Prevalence and Determinants of Myocardial Damage after Occluder Implantation in Patients with Atrial Septal Defect (ASD)

PROJECT REPORT
Submitted during the course of DM Cardiology

Dr. MAHIM SARAN
DM Trainee

DEPARTMENT OF CARDIOLOGY
Jan 2014 – Dec 2016
DECLARATION

I, Dr. Mahim Saran, hereby declare that the project in this book, titled “Prevalence and Determinants of Myocardial Damage after Occluder Implantation in Patients with Atrial Septal Defect (ASD)” was undertaken by me under the supervision of the faculty, Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology.

Thiruvananthapuram

Date: Dr. Mahim Saran
DM Cardiology Trainee

Forwarded

The candidate, Dr Mahim Saran, has carried out the minimum required project.

Thiruvananthapuram

Date: Dr. Ajit Kumar V.K.
Professor and Head
Dept. of Cardiology, SCTIMST
“Prevalence and Determinants of Myocardial Damage after Occluder Implantation in Patients with Atrial Septal Defect (ASD)”

Primary Investigator:
Dr. Mahim Saran,
Senior Resident,
Department of Cardiology, SCTIMST

Guide:
Dr. Sivasankaran Sivasubramonian,
Senior Professor,
Department of Cardiology, SCTIMST

Co-guide:
Dr. Sanjay G.,
Additional Professor,
Department of Cardiology, SCTIMST
ACKNOWLEDGEMENT

In the course of this dissertation I have been benefited greatly from the assistance of many people, without whose help this study would not have been possible. I would like to convey my heartfelt thanks to all of them for their kind support.

I am indebted to my guide and teacher Dr. Sivasankaran Sivasubramonian, Senior Professor, Department of Cardiology, SCTIMST for his constant support, enthusiasm, guidance and personal attention throughout this study and training.

I thank my co-guide Dr. Sanjay G., Additional Professor, Department of Cardiology, SCTIMST for his constant guidance, encouragement and immense support throughout the project.

I am extremely thankful to Dr. Ajit Kumar V.K., Professor and Head, Dept. of Cardiology, SCTIMST for his valuable suggestions, support and encouragement.

I am equally indebted to the Faculty of Cardiology department for having permitted me to include their patients in this study.

I also thank all my colleagues for their support and suggestions, my juniors and seniors for helping me in the study. I express my deep felt gratitude to my family and my friends whose blessings and well wishes have always been a strong support during my entire career. And lastly, I am grateful to all the patients, patient's informants, who willingly participated in my study.

Dr. Mahim Saran
## CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>2. AIMS AND OBJECTIVES</td>
<td>3</td>
</tr>
<tr>
<td>3. REVIEW OF LITERATURE</td>
<td>5</td>
</tr>
<tr>
<td>4. MATERIAL AND METHODS</td>
<td>18</td>
</tr>
<tr>
<td>5. RESULTS</td>
<td>22</td>
</tr>
<tr>
<td>6. DISCUSSION</td>
<td>33</td>
</tr>
<tr>
<td>7. CONCLUSION</td>
<td>37</td>
</tr>
<tr>
<td>8. REFERENCES</td>
<td>39</td>
</tr>
<tr>
<td>APPENDIX i</td>
<td>45</td>
</tr>
</tbody>
</table>
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASD</td>
<td>Atrial septal defect</td>
</tr>
<tr>
<td>ASDDC</td>
<td>Atrial septal defect device closure</td>
</tr>
<tr>
<td>cTnI</td>
<td>Cardiac troponin I</td>
</tr>
<tr>
<td>cTnT</td>
<td>Cardiac troponin T</td>
</tr>
<tr>
<td>ICE</td>
<td>Intracardiac echocardiography</td>
</tr>
<tr>
<td>IVC</td>
<td>Inferior vena cava</td>
</tr>
<tr>
<td>PFO</td>
<td>Patent foramen ovale</td>
</tr>
<tr>
<td>TEE</td>
<td>Transesophageal echocardiography</td>
</tr>
<tr>
<td>TRF</td>
<td>Time resolved fluorometry</td>
</tr>
<tr>
<td>TTE</td>
<td>Transthoracic echocardiography</td>
</tr>
</tbody>
</table>
INTRODUCTION
Manipulation of the heart to treat various congenital malformations could result in myocardial damage which could be minimized by the less invasive interventional procedures by avoiding cardiotomy and cardiopulmonary bypass. (1, 2) Interventional Atrial Septal defect (ASD) occlusion produces much lower myocardial damage (1) than surgical ASD closure. (2) However, little is known about myocardial lesions after occluder implantation in children. There are indications that the sensitivity of the myocardium to surgical trauma is inversely related to the patient’s age, with higher vulnerability among children. (3) Cardiac troponin I (cTnI) is a sensitive and specific marker for myocardial damage. It is detectable only in traces in the peripheral blood of healthy people. (3, 4) Cardiac troponin I increase is widely used for the diagnosis of myocardial infarction (4, 5) and its concentration is increased after cardiac surgery (3, 6, 7) with maximum values 6–10 hours after surgery. (3, 7) Catheter intervention and radiofrequency ablation also lead to myocardial injury with increased cTnI. (8, 9) The specific mechanism of myocardial injury in interventional ASD closure is not fully understood. The influence of the size of the defect and of the closure device has not been studied. It is not clear whether the size of the septal defect also contributes to myocardial damage. So, the purpose of our study is to study the incidence and extent of myocardial damage after occluder implantation in patients with ASD and to determine its relationship with age, device size and size of the ASD.
Aims And Objectives

