

**“Long term outcomes of transcatheter device closure of ostium Secundum
Atrial Septal Defect with moderate and severe pulmonary hypertension.”**



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OF THE DEGREE OF

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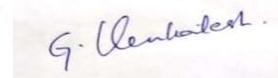
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DECLARATION

I, **Dr. Gurajala Venkatesh**, hereby declare that this thesis entitled “**Long term outcomes of transcatheter device closure of ostium Secundum Atrial Septal Defect with moderate and severe pulmonary hypertension**” was done by me under the supervision and guidance of Dr. K M Krishnamoorthy Professor & Head Dept of Cardiology, Dr. Deepa S Kumar, Associate Professor Dept of Cardiology, Dr. Arun Gopalakrishnan, Assistant Professor, Dept of Cardiology, Dr. Hari Krishnan. K.N., Assistant Professor Dept of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology.

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I hereby certify that the work in this thesis titled **Long term outcomes of transcatheter device closure of ostium Secundum Atrial Septal Defect with moderate and severe pulmonary hypertension”** is a certified original research work, done by *Dr. Gurajala Venkatesh* in the division of Paediatric Cardiology, the Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology in partial fulfilment of requirement for the purpose of award of Post-doctoral fellowship (PDF) in Paediatric cardiology.



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TITLE

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Atrial Septal Defect with moderate and severe pulmonary hypertension”**

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LIST OF ABBREVIATIONS

ACC	The American College of Cardiology /
AF	Atrial fibrillation
AHA	<i>The American Heart Association</i>
ANA test	antinuclear antibody test
ASD	Atrial Septal defects
AVT	Acute vasoreactivity test
BMI	Body mass index
CATH	Cardiac catheterisation
CHD	congenital heart defects CHD
CI	Confidence interval
CT ratio	cardiothoracic ratio
ECG	Electrocardiogram
ESC	The European Society of Cardiology
EPPVDN	The European Paediatric Pulmonary Vascular Disease Network
F-ASO	Fenestrated atrial septal occluder
IQR	Interquartile range
L→R shunt	Left to right shunt
MACCE	Major Adverse Cardiac and Cerebrovascular Events
mPAP	Mean pulmonary artery pressure
MR	Mitral Regurgitation
MVP	Mitral valve prolapse
NYHA	<i>New York Heart Association (NYHA) Functional Classification</i>
OS ASD	Ostium Secundum Atrial Septal Defects
PH	Pulmonary hypertension
PAH	Pulmonary arterial hypertension
PAP	pulmonary artery pressure
PADP	pulmonary artery diastolic pressure
PASP	pulmonary artery systolic pressure
PFO	Patent foramen ovale
PR	pulmonary regurgitation
PVR	pulmonary vascular resistance

PVRI	Pulmonary vascular resistance index
Qp	pulmonary blood flow
Qs	systemic blood flow
Qp: Qs	Ratio of pulmonary blood flow to systemic blood flow
RBBB	Right bundle branch block
ROC	Receiver Operative <i>Characteristic</i> curve
RV	right ventricle
RVSP	right ventricular systolic pressure
R RATIO	Resistance ratio
SCTIMST	Sree Chitra Tirunal Institute of Medical Sciences and Technology
SVR	Systemic Vascular Resistance
SVR _i or SVRI	Systemic Vascular Resistance Index
TR	Tricuspid regurgitation
TEE	Transoesophageal echo
TTE	Transthoracic echo
WSPH	World Symposium on Pulmonary hypertension
WU	Wood units
WU.m ²	Wood units.m ²
2D echo	Two-dimensional echocardiography

Long term outcomes of transcatheter device closure of ostium Secundum Atrial Septal Defect with moderate and severe pulmonary hypertension

INTRODUCTION

Atrial Septal defects (ASDs) account for 8% to 10% of congenital heart defects (CHDs) in the pediatric population and up to 30% of CHDs in adults(1). ASDs are grouped into the ostium secundum ASD, the ostium primum ASD, the sinus venosus type, and the coronary sinus ASD based on their anatomy. OS ASDs are the commonest type comprising 75% of all ASDs, with a 2:1 female: male ratio. Infants with OS ASD usually do not have symptoms unless associated with other shunt lesions or cardiac defects. Children and adolescents with an isolated OS ASD are generally asymptomatic or mildly symptomatic, often ignored by the patient even in the presence of large shunts. Symptoms like exercise intolerance, fatigue, dyspnoea, and palpitations progressively increase with age, and so do pulmonary artery pressures. The prevalence of atrial arrhythmias also increases with age, especially if age is more than 40 years.(2) Only four percent of those over 40 years of age with untreated ASDs did not have any symptoms.(3) If the OS ASD size at birth is >8 mm, spontaneous closure is rare, and also, OS ASDs are unlikely to close after 2–3 years of age. An ASD surgical repair/device closure should be done in cases with ($Q_p: Q_s > 1.5$) a significant left to right shunt and features of right ventricular dilatation without evidence of irreversible pulmonary vascular disease.(4) The efficacy and safety of transcatheter device closure of OS-ASDs have been well documented in multiple studies in children and adults.(2,5–7)

The long-standing significant left to right shunt causes dilatation of right heart chambers and can lead to changes in pulmonary vasculature resulting in the development of pulmonary hypertension. Nearly 8% to 10% of patients with atrial septal defects would develop pulmonary hypertension.(8) At one end of the spectrum, in patients with reversible pulmonary hypertension, ASD closure improves symptoms and reduces pulmonary artery pressures at follow-up. In

contrast, closure of ASD in patients with irreversible pulmonary hypertension is detrimental due to the removal of the pop-off mechanism at an atrial level, causing right ventricular dysfunction and heart failure. Patients with hemodynamically significant ASD ($L \rightarrow R$ shunt $>1.5:1$) without ASD closure have worsening symptoms, atrial arrhythmias, reduced exercise capacity, and eventually severe degrees of PAH.(9) With the development of severe pulmonary artery hypertension, the symptoms worsen and can cause right ventricular dysfunction. The development of the irreversible pulmonary vascular disease can lead to worse patient outcomes and contribute to high morbidity and mortality.(10,11)

“As per the 6th World Symposium on Pulmonary hypertension (WSPH) Task Force(12), Pulmonary artery hypertension is defined as the mean pulmonary artery (PA) pressure ≥ 20 mm Hg and a pulmonary capillary wedge pressure ≤ 15 mm Hg and the pulmonary vascular resistance ≥ 3 Wood units.”

“Pulmonary hypertension (PH) is considered to be present if the estimated Pulmonary arterial systolic pressures (PASP) on echocardiography is > 40 mm Hg. PH is classified according to the baseline PASP by 2D echocardiography as; no PAH (<40 mm Hg), mild PAH group (40 to 49 mm Hg), Moderate PAH group (50 to 59 mm Hg), or Severe PAH group (>60 mm Hg) based on classification used by other studies”.(13)

“As per the ACC/ AHA guidelines(14), ASD with the elevated pulmonary artery systolic pressure (PASP) $>2/3$ rd systemic; pulmonary vascular resistance (PVR) $>2/3$ rd systemic; and or with a net right to left shunt, is considered as a contraindication for the closure”. Multiple studies have shown a notable reduction in pulmonary artery pressures in patients with ASD with a left to right shunt and PH after transcatheter ASD closure.(15–17) Transcatheter ASD closure with the fenestrated device was done in patients with severe pulmonary hypertension with concomitant vasodilator therapy with favorable outcomes and symptomatic improvement in multiple studies.(18,19) In a selected group of non-repairable ASD patients with severe pulmonary

hypertension, a treat to close approach was described with some benefit in selected patients, especially if PVR drops to ≤ 6.5 Wood units post pulmonary vasodilator therapy. (20)

Sree Chitra Tirunal Institute of Medical Sciences and Technology (SCTIMST) is a tertiary care cardiac center in Trivandrum that serves patients from Kerala and Tamil Nadu's border districts. A large cohort of patients underwent transcatheter device closure of ostium Secundum atrial septal defect at our institute. We aim to report the outcome of percutaneous device closure of ostium secundum ASD in patients with moderate and severe pulmonary hypertension.

The outcome variables on long-term follow-up are the change in pulmonary artery systolic pressure with respect to age at the time of device closure, baseline pulmonary artery pressure, baseline PVR and size of the defect, use of pulmonary vasodilator drugs. The percentage of patients with normalisation of pulmonary artery systolic pressure at long-term follow-up, the factors predicting the normalisation of pulmonary artery systolic pressure at long-term follow up are analysed. The percentage of patients with presence or persistence pulmonary hypertension (PASP ≥ 40 mm Hg) and presence or persistence severe pulmonary hypertension (PASP ≥ 60 mm Hg) at long-term follow-up, the factors predicting them are assessed.

Other outcome variables on long-term follow up were NYHA functional class; the prevalence of arrhythmias at baseline and incidence of any new-onset arrhythmia especially atrial fibrillation; the incidence of Major Adverse Cardiac and Cerebrovascular Events (MACCE) and mortality; the incidence of use of pulmonary vasodilators prior to device closure; and percentage of patients taking pulmonary vasodilators after device closure; incidence of device migration, device erosion, infective endocarditis.

REVIEW OF LITERATURE

Atrial Septal defects (ASDs) account for 8% to 10% of congenital heart defects (CHDs) in the pediatric population and up to 30% of CHDs in adults(1). The incidence of ASD is 1.64 per one 1000 live births. OS ASDs are the commonest type comprising 75% of all ASDs, with a 2:1 female: male ratio. Atrial septal defects result in left to right shunt at the inter-atrial level. The direction and volume of the shunt are determined by ASD size and the relative left atrial and right pressures, the left and right ventricular compliance. In large ASDs, the two atrial pressures are equalized, and the shunt depends mainly on the ventricular compliance ratio. The long-standing significant left to right shunt causes dilatation of right heart chambers and the development of pulmonary hypertension. However, Small ASDs do not result in significant dilatation of RV.

Natural History of (OS ASD) ostium secundum atrial septal defect:

Symptoms & Functional status:

Infants with OS ASD usually do not have symptoms unless associated with other shunt lesions or cardiac defects. In a retrospective case series by **Andrews R et al.**(21), six infants with ASD who were symptomatic with very little weight gain had significant left to right shunt and elevated Pulmonary artery pressures. They underwent surgical closure of ASDs. Five of these had significant other pathologies like a small pulmonary artery, anomalous collateral to the lung, pulmonary vein stenosis, Noonan syndrome with lung hypoplasia, and or hypertrophic cardiomyopathy tracheobronchomalacia predisposing to recurrent respiratory infections, pneumonitis.

Children and adolescents with an isolated OS ASD are generally asymptomatic or mildly symptomatic, often ignored by the patient even in the presence of large shunts. Symptoms like exercise intolerance, fatigue, dyspnoea, and palpitations progressively increase with age, and so do pulmonary artery pressures and atrial arrhythmias.(2)

In a study done by **Richard H et al.**(22) review of 481 patients with OS ASD seen during 1957 to 1976, who underwent surgical correction before the age of forty years, 202 (42%) patients were asymptomatic, and the defect was detected on routine examination, more than fifty percent had symptoms of dyspnoea and fatigue.

In a study by **Craig and Selzer**, (23) 128 consecutive adult patients (18-68 years) with OS ASD were analyzed, 87 patients were females, 41 were males, 14 % of patients in the age group 20-40 years, 24% patients in the age group 40-60 years, seventy-five percent of patients with age above 60 years had exertional dyspnoea.

In a study by **James Gault** (24), sixty-two patients, age 40 years or more with ASD, were analyzed. 94% were symptomatic at the initial presentation. Symptoms of dyspnoea were seen in 90%, fatigue was found in 48%, palpitations in 43%, edema in 28%, angina in 8% of patients. Forty-five percent of patients were in NYHA function class II, forty-four percent of patients were in NYHA function class III, eight two percent in NYHA II/III had Pulmonary arterial hypertension. More than fifty percent of symptomatic patients had severe PAH, 13% had a balanced or reversed shunt.

Atrial arrhythmias:

Arrhythmias are uncommon in children with ASDs. Atrial arrhythmias occur late in the natural course of ASD patients. They can cause increased morbidity and mortality, especially in older adult patients, and predispose to the development of heart failure and stroke. “In a prospective study done by **Berger F et al.**(25), the incidence of atrial flutter/fibrillation in adults with atrial septal defect before and after surgery was evaluated”. Two hundred eleven adults with ASD were divided into three groups: 18 - 40 years group, 40 - 60 years group, and >60 years group. The age of the patient cohort without atrial arrhythmias prior or after atrial septal defect closure was (39±13 years) significantly less than that of patients with flutter (54±12 years) or

fibrillation (59 ± 8 years). Preoperatively, in the age group 18 - 40 years, atrial flutter was seen in 1 patient (1%). In the age group 40 – 60 years: 15 % of patients were in atrial flutter. 15 % of patients were in atrial fibrillation. Whereas in patients >60 years: 61% had atrial fibrillation. 19% had atrial flutter. ASD surgical closure did not decrease the incidence of atrial fibrillation but reduced the incidence of the atrial flutter.

In a study by **Gatzoulis et al.** (26), 213 symptomatic adult patients with a significant left to right shunt (82 men and 131 women) underwent surgical closure. They were assessed for incidence of pre and postoperative atrial arrhythmias. Forty patients (19%) had atrial fibrillation or flutter before surgery. Patients with atrial arrhythmias were older compared to patients in sinus rhythm (mean [$\pm$ SD] age, 59 ± 11 vs. 37 ± 13 years, $P < 0.001$), and their mean pulmonary arterial (PA) pressures were high (25.0 ± 9.7 vs. 19.7 ± 8.2 mm Hg, $P = 0.001$). Follow-up duration of 3.8 ± 2.5 years, 60% of patients persistently had atrial arrhythmias. The mean age of patients with persistent atrial arrhythmias was more than that of the 40% of patients who converted to sinus rhythm ($P = 0.02$). New-onset atrial arrhythmias were higher in patients who were greater than 40 years of age at the time of surgery than in those of age 40 years or less (5 of 67 vs. 0 of 106, $P = 0.008$). Six patients had a stroke on follow-up. Multivariate analysis showed that age >40 years at the time of surgery ($P = 0.001$), the presence of pre-operative atrial arrhythmias ($P < 0.001$), and the presence of postoperative junctional rhythm or atrial arrhythmias ($P = 0.02$) were predictive of late postoperative atrial arrhythmias. Patients with atrial fibrillation or flutter were older & also had higher pulmonary arterial pressures and a worse NYHA functional class. However, in patients aged >40 years, surgery had survival benefits and improved functional capacity.

In a study by **Murphy et al.** (27) development of atrial fibrillation, post-surgery depends on the patient's age at the time of surgery and may occur despite surgical closure of ASD in patients more than 25 years of age.

In a study done by **Oliver J et al.**(28), comprising 286 adults with ASD with a mean age of 39.5 ± 19 years, atrial fibrillation was seen in 15% of patients. Age at surgical repair was 47.7 ± 19 years among those patients with persistent atrial fibrillation versus 22.9 ± 18 among those who have had resolution of their atrial arrhythmia following surgery. The sole predictor of atrial fibrillation was late age at the time of operation (>25 years).

Mitral regurgitation:

Mitral Regurgitation (MR) may complicate the late course of an unrepaired OS ASD. The morphology responsible for MR is usually prolapsing mitral valve. In a study by **M Toyono et al.** (29) to evaluate the incidence of MR in adults with ASD before surgery and the outcome of moderate to severe MR after surgical repair, 71 consecutive patients with secundum ASD (47 ± 16 years) who underwent surgery were included, preoperatively 20% patients had moderate to severe MR and 35% patients showed mitral valve prolapse (MVP). The ASD patients with moderate to severe MR had worse symptoms, higher rate of atrial fibrillation and MVP compared to patients with no MR to mild MR.

Paradoxical embolism

Elderly ASD patients are also at higher risk of stroke due to paradoxical embolization. In a study done by **Khositseth A et al.** (30), one hundred three patients with presumed Paradoxical embolism (TIA =22, stroke $n=77$, or peripheral emboli =4) 12 patients had OS ASD and underwent device closure; the remaining patients had Patent foramen ovale (PFO).

Life expectancy and survival:

Hemodynamically significant unrepaired ASDs were associated with high morbidity and mortality with increasing age, as demonstrated by old studies. In a study done by **Campbell** (31), The mortality rates were low in the first two decades, 0.6 % and 0.7 % per year. In the following decades, they increased from 2.7 to 4.5, to 5.4, and 7.5 % per year. 25% of patients have died just before their 27th year, half by their 36th year, 75% by 50, and 90 % by 60 years. The average age

of death was 37.5 +/- 4.5 years. The median age was 37 years. However, this study seems to overstate the poor outcome.

A study by **Murphy *et al.*** (27) was done to look at the long-term outcome of 123 adults with surgical repair of ostium secundum or sinus venosus atrial septal defects. The overall 30-year survival rate of operated ASD patients was 75% versus 84% in the matched control population. When operated on before 25 years of age, the survival rate at 27-year follow-up was (97 % and 93% in < 11 years and 12-24 years, respectively) similar to that of a matched control population. In the patient age groups, 25-41 years and > 41 years survival rates were 84% and 40%, respectively. When operated in older age, higher mortality and morbidity were seen. In this study, patients with pulmonary artery systolic pressure (PASP), more than 40 mm Hg, were classified to have moderate or severe pulmonary hypertension and were higher in the age group >41 years (oldest quartile). Long-term survival was reduced in patients with significant pulmonary hypertension prior to surgery. 25-year survival of patients with age more than 24 years and PASP >40 mm Hg was significantly lower than the control population. Independent predictors of long-term survival were age at surgery and PASP (pulmonary arterial systolic pressure) before operation. Twenty-seven late deaths were reported, with 18 from a cardiovascular cause (13 cardiac and five-stroke deaths). Patients operated on before 25 years of age had a better prognosis, whereas those operated after 25 years of age had a higher risk of atrial fibrillation, stroke, late cardiac failure on follow-up.

The life expectancy of ASD patients with pulmonary hypertension is less compared to those without PH. In a study done by **Dalen *et al.*** (10) (1968), 49 ASD patients, age ranging from 10-61 years with a median age of 32 years, females were 35, males were 14, underwent cardiac catheterization and “were classified to have the pulmonary vascular disease if mean pulmonary artery pressures (mPAP) > 25 mm Hg and pulmonary vascular resistance (PVR) more than

120dynes/sec/cm⁻⁵.” 40% of patients were found to have pulmonary vascular disease and had symptoms and had reduced survival rate.

“**Craig and Selzer**(23) in 1968 reported the natural history and prognosis of 128 adult OS ASD patients. Significant pulmonary artery hypertension (>50 mm Hg) was seen in 22%, of which 15% had high pulmonary vascular resistance (>5Wood units), with significant arterial hypoxemia (<90%) in 14%.” The significant risk factor for ASD patients is a severe pulmonary vascular disease occurring in about 14% of patients and was seen after 20- 40 years of age, leading to the right to left shunt (the Eisenmenger syndrome), disability, and death.

Cherian et al. (32) studied 709 consecutive patients with isolated OS ASD, the pulmonary artery systolic pressure (PASP) was > 50 mmHg in 16.6% of patients. Pulmonary hypertension was seen in 13% of patients < 10 years of age, 14% of those aged 11 to 20 years. PVR > 5.0 units as the criteria of pulmonary hypertension were seen in 12% of those from 0 to 10 years, 10% between 11 and 20 years, 17% from 21 to 30 years, 19% between 31 and 40 years, and 11% > 40 years of age. The Eisenmenger reaction was seen to be 7% in the 1st decade, 8% in the 2nd decade, 10% in the 3rd decade, and 11% in the 4th decade and beyond. In this study development of pulmonary vascular disease was independent of age which was contrary to other studies.

In a study by **Steele et al.** (11), 40 of 702 patients (6%) with ASD (34 women and six men) had the pulmonary vascular obstructive disease, with a total pulmonary resistance greater than 7 U/m²; of these 14 (mean age 44 years) received medical treatment and 26 patients (mean age 47 years) underwent surgical closure. In the surgically managed group, total pulmonary resistance, pulmonary arteriolar resistance, pulmonary to systemic resistance ratio, systemic arterial oxygen saturation, and pulmonary arterial oxygen saturation correlated well with survival.

In a study by **Konstantinides et al.** (33), 179 patients with isolated atrial septal defects diagnosed after the age of 40 were analyzed. The 84 patients (47%) who underwent surgical repair were compared to the 95 patients (53%) who did not undergo surgery. The average duration of

follow-up was 8.9 ± 5.2 years (range, 1 to 26). The surgical correction of the defect resulted in a considerable reduction in mortality (relative risk, 0.31; 95 percent confidence interval, 0.11 to 0.85). The adjusted 10-year survival rate for surgically treated patients was 95%, better compared to 84% who did not undergo surgery. In addition, the surgical treatment prevented worsening of NYHA class (relative risk, 0.21; 95 % confidence interval, 0.08 to 0.55). However, ASD repair after the age of 40 years did not have any benefit in reducing new-onset atrial arrhythmias or stroke events. In comparison to medical treatment, the surgery for an atrial septal defect in patients over 40 years of age improves long-term survival and functional capacity. Closure of the defect after 40 years of age does not reduce the risk of atrial arrhythmias.

Percutaneous device closure in OS ASD patients with pulmonary hypertension:

Percutaneous ASD device closure is preferred to surgery as the treatment of choice when the anatomy is suitable, with less than one percent risk of any complications and more than 95% success rate for device closure.(34)

In a study by De Lezo J et al. (16), 29 adult patients out of 101 patients with OS ASD who underwent transcatheter device closure had a peak systolic pulmonary pressure of >40 mm Hg prior to device closure. Female patients were 24 (83%), and males were 5 (17%), ranging from 17 to 75 years of age, the mean age was 56 ± 14 years, and 25 patients (86%) were >40 years of age. Six patients (20.6%) were asymptomatic. 79.4% had dyspnoea, 48% had NYHA III-IV symptoms. 41% had chronic atrial fibrillation. The patients with sinus rhythm were younger than those with long-standing atrial fibrillation. (51 ± 16 versus 64 ± 6 years, $P < 0.01$). Patients with atrial fibrillation had a higher PASP than those in sinus rhythm (78 ± 27 vs. 54 ± 12 mm Hg, $P < 0.05$). The peak systolic pulmonary pressure dropped from 64 ± 23 to 54 ± 21 mm Hg ($P.001$) when the ASD device was closed, and the systolic pulmonary-to-systolic systemic pressure ratio dropped from 0.66 ± 0.22 to 0.54 ± 0.17 ($P.001$). All symptomatic patients showed improvement in their functional class, especially in those with severe pulmonary hypertension and heart failure.

Only 3 % had residual ASD flow on follow-up. The average peak systolic pulmonary pressure (PASP) by echocardiography further decreased to 34 ± 11 mm Hg ($P < .001$), compared to that of baseline and immediate post device closure.

