study did not give any evidence to this hypothesis. 98.1 % of patients in the cohort had normal LV function to begin with and 96.1 % of patients continued to have normal LV function at the time of PG change after a mean duration of 10 years of pacing. The study also compared the incidence of LV dysfunction between the patients who were reported to have only paced beats on all of their follow up visits and the patients who had own beats on follow up visits. The

difference was not significant (3.5 % vs. 5.3%). But the number of patients who had owns rhythm was much smaller when compared to those who had fully paced rhythm. The analysis of LV function was only qualitative and based on visual impression of the examiner. Significant intra and inter observer variability as well as changes in machines over time would have affected the data.

Status of leads at PG change

89 % in the study cohort were able to retain their leads at the time of PG change. The leads got replaced in 11 % patients. Only in a single patient, the lead got replaced due to inherent lead problem (insulation failure). In this patient, the low lead impedance caused excess current drain and premature battery depletion. Only 5.2 % patients had unacceptably high threshold necessitating lead change. One patient got her endocardial lead changed to epicardial lead. The other reasons which mandated the lead change like size mismatch between the pulse generators and lead, inability to detach the lead from pulse generator have become almost non-existent with standardised hardware in present use. Though the leads had a significantly higher mean threshold at the time of PG change, this remained still in the acceptable range for most of the patients.

The implantation threshold as well as the impedance had impact on the longevity of the pulse generator. But the data on thresholds and amplitudes at the first or subsequent programming was not available in most of the patients. This data is essential for a meaningful analysis of the impact of the lead characteristics on the longevity of pulse generator because the thresholds invariably rise by lead maturation and the programmed parameters at this stage will have a significant impact on the longevity rather than the values available at implantation. The study showed that longevity is significantly correlated to lead factors like threshold and impedance available even at implantation also.

Conclusions

CONCLUSIONS

Follow up evaluation of pacemakers and anticipation and detection of various types of pacemaker malfunction remains far from satisfactory in the studied cohort of patients. Follow up intervals are longer and evaluation beyond the surface ECG and magnet rate is very less. 7.1 % of patients were lost to follow up after the pacemaker implantation till the time of PG change.

This has resulted in development of a pacing failure due to battery depletion in 20 % total patients in the study cohort. Pacing failure developed in 18 % of patients who were not lost to follow up. The failed detection and development of pacing failure has no relation ship with the basic diagnosis of the patient or with the serial change in magnet rates, whether it is abrupt or gradual. A minimum 6 monthly follow up visits for a minimum duration of 25 % of the lifespan of pulse generator may help to significantly reduce the incidence of development of pacing failure.

After the detection of battery depletion by magnet rate or telemetry, the patients are free of and adverse outcomes if their pulse generators are replaced within 3 months. 46.42 % of the patients who went past the 3 months developed pacemaker malfunction and had developed symptoms. Among them, half of the patients had developed total loss of pacing.

Old leads were retained in 89 % patients in the study cohort. A high threshold was the commonest cause of lead replacement. Longevity of the pulse generator was found to be directly correlating with threshold at implantation and inversely correlating with impedance at implantation.

Despite a prolonged period of duration of the right ventricular pacing, left ventricular function remains to be normal in most of the patients whether or not they had stable own rhythms at some point of time.

Increasing the frequency of follow up visits, establishing an effective trans-telephonic monitoring system and establishment of a fully functioning pacemaker clinic will increase the detection rates of battery depletion and prevent sudden loss of pacing.

LIMITATIONS

The population was very heterogeneous with respect to the manufacturers and models and a subgroup analysis was not possible. But the emphasis was not on performance of pacemakers but on the ability of follow up program to detect time of PG replacement.

Study was only a retrospective observational study based on medical records and only those who underwent a PG replacement in our centre were included. The patients who were either on follow up or lost to follow up and suffered an event outside and had mortality or a PG replacement in some other place was not included.

Bibliography

BIBLIOGRAPHY

1) Dwivedi SK, Sandeep Bansal, Aniket Puri, Makharia MK, Narain VS, Saran RK, Hasan M, Puri VK. Diastolic and Systolic Right Ventricular Dysfunction Precedes Left Ventricular Dysfunction in Patients Paced From Right Ventricular Apex. *Indian Pacing Electrophysiol J.* 2006; 6(3):142-152.

2) Hauser RG, et al. Clinical experience with pacemaker pulse generators and transvenous leads: An 8-year prospective multicenter study. *Heart Rhythm.* 2007; 4(2):154-60.

3) Vijayaaman P, Vaidya K, et al. Runaway pulse generator malfunction resulting from undetected battery depletion. *Pacing Clin Electrophysiol.* 2002; 25(2): 220-2.

4) Kindermann M, et al. Do battery depletion indicators reliably predict the need for pulse generator replacement? *Pacing Clin Electrophysiol.* 2001; 24(6): 945-9.

5) Kindermann M, et al. Longevity of dual chamber pacemakers: device and patient related determinants. *Pacing Clin Electrophysiol.* 2001; 24(5):810-5.

6) Kraus M, et al. High thresholds may alter end-of-life behavior in a dual chamber pacemaker. *Pacing Clin Electrophysiol.* 1997; 20(6):1691-7.

7) Scheibelhofer, et al. Reversible end-of-life indicator leading to erroneous pacemaker replacement-pitfalls of telemetry. *Pacing Clin Electrophysiol.* 1984; 7(6 Pt 1):952-4.

8) Victoria M, Tantengco T, Ronald L. Thomas, et al. Left ventricular dysfunction after long-term right ventricular apical pacing in the young. *Journal of American College of Cardiology*, 2001; 37(8): 2093-2100.

9) Bohm A, et al. Runaway pacemaker syndrome and intermittent non output as manifestations of end of life of a VVI pacemaker. *PACE.* 2000; 23: 2143.

10) Mantini EL, et al. A recommended protocol for pacemaker follow-up: Analysis of 1705 implanted pacemakers. *The Annals of Thoracic Surgery.* 1977; 24:62.

11) Parsonnet V. et al. Prediction of impending pacemaker failure in a pacemaker clinic. *The American Journal of Cardiology.* 1970; 25: 317.

12) Griffin JC, et al. Pace maker Follow–up: Its role in the detection and correction of pacemaker system malfunction. *PACE.* 1986; 9: 387.

13) Luceri RL, et al. Follow-up of DDD pacemakers. *PACE.* 1984; (7): 1187.

14) Schughert A. et al. Reliability and variability of impedance measured by real time telemetry. *PACE*. 1996; 19: 265.

15) Guidelines of Pacemaker follow-up. Report of a British pacing and electrophysiology group. *Heart*. 1996; 76: 458.

16) Vallario L. et al. Pacemaker follow–up and adequacy of medicare guidelines. *American Heart Journal*. 1988; 11.

17) Kamath PK. Pacemaker follow-up guidelines for physicians. *JAPI*. 2007; 35: 66.

18) Cardiac Pacing for the Clinician. Second edition. 2008. Springer Science plus Business Media, LLC.

19) Allenbogen K. Clinical cardiac pacing, defibrillation and re synchronisation therapy. Third Edition, 2007. Elsevier Publishers.