To study the incidence and extent of myocardial damage following occluder implantation in patients with atrial septal defects (ASD) and to correlate the same with baseline parameters like

1. Age
2. Atrial septal defect size and
3. Device / occluder size
REVIEW

OF

LITERATURE
Atrial septal defect (ASD) accounts for 8-10% of congenital heart defects with an incidence of 56 per 100,000 live births. (10) Although the total prevalence was 46 per 100,000 births from 1968-1997, it showed an approximately 9-fold increase to 100 per 100,000 live births in 1995-1997. (11) This recent trend may be attributed to the increasing use of echocardiography, compared to earlier studies where ASDs were diagnosed using autopsy reports, death certificates, physical examination, x-rays, catheterization, and surgical reports. (12)

**Etiology:**

Atrial septal defect is a congenital defect arising from malformation of the interatrial septum allowing pulmonary venous return from left atrium to directly enter the right atrium. The interatrial septum starts developing by 5th week of gestation and descends from the roof of the atrium to the endocardial cushion. Before the septum primum fuses with the endocardial cushion, the cephalad portion develops small perforation which coalesce to form a larger defect. The septum secundum which starts forming as a fold from the atrial roof stops growing by the seventh week of gestation leaving a flap like foramen ovale which closes at birth due to higher left atrial pressures. (13)

Ostium secundum ASD, the commonest form of atrial septal defect results from incomplete formation of septum secundum or excessive apoptosis of the cephalad portion of septum primum. Incomplete fusion of the septum primum with endocardial cushion on the other hand, leads to ostium primum ASD. (13) Sinus venosus ASD occurs due to lack of septation between right upper pulmonary vein and right atrium. (14) And, a rare occurrence of a defect between coronary sinus and left atrium is referred to as the coronary sinus ASD. (15)
**Echocardiographic assessment:**

Before planning for defect closure, the size and residual rims of the ASD should be properly assessed as some of the deficient rims (pulmonary vein, inferior vena cava or posterior rims) may preclude ASD device closure and deficiency of aortic rim may be the reason for erosion later. Echocardiographic assessment remains the gold standard for evaluation of ASD. (16) Transthoracic echo (TTE) is helpful in children for complete evaluation as the window is good however, in adults transesophageal echo (TEE) may be required.

**Transthoracic echocardiography:**

Subcostal frontal view is the best view to visualise the defect as the atrial septum is perpendicular to the ultrasound beam, visualising the septum in its antero-posterior axis. (17) Placing the beam perpendicular to the septum helps differentiate a true ASD from an echo drop out.

Analysis of the septum in supero-inferior axis via subcostal sagittal view is the best technique for sinus venosus ASDs. It also helps in assessment of the inferior vena cava (IVC) rim and shape of the ASD. (16)

Apical four chamber view is used to assess the mitral and the pulmonary venous rims and the size and pressures of the right sided chambers. (16)

Parasternal short axis view helps visualise the aortic and posterior rims. It also aids assessment of pulmonary artery hypertension, by measuring the pulmonary regurgitation jet. (16)
Transesophageal echocardiography:

Transesophageal echocardiography is used for complete assessment of the defect and during ASD closure. Multiple views have been suggested (16):

- **Mid esophageal four chamber view:**
  
  This view helps in assessment of mitral rim and detection of device impingement over the atrioventricular valves in case of a larger device. The multiplane probe is kept at zero degree and swept up to 15-30 degrees.

- **Mid esophageal Aortic valve short axis view:**
  
  This view is used to assess the aortic and posterior rims. The probe is kept at 30 degrees and swept 15-30 degrees.