In a study done by **Balint et al.** (13), 54 patients who underwent device closure of ASD with moderate and severe PAH from 1999 to 2004 were included. “Pulmonary hypertension was labeled as moderate (50–59 mm Hg) or severe (>60 mm Hg) according to RVSP (right ventricular systolic pressure) measured by echocardiography”. 49% of the patients had symptoms of NYHA class $> II$, and 22 % of patients had atrial arrhythmias at the time of device closure, 11% patients had persistent AF, 11% patients had paroxysmal AF. 96% of patients had dilated right heart chambers, and 41% had more than mild right ventricle (RV) dysfunction. Cardiovascular drugs were used by 63% of patients. 26% were using oral anticoagulants. The (mean $\pm$ SD) baseline RVSP was 57 ± 11 mm Hg (range 50–95). 63% of cases had moderate PAH, and 37% had severe PAH at baseline. There was no relationship between average RVSP (right ventricular systolic pressure) and female sex (female 58 ± 9 mm Hg and male 58 ± 11 mm Hg, $p = 0.91$). It correlated with age at time of device closure ($r = 0.73$, $p = 0.05$). The pulmonary hypertension did not correlate with the ASD size ($r = 0.66$, $p = 0.06$). The average RVSP did not differ between individuals with and without systemic hypertension (53 ± 21) versus (51 ± 16), $p = 0.79$. Extra possible contributory factors of PAH (venous thromboembolic disease, and left ventricular dysfunction, respiratory diseases like chronic obstructive pulmonary disease, sarcoidosis, pulmonary tuberculosis) were noted in 19% of individuals. There was gender difference with respect to secondary causes of PAH (25% vs 40%, $p = 0.29$).

At the early follow-up (mean 2.3 ± 1.2 months), the systolic pulmonary artery pressure reduced from 57 ± 11 mm Hg to 51 ± 17 mm Hg ($p = 0.003$), and there was no mortality. At the late follow-up ($n = 39$, mean duration 31 ± 15 months), the systolic pulmonary artery pressure reduced from 58 ± 10 mm Hg to 44 ± 16 mm Hg ($p = 0.004$), and there were two deaths. In only

43.6% of patients, the RVSP reduced to normal (<40 mm Hg), and 15.4% of patients continued to have severe PAH. Two deaths occurred during late follow-up: the cause of death in one patient was recurrent pulmonary thromboembolism, and the second was non-cardiac (bowel obstruction). There was no incidence of newly detected AF at late follow-up. Compared to patients with $RVSP < 60$ mm Hg, patients with persistently severe PAH ($RVSP > 60$ mm Hg) were more likely to have persistent symptoms after device closure (15% vs. 67%, $p = 0.02$).

Yong et al. (35) did a cohort study on 215 adults with attempted transcatheter ASD device closure from 1999 to 2006. “Patients were classified as having no PAH (<40 mm Hg), mild PAH (40 to 49 mm Hg), moderate PAH (50 to 59 mm Hg), or severe PAH (≥ 60 mm Hg) based on their baseline systolic pulmonary artery pressures”. Older age (odds ratio [OR], 1.10 per year; $P < 0.0001$), large defect (OR, 1.13 per mm; $P < 0.0052$), female gender (OR, 3.9 ; $P < 0.0313$), and at least moderate tricuspid regurgitation were all independent predictors of moderate or severe PAH (OR, 3.6 ; $P < 0.0043$). At 15 months of follow-up (interquartile range 8 to 43), reduction of systolic pulmonary artery pressures to <40 mm Hg was least in patients with severe PAH (90.2% ; 71.7% ; 66.7% ; and 23.5% $P < 0.0001$). Among patients with moderate or severe PAH, independent predictors of reduction of systolic pulmonary artery pressures to a normal level were lower baseline PASP (OR, 0.91 per mm Hg; $P < 0.0418$) and mild tricuspid regurgitation (OR, 0.14 ; $P < 0.0420$).

Huang et al. (39) examined the short and intermediate-term outcomes of 15 ASD patients with severe pulmonary arterial hypertension (PAH) who had transcatheter closure between 2007 and 2010. Clinical, echocardiographic, and hemodynamic data were analyzed. “15 patients with pulmonary arterial systolic pressure measured by catheterization ≥ 60 mmHg and pulmonary vascular resistance (PVR) ≥ 6 and <15 Wood Units (WU) underwent vasoreactivity test with inhaled iloprost for 15 min and deemed operable underwent a trial occlusion of the defect with ASD device for one hour and met criteria of fall in mPAP by 20%, then the device was released.” The 6-min walk distance improved by 29.7 ± 26.3 m ($P < 0.001$) at three months (short-term) and

65.4 ± 63.6 m (P 0.001) at 23.4 ± 9.7 months (intermediate-term) as compared to baseline. The function class improved dramatically following the short-and medium-term closure of the ASD device. On follow-up of 12 months, repeat cardiac catheterization (n=7) revealed that mean pulmonary artery pressure (mPAP) decreased from 51.6±9.4 mmHg at baseline to 21.0±3.8 mmHg (P0.001). The PVR was reduced by 5.6±1.1 WU (P0.001), indicating that transcatheter closure can be safely performed in selected OS ASD patients with severe PAH, with a promising short-and medium-term result. Trial occlusion of the defect is a useful way to determine whether severe PAH in ASD patients is reversible or not.

A study by **Lauren et al.** (36) was done to look at the impact of pulmonary hypertension on survival following device closure of atrial septal defects. The study looked at 228 adults (mean age 49.1±16.2) who had transcatheter ASD closure. Pulmonary hypertension (PH) was seen in 48 patients (21.1 percent). At the time of intervention, 113 of the 228 patients in this cohort were younger than the cohort's median age (48 years), while 115 were older. PH was more likely to be present in patients above the age of 48 years (31.3 percent versus 10.6 percent, p0.01). Older patients had similar sized ASDs (18.3±6.9 vs. 19.1±6.3 mm, p=0.35) but many medical comorbidities such as diabetes (10.4 percentage vs. 2.7 percent, p=0.02), hyperlipidemia (49.6 percent vs 12.4%, p0.01), and systemic hypertension (55.7 percent vs. 15.0 percent, p0.01). PH had no effect on survival in individuals under the age of 48 years, while it was linked with a five times greater risk of mortality in patients above the age of 48 years (p0.01). At 3-month follow-up, patients with preprocedural PH and RVSP 40 mm Hg remained to have an elevated risk of mortality (p0.01), although those with PH resolution had similar survival to those without PH at the time of closure. PH is frequent in individuals with unrepaired ASDs and was found to be unrelated to the size of the defect. PH in older persons, as well as its persistence following ASD closure, are substantial indicators of a poor clinical outcome.

“Treat-to-close approach for non-repairable ASD-PAH in the adult was described in a study by **Bradley et al.**” (20). Adults with unrepaired ASD-PAH who did not fulfill repair recommendations at initial presentation (1996–2017) were analyzed retrospectively at nine tertiary care centers in North America. 69 patients (women 51 (74 percent), age 40 ± 15 years, mean pulmonary artery pressure (mPAP) 51 ± 13 mmHg), pulmonary vascular resistance (PVR) 8.7 ± 4.9 Wood units, Qp: Qs 1.6 ± 0.4) were included. All patients had PAH targeted therapy, and 19 (28%) had late shunt repair (women 15(29%) vs. men 4(22%), $p = 0.6$). At the long-term follow-up (4.4 ± 2.9 years), the 6-minute walk test distance was considerably higher in the repair group (486 ± 89 m vs. 375 ± 139 m, $p = 0.05$). Echo demonstrated a considerable recovery in right ventricular (RV) function (severe RV dysfunction in repaired groups 8(40%) versus unrepaired groups 35(69%), $p = 0.05$). There were differences in survival between the repaired and unrepaired groups, but they were not statistically significant. (Repaired: 17(94%) vs. unrepaired: 32(81%), $p = 0.18$). If the post-therapy PVR is ≤ 6.5 Wood units in a properly selected patient with non-correctable ASD-PAH, effective shunt repair is feasible. Patients who underwent repair exhibited improved RV function after PAH targeted therapy.

In a study by **Dalvi et al.** (37), Six patients with large OS ASD associated with severe Pulmonary hypertension underwent successful fenestrated device closure. The basal Qp: Qs ratio was 2.8 ± 0.3 while the systolic PAP and the PVR index (PVRI) were 102.6 ± 11.5 mm Hg and 9.6 ± 1.6 Wu.m², respectively. Following a vasoreactivity test with 100% oxygen, the Qp: Qs rose to 3.5 ± 0.3 , the systolic PAP was 103.5 ± 7.6 mm Hg, and indeed the PVRI fell to 5.4 ± 1.1 Wu.m². The systolic PAP after balloon occlusion fell to 86.6 ± 8.8 mm Hg. On follow-up of 45.3 ± 13.3 months, their systolic PAP decreased significantly from 105.6 ± 12.6 mm Hg at baseline to 45 ± 7 mm Hg following device closure as measured by a 2D echo. All of the patients had right ventricle remodeling. In four patients who had a follow-up cardiac catheterization, the systolic PAP and PVRI were 55.7 ± 9.2 mm Hg and 3.2 ± 0.4 , respectively.

In a study by **Song J et al.**, (38) Follow up of patients after partial closure of atrial septal defects with pulmonary hypertension using **fenestrated device/ fenestrated patch closure**. The cardiac catheterization data and clinical parameters of 17 adult patients were analyzed before and after closure and at follow-up. At the time of closure, the median age was 29 years. The initial Qp/Qs ratio was 1.9 ± 0.6 . The median time elapsed between ASD closure and cardiac catheterization was 27 months. The CT (cardiothoracic) ratio also reduced from 0.55 ± 0.07 to 0.48 ± 0.06 ($p < 0.05$). The pulmonary vascular resistance index (PVRI) fell from 9.2 ± 3.6 Wood units $\cdot$ m² to 6.3 ± 3.8 Wood units $\cdot$ m². The pulmonary artery means pressure reduced from 50.0 ± 11.5 mm Hg to 32.5 ± 14.4 mm Hg ($p < 0.05$). At follow up 64.7 percent still had high pulmonary resistance more than 3.0 Wood units $\cdot$ m², and prior to the partial closures, these individuals exhibited significantly greater pulmonary resistance indices and mean pulmonary arterial pressures ($p < 0.05$). Predictors of post-closure PH were not detected. On follow-up echocardiography, one patient experienced spontaneous closure of fenestration.

Yan et al.(39) did a study to analyze **the combined use of pulmonary vasodilator therapy and fenestrated atrial septal occluder (F-ASO)** in 56 patients with OS ASD with severe PAH (7 men, 49 women; median age 50.5 years; mean ASD size 26.94.6 mm). After three months of pulmonary vasodilator therapy, percutaneous closure was done using F-ASO in patients with Qp/Qs > 1.5 . Pulmonary vasodilator therapy was continued post device closure. The hemodynamic characteristics were compared during baseline, pulmonary vasodilator therapy alone, and concomitant treatment with F-ASO. The systolic pulmonary arterial pressure (decline of 14.5 mm Hg; $p < 0.001$), pulmonary vascular resistance (decline of 3.9 Wood units; $p < 0.001$), and exercise capacity (rise in 6min walk distance by 72.0 m; $p < 0.001$) improved after pulmonary vasodilator therapy alone. Fenestrated atrial septal occluder (median size 34.0 mm) resulted in a further drop in systolic pulmonary artery pressure (6.0 mm Hg; $p < 0.001$). Follow-up (median length ten months) revealed a tremendous rise in exercise capacity (by 60.5 m; $p < 0.001$), as well as a 9.9

mm decrease in right ventricular size ($p < 0.001$). All fenestrations were patent with a minimal shunt (Qp/Qs median ratio of 1.1) and no complications. One year later, pulmonary artery pressure was normalized in 8 of 19 patients, and PAH recurred in 5 patients after discontinuation of pulmonary vasodilator therapy. A combination of F-ASO and pulmonary vasodilator therapy proved a safe and successful method in patients with ASD and severe PAH. When compared to pulmonary vasodilator therapy alone, the combination treatment improved exercise capacity even more, with better right ventricular remodeling.

In a study by **Wang et al.** (40), the **close and treat approach** was assessed. 51 ASD patients (10 males, 41 females, age 46 ± 18 years) with a mean pulmonary artery pressure (mPAP) ≥ 35 mm Hg and/or systolic PAP ≥ 60 mm Hg underwent closure with a fenestrated device. The mean Qp/Qs ratio, mean PAP, systolic PAP, and were, respectively, 2.6, 44.8 mm Hg, 73.14 mm Hg. Following the closure of the fenestrated device, 35 patients were given pulmonary vasodilator treatment. The New York Heart Association (NYHA) functional class improved follow-up duration of 3 to 6 months ($p < 0.001$) 19 patients underwent repeat catheterization at follow-up. The hemodynamic parameters between baseline and repeat catheterization were compared showed a significant decrease in both mean PAP and systolic PAP (48 ± 7 vs 37 ± 8 mm Hg, $p = 0.001$ & 77 ± 11 vs 55 ± 14 mm Hg, $p < 0.0001$ respectively). PVRI and PVR also decreased (7.7 ± 3.3 vs 6.2 ± 2.4 WU $\cdot$ m², $p = 0.024$) and (5.1 ± 2.3 vs 4.0 ± 1.7 WU, $p = 0.011$), respectively. On long term follow-up of 84 ± 45 months, 6 patients died; 2 were due to cardiac causes. This study concluded that fenestrated device closure of ASD in patients with PAH followed by vasodilator therapy (close and treat approach) can be done without any safety issues.

As per 2018, ACC/AHA guidelines,(14) recommendations on the management of OS ASD in adults is as follows.

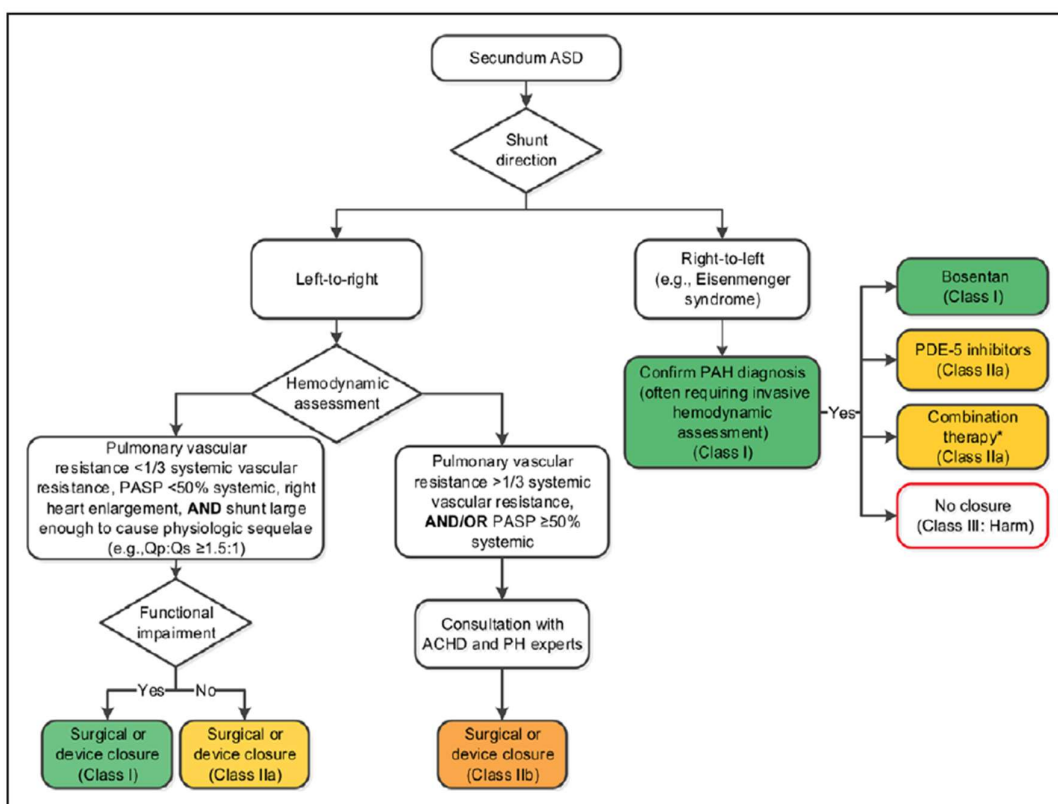


Figure:1 Management guidelines(14) of OS ASD in adults as per ACC/AHA

“As per 2020 ESC guidelines for the management of adult congenital heart diseases)(41), cardiac catheterization and calculation of PVR are mandatory. In patients with $PVR < 5WU$, ASD closure is safe and associated with a reduction in Pulmonary artery pressures and improvement of symptoms. However, even if $PVR < 5WU$, the extent of improvement reduces with increasing pulmonary artery pressures”. Patients with $PVR > 5WU$ are likely to have a worse outcome with complete ASD closure, and in this group, however, in order to decide whether to close or not, vasoreactivity testing is not recommended. It is safer to treat patients with $PVR > 5WU$ using pulmonary vasodilators, re-evaluate PVR and PAP during follow-up and consider fenestrated closure only when PVR falls below $5WU$ and $Qp/Qs > 1.5:1$; if not, ASD closure should not be done.

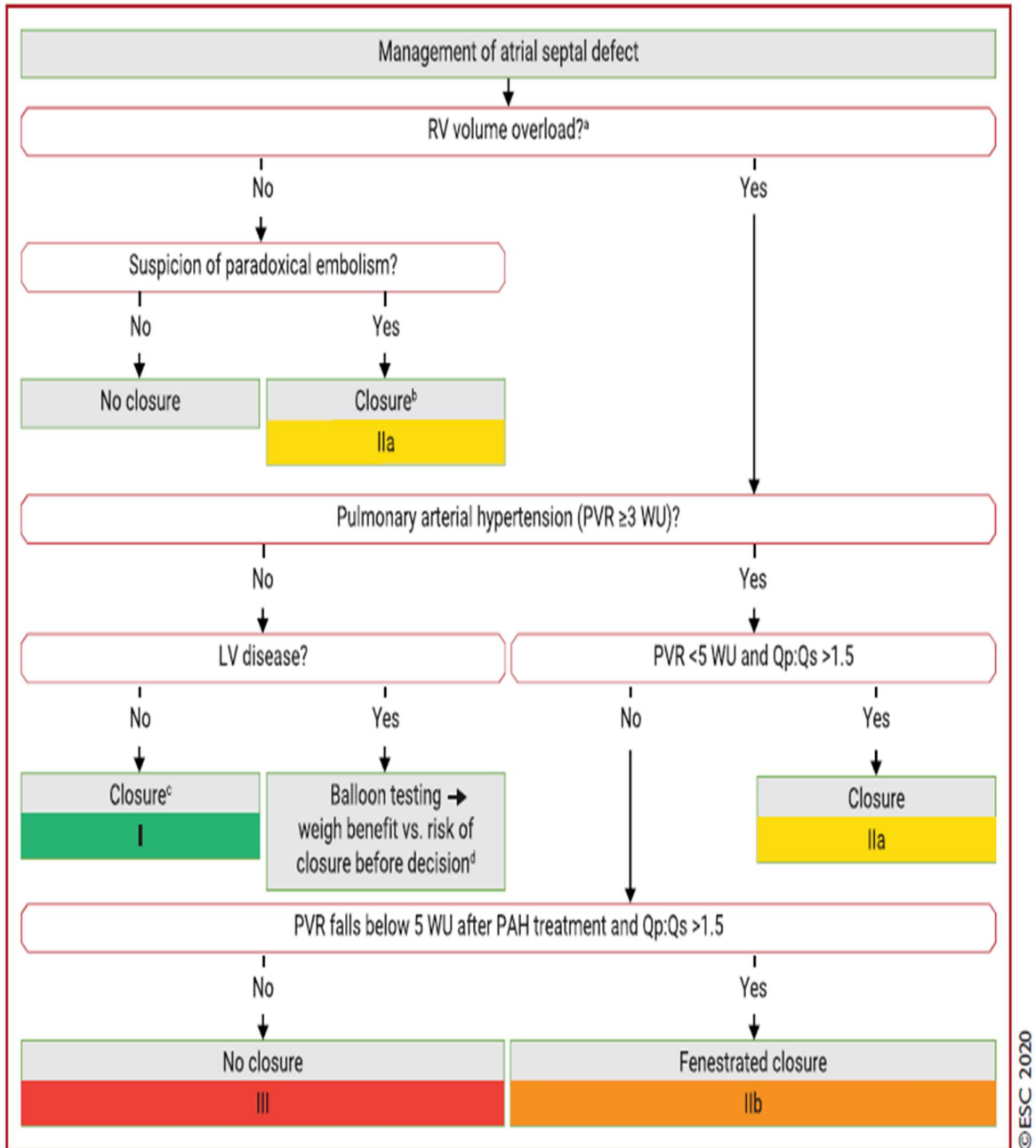


Figure 2: Management of ASD (atrial septal defect) as per 2020 ESC guidelines(41)

“As per the 2019 updated consensus statement on the diagnosis and treatment of pediatric pulmonary hypertension by **The European Paediatric Pulmonary Vascular Disease Network (EPPVDN)**” (42) recommendations are:

Recommendations on the Management of PH in Children and Young Adults with CHD	COR	LOR
• Children with $PVRi < 6 \text{ WU} \cdot \text{m}^2$ and a PVR/SVR ratio < 0.3 , in the absence of additional risk factors, are eligible for standard management/surgical shunt closure/percutaneous interventional device closure	I	C
• Children with $PVRi \geq 6 \text{ WU} \cdot \text{m}^2$ and a PVR/SVR ratio ≥ 0.3 should be evaluated by AVT	I	C
• Individual patient assessment in tertiary pediatric PH centers is particularly needed when $PVRi$ is between 6 and $8 \text{ WU} \cdot \text{m}^2$ (gray zone)	I	C
• A treat-to-close (treat-and-repair) approach (defined as PAH-targeted pharmacotherapy with 1–2 medications followed by partial or complete defect closure) might be considered in highly selected patients with pre- or post-tricuspid shunt (ASD, VSD, PDA) from the gray zone ($PVRi$ 6–8 $\text{WU} \cdot \text{m}^2$), and potentially even in children with PAH with $PVRi > 8 \text{ WU} \cdot \text{m}^2$, with the goal to decrease $PVRi < 8 \text{ WU} \cdot \text{m}^2$. After (complete or partial) closure, such patients must stay under long-term tertiary follow-up and be reassessed by cardiac catheterization, in addition to non-invasive measures, to assess for PVR after shunt closure.	IIb	C
• A partial defect closure (fenestrated patch or device) may be considered in selected patients with PAH-CHD from the gray zone ($PVRi$ 6–8 $\text{WU} \cdot \text{m}^2$), with or without preceding treat-to-close (treat-and-repair) approach. The impact of PVR numbers alone for clinical decision making differs between patients at different ages (e.g., infants with VSD vs young adults with ASD) class IIb	IIb	C
• A cardiovascular shunt defect (ASD, VSD, PDA) generally must not be closed when $PVRi > 8 \text{ WU} \cdot \text{m}^2$ in children ($PVR > 4.6 \text{ WU}$ in adults).	III harm	C

Table 1: Recommendations on the management of PH in Children and Young Adults with CHD as per EPPVDN (42)

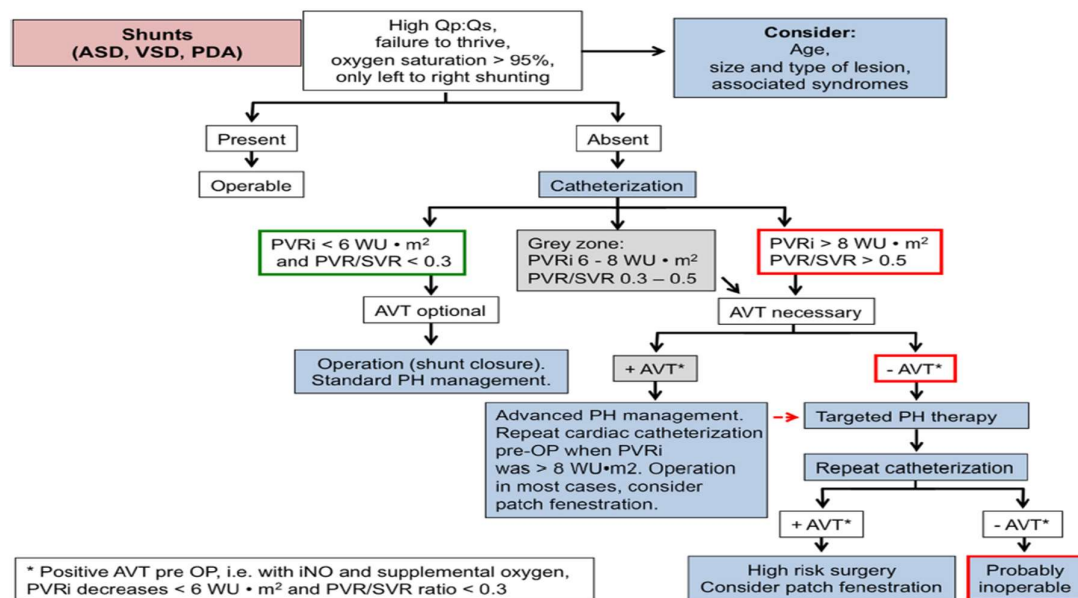


Figure 3: Flow chart for management of PH in Children and Young Adults with CHD as per EPPVDN (42)

AIMS, OBJECTIVES, and METHODOLOGY:

Design: A retrospective observational study.