- **Mid esophageal bicaval view:**
  
  This view aids in assessment of sinus venosus ASD and the IVC rim. It also helps in guiding the wire into left atrium through the septum. The probe is kept at 90 degrees and swept through 105 and 120 degrees.

Other modalities like 3-dimensional echocardiography and intra cardiac echocardiography have been used but not commonly available. Computerised tomography (CT) or magnetic resonance imaging (MRI) may be helpful in complex or sinus venosus ASDs and in delineating the pulmonary vein anatomy if not clear by echo.
Figure 1 demonstrates different morphological variations of atrial septal defects on transesophageal echocardiography.

**Figure 1:** Different Morphological Variations of Atrial Septal Defects on TEE; A: Centrally located ASD imaged at zero degree; the posterior (Post) and the mitral rims are demonstrated (arrows). B: ASD with deficient Aortic rim (arrow) imaged at 45 degrees. Both of these types of ASDs can be easily closed using the trans catheter technique. C: A large ASD with deficient posterior and aortic rims (arrows). These ASDs are technically challenging for device closure and are associated with complications. D: Multiple ASDs; there is a larger anterior defect (block arrow) and a smaller posterior defect (thin arrow). Post=posterior, Ant=anterior, Ao=aortic

**Closure of the Atrial septal defect**

The gold standard in the treatment of atrial septal defect (ASD) is direct surgical closure of the defect. (18) Although surgical closure is associated with low morbidity and mortality and excellent long-term results, sternotomy and cardiopulmonary bypass are required. Hence, in recent times, secundum ASD are being increasingly closed by trans catheter implantation of occluder devices.
Percutaneous transcatheter closure

Overall utilisation rates of atrial septal defect (ASD) and patent foramen ovale (PFO) repair have increased over time. This has mainly been due to the dramatic rise in the percutaneous closure rates. (19) The fact that surgical mortality rates for ASD closure are similar or higher than transcatheter mortality rates even when accounting for erosion-related mortality might have led to this substantial increase in its utilisation. (20, 21) In addition lower cost, better medical outcome, avoidance of unnecessary blood transfusions and the complications that accompany extracorporeal circulation make transcatheter closure a better option. (22, 23) The absence of skin scars and a shorter hospital stay are also more appreciated.

American college of cardiology/American heart association guideline published in 2008 have clearly outlined the guidelines for secundum ASD closure (Table 1). (24) However, even if the criteria are met, concurrent data may preclude closure in some cases, like a defect larger that 40mm or a concomitant cardiac lesion that requires surgery. Also, ASD closure should not be attempted in irreversible pulmonary hypertension where the defect act as a “pop-off” mechanism decompressing the right heart during pulmonary hypertensive crisis. (25)

Major contra-indications to device placement in secundum ASD are summarised in table 2.
Table 1: Indications for Atrial Septal Defect (ASD) device closure, (24)

<table>
<thead>
<tr>
<th>Indications for closure of ASD</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right atrial and right ventricular enlargement by echocardiography with or without symptoms.</td>
<td>Class I</td>
</tr>
<tr>
<td>Minimum diameter &gt; 5 mm and &lt; 40 mm on echo.</td>
<td></td>
</tr>
<tr>
<td>Adequate rims of tissue (&gt; 5 mm) from the defect to surrounding structures such as the coronary sinus, SVC, IVC, and AV valves, as well as the pulmonary veins.</td>
<td></td>
</tr>
<tr>
<td>Presence of an ASD with documented or verified paradoxical embolization and/or documented orthodeoxia-platypnea.</td>
<td>Class IIa</td>
</tr>
<tr>
<td>Net left-to-right shunting, pulmonary artery pressures less than two-thirds systemic levels, pulmonary vascular resistance less than two-thirds systemic vascular resistance, when either is responsive to pulmonary vasodilators, or test occlusion of the defect is successful.</td>
<td>Class IIb</td>
</tr>
</tbody>
</table>
Table 2: Contraindications to Atrial Septal Defect (ASD) device closure (25)

<table>
<thead>
<tr>
<th>Contraindications to ASD closure</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Aortic rim absence or severe deficiency confirmed in multiple TEE views. Absence of rims documented in <em>multiple</em> views of 30°, 40°, 50°+.</td>
</tr>
<tr>
<td>• IVC rim absence or severe deficiency.</td>
</tr>
<tr>
<td>• Pulmonary vascular resistance &gt; 15 Woods units is an absolute contraindication.</td>
</tr>
<tr>
<td>• Coronary sinus rim absence with evidence of coronary sinus impingement by the device in the catheterization laboratory.</td>
</tr>
<tr>
<td>• Mitral valve impingement by the device with evidence of new-onset or increasing mitral insufficiency. Try a smaller device, if feasible.</td>
</tr>
<tr>
<td>• Development of AV block after device deployment.</td>
</tr>
</tbody>
</table>