Setting: A tertiary level single-center (Sree Chitra Tirunal Institute for Medical Sciences and Technology-SCTIMST).

AIM: To study the long-term outcome of percutaneous device closure of ostium secundum ASD in patients associated with moderate and severe pulmonary hypertension.

Hypothesis:

We hypothesize that the pulmonary artery pressures decrease after ASD device closure in patients with OS ASD associated with moderate and severe pulmonary hypertension.

OBJECTIVES

1. To assess the change in pulmonary artery pressures by echocardiography in OS ASD patients with moderate and severe pulmonary hypertension who underwent ASD device closure at early, intermediate, and long-term follow-up.
2. To look at the prevalence of arrhythmias at baseline and incidence of any new-onset arrhythmia, especially atrial fibrillation in these patients.
3. To assess the incidence of Major Adverse Cardiac and Cerebrovascular Events (MACCE) and mortality on long-term follow-up.
4. To assess the incidence of use of pulmonary vasodilators prior to device closure and the percentage of patients requiring pulmonary vasodilators on long-term follow-up.

Sample Size: All ASD patients with moderate and severe pulmonary hypertension underwent ASD device closure at SCTIMST from Jan 1998 to June 2020 and met inclusion and exclusion criteria.

INCLUSION CRITERIA:

All patients with ostium secundum ASD with mean PA pressure ≥ 30 mm Hg or PA systolic pressure ≥ 50 , as documented by right heart catheterization, and underwent ASD device closure at SCTIMST between Jan 1998 and June 2020.

EXCLUSION CRITERIA:

1. Patients with coexisting shunt lesions or significant left heart disease.
2. Patients not who don't meet the criteria of positive response on acute vasoreactivity test on cardiac catheterization. A positive response to AVT in PAH is defined as $>20\%$ fall in PVR to less than 6 Wood units and or PVR/SVR to <0.3 .²¹
3. Patients whose data is incomplete or unavailable.

DATA COLLECTION:

All ostium secundum ASD patients with moderate and severe pulmonary hypertension who underwent device closure, satisfying inclusion Criteria/ exclusion criteria, were included in the study. A consent form, written either in English or in the Malayalam language, was signed by the parent and a witness. Data were collected by the principal investigator. Clinical and echocardiographic data at baseline evaluation, catheterization data, and procedure details of device closure were obtained by retrospective review of electronic medical records (EMR).

Patient's characteristics evaluated include age at the time of device closure, symptom status and size of the ASD, any additional ASD, the presence of contributory risk factors for PH. Cardiac catheterization details like Qp, Qs, Qp/Qs ratio, PVR, SVR, and PVR/SVR ratio at baseline and after acute vasoreactivity test were collected. The values were indexed to body surface area for children with body surface area <1 to obtain PVRI, SVRI. Procedural characteristics like size of the atrial septal defect, Device size used, whether fenestration of device is done or not were noted. Patients were categorized into moderate pulmonary hypertension group if mean PA pressure is between 30 - 40 mm Hg or PA systolic pressure is between 50 – 60 mm Hg and severe pulmonary

hypertension group if mean PA pressure is ≥ 40 mm Hg or PA systolic pressure is ≥ 60 mm Hg, as measured by Right heart catheterization.

Information about arrhythmias and the use of pulmonary vasodilators to treat pulmonary hypertension before or after device closure was collected at baseline and at follow-up. The symptomatic status, NYHA functional class, echo parameters like right ventricular dimension, right ventricular dimension, PASP, the severity of MR and TR were collected. Additional details like patient's rhythm, use of pulmonary vasodilators, at early, intermediate and long term follow up. 2D echocardiography was done on their follow-up. The data on left and right ventricular systolic function, right ventricular size, and the degree of tricuspid regurgitation, right ventricular systolic pressure, PA mean pressure assessed by transthoracic echocardiography were documented. RVSP is derived from right ventricular systolic pressure estimates using tricuspid regurgitation jet velocity (v) and the Bernoulli equation as $4v^2$, mean pulmonary artery pressure derived from peak pressure of pulmonary regurgitation (PR) signal is obtained in the parasternal short-axis view^{22,23}.

The outcome variables on long-term follow-up are the change in pulmonary artery systolic pressure with respect to age at the time of device closure, baseline pulmonary artery pressure, baseline PVR and size of the defect, use of pulmonary vasodilator drugs. The percentage of patients with normalisation of pulmonary artery systolic pressure at long-term follow-up, the factors predicting the normalisation of pulmonary artery systolic pressure at long-term follow up are analysed. The percentage of patients with presence or persistence pulmonary hypertension (PASP ≥ 40 mm Hg) and presence or persistence severe pulmonary hypertension (PASP ≥ 60 mm Hg) at long-term follow-up, the factors predicting them are assessed.

Other outcome variables on long-term follow up were NYHA functional class; the prevalence of arrhythmias at baseline and incidence of any new-onset arrhythmia especially atrial fibrillation; the incidence of Major Adverse Cardiac and Cerebrovascular Events (MACCE) and

mortality; the incidence of use of pulmonary vasodilators prior to device closure; and percentage of patients taking pulmonary vasodilators after device closure; incidence of device migration, device erosion, infective endocarditis.

STATISTICAL METHODS

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Non normally distributed quantitative variables were summarized by the median and interquartile range (IQR). Data was also represented using appropriate diagrams like bar diagrams, pie charts etc.

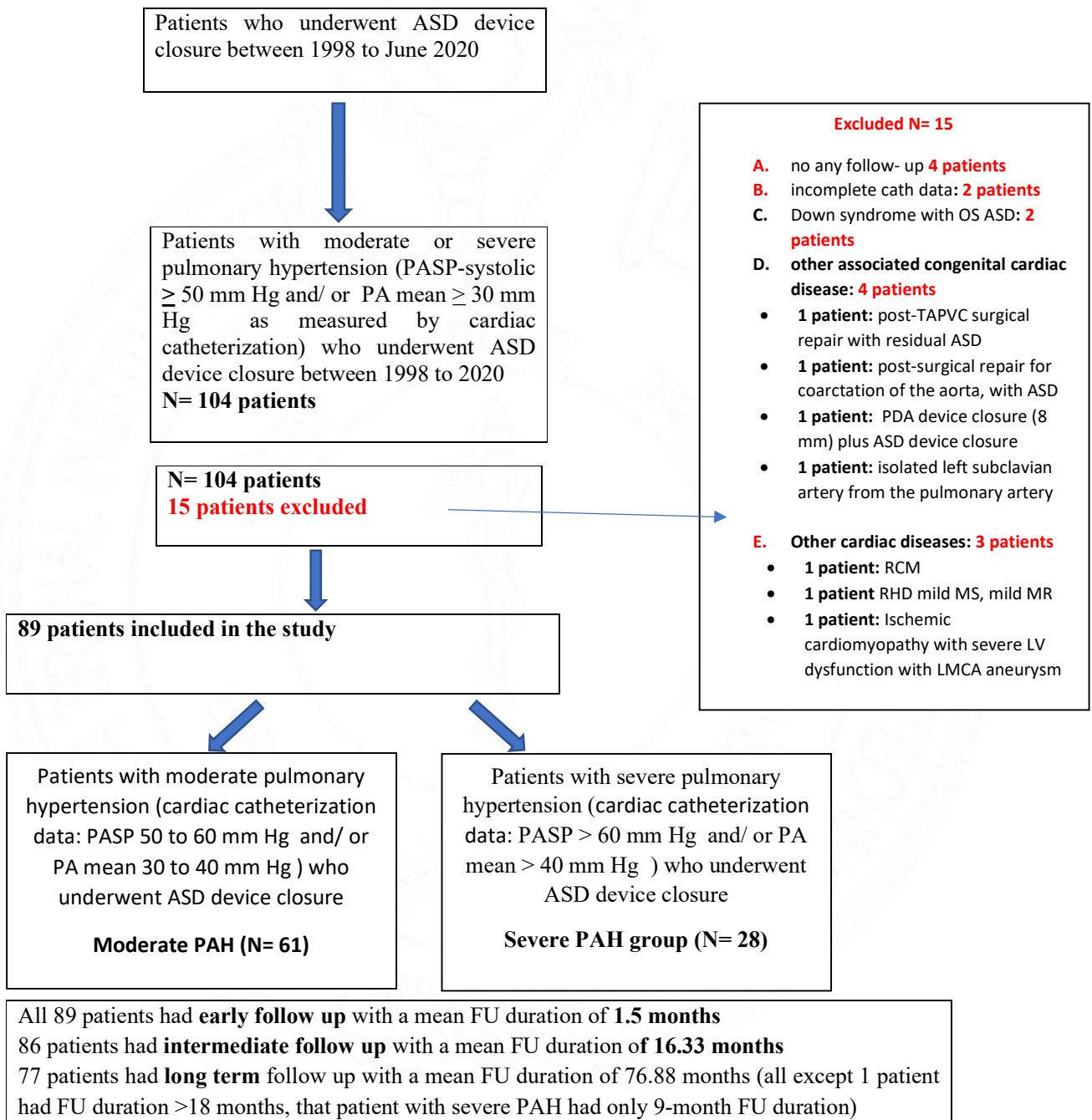
All Quantitative variables were checked for normal distribution within each category of the explanatory variable by using visual inspection of histograms and normality Q-Q plots. For normally distributed Quantitative parameters, the mean values were compared between study groups using an independent sample t-test (2 groups). Categorical outcomes were compared between study groups using the Chi-square test. Association between quantitative explanatory and outcome variables was assessed by calculating the Spearman correlation coefficient.

Univariate binary logistic regression analysis was performed to test the association between the explanatory variables and outcome variables. An unadjusted Odds ratio along with 95% CI is presented. Variables with statistical significance in univariate analysis were used to compute multivariate regression analysis. Adjusted odds ratio along with their 95% CI is presented.

Receiver operating characteristic curve, *or* ROC curve analysis was done to estimate the predictive validity of cardiac catheterisation data in predicting the persistence /presence of pulmonary artery hypertension at long-term follow-up and severe pulmonary artery hypertension. The cut-off value was estimated by **The Youden index (J)** from the ROC curve.

The sensitivity, specificity, predictive values, and diagnostic accuracy of the screening test with the decided cut-off values along with their 95% CI were presented. P-value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.

Figure 4: Consort diagram



RESULTS:

A total of 89 subjects were included in the study for final analysis. Clinical, 2D echo, and cardiac catheterization parameters at baseline, ASD device closure procedural details are compiled in Table 1. Based on cardiac catheterisation, 89 patients are categorized into two groups: **group 1 moderate PAH-** (cardiac catheterization data: - PASP 50-60 and/ or PA mean pressure :30-40) (N=61, 68.5%) and **group 2 severe PAH** (cardiac catheterization data: - PASP >60 and/ or PA mean pressure >40 (N= 28, 31.5%)

Descriptive analysis of baseline parameters in the study population (N=89) and comparison between Moderate PAH and ASD Severe PAH groups

Table 1: Demographic parameters of the study population

Baseline parameters	PH			P-Value
	Total population (N=89)	Group 1 Moderate PAH (N=61)	Group 2 Severe PAH (N=28)	
Age (mean) years	45.52 (range 3, 71) 95% C.I (42.41, 48.63)	44.66 ± 15.83	47.39 ± 12.15	0.375
Age group				
<11 years	5 (5.6%)	5 (8.2%)	0 (0.00%)	*
11-24 years	4 (4.4%)	2 (3.3%)	2 (7.1%)	
25- 39 years	13(14.6%)	9 (14.7%)	4 (14.3%)	
40 -60 years	55(61.7%)	37 (60.6%)	18 (64.3%)	
>60 years	12(13.4%)	8 (13.1%)	4 (14.3%)	
Gender				
Male	21(23.6%)	18 (29.5%)	3 (10.7%)	0.052
Female	68(76.4%)	43 (70.5%)	25 (9.3%)	

The mean age of the whole study population was 45.52 years (range 3, 71) with 95% Confidence interval (42.41, 48.63), whereas the mean ±standard deviation of group 1 was 44.66

± 15.83 years, group 2 was 47.39 ± 12.15 years. The mean age of the ASD Severe PAH group was slightly higher than ASD Moderate PAH group but not statistically significant ($P 0.375$).

Of 89 patients, 5 patients (5.6%) were less than 11 years (group 1 Moderate PAH- 5, group 2 severe PAH -0), 4 (4.4%) belonged to 11 to 24 years age (2 each in both PH groups), 13(14.6%) belonged to 25 to 39 years age (9 in group 1, 4 in group 2), 55(61.7%) were between 40 -60 years (37 in group 1, 18 in group 2), 12(13.4%) were more than 60 years (8 in group 1, 4 in group 2).

Figure 5: Stacked bar chart for comparison of age group with PH in the study population (N=89)

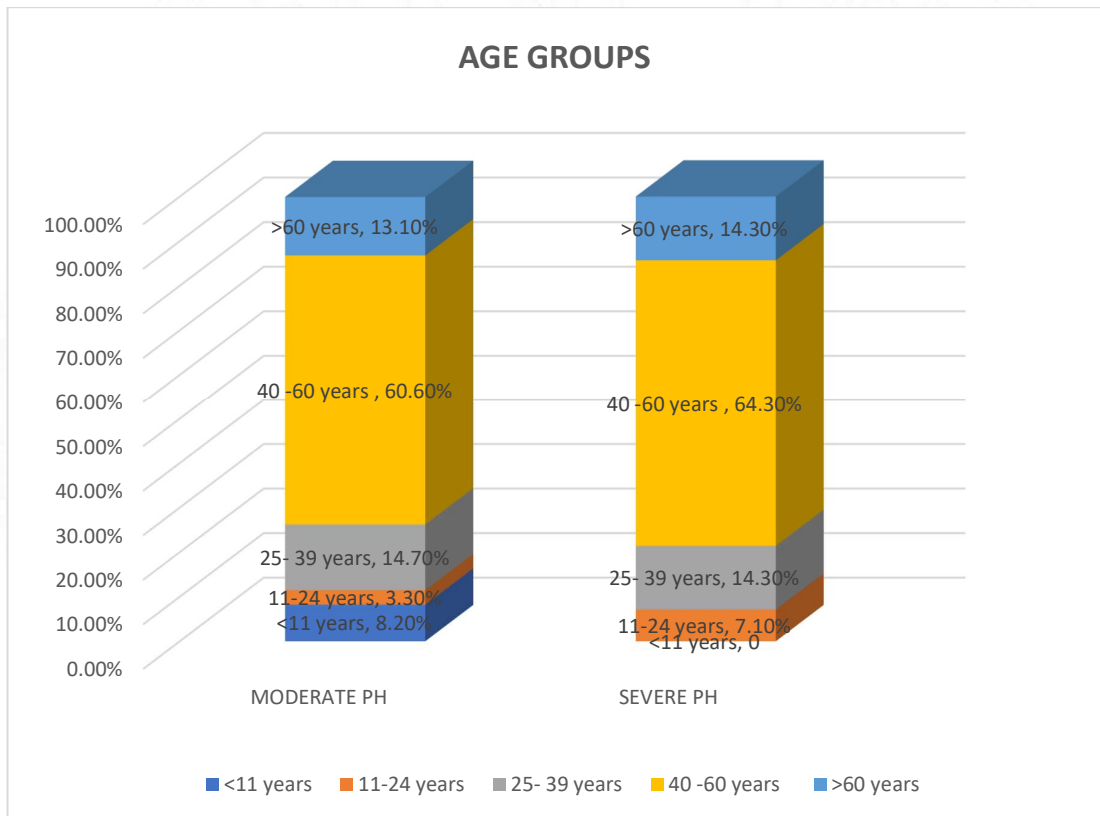
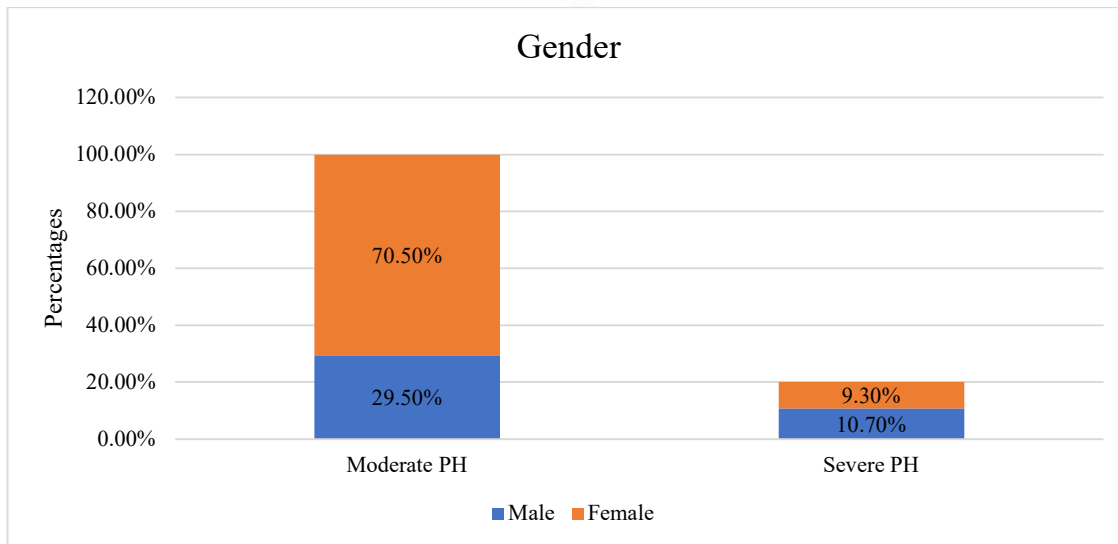


Figure 6: Stacked bar chart for comparison of Gender with PH in the study population (N=89)



There was female preponderance with a ratio of 2.4:1 in the study. Females were 68 out of 89 patients (76.4%) (group 1 – 43, group 2- 25).

Body mass index (BMI) & size of the OS ASD on transthoracic echo and transoesophageal echo

Table 2: BMI & size of the OS ASD on transthoracic echo and transoesophageal echo

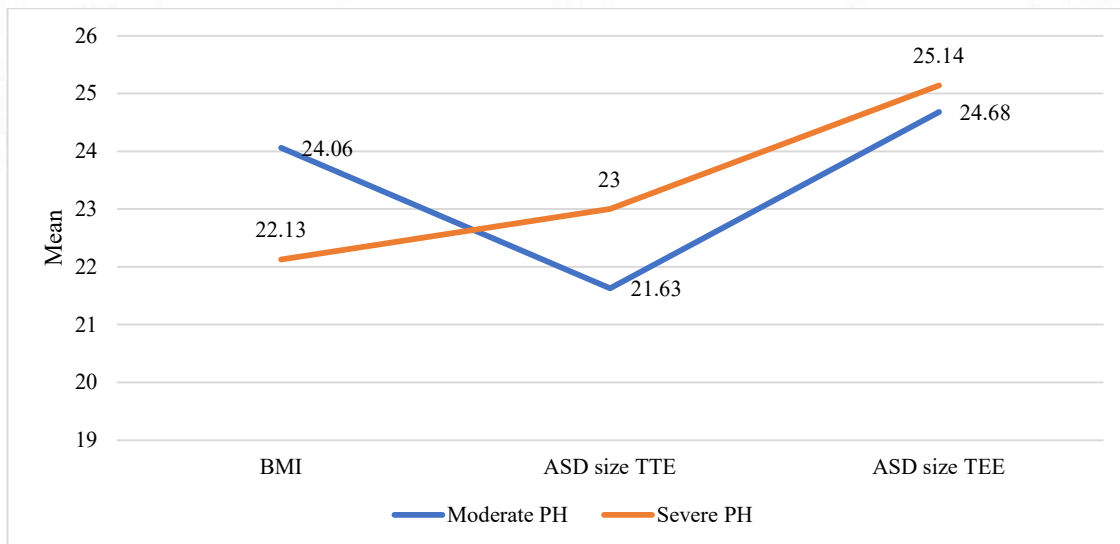
Baseline parameters	PH			P-Value
	Total population (N=89)	Group 1 Moderate PAH (N=61)	Group 2 Severe PAH (N=28)	
BMI (kg/m²)	23.45 (12.76, 33.75) 95% C.I (22.44, 24.46)	24.06 ± 4.86	22.13 ± 4.43	0.070
ASD size TTE mm	22.07 (8, 36) 95% C.I (20.81, 23.33)	21.63 ± 5.97	23 ± 5.88	0.317
ASD size TEE mm	24.83 (9, 43) 95% C.I (23.49, 26.17)	24.68 ± 6.53	25.14 ± 5.96	0.745

The mean body mass index of the whole cohort was 23.45 kg/m² (range 12.76- 33.75) with 95% Confidence interval of (22.44, 24.46). The mean ($\pm$ SD) BMI of the moderate PAH group was 24.06 $\pm$ 4.86 kg/m², marginally higher than severe PAH group 22.13 $\pm$ 4.43 kg/m² but not statistically significant.

The mean ASD size measured by transthoracic echo (TTE) of the whole cohort was 22.07 mm (range 8- 36) with 95% Confidence interval of (20.81, 23.33). The mean ($\pm$ SD) of the defect in moderate PAH group was 21.63 $\pm$ 5.97 mm and severe PAH group was 23 $\pm$ 5.88 mm but not statistically significant.

The mean ASD size measured by transoesophageal echo (TEE) of the whole cohort was 24.83 mm (range 9- 43) with 95% Confidence interval of (23.49, 26.17). The mean ($\pm$ SD) of the defect in moderate PAH group was 24.68 $\pm$ 6.53 mm and severe PAH group was 25.14 $\pm$ 5.96 mm but not statistically significant.

Figure 7: Line chart for comparison of parameters with PH in the study population (N=89)

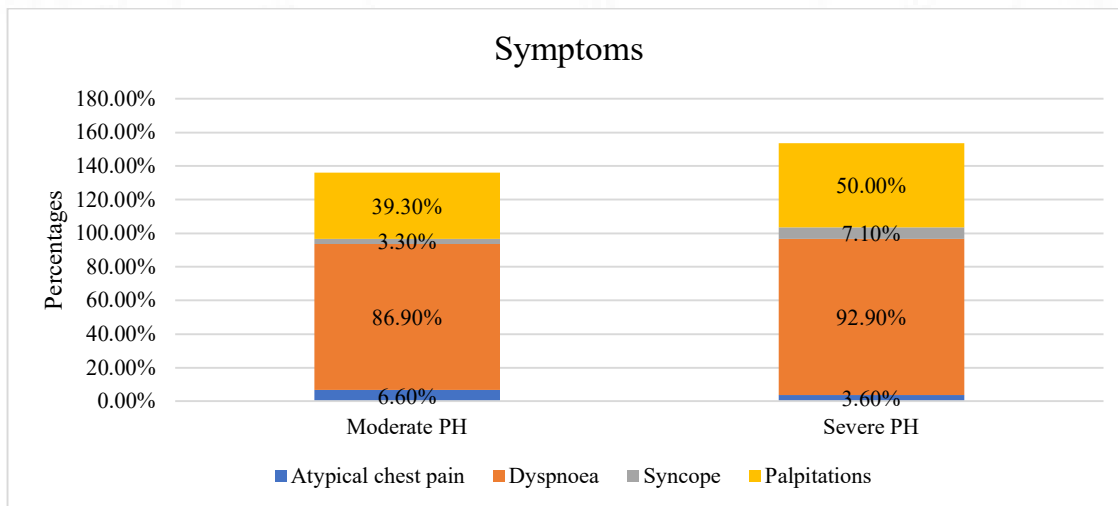


Symptoms & NYHA functional class at baseline in the study population

Table 3: Symptoms & NYHA functional class at baseline

Baseline parameters	PH			P-Value
	Total population (N=89)	Group 1 Moderate PAH (N=61)	Group 2 Severe PAH (N=28)	
Symptoms				
Non-anginal chest pain	5(5.6%)	4 (6.6%)	1 (3.6%)	0.570
Dyspnoea	79(88.8%)	53 (86.9%)	26 (92.9%)	0.407
Syncope	4(4.5%)	2 (3.3%)	2 (7.1%)	0.414
Palpitations	38(42.7%)	24 (39.3%)	14 (50%)	0.345
NYHA functional CLASS				
Class -1	9(10.1%)	8 (13.1%)	1 (3.6%)	0.355
Class -2	76(85.4%)	50 (82%)	26 (92.9%)	
Class -3	4(4.5%)	3 (4.9%)	1 (3.6%)	
Duration of symptoms (years)	2.48 (0, 15) 95% C.I (1.96, 2.99)	2.33 ± 2.09	2.80 ± 3.12	0.470

Figure 8: Stacked bar chart for comparison of Symptoms with PH in the study population (N=89)



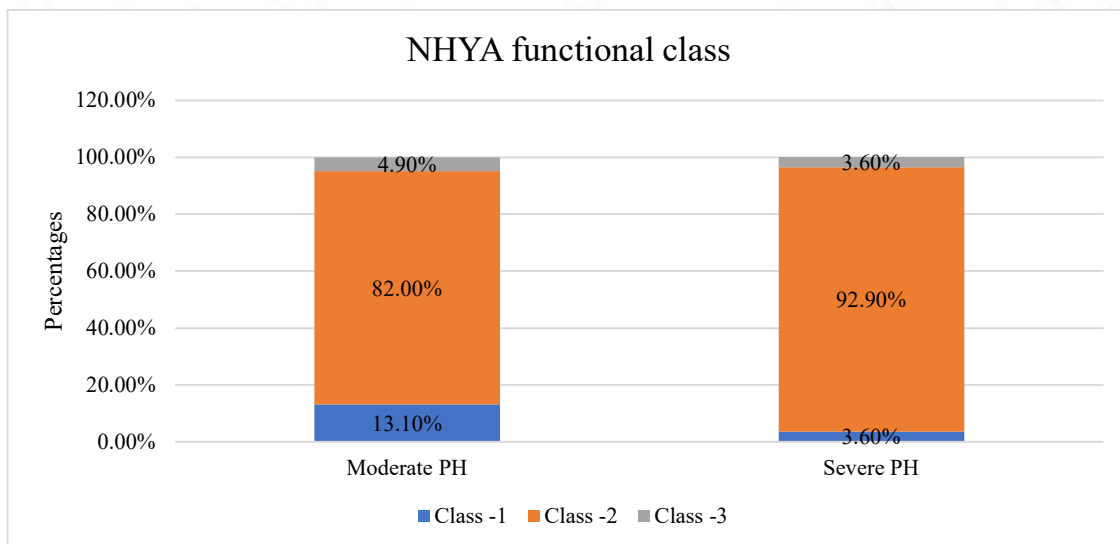
The mean duration of symptoms is 2.48 years (range 0- 15) 95% Confidence interval of (1.96, 2.99) among the whole study patients. In patients with moderate PAH (N=61) and severe PAH(N=28), the mean symptom duration ($\pm$ SD) is 2.33 ± 2.09 years & 2.80 ± 3.12 years, respectively

The predominant symptom was dyspnoea (n= 79, 88.8%), followed by palpitations seen in 42.7%. Out of 38 patients with palpitations, only 9 had atrial fibrillation. Exertional palpitations were seen in 29 patients. Non-anginal chest pain was seen in 5 patients (5.6%). Syncope was seen in 4 patients (4.5%).

Among patients with moderate PAH (N=61), dyspnoea was the predominant symptom seen in 53 (86.9%), followed by palpitations (24, 39.3%). Non-anginal chest pain was seen in 4 patients (6.6 %). Syncope was seen in 2 patients (3.3%).

In severe PAH(N=28), group also, dyspnoea was predominant symptom seen in 26 (92.9%), followed by palpitations 14 (50%). Syncope was seen in 2 patients (7.1%). Non-anginal chest pain was seen in 1 patient (3.6%).

Figure 9: Stacked bar chart for comparison of NYHA with PH in the study population (N=89)



In the whole study population, 10.1% of patients (9/89) were asymptomatic, and in NYHA class I, 88.8% (76/89) of patients had NYHA class II functional limitations. However, only 4.5% (4/89) patients had NYHA class III functional limitations, and no patients had NYHA class IV symptoms. 89.9% of patients (80/89) had NYHA functional class $\geq$ II.

In ASD Moderate PAH group, 13.1% of patients (8/61) were asymptomatic with NYHA class I, 86.9% (53/61) of patients had NYHA class II functional limitations. However, only 4.9% (3/61) patients had NYHA class III functional limitation and no patient had NYHA class IV symptoms. 86.9% of patients (53/61) had NYHA functional class $\geq$ II.

In ASD Severe PAH group, only one patient was asymptomatic; 92.9% (26/28) of patients had NYHA class II, one patient had NYHA class III functional limitation, and no patient had NYHA class IV symptoms. 98.5% of patients (27/28) had NYHA functional class $\geq$ II.

The percentage of patients with symptoms and NYHA functional class $\geq$ II increased, with an increase in severity of PAH; however, it was not statistically significant.

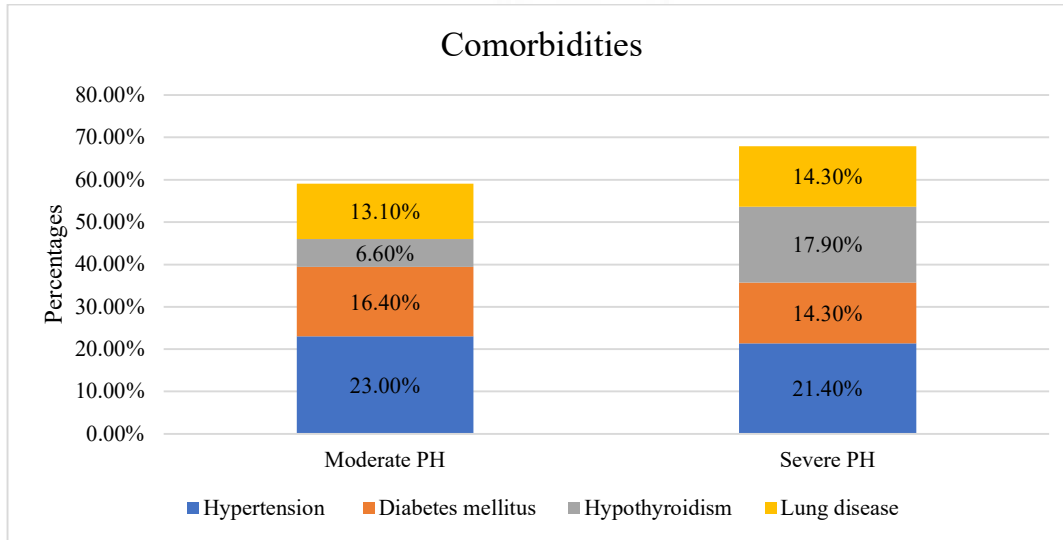
Comorbidities at baseline in the study population

Table 4: patient comorbidities at baseline

Baseline parameters	PH			P-Value
	Total population (N=89)	Group 1 Moderate PAH (N=61)	Group 2 Severe PAH (N=28)	
Hypertension	20(22.5%)	14 (23%)	6 (21.4%)	0.873
Diabetes mellitus	14(15.7%)	10 (16.4%)	4 (14.3%)	0.800
Hypothyroidism	9(10.1%)	4 (6.6%)	5 (17.9%)	0.101
Lung disease	12(13.5%)	8 (13.1%)	4 (14.3%)	0.881

At baseline, 20 patients (22.5%) had **Hypertension**, 14(15.7%) had **Diabetes mellitus**, 9(10.1%) had **Hypothyroidism**, 12(13.5%) had lung disease (asthma/ COPD). There was no significant difference in comorbidities between moderate PAH and severe PAH groups.

Figure 10: Stacked bar chart for comparison of Comorbidities with PH in the study population (N=89)



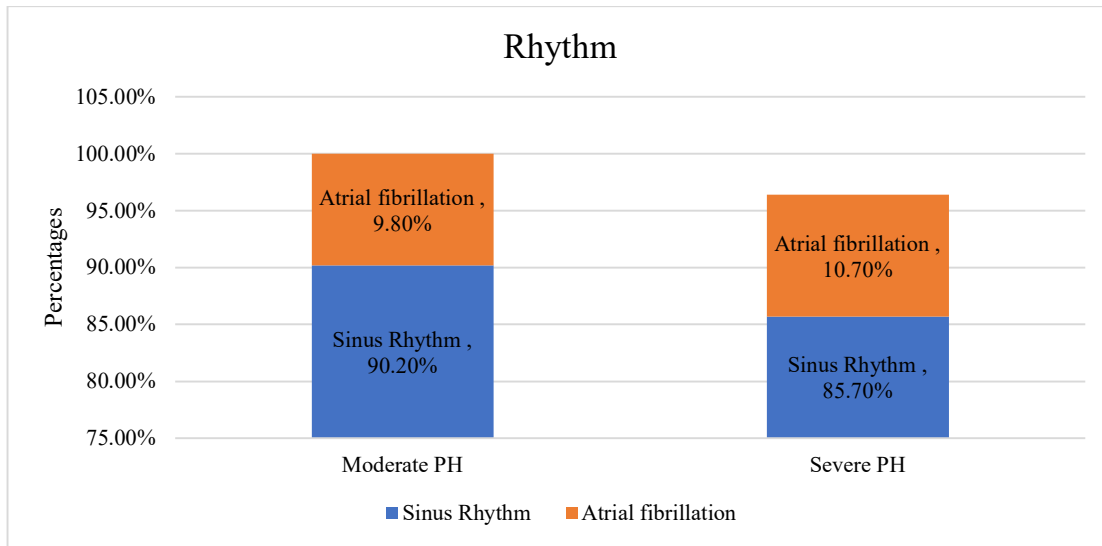
Electrocardiographic parameters and prevalence of atrial fibrillation in the study patients

Table 5: ECG parameters and prevalence of atrial fibrillation in the study patients

Baseline parameters	PH			P-Value
	Total population (N=89)	Group 1 Moderate PAH (N=61)	Group 2 Severe PAH (N=28)	
Rhythm				
Sinus Rhythm	79(88.8%)	55 (90.2%)	24 (85.7%)	0.327
Atrial fibrillation	9 (10.2 %)	6 (9.8%)	3 (10.7%)	
Incomplete RBBB	83(93.3%)	57 (93.5%)	26 (92.9%)	0.921
QRS Axis (median)	90 (30, 150) 95% C.I (84.07, 94.36)	90 (105, 65)	100 (90, 110)	0.008

In the whole study population, 9 (10.2 %) of patients had atrial fibrillation at baseline. 88.8% of patients (79/89) had sinus rhythm. 1 patient had a junctional rhythm. **Incomplete RBBB** was seen in 93.3% (83/89) patients. The median QRS axis was 90 degrees (range 30, 150) 95% confidence interval (84.07, 94.36).

Figure 11: Stacked bar chart for comparison of Rhythm with PH in the study population (N=89)



In ASD Moderate PAH group, 9.8% of patients (6/61) had atrial fibrillation at baseline. 90.2 % of patients (5/61) had sinus rhythm. **Incomplete RBBB** was seen in 93.5% (57/61) patients. The mean QRS axis was 90 degrees.

In ASD Severe PAH group, 10.7% of patients (3/28) had atrial fibrillation at baseline. 85.7 % of patients (24/24) had sinus rhythm. **Incomplete RBBB** was seen in 92.9% (26/28) patients. The mean QRS axis was 100 degrees.

The 2D echocardiographic parameters in the total study population at baseline were analyzed. RV dilatation on echo was seen in 98.8% (88/89) of patients. The mean RVIDD was 35.02 mm (range 18, 55) with 95% Confidence interval of (33.69, 36.35 mm). The average Pulmonary artery pressure (PASP) was 62.49 mm Hg (range 40, 110) with 95% Confidence interval of (59.10, 65.89). All patients had normal left ventricular ejection fraction. 2 patients with Severe PAH had RV dysfunction at baseline prior to device closure.

2D Echocardiographic parameters at baseline in the study population

Table 6: Baseline 2D Echocardiographic parameters

Baseline parameters	PH			P-Value
	Total population (N=89)	Group 1 Moderate PAH (N=61)	Group 2 Severe PAH (N=28)	
Echo				
ASD size TTE mm	22.07 (8, 36) 95% C. I (20.81, 23.33)	21.63 ± 5.97	23 ± 5.88	0.317
RV dilatation	88(98.8%)	60 (98.3%)	28 (100%)	*
RVID mean mm	35.02 (18, 55) 95% C.I (33.69, 36.35)	33.72 ± 5.94	37.82 ± 6.15	0.005
PASP mean (TTE) mm Hg	62.49 (40, 110) 95% C.I (59.10, 65.89)	55.05 ± 10.02	78.71 ± 15.04	
RV dysfunction	2 (2.2%)	0 (0.00%)	2 (7.1%)	*
TR severity				
Mild	56(62.9%)	52 (85.2%)	4 (14.3%)	<0.001
Moderate	33(37.1%)	9 (14.8%)	24 (85.7%)	
MR severity				
No MR	41(46.1%)	29 (47.5%)	12 (42.9%)	*
Mild	47(52.8%)	31 (50.8%)	16 (57.1%)	
Moderate	1(1.1%)	1 (1.6%)	0 (0.00%)	
LV EF	67.16 (55, 86) 95% C.I (65.78, 68.54)	66.84 ± 6.13	67.86 ± 7.47	0.531

In ASD Moderate PAH group, RV dilatation on echo was seen in 98.3% (60/61) of patients. The mean ± SD of RVIDD was 33.72 ± 5.94 mm. The mean ± SD of Pulmonary artery pressure (PASP) estimated by echo was 55.05 ± 10.02 mm Hg.

In ASD Severe PAH group, all patients had dilated RV on echo. The mean ± SD of RVIDD was 37.82 ± 6.15mm, which was higher than ASD Moderate PAH group with statistically significant difference (P 0.005). The mean ± SD of Pulmonary artery pressure (PASP) estimated

by echo was 78.71 ± 15.04 mm Hg, which was higher than ASD Moderate PAH group with statistically significant difference ($P < 0.001$).

Figure 12: Line chart for comparison of parameters with PH in the study population (N=89)

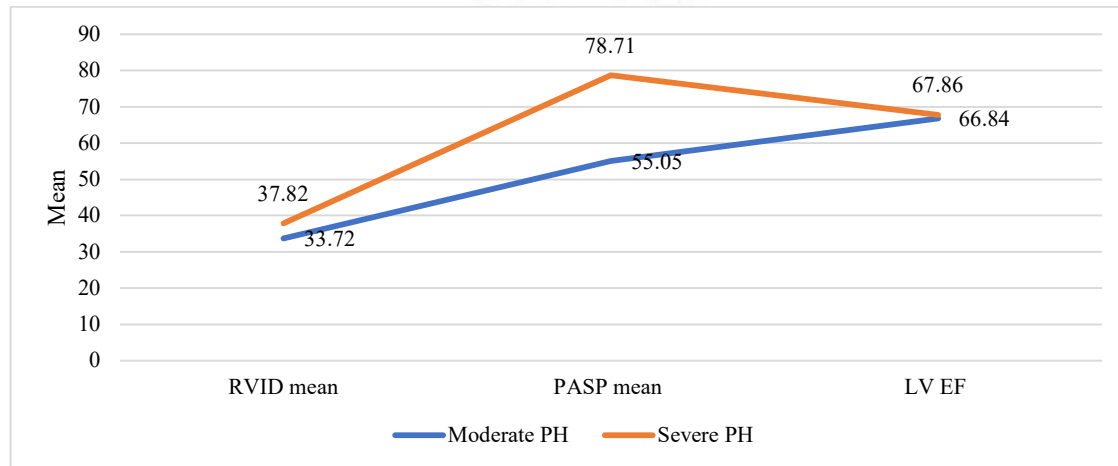
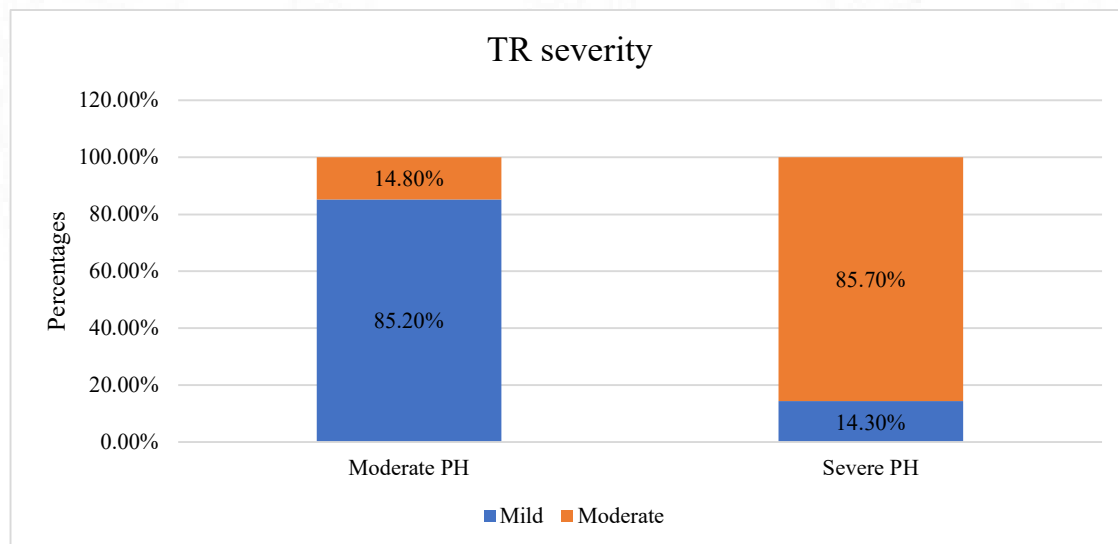


Figure 13: Stacked bar chart for comparison of TR severity with PH in the study population (N=89)



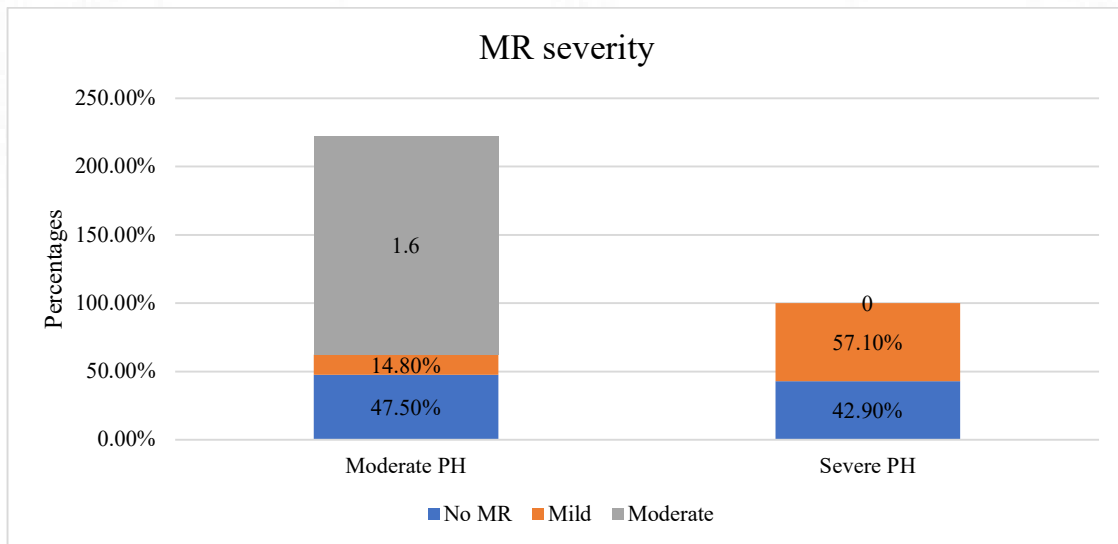
Among the whole study population, 62.9% (56/89) had mild tricuspid regurgitation. 37.1% (31/89) had moderate tricuspid regurgitation. No patients had severe tricuspid regurgitation. 46.1% (41/89) patients did not have any mitral regurgitation. 52.8% (47/89) of patients had mild

mitral regurgitation. One patient (1.1%) had moderate mitral regurgitation. No patient had severe MR.