**ASD closure devices**

There are two devices approved by the US Food and Drug Administration (FDA) to close ASDs—the Amplatzer septal occluder and the Helex septal occluder. While the Helex septal occluder has a non-self-centering design requiring the disc size to be twice the size of the defect for effective closure, the Amplatzer septal occluder is a self-centering device. The waist of the device sits in the ASD not leaving much wiggle room after placement. The requirement of device size to be as close to the defect size as possible makes Amplatzer septal occlude suitable for defects as large as 40mm.

Various complications of percutaneous occluder implantation have been reported including device embolization and malpositioning, arrhythmias, thrombus formation, erosion and residual shunts. (26) While, device embolization is the most common complication requiring
surgical intervention, (27) little is known about myocardial lesions after occluder implantation in children.

**Device related myocardial injury**

Device-related erosion or device-related cardiac tissue injury is quite rare in the cardiac catheterization laboratory (0.1%-0.3%). (28)

In a review of registry of complication the incidence of device erosion in the United States was 0.1%. All erosions occurred at the dome of the atria, near the aortic root. Deficient aortic rim, superior rim and larger device to unstretched ASD ratio were considered risk factors for device erosion, on follow up. It was suggested not to overstretch the defect during balloon sizing. Patients with small pericardial effusion at 24 hr required closer follow-up.(28)

Cardiac troponin I (cTnI) is a very specific and sensitive marker of myocardial injury.(29,30) Cardiac surgery in known to cause a transient increase in cTnI serum concentration.(6,7) However, in a study by Tarnok et al. (31) transient mild elevations of cTnI concentration were also observed after occluder implantation. These changes lasted for up to 1 day after the procedure and were more pronounced in children than adults. Mere diagnostic cardiac catheterisation did not contribute to these results. They considered these changes to be the result of transient, clinically silent myocardial damage caused by the procedure. Similar post procedure cTnI elevation were also reported by Pees and colleagues. (1) They regarded transient, reversible myocardial membrane instability caused by the device as the cause. Their study focused on older patients (mean age 43.5 years) and did not examine correlations with age or device size. The specific mechanism of myocardial injury in interventional ASD closure in not yet fully understood.
Taggart et al. demonstrated that the sensitivity of the myocardium to surgical trauma is inversely related to the patient’s age, with higher vulnerability among children. (3) cTnI at +1 hour, +4 hours, and +1 day, and the cTnI-AUCs after occluder implantation also correlated negatively with the patient’s age in a study by Tarnok and company. However, the total amount of released cTnI was not age related in this study. It is suggested that child’s myocardium is more susceptible to trauma than adults. (3)

Few studies have also demonstrated that myocardial damage after ASD device closure (ASDDC) depends upon the occluder size (31) and occluder size/body surface area ratio. (32) These studies failed to show any influence of body weight and duration of the procedure on cTnI levels.

The rim of the atrial septum is formed by various vital cardiac structure – the ascending aorta and aortic sinuses anteriorly (towards the sternum), superior vena cava superiorly and slightly posterior, pulmonary veins posteriorly, inferior vena cava inferiorly and atrioventricular valves antero-inferiorly. (Figure 2)

Since the discs of the device lie on these rims, deficiency or absence of these rims effect the safety and efficacy of the closure. Although other rims are also important the aortic rim is the most important rim when it comes to device-related complications such as erosion. (28)If 5 mm is considered to be an adequate rim size, more than 40% of patients with ASD have an aortic rim that is < 5 mm. However, aortic rim deficiency is not a generalised contra-indication for device closure (table 2). (33)
The absence or deficiency of the IVC rim may cause the device edge to impinge upon the conduction system causing arrhythmias. Risk of device embolization is also increased in these situations. In case of deficiency of the atrioventricular valve rim the device may impinge on mitral or tricuspid valve leaflet resulting in restriction and/or regurgitation. (34)

The atrial septum being a three-dimensional structure, a defect may result in malalignment of the rims, especially the aortic and posterior rims. In an eccentric and leftward displaced aortic rim the right atrial disc will be slightly tilted, not straddling the aorta evenly and its edge will dig into the adjacent atria. Thus, increasing the chances of atrial free wall injury by the right atrial disc. (35)