In ASD Moderate PAH group, 85.2% (52/61) had mild tricuspid regurgitation. 14.8 % (9/61) had moderate tricuspid regurgitation. No patients had severe tricuspid regurgitation. 47.5% (29/61) patients did not have any mitral regurgitation. 50.8% (31/61) of patients had mild mitral regurgitation. One patient (1.6%) had moderate mitral regurgitation.

In ASD Severe PAH group 14.3%,) (4/28) had mild tricuspid regurgitation. 85.7 % (24/28) had moderate tricuspid regurgitation. No patients had severe tricuspid regurgitation. 42.9% (12/24) patients did not have any mitral regurgitation. 57.1% (16/28) of patients had mild mitral regurgitation. No patients in the severe PAH group had more than moderate or severe MR. the prevalence of Moderate tricuspid regurgitation was higher in ASD Severe PAH group compared to ASD Moderate PAH group and statistically significant ($P<0.001$)

Figure 14: Stacked bar chart for comparison of MR severity with PH in the study population (N=89)



Baseline cardiac catheterization data

The median aortic saturation as measured by catheterization study (SpO_2) for the whole cohort was 97% (range 89, 100) 95% Confidence interval of (95.76, 96.97). In ASD Moderate

PAH group, the median aortic saturation was 97% which was higher than that of the ASD Severe PAH group 95%. This difference was statistically significant. ($P < 0.001$)

All the patients underwent baseline cardiac catheterization study prior to ASD device closure. In the total study population, the mean of PASP (pulmonary artery systolic pressure) was 58.56 mm Hg, 95% C. I (55.23, 61.90), the mean of PA diastolic pressure was 23.17 mm Hg, 95% C. I (21.95, 24.38), average PA mean pressure was 36.04 mm Hg, 95% C. I (34.51, 37.58), the average value for the ratio of pulmonary systolic pressure and systolic aortic pressure was 0.45, 95% C.I (0.42, 0.47). The average value for pulmonary blood flow and systemic blood flow (Qp/Qs) ratio is 2.16, 95% C.I (1.98, 2.34). The mean PVR (pulmonary vascular resistance) was 3.51 WU (wood units) (range 0.7- 16.78) 95% C.I (2.98, 4.04). The mean value of pulmonary resistance to systemic resistance ratio of was 0.16, 95% C.I (0.14, 0.19).

Table 7: Baseline cardiac catheterization data

Baseline parameters	PH			P-Value
	Total population (N=89)	Group 1 Moderate PAH (N=61)	Group 2 Severe PAH (N=28)	
Cath data (Baseline) (N= 89, 100%)				
Aorta saturation by blood gas analysis (median)	97 (89, 100) 95% C.I (95.76, 96.97)	97 (95, 99)	95 (96, 92.25)	<0.001
PA systolic mm Hg	58.56, 95% C.I (55.23, 61.90)	50.08 ± 6.83	77.04 ± 14.01	<0.001
PA diastolic mm Hg	23.17, 95% C.I (21.95, 24.38)	21.26 ± 3.76	27.32 ± 7.15	<0.001
PA mean mm Hg	36.04, 95% C.I (34.51, 37.58)	32.33 ± 3.03	44.14 ± 7.29	<0.001
AO systolic mm Hg	132.99, 95% C.I (128.23, 137.74)	129.02 ± 21.34	141.64 ± 23.13	0.018
PASP/AO systolic	0.45, 95% C.I (0.42, 0.47)	0.40 ± 0.08	0.56 ± 0.13	<0.001
QP/QS	2.16, 95% C.I (1.98, 2.34)	2.26 ± 0.85	1.94 ± 0.83	0.107
PVR (WU)	3.51 (0.7, 16.78) 95% C.I (2.98, 4.04)	2.50 ± 0.98	5.73 ± 3.33	<0.001
SVR (WU)	21.59, 95% C.I (20.09, 23.08)	20.20 ± 6.40	24.62 ± 7.65	0.011
R RATIO	0.16, 95% C.I (0.14, 0.19)	0.13 ± 0.05	0.25 ± 0.15	<0.001

The mean $\pm$ SD of PASP (pulmonary artery systolic pressure) in the ASD Moderate PAH group was $(50.08 \pm 6.83 \text{ mm Hg})$ lower compared to that of the ASD Severe PAH group, and it was statistically significant ($P < 0.001$).

The mean $\pm$ SD of PA diastolic pressure was $21.26 \pm 3.76 \text{ mm Hg}$ in ASD Moderate PAH group and $27.32 \pm 7.15 \text{ mm Hg}$ in ASD Severe PAH group and had a statistically significant difference ($P < 0.001$).

The mean $\pm$ SD of PA mean pressure was $32.33 \pm 3.03 \text{ mm Hg}$ in ASD Moderate PAH group and $44.14 \pm 7.29 \text{ mm Hg}$ in ASD Severe PAH group and had statistically significant difference ($P < 0.001$).

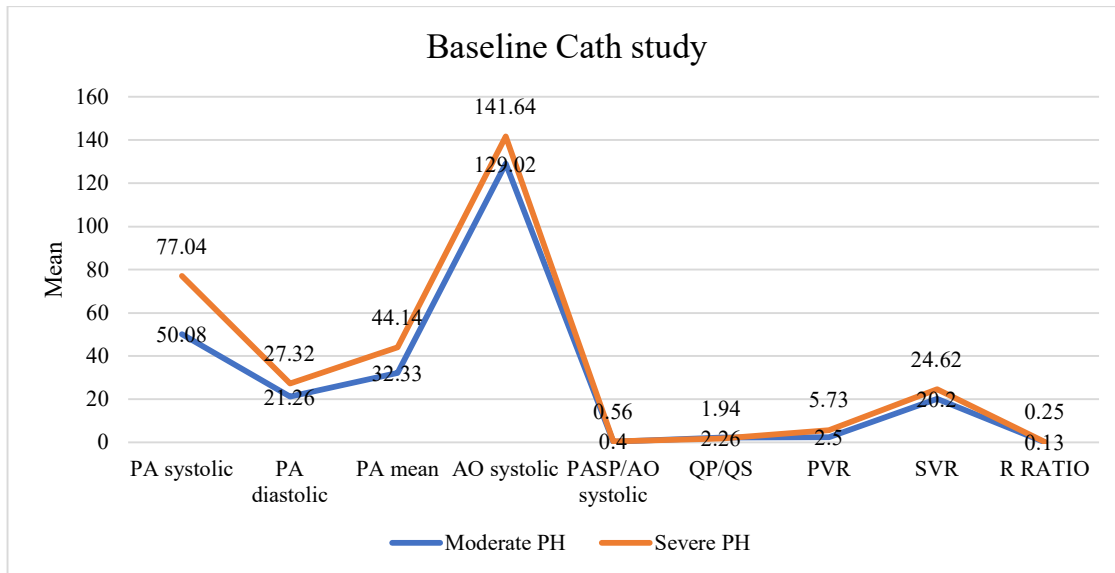
The mean $\pm$ SD of the ratio of pulmonary systolic pressure and systolic aortic pressure was 0.40 ± 0.08 in ASD Moderate PAH group and 0.56 ± 0.13 in ASD Severe PAH group and had a statistically significant difference ($P < 0.001$).

The mean $\pm$ SD of the ratio of pulmonary blood flow and systemic blood flow (Q_p/Q_s) was higher (2.26 ± 0.85) in ASD Moderate PAH group compared to that (1.94 ± 0.83) in ASD Severe PAH group and had a statistically significant difference ($P < 0.001$).

The mean $\pm$ SD of PVR (pulmonary vascular resistance) was lower ($2.50 \pm 0.98 \text{ WU}$) in ASD Moderate PAH group compared to that ($5.73 \pm 3.33 \text{ WU}$) in ASD Severe PAH group and had a statistically significant difference ($P < 0.001$).

The mean $\pm$ SD of PVR/SVR ratio (ratio of pulmonary resistance to systemic resistance) was lower (0.13 ± 0.05) in ASD Moderate PAH group compared to that (0.25 ± 0.15) in ASD Severe PAH group and had a statistically significant difference ($P < 0.001$).

Figure 15: Line chart for comparison of Cath variables (baseline) with PH in the study population (N=89)



33.7% of patients (30/ 89) underwent pulmonary vasoreactivity testing with 100% oxygen inhalation for 15 min. Of the 16 patients had PVR >5 WU in baseline cardiac catheterization. The cardiac catheterization data pre and post pulmonary vasoreactivity testing was compared in patients with PVR > 5 WU.

Table 8: Comparison of cardiac catheterization data pre and post pulmonary vasoreactivity testing in patients with baseline PVR > 5 WU (N=16)

Parameters	Without Oxygen study (P)	With Oxygen study (P2)	P-value
PASP	82.56 ± 15.20	73.13 ± 14.52	<0.001
PADP	30.69 ± 6.25	26.81 ± 5.73	<0.001
PA MEAN	48.19 ± 6.56	42.88 ± 6.79	<0.001
AO SYSTOLIC	135.63 ± 20.86	132.44 ± 22.35	0.343
PASP/ Aorta Systolic pressure	0.62 ± 0.13	0.57 ± 0.15	0.003
PVR	7.73 ± 3.00	3.49 ± 2.04	<0.001
SVR	24.62 ± 5.33	24.19 ± 5.52	0.823
PVRI	11.12 ± 4.53	5.00 ± 3.03	<0.001
SVRI	34.99 ± 5.97	35.11 ± 10.23	0.966
R RATIO	0.33 ± 0.16	0.16 ± 0.08	<0.001

17.9% (16/89) patients had PVR value >5 WU at baseline cath study, all of them underwent pulmonary vasoreactivity testing. The Cath parameters pre and post-oxygen study were analyzed (Table 8). Post oxygen study, there was a significant decrease in the mean $\pm$ SD values of PASP (pulmonary artery systolic pressure), PA diastolic pressure, PA mean pressure, the ratio of pulmonary systolic pressure, and systolic aortic pressure, pulmonary vascular resistance, PVR/SVR ratio.

3 patients had persistently high PVR (>5WU) even after oxygen study. (6.72WU, 6.57WU, 6.99 WU). The first patient underwent ASD device closure without fenestration in the year 2000 and also was not on pulmonary vasodilator therapy, then later developed RV dysfunction at nine months of follow up after ASD device closure, after that lost for follow up. The remaining two of three patients underwent fenestrated ASD device closure and were on pulmonary vasodilators; they had good RV function, mild PAH at 58 months and 33 months of follow up respectively and using pulmonary vasodilators.

The procedure-related parameters:

Table 9: The procedure-related parameters:

Baseline parameters	PH			P-Value
	Total population (N=89)	Group 1 Moderate PAH (N=61)	Group 2 Severe PAH (N=28)	
Procedural details				
ASD device closure				
ASD size on TTE (mm)	22.07 (8, 36) 95% C.I (20.81, 23.33)	21.63 ± 5.97	23 ± 5.88	0.317
ASD size on TEE (mm)	24.83 (9, 43) 95% C.I (23.49, 26.17)	24.68 ± 6.53	25.14 ± 5.96	0.745
Device size	28.30 (12, 44) 95% C.I (26.99, 29.60)	27.67 ± 6.33	29.64 ± 5.61	0.145

Fenestrated device	4 (4.5%)	1 (1.6%)	3 (10.7%)	0.055
Procedural success	89(100%)	61 (100%)	28 (100%)	*
Complications				
Device embolization immediate	1(1.1%)	1 (1.6%)	0 (0.0%)	*
Late embolization	0	0	0	
Rhythm disturbance	3(3.3%)	3 (4.9%)	0 (0.00%)	
Other complications	2(2.2%)	1 (1.6%)	1 (1.6%)	
Residual flow / flow through fenestration	6(6.7%)	3 (4.9%)	3 (10.7%)	0.311
PASP (mm Hg) immediate post device closure	50.53 (28, 90) 95% C.I (47.46, 53.61)	43.68 ± 9.34	65.21 ± 12.69	<0.001
PAH drugs (pulmonary vasodilators) at discharge	10 11.2%	2 (3.3%)	8 (28.6%)	0.026

The **procedural success rate** of ASD device closure was 100%. **Device fenestration** was done prior to device implantation manually with 14 F dilator in **4 patients** in the whole study cohort. Of the one who had PASP > 60 mm Hg, as estimated by echo, was given pulmonary vasodilators for 3 months and later underwent cardiac catheterization, and ASD device closure had PASP on baseline cath study equal to 60 mm Hg and other patients had PASP >60 on baseline cath study.

Post ASD device closure, 2D echo prior to discharge showed residual flow in a total of 6 patients (in 4 patients, the residual flow was due to device fenestration). The mean value of PASP estimated from 2D echo within 24 hours of procedure was 50.53 (range 28- 90) 95% C. I (47.46, 53.61)

In 88 patients single ASD device was used; only one patient having two atrial septal defects with significant intervening atrial septal length underwent device closure with two separate devices.

The use of Pulmonary vasodilators was seen in (10/89) 11.2% of patients. Of the, 8 patients were in Severe PAH group, 2 patients were in Moderate PAH group.

The procedure-related complications:

One patient (1.1%) (with 22 mm defect size on TTE, 26 mm measured on TEE) had 26 mm device embolization to RPA immediately after deploying. The embolised device was snared and a bigger device (34 mm) was deployed successfully.

(3/89) 3.3% of patients' rhythm disturbance during the procedure. Atrial fibrillation during the procedure was seen in 1 patient, and it was reverted to sinus rhythm after DC cardioversion. The second patient had periprocedural SVT terminated with adenosine; the third patient had transient junctional rhythm reverted to sinus rhythm.

One patient had TEE-related oesophageal injury with hematemesis and oesophageal hematoma confirmed by CT thorax. She was managed conservatively and recovered.

One patient had retroperitoneal hematoma related to femoral access for Cath study, managed conservatively, and then underwent device closure one month later.

Comparison of baseline parameters with PVR category in the study population:

There was no significant difference in size of the ASD between the groups. Pulmonary artery pressures, resistance ratio, pulmonary artery systolic to aortic systolic pressures, RVIDD, severity of TR increased with increase in PVR (statistically significant).

Table 10: Comparison of baseline parameters with PVR category in the study population (N=89)

Baseline parameters	PVR			P-Value
	<3 WU (N=51)	3 to 5 WU (N=22)	>5 WU (N=16)	
Age (mean) years	46.90 ± 14.08	44.32 ± 17.93	42.75 ± 12.26	0.566
ASD size TTE mm	23.26 ± 6.17	20.00 ± 5.49	22.07 ± 5.94	0.080
ASD size TEE mm	26.62 ± 6.62	21.55 ± 5.19	23.75 ± 4.78	0.004
RVID mean mm	34.36 ± 5.97	34.09 ± 7.96	36.50 ± 4.46	0.508
PASP mean mm Hg	55.25 ± 10.83	64.73 ± 15.92	82.50 ± 12.95	<0.001
RV dysfunction	0 (0.00%)	0 (0.00%)	2 (12.5%)	*
TR severity				
Mild	39 (76.5%)	16 (72.7%)	1 (6.3%)	<0.001
Moderate	12 (23.5%)	6 (27.3%)	15 (93.8%)	
LV EF	66.51 ± 6.38	67.00 ± 6.46	67.16 ± 6.55	0.297
Cath data (Baseline)				
AO saturation (median)	98 (95.5, 99)	96 (93.75, 97.5)	94.5 (90.75, 95.88)	<0.001
PA systolic mm Hg	51.29 ± 8.48	57.95 ± 12.08	82.56 ± 15.20	<0.001
PA diastolic mm Hg	21.61 ± 3.98	21.32 ± 4.63	30.69 ± 6.25	<0.001
PA mean mm Hg	32.57 ± 3.41	35.27 ± 4.63	48.19 ± 6.56	<0.001
AO systolic mm Hg	76.75 ± 10.59	79.05 ± 10.84	73.94 ± 10.01	0.342
PASP/AO systolic	0.40 ± 0.08	0.43 ± 0.07	0.62 ± 0.13	<0.001
QP/QS	2.43 ± 0.96	1.96 ± 0.45	1.57 ± 0.41	0.001
PVR (WU)	2.03 ± 0.57	3.87 ± 0.57	7.73 ± 3.00	<0.001
SVR (WU)	18.55 ± 5.42	26.43 ± 8.10	24.61 ± 5.33	<0.001
R RATIO	0.12 ± 0.05	0.16 ± 0.05	0.33 ± 0.11	<0.001
Procedural details				
ASD device closure				
Fenestrated device	1 (2.0%)	0 (0.00%)	3 (18.8%)	*
Procedural success	51 (100%)	22 (100%)	16 (100%)	*
PASP immediate post device closure mm Hg	44.16 ± 10.56	51.55 ± 13.01	69.06 ± 10.87	<0.001
PAH drugs (pulmonary vasodilators) at baseline	1 (2%) (This patient was started on pulmonary vasodilators based on echo estimate of PASP and later underwent Cath study followed by fenestrated device closure)	2 (9.1%)	7 (43.8%)	0.011

Follow-up analysis of all patients.

We analyzed parameters in the early, intermediate, and long term. All 89 patients (100%) had an early follow-up with a mean duration of **1.51 months**. 86 patients (96.6%) had an intermediate follow-up with a mean duration of **16.33 months**. 77 patients (86.5%) had a **long-term follow-up** with a mean duration of **76.88 months**.

Table 11: Follow up analysis of the whole cohort of patients

Parameters	Baseline (N=89)	Early FU (N=89)	Intermediate FU (N=86)	Long term FU (N=77)
Duration of follow up months (mean & range)	Not applicable	1.51 (0.1, 4.7)	16.33 (2, 65)	76.88 (9, 198)
NYHA functional CLASS				
Class -1	9 (10.1%)	60 (67.4%)	70 (81.4%)	60 (77.9%)
Class -2	76 (85.4%)	29 (32.6%)	16 (18.6%)	16 (20.8%)
Class -3	4 (4.5%)	0	0	1 (1.3%)
Echo RVIDD (mm) (mean & range)	35.02 (18, 55)	30.89 (18, 50) *P <0.001	28.3 (18, 45) *P <0.001	28.23 (18, 40) *P <0.001
ECHO RV dysfunction	2 (2.2%)	2 (2.2%)	1 (1.2%)	1 (1.3%)
Pulmonary artery systolic pressure echo (mm Hg) (mean & range)	62.49 (40, 110)	46.25 (25, 89) *P < 0.001	41.09 (22, 90) *P < 0.001	40.4 (24, 82) *P <0.001
Number of patients with echo PASP <40	Not applicable	24 (27%)	45 (52.3%)	46 (59.7%)
Number of patients with severe PAH (echo PASP 60 or more)	44 (49.4%)	17 (19.1%)	7 (8.1%)	6 (7.8%)
Number of patients with PAH (Echo PASP>=40)	89(100%)	65(73%)	41(47.6%)	31(40.2%)
TR severity				
Mild	56 (62.9%)	82 (92.1%)	84 (97.7%)	72 (96%)
Moderate	33 (37.1%)	7 (7.9%)	2 (2.3%)	3 (4%)
MR severity				
No MR	41 (46.1%)	51 (57.3%)	54 (62.8%)	47 (61.8%)
Mild	47 (52.8%)	38 (42.7%)	32 (37.2%)	27 (35.5%)
Moderate	1 (1.1%)	0	0	2 (2.6%)
LV EF	67.16 (55, 86)	67.17 (54, 85)	66.71 (56, 78)	66.88 (60, 86)
Flow across the fenestration of device/ residual flow	Not applicable	2	1	1
Sinus rhythm	79 (88.8%)	79 (88.8%)	78 (90.7%)	65 (84.4%)
AF	9 (10.1%)	10 (11.2%)	7 (8.1%)	10 (13%)
PAH drugs	10 (11.2%)	8 (9%)	9 (10.6%)	9 (11.7%)
MACCE	-	-	-	5 (5.6%)
Mortality	-	-	-	3 (3.4%)

All patients (moderate and Severe PAH analyzed together) symptoms, NYHA class, echo, and other parameters at each follow-up are described in the above table. On long-term follow up 16/77 (21.1%) patients had NYHA functional class II. One patient had NYHA functional class III. The mean RVIDD reduced from 35.02 mm at baseline to 28.23 mm at long-term follow-up, and the reduction was statistically significant. The mean pulmonary artery systolic pressure as

measured by 2D echocardiography reduced from 62.49 mm Hg at baseline to 40.4 mm Hg, at last, follow up, and the reduction was statistically significant. RV dysfunction in one patient resolved, whereas in another patient, it persisted at her follow-up of nine months, and after that, she had lost to follow-up.

At long-term follow-up, 51.7% (46/77) patients had normalization of pulmonary artery systolic pressures, whereas 7.7% (6/77) patients persisted in having pulmonary artery systolic pressures ≥ 60 mm Hg. Only 4% (3/77) patients had moderate TR. No patients had severe TR. LV systolic function was normal in all patients. All patients with device fenestration did not have flow across the device at the long-term follow-up. Only one patient had residual flow at long-term follow-up. Atrial fibrillation (AF) was seen in (10/77) 13% of patients. New-onset AF was seen in 2.6% (2/77) patients. One patient had new-onset atrial bigeminy.

5 MACCE events occurred in the study cohort on long-term follow-up, which was three deaths, 1 Myocardial infarction, 1 heart failure. Causes of death were massive GI bleed with refractory shock and acute kidney injury due to oral anticoagulation for AF in 1 patient, stroke in 1 patient. In the third patient cause of death was not known. 1 patient had MI on follow-up.

Follow up analysis of ASD Moderate PAH (group 1)

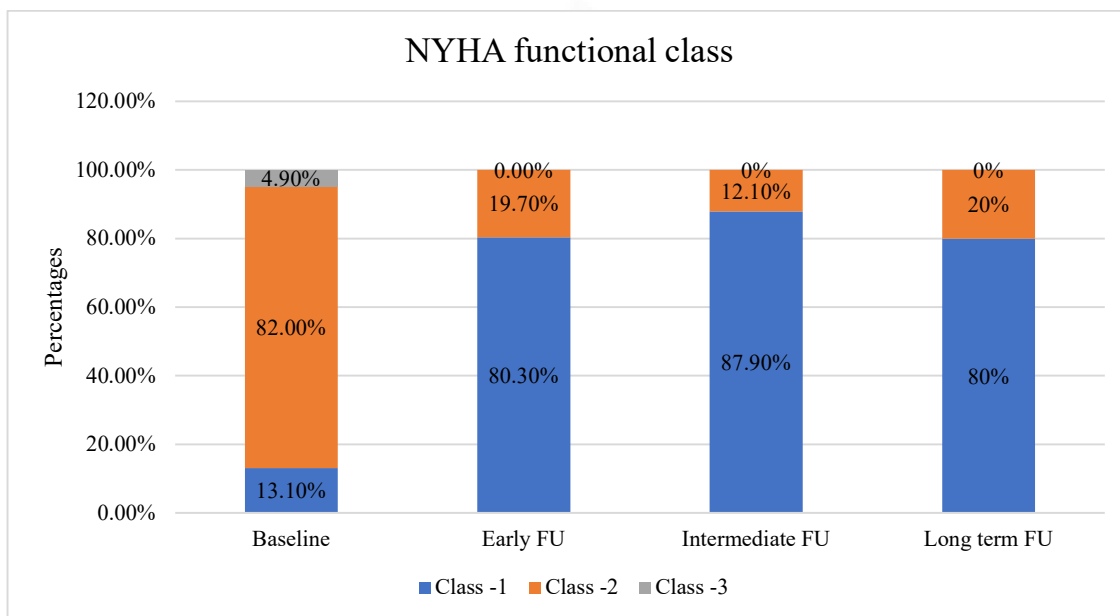
Table 12: NYHA functional class at each follow up in ASD moderate PAH group 1

Parameter (Moderate PAH group)	Baseline (N=61)	Early FU (N=61)	Intermediate FU (N=58)	Long term FU (N=51)
Duration of follow up (months) (mean & range)	Not applicable	1.23 (0.1, 4.7)	18.19 (2, 65)	84.33 (12, 198)
NYHA functional CLASS				
Class -1	8 (13.1%)	49 (80.3%)	51 (87.9%)	40 (80%)
Class -2	50 (82%)	12 (19.7%)	7 (12.1%)	10 (20%)
Class -3	3 (4.9%)	0	0	0

**No statistical test is performed due to zero subjects in the cells.*

The functional status was assessed by the NYHA classification improved at early follow-up, and the improvement was persistent at long-term follow-up.

Figure 16: Stacked bar chart for comparison of NYHA functional class with Moderate PAH in the study population (N=61)



Echo parameters at each follow up in ASD moderate PAH group

Figure 17: Line chart for comparison of echo parameters with Moderate PAH in the study population (N=61)

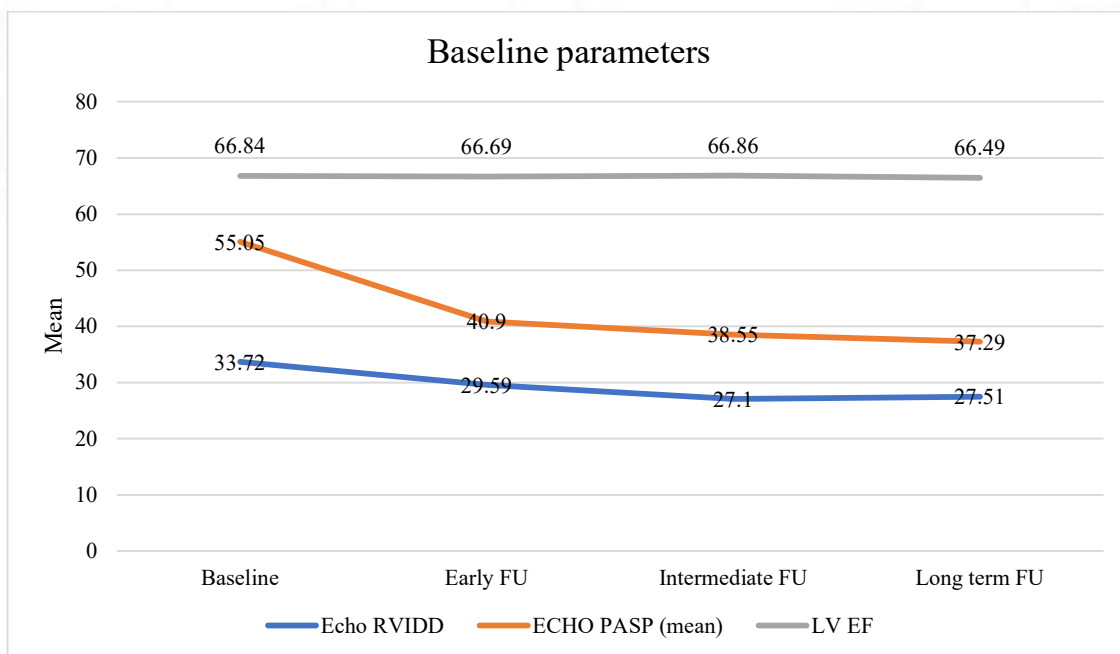


Table 13: Echo parameters at each follow up in ASD moderate PAH group 1

Parameter (Moderate PAH)	Baseline (N=61)	Early FU (N=61)	Intermediate FU (N=58)	Long term FU (N=51)
Duration of follow up (months)	Not applicable	1.23 (0.1, 4.7)	18.19 (2, 65)	84.33 (12, 198)
Echo RVIDD (mean) mm (mean & range)	33.72 (18, 45)	29.59 (18, 43) *P<0.001	27.10 (18, 38) *P = 0.001	27.51 (19, 40) *P=0.001
ECHO RV dysfunction	0	0	0	0
Pulmonary artery systolic pressure (PASP) echo (mean & range) mm Hg	55.05 (40, 78)	40.90 (25, 70) *P<0.001	38.55 (22, 90) *P<0.001	37.29 (25, 77) *P =0.002
Number of patients with PASP <40	Not applicable	23 (37.7%)	42 (72.4%)	40 (78.4%)
Number of patients with PASP >40 (PH present)	61(100%)	38(62.3%)	16(36%)	11(21.6%)
Number of patients with PASP 60 or more (SEVERE PAH)		4 (6.6%)	4 (6.9%)	4 (7.8%)

***Compared with baseline**

The decrease in RVIDD, Pulmonary artery systolic pressure (PASP) assessed by 2D echo was statistically significant.

Table 14: Echo parameters (TR, MR, residual flow/ device fenestration flow) at each follow up in ASD moderate PAH group 1

Parameter (Moderate PAH)	Baseline (N=61)	Early FU (N=61)	Intermediate FU (N=58)	Long term FU (N=51)
Duration of follow up (months)	Not applicable	1.23 (0.1, 4.7)	18.19 (2, 65)	84.33 (12, 198)
TR severity				
Mild	52 (85.2%)	58 (95.1%)	56 (96.6%)	48 (96%)
Moderate	9 (14.8%)	3 (4.9%)	2 (3.4%)	2 (4%)
MR severity				
No MR	29 (47.5%)	37 (60.7%)	38 (65.5%)	35 (70%)
Mild	31 (50.8%)	24 (39.3%)	20 (34.5%)	14 (28%)
Moderate	1 (1.6%)	0	0	1 (2%)
LV EF	66.84 (55, 79)	66.69 (54, 80)	66.86 (56, 78)	66.49 (60, 79)
residual flow/ device fenestration flow	Not applicable	1 (1.6%)	0	0

The decrease in the severity of TR and MR was not statistically significant at each follow-up.

Figure 18: Stacked bar chart for comparison of TR severity at each follow up in Moderate PAH group (N=61) in the study population

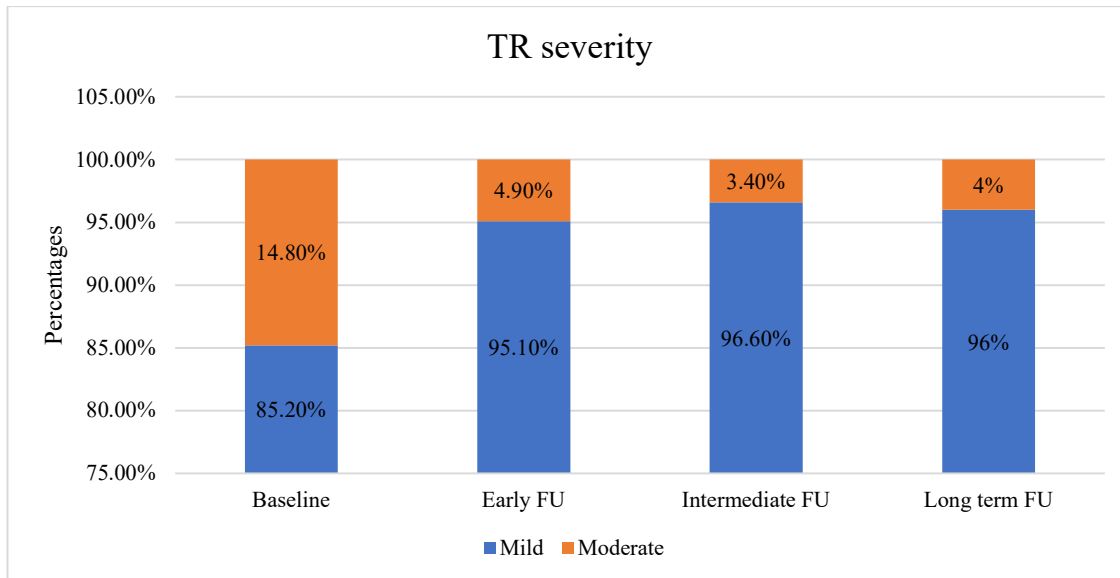
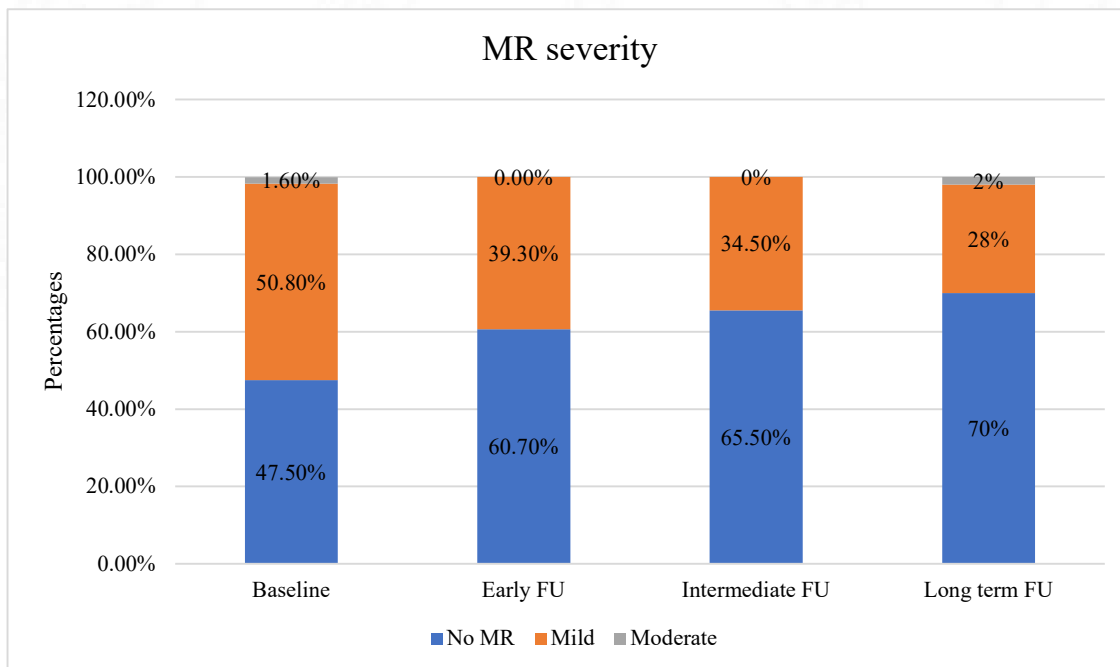


Figure 19: Stacked bar chart for comparison of MR severity at each follow up in ASD moderate PAH group



Prevalence of Atrial fibrillation at each follow up in **ASD moderate PAH group 1**

Table 15: Prevalence of Atrial fibrillation at each follow up in ASD moderate PAH group (N=61)

Parameter (Moderate PAH)	Baseline (N=61)	Early FU (N=61)	Intermediate FU (N=58)	Long term FU (N=51)
Duration of follow up (months)	Not applicable	1.23 (0.1, 4.7)	18.19 (2, 65)	84.33 (12, 198)
Sinus rhythm	55 (90.2%)	54 (88.5%)	54 (93.1%)	45 (88.2%)
AF	6 (9.8%)	7 (11.5%)	4 (6.9%)	6 (11.8%)

There was no statistically significant change in the number of patients with AF at each follow-up. Two patients with AF at baseline reverted to sinus rhythm after treatment; however, recurrence of AF was seen in one of them at further follow-up visits. Two patients in group 1 had new-onset AF on early follow up which got reverted to sinus rhythm after treatment.

Figure 20: Stacked bar chart for comparison of Rhythm with Moderate PAH in the study population (N=61)

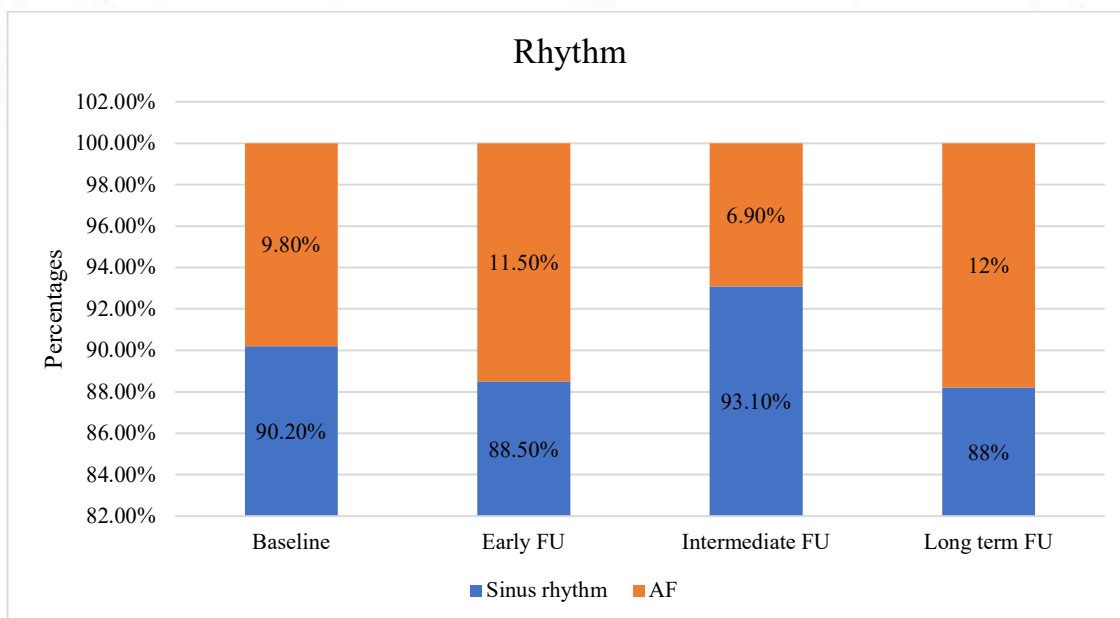


Table 16: Use of pulmonary vasodilators in ASD moderate PAH group 1

Parameter (Moderate PAH)	Baseline (N=61)	Early FU (N=61)	Intermediate FU (N=58)	Long term FU (N=51)
Pulmonary vasodilator use	2 (3.3%)	1 (1.6%)	2 (3.5%)	3 (5.9%)

2 patients were given oral pulmonary vasodilators for 3 months prior to device closure in the moderate PAH group as their PASP estimated was >60mm Hg by 2D echocardiography. The pulmonary vasodilators were stopped after device closure.

On long-term follow-up, 3 new patients in the moderate PAH group were started on pulmonary vasodilators. (Two patients had contributory factors for pulmonary hypertension, one patient had poorly controlled chronic asthma, another patient with chronic asthma had worsening PA pressures at follow-up after delivery with suspected autoimmune disease (Antinuclear antibodies positive)).

Table 17: MACCE and mortality in in ASD moderate PAH group 1

Parameter (ASD Moderate PAH)	Long term FU (N=51)
MACCE & deaths	4 (4.9%)
mortality	3 (4.9%)

There were 3 deaths on follow-up in the Moderate PAH group; causes of death were massive Gastrointestinal bleed with refractory shock and acute kidney injury due to oral anticoagulation for AF), stroke in 1 patient. In the third patient cause of death was not known. 1 patient had MI on follow-up.

Follow up analysis of ASD Severe PAH group

Table 18: FOLLOW UP of ASD Severe PAH group 2:

Parameter (Severe PAH)	Baseline (N=28)	Early FU (N=28)	Intermediate FU (N=28)	Long term FU (N=26)
Duration of follow up (months)	Not applicable	0.968 (0.1, 1.5)	12.46 (3, 35)	62.27 (9, 119)
NYHA CLASS				
Class -1	1 (3.6%)	11 (39.3%)	19 (67.9%)	19 (73.1%)
Class -2	26 (92.9%)	17 (60.7%)	9 (32.21%)	6 (23.1%)
Class -3	1 (3.6%)	0	0	1 (3.8%)

**No statistical test is performed due to zero subjects in the cells.*

The functional status as assessed by the NYHA classification improved at early follow-up, and the improvement was persistent at long-term follow-up.

Figure 21: Stacked bar chart for comparison of NYHA with Severe PAH in the study population (N=28)

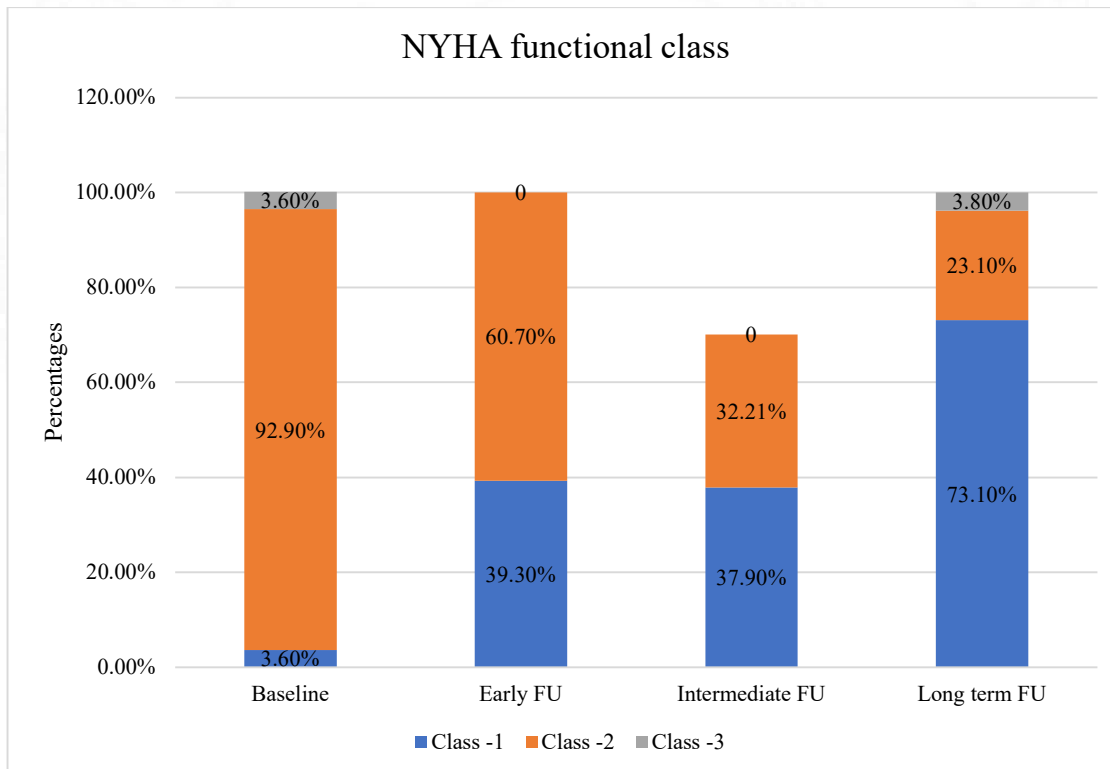


Table 19: Echo parameters at each follow up in **ASD Severe PAH group 2**

Parameter (Severe PAH)	Baseline (N=28)	Early FU (N=28)	Intermediate FU (N=28)	Long term FU (N=26)
Duration of follow up (months) mean range	Not applicable	0.968 (0.1, 1.5)	12.46 (3, 35)	62.27 (9, 119)
Echo RVIDD mm (range)	37.82 (28, 55)	33.71 (23, 50) *P= 0.026	30.79 (20, 45) *P= 0.001	29.65 (18, 40)
ECHO RV dysfunction	2 (7.1%)	2 (7.1%)	1 (3.6%)	1 (3.8%)
Pulmonary artery systolic pressure echo mm Hg mean (range)	78.71 (40, 110)	57.89 (30, 89) *P= 0.007	46.36 (30, 75) *P= 0.036	45.42 (24, 82) *P= 0.07
Number of patients with PASP <40	Not applicable	1 (3.6%)	3 (10.7%)	6 (21.4%)
Number of patients with PASP 60 or more	24 (85.7%)	13 (46.4%)	3 (10.7%)	2 (7.1%)
Number of patients with PASP >=40 (PH present)	28(100%)	27(96.4%)	25(89.2)	20(76.9%)

***Compared with baseline**

The decrease in RVIDD, Pulmonary artery systolic pressure (PASP) assessed by 2D echo was statistically significant on early and intermediate follow-ups. The PASP and RVIDD were further reduced on long-term follow-up.

Of 26 patients, only 2 patients (7.6 %) continued to have severe PAH (PASP 60 or more on echo) at long-term follow-up.