Hyperdynamic defect, where the ASD size changes by more than 50% between atrial systole and diastole poses an increased risk of atrial wall trauma as the device is too large during systole and appropriately sized during diastole. (35)
An eccentric ASD located high in the atrial septum will be closer to the aorta and hence, device closure may increase the risk of tissue trauma. (35)

In a study by Amin Z, pre-procedural, intra-procedural and/or post-procedural echocardiograms of 12 device erosions from 2005 through 2012 were reviewed. Aortic rim absence in multiple views, poor posterior rim consistency, septal mal-alignment, and dynamic ASD were found to increase the risk of erosion significantly. In cases of bloody pericardial effusion with device in place, thorough assessment of the device edge by echocardiography in short-axis view showed tenting of the atrial free was into the transverse sinus by the device. (35)

Echocardiography being the primary modality on which the interventionists depend to determine whether a particular defect is suitable for transcatheter closure or not, in 2011, Bell-Cheddar and Amin (25) published criteria for effective echocardiographic evaluation of ASD.

Although transthoracic echocardiography is a useful tool in paediatric age group, adults generally have a poor acoustic window. In these patients, trans-esophageal echocardiography (TEE) provides a better delineation of the anatomy of the atrial septum, its nearby structures and pulmonary venous drainage. Intracardiac echocardiography (ICE) provides very similar information. Apart from the logistic issues, ICE has a disadvantage of not being able to form a four-chamber view. But, it has a greater ability to clearly delineate IVC and superior rims.

Bell-Cheddar and Amin (25) recommended that if using TEE, the defect should be evaluated in three views: aortic short-axis view, four-chamber view, and bicaval view. The aortic short-
axis view should be further evaluated sequentially from 30° through 80° in 10°- to 15°-increment. This evaluation is crucial as the aortic rim spans approximately 20% to 25% of the circumference of the ASD. If using ICE, evaluation in two views (shot axis and bicaval) was recommended. (25) Thorough evaluation should be done to ensure absence of any obstruction to surrounding structures such as AV valves, the right upper pulmonary vein, and coronary sinus after placement of the device.

TEE has also been used to successfully guide transcatheter closure of secundum ASD and PFO. (25, 36) ICE is thought superior to TEE in some centers (37). However, at this time, TEE remains the gold standard for ASD closure. (38)

Device closure being a technically simple procedure, morbidity and mortality rates associated with the procedure should be as low as possible. The importance of detailed clinical and echocardiographic evaluation, anticipation of hemodynamic consequences of ASD closure, a better understanding of the structure and limitations of the available devices and expertise of the interventionist in unquestionable. However, we lack enough data to lay down definite criteria to determine the type of defects where surgical closure should be preferred and to rule out the defects where closure should not be attempted.

In the absence of meaningful benchmarks, larger studies are needed to compare the outcome of surgical versus trans-catheter approaches based on defect type and patient characteristics, determine the high risk patients and identify the defects where closure should not be attempted.
MATERIAL AND METHODS
This study is a retrospective observational study on consecutive patients with atrial septal defect (ASD) admitted ASDDC (ASD device closure) from May 2015 to June 2016.

Standard procedure was adopted to close the defect in the catheterization laboratory by experienced operators under general anaesthesia and transesophageal echocardiography guidance, assisted by fluoroscopy after informed consent.

In all patients, device was implanted under general anaesthesia. Before starting the cardiac catheterization a detailed TEE examination was done using a multiplane probe. Standard technique for right heart catheterization was then performed via the right femoral vein, recording the pressures and blood samples to calculate the pulmonary to systemic blood flow (Qp/Qs) ratio. Antibiotic prophylaxis and unfractionated heparin (100U/kg) were given routinely. Implantation was performed under fluoroscopic and echocardiographic guidance. Mullin’s sheath was positioned in the left atrium after which the device was connected to its delivery system and advanced within the sheath until the left atrial disc was deployed. The complete system was then slowly withdrawn towards the atrial septum and proper positioning of the disc was confirmed on TEE. Then the proximal disc was deployed under TEE and fluoroscopic control in the right atrium. Appropriate device position was confirmed before releasing the device.