Figure 22: Line chart for comparison of parameters with Severe PAH in the study population (N=28)

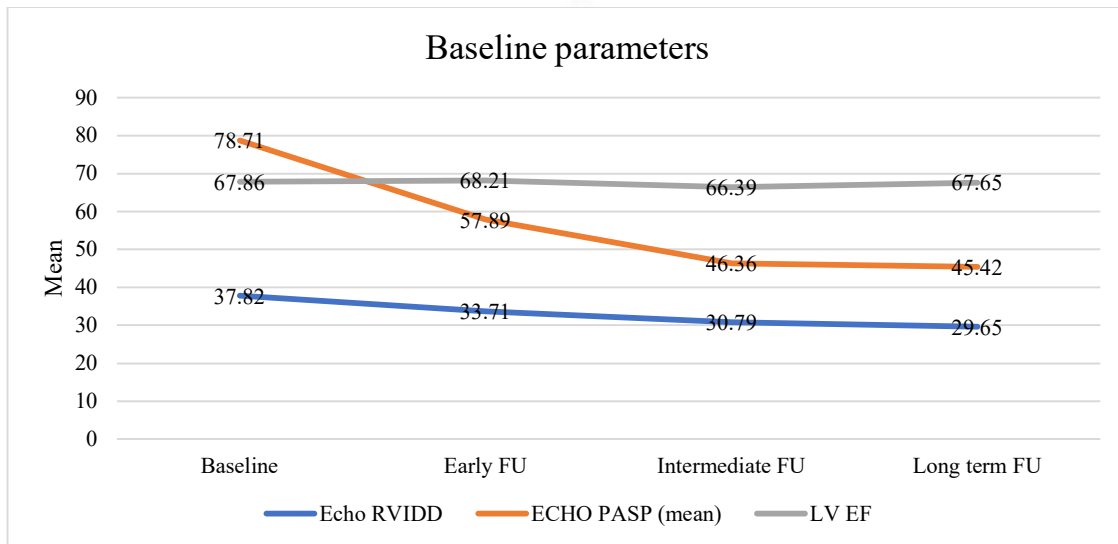


Table 20: Echo parameters (TR, MR, residual flow/ device fenestration flow) at each follow up in ASD Severe PAH (group 2)

Parameter (Severe PAH)	Baseline (N=28)	Early FU (N=28)	Intermediate FU (N=28)	Long term FU (N=26)
Duration of follow up (months)	Not applicable	0.968 (0.1, 1.5)	12.46 (3, 35)	62.27 (9, 119)
TR severity				
Mild	4 (14.3%)	24 (85.7%)	28 (100%)	24 (96%)
Moderate	24 (85.7%)	4 (14.3%)	0	1 (4%)
MR severity				
No MR	12 (42.9%)	14 (50%)	16 (57.1%)	12 (46.2%)
Mild	16 (57.1%)	14 (50%)	12 (42.9%)	13 (50%)
Moderate	0 (0.00%)	0	0	1 (3.8%)
LV EF	67.86 (55, 86)	68.21 (60, 85)	66.39 (59, 77)	67.65 (60, 86)
residual flow/ device fenestration flow	Not applicable	1 (3.6%)	1 (3.6%)	1 (3.6%)

The decrease in the severity of TR and MR was not statistically significant at each follow-up.

Figure 23: Stacked bar chart for comparison of TR severity with Severe PAH in the study population (N=28)

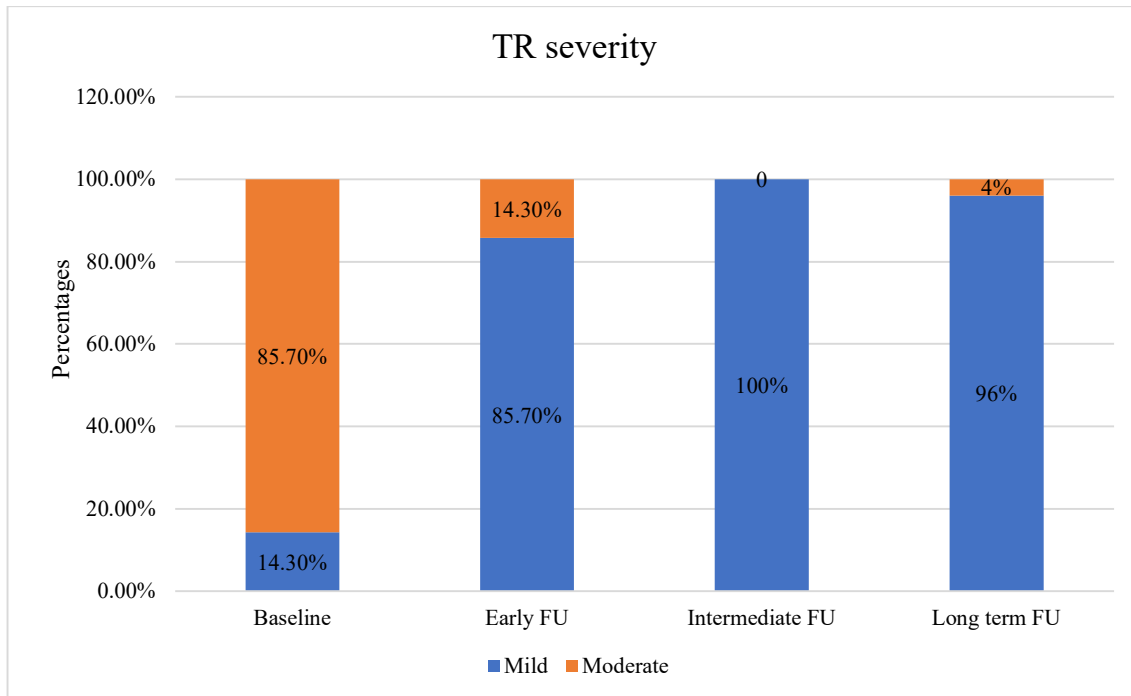
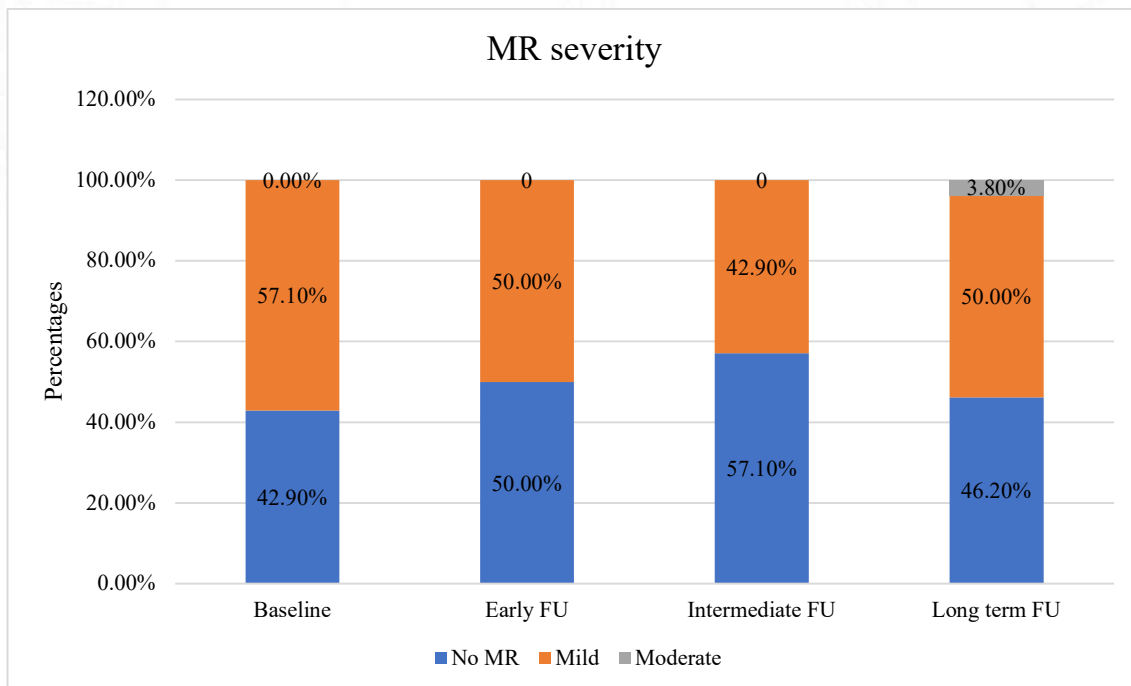


Figure 24: Stacked bar chart for comparison of MR severity with Severe PAH in the study population (N=28)



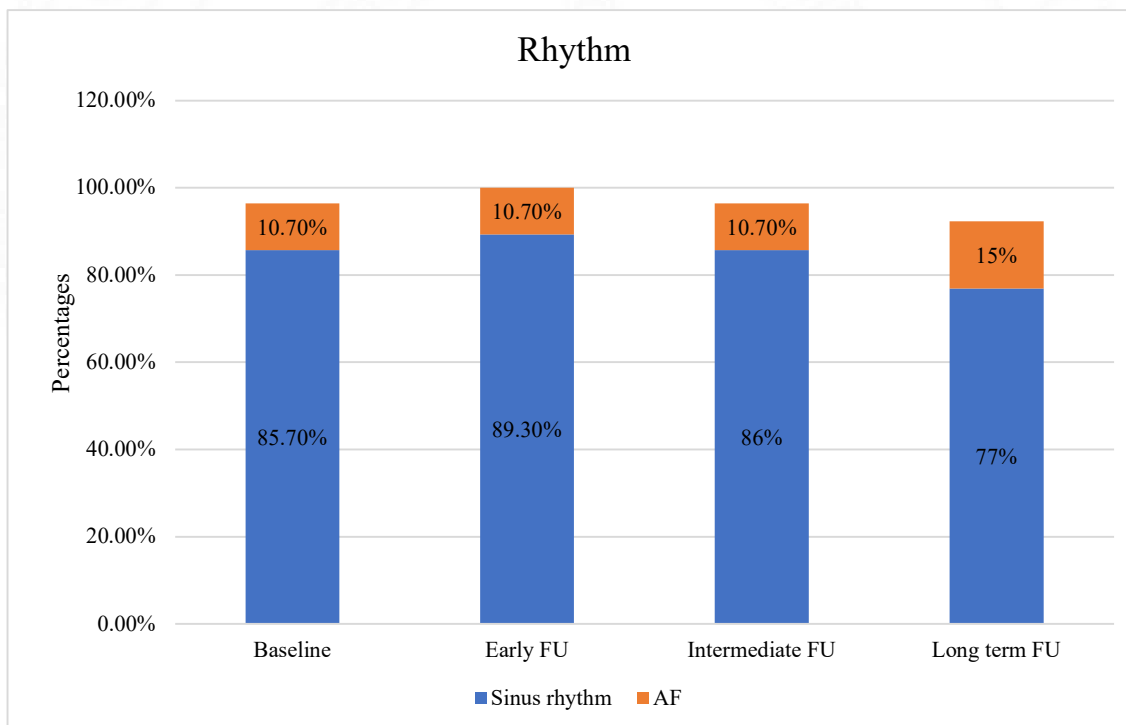
Prevalence of Atrial fibrillation at each follow up in the ASD Severe PAH group 2

Table 21: Prevalence of Atrial fibrillation at each follow up in the ASD Severe PAH (group 2) in the study population

Parameter (Severe PAH)	Baseline (N=28)	Early FU (N=28)	Intermediate FU (N=28)	Long term FU (N=26)
Duration of follow up (months)	Not applicable	0.968 (0.1, 1.5)	12.46 (3, 35)	62.27 (9, 119)
Sinus rhythm	24 (85.7%)	25 (89.3%)	24 (85.7%)	20 (76.9%)
AF	3 (10.7%)	3 (10.7%)	3 (10.7%)	4 (15.4%)

There was no statistically significant change in the number of patients with AF at each follow-up. One patient with AF at baseline in group 2 developed a complete heart block on follow-up and underwent permanent pacemaker insertion. Two patients had new-onset AF in this group.

Figure 25: Stacked bar chart for comparison of Rhythm with Severe PAH in the study population (N=28)



Use of pulmonary vasodilators in the ASD Severe PAH (group 2)

Table 22: Use of pulmonary vasodilators in the ASD Severe PAH (group 2):

Parameter (Severe PAH)	Baseline (N=28)	Early FU (N=28)	Intermediate FU (N=28)	Long term FU (N=26)
Duration of follow up (months) mean range	Not applicable	0.968 (0.1, 1.5)	12.46 (3, 35)	62.27 (9, 119)
PAH drugs	8 (28.6%)	7 (25%)	7 (25%)	6 (23.1%)

28.6% (8/28) of patients in ASD Severe PAH were on pulmonary vasodilators. Pulmonary vasodilators were stopped in one patient in this group as their pulmonary artery systolic pressures fell into mild PAH level. One patient on pulmonary vasodilators was lost for long-term follow-up.

MACCE and mortality in Group 2 ASD severe PAH: one patient had heart failure hospitalization. There was no death in this group.

There was no incidence of device migration, device erosion, infective endocarditis at long-term follow-up.

Categorisation of patients according to pulmonary artery systolic pressure (PASP) at Long term follow up:

Subgroup analysis at long term follow-up by categorizing the patients based on the pulmonary artery systolic pressure estimated by 2D echocardiography into 4 groups: No PAH (PASP < 40 mm Hg), mild PAH (PASP 40-49 mm Hg), moderate PAH (PASP 50-59 mm Hg), severe PAH (PASP $\geq$ 60 mm Hg). There was no significant difference in the defect size, age at device closure among the sub-groups. The baseline pulmonary artery pressures, PVR and PVR/SVR ratio was higher in patients with persistently high pulmonary artery pressures at long term follow up which was statistically significant.

Table 23: Categorisation of patients according to PASP at Long term follow up (N=77)

Parameter	PASP<40 (N=46)	PASP 40-49 (N=18)	PASP 50-59 (N=7)	PASP 60 or more (N=6)	P values
BASELINE DATA					
Age at device closure	43.74 (3, 71)	50.22 (22, 70)	49.86 (34, 63)	43.67 (5, 67)	0.364
Follow up duration Months mean, range	80.80±43.53 (12, 195)	64.83±31.68 (22, 136)	89.57±37.04 (20, 128)	68.17±73.20 (9, 198)	0.468
Defect size mm	24.62 (9, 38)	27.5 (20, 43)	20.71 (17, 26)	24.28 (15, 36)	
Baseline ECHO PASP (mean) mm Hg	55.36 (40, 95)	74.72 (45, 96)	73.43 (56, 85)	64.67 (46, 110)	<0.001
Baseline ECHO RV dysfunction	0	0	1 (14.3%)	1 (5.6%)	*
BASELINE CATH DATA					
PA systolic mm Hg	51.91 (37, 110)	71.5 (55, 105)	61 (51, 70)	61.67 (44, 110)	<0.001
PA diastolic mm Hg	22.04 (11, 38)	24.89 (11, 36)	24.57 (15, 32)	23.78 (13, 38)	0.191
PA mean mm Hg	33.22 (24, 54)	40.94 (32, 58)	38.29 (28, 45)	37.5 (30, 62)	<0.001
AO systolic mm Hg	128.72 (80, 176)	145 (108, 180)	139.71 (110, 170)	129.28 (85, 193)	0.031
PASP/AO systolic	0.41 (0.27, 0.79)	0.50 (0.38, 0.74)	0.44 (0.35, 0.57)	0.49 (0.31, 0.85)	0.027
QP/QS	2.35 (1.20, 5.76)	2.19 (1.1, 4.3)	1.48 (0.16, 2)	1.90 (1.23, 2.96)	0.032
PVR (basal) (WU)	2.69 (0.86, 8.6)	4.48 (1.47, 11.2)	4.26 (1.9, 5.78)	4.37 (0.7, 16.78)	0.003
SVR (WU)	20.35 (10, 38.4)	25.69 (16.4, 48)	21.23 (8.8, 29.5)	20.79 (14, 34)	0.064
R RATIO	0.13 (0.04, 0.28)	0.19 (0.06, 0.51)	0.21 (0.14, 0.31)	0.21 (0.02, 0.76)	
Long term follow up data					
RVIDD at FU 3	26.93±3.57	28.94±5.19	31.14±5.27	32.67±4.54	0.004
Use of PAH drugs at FU 3	0	4 (22.2%)	2 (28.6%)	3 (16.7%)	
RV dysfunction at FU 3	0	0	0	1	

Categorisation of patients according presence or absence of pulmonarty artery hypertension at Long term follow up:

Table 24: Categorisation of patients according presence or absence of pulmonarty artery hypertension at Long term follow up (N=77)

Parameter	NO PAH PASP<40 at long term (N=46)	PAH present PASP >= 40 at long term (N= 31)	P values
Age at device closure	43.74±15.12	49.23±12.57	0.088
Follow up duration	80.80±44.07	71.06±42.91	0.337
BMI	23.35±5.10	23.65±4.20	0.781
Defect size	24.62±6.54	24.65±5.84	0.987
Hypertension at FU 3	18 (39.1%)	15 (48.4%)	0.421
DM at FU 3	10 (21.7%)	8 (25.8%)	0.679
Hypothyroidism at fu 3	6 (13%)	4 (12.9%)	0.986
Lung disease at fu 3	4 (8.7%)	3 (9.7%)	0.883
NYHA functional CLASS at long term follow up FU 3			
Class -1	42 (93.3%)	17 (54.8%)	0.003
Class -2 or more	3 (6.7%)	14 (45.1%)	
Baseline Echo RVIDD	33.18±5.82	37.61±6.18	0.003
Baseline ECHO PASP (mean)	55.36±11.87	74±13.68	<0.001
Baseline ECHO RV dysfunction	0	1 (3.2%)	*
BASELINE CATH DATA			
PA systolic	51.91±13.34	68.13±3.76	<0.001
PA diastolic	22.04±4.73	24.97± 6.91	0.045
PA mean	33.22±5.57	39.90±7.40	<0.001
AO systolic	128.72±19.09	143.29±22.79	0.005
PASP/AO systolic	0.41±0.11	0.49±0.12	0.006
QP/QS	2.35±0.89	1.91±0.84	0.032
PVR (basal)	2.69±1.61	4.53±2.49	0.001
SVR	20.35±6.65	24.08±7.59	0.030
Number of patients with baseline PVR <3 WU	35 (76.1%)	9 (29%)	<0.001
Number of patients with baseline PVR 3-5 WU	6 (13%)	12 (38.7%)	
Number of patients with baseline PVR >5 WU	5 (10.9%)	10 (32.3%)	
Number of Group 1 patients (Moderate PH)	40 (87%)	11 (35.5%)	<0.001
Number of group 2 patients (Severe PH)	6 (13%)	20 (64.5%)	
R RATIO	0.13±0.06	0.19±0.12	0.004
RVIDD at FU 3	26.93±3.57	30.16±5.16	0.004
Number of patients with RVIDD >= 28 mm at FU 3	20 (43.5%)	22 (71%)	0.018
Fate of fenestration of device/ residual at FU 3	0	1 (3.2%)	*
Sinus rhythm at FU 3	42 (91.3%)	11 (61.1%)	0.156
AF at FU 3	4 (8.7%)	5 (27.8%)	
PAH drugs at FU 3	0	4 (22.2%)	*

Subgroup analysis at long term follow-up by categorizing the patients based on the pulmonary artery systolic pressure estimated by 2D echocardiography into 2 groups: *No pulmonarty artery hypertension* (PASP<40 mm Hg), *pulmonarty artery hypertension present* (PASP $\geq$ 40 mm Hg), was done. There was no significant difference in the defect size, age at device closure among the two sub-groups. The baseline pulmonary artery pressures, PVR and PVR/SVR ratio, PASP/ Aorta systolic pressure ratio, RVIDD was higher in patients with persistence or presence of pulmonary artery hypertension at long term follow up which was statistically significant

Long term follow-up characteristics: comparison between the ASD moderate PAH group 1 and the ASD Severe PAH group 2:

At the long-term follow- up in the ASD Severe PAH group, the average pulmonary artery systolic pressure was higher than that of the Moderate PAH group (P= 0.004)

In ASD moderate PAH group, at long term follow up 78% (40/51) of patients had normalization of pulmonary artery systolic pressures as estimated by 2D echocardiography, 13.7% (7/51) had PA systolic pressures in mild to moderate PAH range, 7.8% (4/51) of patients had worsened PA systolic pressures to severe PAH range, whereas in the ASD severe PAH group 23.4% (6/26) of patients had normalization of pulmonary artery systolic pressures, 69.2% (18.26) of patients had a decrease in PA systolic pressures into mild to moderate PAH range. 7.7% (2/26%) continued to have a persistently severe degree of PAH. There is a statistically difference between the two groups in the number of patients with normalization of pulmonary artery pressures at long term follow up. (P <0.001)

Table 25: Long term follow up characteristics: comparison of ASD moderate PAH group and ASD Severe PAH groups

Parameters	Moderate PAH group 1 (N=51)	Severe PAH group 2 (N=26)	P-value
Duration of follow up (months)	84.33 ± 46.68	62.27 ± 32.88	0.019
Echo RVIDD (mm) on long term follow up	27.51 ± 4.12	29.65 ± 5.04	0.068
ECHO RV dysfunction On long term follow up	0	1 (3.8%)	*
Pulmonary artery systolic pressure echo (mm Hg) on long-term follow up	37.29± 10.63	45.42 ± 11.57	0.004
Number of patients with PASP <40 (n= 46) at long-term	40 (78.4%)	6 (23.4%)	<0.001
Number of patients with PASP 40-49 (n=18) at long-term	4 (7.8%)	14 (50%)	
Number of patients with PASP 50-59 (n= 7) at long-term	3 (5.9%)	4 (14.3%)	
Number of patients with PASP 60 or more (n= 6) at long-term	4 (7.8%)	2 (7.1%)	
PAH drugs	3 (5.9%)	6 (23.1%)	0.026
MACE	4 events (3 deaths, 1 MI)	1 event (HF hospitalisation)	
Mortality	3 (4.9%)	0	*

**No test is performed due to zero subjects in the cells.*

Univariate analysis for the independent predictors of severe PAH (at baseline) prior to device closure in OS ASD patients

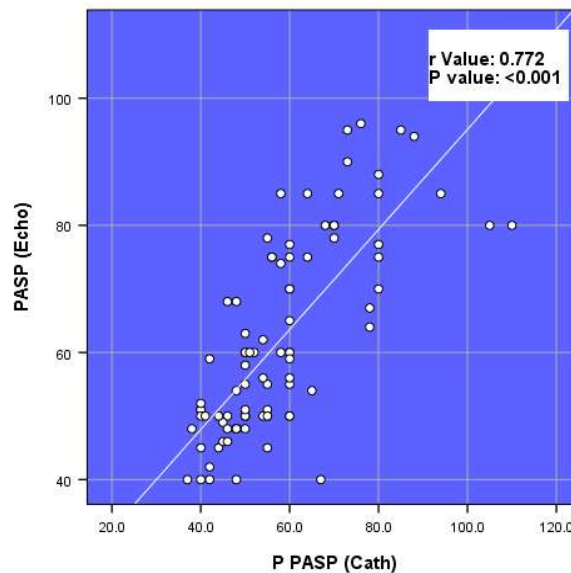
Univariate analysis showed the independent predictors of severe PAH prior to device closure in OS ASD patients were baseline PVR, baseline PVR/SVR ratio, pulmonary artery systolic/ aorta systolic pressure ratio and on **multivariate analysis** the variables were baseline PVR baseline PVR/SVR ratio, pulmonary artery systolic/ aorta systolic pressure ratio. Age at device closure and the defect size was not the independent predictors of severe PAH prior to device closure in OS ASD patients.

Table 26: Baseline variables associated with severe PAH (CATH - PASP >60 and/ or PA MEAN >40) at baseline (N=28)

Severe PAH (N=28)	Univariate factors			Multivariate factors		
	Odds Ratio	95% C. I	P-value	Odds Ratio	95% C. I	P-value
Age at device closure	1.013	0.981-1.046	0.416			
Defect size	1.012	0.942-1.086	0.749			
Baseline PVR	2.777	1.769-4.357	<0.001	2.695	1.344-5.404	0.005
Baseline PASP/AO systolic pressure	2497793.086	3650.17-1709226374	<0.001	90466.753	41.305-198143311.4	0.004
Baseline R RATIO	85539122.32	8235.99-8.884E+11	<0.001			
Hypertension	0.856	0.339-2.167	0.744			
DM	0.730	0.234-2.274	0.587			
Hypothyroidism	1.993	0.533-7.187	0.292			
Lung disease	1.71	0.356-8.212	0.503			
BMI	0.918	0.833-1.011	0.082			

Correlation PASP (pulmonary artery systolic pressure) estimated by 2D echocardiography and cardiac catheterisation at baseline

Figure 26: Scatter plot between PASO (Echo) and P PASP in the study population (N= 89)



The baseline pulmonary artery pressures estimated by 2D echocardiography and measured by cardiac catheterization had a good correlation with correlation coefficient (r value) of 0.772.