All patients were kept on dual antiplatelets for 6 months post procedure. Cardiac troponin T (cTnT) was measured 1 day before or at the time of sheath insertion (T1) and 4-6 hrs after the procedure (T2). Cardiac troponin T was measured using Radiometer's AQT90 FLEX bench-top immunoassay analyser (which has a cut off value of 0.017ng/ml) in all cases. Troponin T
assay is done automatically by the machine which contains an assay solution and a cartridge containing a cup with assay specific reagents. The blood sample is collected in an EDTA sample bottle (minimum 2ml) and set in the introducer panel. In the assay process, the sample and the assay solution are automatically added to the cup containing the assay-specific reagents. During the incubation period, the tracer and capture antibodies form sandwich complexes with the Troponin T present in the sample. After the incubation, the assay cup is washed with the assay solution and dried. The signal from the tracer antibody is then measured by means of time-resolved fluorometry (TRF), directly from the dry surface of the assay cup. The concentration of the analyte in the blood is directly proportional to the measured signal. The measured signal is converted to concentration using the calibration curve stored in the memory of the instrument.

Case sheets of all patients who underwent ASD device closure between May 2015 and July 2016 and had negative T1 and positive T2, who did not meet the exclusion criteria were studied using a pre-specified proforma for the study (appendix i). The data thus collected was analysed using SPSS.

**Statistical analysis**

Multivariate linear regression was used to determine the significance of relationship between the baseline parameters and Trop T elevation. In the group with Trop T > 50ng/L, linear regression was used to determine the relationship between baseline parameters and Trop T values. Association was considered significant if p < 0.05.
**Exclusion criteria**

All patients with other causes of Troponin T elevation were excluded from the study:

- Acute coronary syndrome
- Pre-procedure Renal failure (acute or chronic)
- Pericarditis/myocarditis
- Acute or chronic heart failure
- Cardiotoxic chemotherapy
- Current cardioversion defibrillation

This retrospective study on myocardial troponin elevation was approved by the ethical committee on 27th May, 2016.
RESULTS
A total of 200 ASD device closures were done from May 2015 to June 2016 with a median age of 12 years. Females constituted 64.5% of the patients. Baseline characteristics of the patients is mentioned in table 3.

Table 3: Baseline characteristics of the patients undergoing ASD device closure from May 2015 to June 2016 (n=200)

<table>
<thead>
<tr>
<th></th>
<th>Mean(standard deviation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>18.42+/−16.57</td>
</tr>
<tr>
<td>Male [nos. (%)]</td>
<td>71(35.5)</td>
</tr>
<tr>
<td>Female [nos. (%)]</td>
<td>129(64.5)</td>
</tr>
<tr>
<td>BSA</td>
<td>1.46+/−1</td>
</tr>
<tr>
<td>Height</td>
<td>136.1+/−24.8</td>
</tr>
<tr>
<td>Weight</td>
<td>35.65+/−1.99</td>
</tr>
<tr>
<td>Device size</td>
<td>21.31+/−7.5</td>
</tr>
<tr>
<td>ASD Size</td>
<td>17.51+/−17.31</td>
</tr>
<tr>
<td>Device Size/BSA</td>
<td>21.70+/−13.9</td>
</tr>
<tr>
<td>ASD Size/BSA</td>
<td>17.66+/−12.05</td>
</tr>
<tr>
<td>Complex ASD [nos. (%)]</td>
<td>61(30.5)</td>
</tr>
</tbody>
</table>
Of these patients 32 (16%) developed Trop T value ≥ 50ng/L 6 hours after the procedure. Baseline characteristics of the two groups (Trop T ≥ 50ng/L = Group 1; Trop T < 50ng/L = Group 2) were studied (Table 4).

Table 4: Baseline characteristics patients with Trop T ≥ 50ng/L and Trop T < 50ng/L

<table>
<thead>
<tr>
<th></th>
<th>Trop T&gt;=50</th>
<th>Trop T&lt;50</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>17.03+/-14.1</td>
<td>18.68+/-16.93</td>
<td>0.602</td>
</tr>
<tr>
<td>≤18years</td>
<td>23</td>
<td>110</td>
<td>0.517</td>
</tr>
<tr>
<td>&gt;18years</td>
<td>9</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>Sex- Male</td>
<td>13</td>
<td>58</td>
<td>0.86</td>
</tr>
<tr>
<td>Female</td>
<td>19</td>
<td>110</td>
<td></td>
</tr>
<tr>
<td>BSA</td>
<td>1.41+/-0.8</td>
<td>1.48+/1.05</td>
<td>0.631</td>
</tr>
<tr>
<td>Height</td>
<td>138+/-25.179</td>
<td>135.68+/-24.78</td>
<td>0.302</td>
</tr>
<tr>
<td>Weight</td>
<td>34.36+/-1.56</td>
<td>35.90+/-2.07</td>
<td>0.846</td>
</tr>
<tr>
<td>Device size</td>
<td>23.25+/-7.83</td>
<td>20.94+/-7.43</td>
<td>0.70</td>
</tr>
<tr>
<td>ASD Size</td>
<td>19.66+/-8.28</td>
<td>17.11+/-7.06</td>
<td>0.089</td>
</tr>
<tr>
<td>Device Size/BSA</td>
<td>22.10+/-12.84</td>
<td>21.63+/-14.16</td>
<td>0.189</td>
</tr>
<tr>
<td>ASD Size/BSA</td>
<td>18.22+/-11.87</td>
<td>17.57+/-12.12</td>
<td>0.112</td>
</tr>
<tr>
<td>Complex ASD</td>
<td>17/32</td>
<td>44/168</td>
<td>0.004</td>
</tr>
</tbody>
</table>

After multivariate logistic regression analysis complex ASDs were found to be significantly associated with positive Trop T values. Of the 32 patients with evidence of myocardial injury 17(53.1%) had complex ASD. Of the complex ASDs, multiple ASDs and deficient posterior rim were significantly associated with myocardial injury (Table 5).
Table 5: Subsets of complex ASDs

<table>
<thead>
<tr>
<th></th>
<th>Trop T≥50</th>
<th>Trop T&lt;50</th>
<th>Total</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deficient rim</td>
<td>3</td>
<td>8</td>
<td>11</td>
<td>0.96</td>
</tr>
<tr>
<td>Floppy rim</td>
<td>3</td>
<td>13</td>
<td>16</td>
<td>0.51</td>
</tr>
<tr>
<td>Multiple ASD</td>
<td>4</td>
<td>1</td>
<td>5</td>
<td>13.23</td>
</tr>
<tr>
<td>Deficient Aortic rim</td>
<td>2</td>
<td>7</td>
<td>9</td>
<td>0.70</td>
</tr>
<tr>
<td>Deficient posterior rim</td>
<td>4</td>
<td>1</td>
<td>5</td>
<td>13.23</td>
</tr>
<tr>
<td>Malaligned ASD</td>
<td>1</td>
<td>8</td>
<td>9</td>
<td>0.28</td>
</tr>
<tr>
<td>Large ASD</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>IAS aneurysm</td>
<td>0</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>44</td>
<td>61</td>
<td></td>
</tr>
</tbody>
</table>
Correlation of myocardial damage with baseline parameters was assessed by linear regression analysis (Figures 3-8)

Figure 3: Correlation of myocardial damage with ASD size

\[ P = 0.185, R^2 = 0.058 \]
Figure 4: Correlation of myocardial damage with Device size

P=0.047, R^2 = 0.125
Figure 5: Correlation of myocardial damage with Device size/BSA

P=0.819, $R^2 = 0.002$
Figure 6: Correlation of myocardial damage with ASD size/BSA

P=0.472, $R^2 = 0.017$
Figure 7: Correlation of myocardial damage with age

P=0.394, $R^2 = 0.024$
Figure 8: Correlation of myocardial damage with BSA

P=0.45, $R^2 = 0.019$
The relationship between the baseline parameters and extent of myocardial damage was analysed separately in the paediatric population as well. (Table 6)

Table 6: Correlation between extent of myocardial damage and baseline parameters in paediatric population (≤18years) via linear regression analysis

<table>
<thead>
<tr>
<th>Parameters studied</th>
<th>R sq</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device size</td>
<td>0.018</td>
<td>0.04</td>
</tr>
<tr>
<td>ASD size</td>
<td>0.053</td>
<td>0.291</td>
</tr>
<tr>
<td>Device size/BSA</td>
<td>0.008</td>
<td>0.68</td>
</tr>
<tr>
<td>ASD/BSA</td>
<td>0.043</td>
<td>0.34</td>
</tr>
<tr>
<td>BSA</td>
<td>0.077</td>
<td>0.19</td>
</tr>
<tr>
<td>Age</td>
<td>0.044</td>
<td>0.337</td>
</tr>
</tbody>
</table>
DISCUSSION
Surgical closure of ASDs had been the traditional method of treatment till 1976 when King et. al. first documented successful device closure of fossa ovalis ASD. (39) This technique has gradually been widely accepted and practiced in most centres. Various complications have been reported with the procedure, the most common being device embolization. Device related erosion on the other hand is relatively rare and usually a late complication. (35) The risk is less in cardiac catheterisation laboratory but tends to increase during the first 96 hours and decreases thereafter. (35) Our centre had only one documented erosion of the mitral valve out of 2000 device implantations for atrial septal defect over the last 15 years.

Cases of erosion started to emerge after the Amplatzer device received premarket approval. Unfortunately, we do not have the exact data on the total number of devices placed. In the absence of sufficient data the risk of erosion may be lower or higher than that demonstrated by Amin et al. in their review of registry of complications (0.1%-0.3%). (28) Hung-Tao Chung et al. in their study took cardiac troponin I (cTnI) as a marker of myocardial injury. (32) In their study, out of the 71 successful transcatheter closures, 50 children (70.4%) had cTnI elevation greater than the WHO criterion for myocardial cell damage (>0.4 mg/L) within 12 hours after the procedure. (40) In our study 16% patients had evidence of myocardial injury following device closure as demonstrated by cardiac troponin T (cTnT) values >50ng/L. Lack of adequate data, failure of initial studies to use cardiac biomarkers to determine myocardial injury and observation that a child’s myocardium is more susceptible to trauma(3) explains the disparities in the results.

Various studies have attempted to identify the risk factors associated with myocardial injury secondary to percutaneous device closure. These studies have taken cardiac troponins as markers of myocardial injury. Chung et al. (32) in their study observed that positive cTnI (>40ng/L) after transcatheter ASD closure depends upon device size/BSA, device size and
patients height. However, this study was limited to the paediatric population. We found a positive association between complex ASDs and a positive cTnT value (>50ng/L). There was no significant association between device size and positive troponin values in our study. The mean device size in patients with negative troponin values in our study was 20.94mm which was much higher than 14.24mm in Chung’s study.

Amin Z et al. studied echocardiographic parameters of 12 patients with device related erosion and found that absence of the aortic rim in multiple views, poor posterior rim consistency, septal malalignment, and dynamic ASDs, significantly increased the risk of erosions. (35) However, in the absence of a control group a significant association could not be established. We observed a significant association of multiple ASDs and deficient posteriors rims with myocardial injury. Definite criteria to determine which ASDs should be directly taken up for surgical closure still need to be established.

We also analysed the determinants of the extent of myocardial injury (in terms of cTnT values) and found that larger device size was significantly associated with greater cTnT release (p=0.048). The results were similar to those obtained by Tarnok et al. (31). Similar to their observation we also observed that cardiac troponin release does not depend upon the patient’s age. We did not find any correlation between cTnT release and ratio of device size to BSA as observed by Chung et al. (32) However, in their study they used overall troponin release rather than a single value as in our study.

Embolization or hemodynamic instability during the procedure can be another reason for troponin release. However, none of our patients had any episode of hypotension or ST-T changes during the procedure as an evidence for the same. Duration of anesthesia and drugs
used were standard in all subjects and hence we do not consider any of the factors could have contributed to inadvertent myocardial damage and troponin release. None of the subjects had any evidence for any adverse drug reaction and hence it is also not likely to have caused the troponin release.

The need for thorough echocardiographic evaluation, assessment of the ASD anatomy and anticipation of the hemodynamic changes occurring on its closure is of paramount importance in our attempt to reduce the morbidity associated with this relatively simple procedure. Not only will it reduce the risk associated with device closure to a minimum, but will also help in ruling out ASDs where percutaneous closure should not be attempted.

Our retrospective study failed to capture the finer procedural details like duration of procedure, no of attempts and whether right pulmonary vein deployment was associated with higher troponin release. The need for more prospective studies and the importance of a good surgical backup cannot be stressed enough.
CONCLUSION
Incidence of myocardial injury is more in patients with complex ASDs. Of the complex ASDs, multiple ASDs and deficient posterior rim are more likely to produce myocardial damage.

The extent of myocardial damage as reflected by larger cTnT release depends on occluder size.

Myocardial injury following ASD device closure does not depend on patient’s age or ASD size.


References


Appendix i

PROFORMA

• NAME
• AGE
• SEX
• HOSP NO
• HISTORY
  – SYMPTOMS
  – PREMORBIDITIES
  – SIGNIFICANT FAMILY HISTORY
• EXAMINATION
  – PR
  – BP
  – RR
  – CARDIOVASCULAR EXAMINATION FINDINGS
  – RESPIRATORY SYSTEM FINDING (SIGNS OF CONGESTION AND CONSOLIDATION)
  – SIGNIFICANT PERABDOMEN FINDING
  – FOCAL NEUROLOGICAL DEFICITS
• ASD SIZE BY TEE
• COMPLEXITY OF ASD

• Qp/Qs

• ASD DEVICE SIZE

• DURATION OF PROCEDURE

• ADDITIONAL PROCEDURES

• BASELINE TROP T

• POST PROCEDURE TROP T

• Other Lab investigations
  – Urea
  – Creatinine
  – Hemoglobin
  – Others

• ECG

• Imaging
  – CXR
  – Other significant ECHO findings
  – Others

• Complications