Univariate analysis for predictors of normalisation of PASP on long-term follow-up.

Univariate analysis showed Baseline PVR, Baseline PASP/AO systolic pressure, Baseline Resistance Ratio, Use of pulmonary vasodilators were independent predictors of normalisation of PASP on long-term follow-up.

Table 27: Factors associated decrease in PASP to < 40 on long term follow up (N=46)

	Univariate factors		
	Odds Ratio	95% C. I	P-value
Age at device closure	0.983	0.954-1.012	0.983
Defect size	0.989	0.926-1.057	0.752
Baseline PVR	0.666	0.507-0.874	0.003
Baseline PASP/AO systolic pressure	0.002	0.0001-0.149	0.004
Baseline R RATIO	0.0001	0.00001-0.073	0.006
Hypertension	0.922	0.392-2.170	0.852
DM	0.953	0.345-2.630	0.926
Hypothyroidism	0.877	0.247-3.115	0.839
Lung disease	1.270	0.267-6.033	0.764
BMI	0.991	0.908-1.081	0.833
Use of PAH drugs	11.912	1.439-98.590	0.022

Table 28: Factors affecting elevated PASP of >=40 on long term follow up (N=31)

	Univariate factors		
	Odds Ratio	95% C. I	P-value
Age at device closure	1.018	0.988-1.048	0.242
Defect size	1.011	0.946-1.080	0.752
Baseline PVR	1.502	1.144-1.972	0.003
Baseline PASP/AO systolic pressure	458.026	6.707-31281.136	0.004
Baseline R RATIO	9120.377	13.742-6053130.884	0.006
Hypertension	1.085	0.461-2.554	0.852
DM	1.049	0.380-2.896	0.926
Hypothyroidism	1.140	0.321-4.048	0.839
Lung disease	0.788	0.166-3.741	0.764
BMI	1.009	0.925-1.102	0.833
Use of PAH drugs	11.912	1.439-98.590	0.022

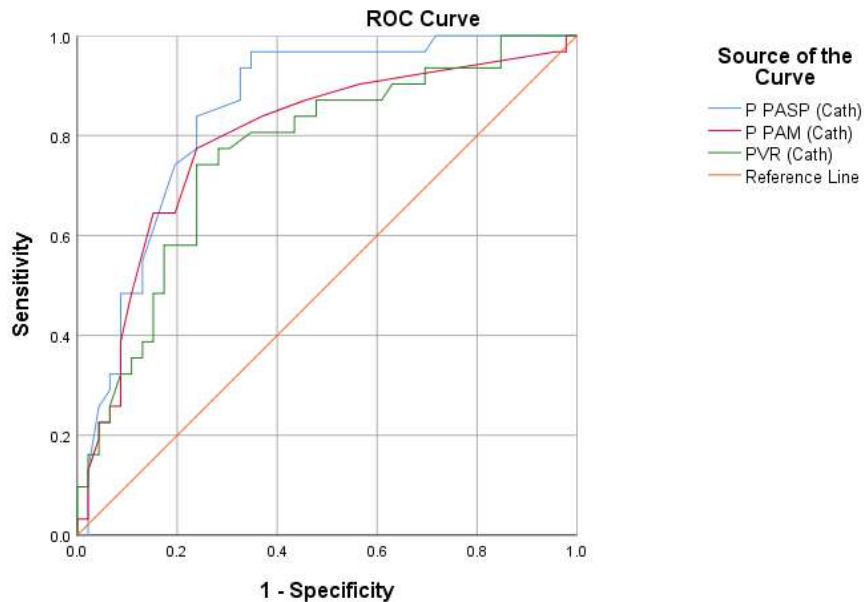
ROC CURVE ANALYSIS for Predictive validity of cardiac catheterisation parameters in predicting the persistence of PULMONARY HYPERTENSION at long term follow-up

1. Predictive validity of

- baseline pulmonary artery systolic pressure (P PASP),
- baseline mean pulmonary artery pressure (P PAM) and
- baseline pulmonary vascular resistance (PVR) -

measured by cardiac catheterisation for predicting the persistence of pulmonary hypertension at long term follow-up - (PASP estimated by 2D echocardiography ≥ 40 mm Hg = PAH present) at long term (ROC analysis):

Figure 27: Predictive validity of Cath PASP, PAM, PVR in predicting long term PASP (ROC analysis) (N=77)



Diagonal segments are produced by ties.

Test Result variables	Area Under the Curve	Std. Error	95% Confidence Interval of AUC		P value
			Lower Bound	Upper Bound	
P PASP (Cath)	0.849	0.044	0.762	0.935	<0.001
P PAM (Cath)	0.792	0.055	0.685	0.900	<0.001
P PVR (Cath)	0.765	0.056	0.655	0.874	<0.001

The optimal cut-off value was estimated by **The Youden index (J)** from the ROC curve.

Table 29: Comparison of presence of pulmonary arterial hypertension at long term with baseline cardiac catheterization data - P PASP, P PAM, PVR (N=77)

Cath variables (baseline) cut-off value	Long term PASP		Chi square	P value
	>=40 (N=31)	<40 (N=46)		
P PASP				
>=50.5 mm Hg	30 (96.77%)	16 (34.78%)	29.591	<0.001
<50.5 mm Hg	1 (3.23%)	30 (65.22%)		
P PAM				
>=34.5 mm Hg	24 (77.42%)	11 (23.91%)	21.385	<0.001
<34.5 mm Hg	7 (22.58%)	35 (76.09%)		
PVR				
>=2.81 WU	23 (74.19%)	11 (23.91%)	18.987	<0.001
<2.81 WU	8 (25.81%)	35 (76.09%)		

Table 30: Predictive validity of baseline cardiac catheterization data -P PASP, P PAM, PVR in predicting the long-term presence of pulmonary arterial hypertension (N=77)

Parameter	P PASP (Cath)	P PAM (Cath)	PVR (Cath)
Sensitivity	96.77% (83.30%-99.92%)	77.42% (58.90%-90.41%)	74.19% (55.39%-88.14%)
Specificity	65.22% (49.75%-78.65%)	76.09% (61.23%-87.41%)	76.09% (61.23%-87.41%)
False positive rate	34.78% (21.35%-50.25%)	23.91% (12.59%-38.77%)	23.91% (12.59%-38.77%)
False negative rate	3.23% (0.08%-16.70%)	22.58% (9.59%-41.10%)	25.81% (11.86%-44.61%)
Positive predictive value	65.22% (49.75%-78.65%)	68.57% (50.71%-83.15%)	67.65% (49.47%-82.61%)
Negative predictive value	96.77% (83.30%-99.92%)	83.33% (68.64%-93.03%)	81.40% (66.60%-91.61%)
Diagnostic accuracy	77.92% (67.02%-86.58%)	76.62% (65.59%-85.52%)	75.32% (64.18%-84.44%)
Positive likelihood ratio	2.78 (1.7-19.353)	3.24 (1.54-6.337)	3.10 (1.44-5.759)
Negative likelihood ratio	0.05 (0-0.344)	0.30 (0.03-0.581)	0.34 (0.04-0.63)

Predictive validity of baseline pulmonary artery systolic pressure (P PASP), measured by cardiac catheterisation for predicting [the persistence of pulmonary hypertension](#) at long term follow-up

ROC analysis showed that **baseline pulmonary artery systolic pressure** measured by cardiac catheterisation prior to device closure [AUC= 0.849, 95% Confidence Interval: 0.762 to 0.935, P value <0.001] was able to predict **the persistence of pulmonary hypertension at long term follow-up, with ≥ 50.5 mm Hg as the optimal cut-off** having 96.77% sensitivity and 65.22% specificity.

Predictive validity of baseline mean pulmonary artery pressure (P PAM) measured by cardiac catheterisation for predicting [the persistence of pulmonary hypertension](#) at long term follow-up

ROC analysis showed that **baseline pulmonary artery mean pressure** measured by cardiac catheterisation prior to device closure [AUC= 0.792, 95% Confidence Interval: 0.685 to 0.900, P value <0.001] was able to predict **the persistence of pulmonary hypertension at long term follow-up, with ≥ 34.5 mm Hg as the optimal cut-off** having 77.42% sensitivity and 76.09% specificity.

Predictive validity of baseline pulmonary vascular resistance (PVR), measured by cardiac catheterisation for predicting [the persistence of pulmonary hypertension](#) at long term follow-up

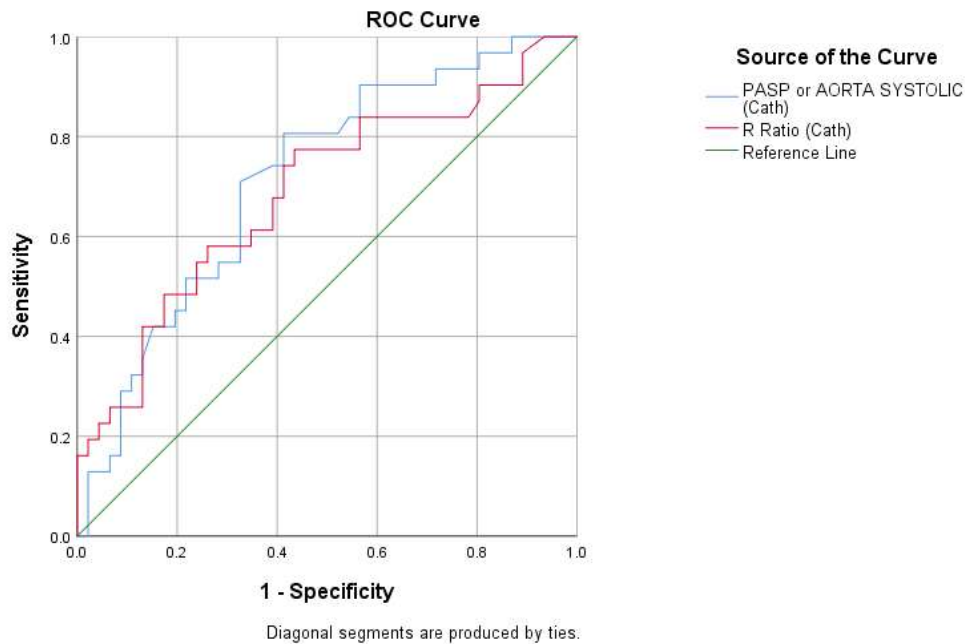
ROC analysis showed that **baseline pulmonary vascular resistance (PVR)** measured by cardiac catheterisation prior to device closure [AUC= 0.765, 95% Confidence Interval: 0.655 to 0.874, P value <0.001] was able to predict **the persistence of pulmonary hypertension at long term follow-up, with ≥ 2.81 WU as the optimal cut-off** having 74.19% sensitivity and 76.09% specificity.

2. Predictive validity of

- baseline ratio of pulmonary artery systolic pressure to systolic aortic pressure and
- baseline resistance ratio (PVR/SVR ratio) -

measured by cardiac catheterisation for predicting the **persistence of pulmonary hypertension at long term follow-up** (PASP estimated by 2D echocardiography ≥ 40 mm Hg = PAH present) at long term (ROC analysis):

Figure 28: Predictive validity of Cath PASP/AORTA systolic pressure ratio , Resistance ratio (R Ratio) in predicting the long-term presence of pulmonary arterial hypertension (N=77) (ROC analysis)



Test Result variables	Area Under the Curve	Std. Error	95% Confidence Interval of AUC		P value
			Lower Bound	Upper Bound	
PASP/AORTA Systolic (Cath)	0.716	0.059	0.61	0.831	0.001
R Ratio (Cath)	0.688	0.063	0.564	0.811	0.005

The optimal cut-off value was estimated by **The Youden index (J)** from the ROC curve.

Table 31: Comparison presence of pulmonary arterial hypertension at long term with baseline cardiac catheterization data with Cath PASP/AORTA systolic, R Ratio (N=77)

Cath variables (baseline) cut-off value	Long term PASP		Chi square	P value
	>=40 (N=31)	<40 (N=46)		
Cath PASP/AORTA systolic				
>=0.3878	25 (80.65%)	19 (41.3%)	11.704	<0.001
<0.3878	6 (19.35%)	27 (58.7%)		
R Ratio				
>=0.1264	24 (77.42%)	20 (43.48%)	8.712	0.003
<0.1264	7 (22.58%)	26 (56.52%)		

Predictive validity of baseline ratio of pulmonary artery systolic pressure to systolic aortic pressure, measured by cardiac catheterisation for predicting the persistence of pulmonary hypertension at long term follow-up

ROC curve analysis showed baseline ratio of pulmonary artery systolic pressure to systolic aortic pressure measured by cardiac catheterisation prior to device closure [AUC= 0.716, 95% Confidence Interval: 0.61 to 0.831, P value 0.001] was able to predict the persistence of pulmonary hypertension at long term follow-up with value ≥ 0.39 as the optimal cut-off having 80.65% sensitivity and 58.7% specificity.

Predictive validity of baseline resistance ratio (PVR/SVR ratio), measured by cardiac catheterisation for predicting the persistence of pulmonary hypertension at long term follow-up

ROC curve analysis showed baseline resistance ratio (PVR/SVR ratio) measured by cardiac catheterisation prior to device closure [AUC= 0.688, 95% Confidence Interval: 0.564 to 0.811, P value 0.005] was able to predict the persistence of pulmonary hypertension at long term follow-up, with value ≥ 0.13 as the optimal cut-off having 77.42% sensitivity and 56.52% specificity.

Table 32: Predictive validity of Cath PASP/AORTA systolic, R Ratio in predicting in predicting the long-term presence of pulmonary arterial hypertension (N=77)

Parameter	Cath PASP/AORTA systolic	R Ratio
Sensitivity	80.65% (62.53%-92.55%)	77.42% (58.90%-90.41%)
Specificity	58.70% (43.23%-73%)	56.52% (41.11%-71.07%)
False positive rate	19.35% (7.45%-37.47%)	43.48% (28.93%-58.89%)
False negative rate	19.35% (7.45%-37.47%)	22.58% (9.59%-41.10%)
Positive predictive value	56.82% (41.03%-71.65%)	54.55% (38.85%-69.61%)
Negative predictive value	81.82% (64.54%-93.02%)	78.79% (61.09%-91.02%)
Diagnostic accuracy	67.53% (55.90%-77.77%)	64.94% (53.22%-75.47%)
Positive likelihood ratio	1.95 (1.18-4.168)	1.78 (1.07-3.583)
Negative likelihood ratio	0.33 (0.01-0.704)	0.40 (0.02-0.804)

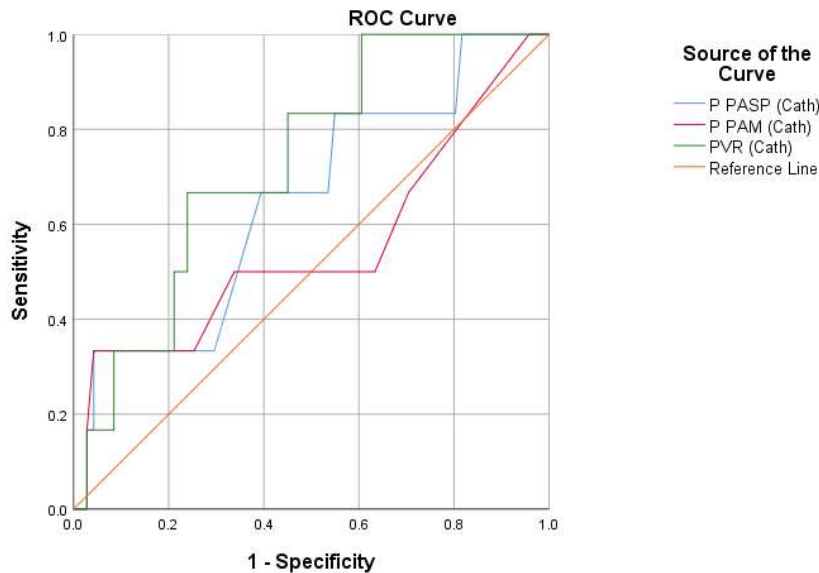
ROC CURVE ANALYSIS for Predictive validity of cardiac catheterisation parameters in predicting the persistence/ presence of SEVERE PULMONARY HYPERTENSION at long term follow-up

A. Predictive validity of

- baseline pulmonary artery systolic pressure (P PASP),
- baseline mean pulmonary artery pressure (P PAM) and
- baseline pulmonary vascular resistance (P PVR)

measured by cardiac catheterisation for predicting the persistence/presence of severe pulmonary hypertension at long term follow-up - (PASP estimated by 2D echocardiography ≥ 60 mm Hg = PAH present) at long term (ROC analysis):

Figure 29: Predictive validity of cardiac catheterisation parameters PASP, PAM, PVR in predicting the persistence/ presence of SEVERE PULMONARY HYPERTENSION at long term follow-up



Diagonal segments are produced by ties.

Test Result variables	Area Under the Curve	Std. Error	95% Confidence Interval of AUC		P value
			Lower Bound	Upper Bound	
P PASP (Cath)	0.648	0.117	0.418	0.877	0.231
P PAM (Cath)	0.552	0.145	0.267	0.836	0.676
P PVR (Cath)	0.730	0.090	0.554	0.907	0.063

ROC curve analysis showed the Area Under Curve (AUC) for baseline pulmonary artery systolic pressure (P PASP), and baseline mean pulmonary artery pressure (P PAM) in predicting the persistence/ presence of [severe pulmonary hypertension](#) at long term follow-up is not significant, (lower bound of confidence interval is <0.5) probably due to underpower of the study in predicting severe PAH at long term follow-up.

ROC curve analysis showed the Area Under Curve (AUC) for **baseline pulmonary vascular resistance (PVR)** in predicting the persistence/ presence of [severe pulmonary hypertension](#) at long term follow-up is [AUC= 0.730, 95% Confidence Interval: 0.554 to 0.907, P value 0.063]. though the P value is 0.063, the lower bound of the AUC is 0.554 which is greater than 0.5, so this is considered significant.

The optimal cut-off value for baseline pulmonary vascular resistance (PVR) was estimated by The Youden index (J) from the ROC curve.

Table 35: Comparison presence of severe pulmonary arterial hypertension at long term with baseline cardiac catheterization data with PVR (N=77)

Cath variable (baseline) PVR Cut-off value	Long term PASP		Chi square	P value
	>=60 (N=6)	<60 (N=71)		
>=4.15 WU	4 (66.67%)	17 (23.94%)	5.091	0.024
<4.15 WU	2 (33.33%)	54 (76.06%)		

Predictive validity of baseline pulmonary vascular resistance (PVR), measured by cardiac catheterisation for predicting [the persistence of severe pulmonary hypertension](#) at long term follow-up

ROC analysis showed that **baseline pulmonary vascular resistance (PVR)** measured by cardiac catheterisation prior to device closure [AUC= 0.730, 95% Confidence Interval: 0.554 to 0.907].

was able to predict **the persistence of severe pulmonary hypertension at long term follow-up**, with **≥ 4.15 WU as the optimal cut-off** having 66.6% sensitivity and 76.06 % specificity.

Table 36: Predictive validity of baseline cardiac catheterization data - PVR in predicting the long-term presence of severe pulmonary arterial hypertension (N=77)

Parameter	PVR (Cath)
Sensitivity	66.67% (22.28%-95.67%)
Specificity	76.06% (64.46%-85.39%)
False positive rate	23.94% (14.61%-35.54%)
False negative rate	33.33% (4.33%-77.72%)
Positive predictive value	19.05% (5.45%-41.91%)
Negative predictive value	96.43% (87.69%-99.56%)
Diagnostic accuracy	75.32% (64.18%-84.44%)
Positive likelihood ratio	2.78 (0.43-8.698)
Negative likelihood ratio	0.44 (0.06-1.369)

DISCUSSION:

We conducted a retrospective observational study to assess the change in pulmonary artery pressures estimated by 2D echocardiography at early, intermediate, and long-term follow-up in ostium Secundum atrial septal defect (OS ASD) patients with moderate and severe pulmonary hypertension who underwent ASD device closure.

After device closure in patients with OS ASD with moderate or severe pulmonary hypertension, it is not clear what fraction of patients have complete normalization pulmonary artery pressures or continue to have persistently elevated pulmonary artery pressures on long-term follow-up.

All patients with ostium secundum ASD with Pulmonary artery mean pressure ≥ 30 mm Hg or pulmonary artery systolic pressure ≥ 50 mm Hg, as documented by right heart catheterization prior to ASD device closure, were included in the study. Patients were categorized based on cardiac catheterization data into **moderate pulmonary arterial hypertension (moderate PAH group-** if mean PA pressure is between 30 - 40 mm Hg or PA systolic pressure is between 50 – 60 mm Hg) and **severe pulmonary arterial hypertension group (severe PAH group-**if mean PA pressure is >40 mm Hg or PA systolic pressure is >60 mm Hg). The mean follow-up duration for early, intermediate, and long-term follow-ups were 1.5 months, 16.3 months, 76.9 months, respectively.

The mean age of patients with OS ASD with moderate or severe pulmonary hypertension was 45.52 years (more than 40 years) which is consistent with multiple previous studies.(13,16,43) The mean age of the ASD moderate PAH group was 44.66 ± 15.83 years; group 2 was 47.39 ± 12.15 years. However, the mean age of the ASD Severe PAH group was slightly higher than ASD Moderate PAH group but not statistically significant (P 0.375).

There was female preponderance with a ratio of 2.4:1 in the study, which is slightly higher than that described in the literature (2:1).

The mean ASD size measured by transthoracic echo (TTE) and transoesophageal echo (TEE) of the whole cohort was 22.07 mm and 24.83 mm, respectively. There was no statistically significant difference in the size of the defect between ASD moderate PAH group and ASD Severe PAH group (by TTE 21.63 ± 5.97 mm versus 23 ± 5.88 mm respectively and by TEE was 24.68 ± 6.53 versus 25.14 ± 5.96 respectively). Similar to the older studies, there was no correlation between the ASD size and severity of pulmonary arterial hypertension.

In multiple older studies which have taken cut-off values for defining pulmonary hypertension as either $PASP \geq 40$ mm Hg or mean pulmonary artery pressure ≥ 25 mm Hg (13,16,35,40,43–45), the mean/median defect size was more than 18 mm. However, in one study(17), the mean $\pm$ standard deviation of the defect size was 13 ± 4 mm.

The age at device closure, the defect size, presence of diabetes, systemic hypertension, hypothyroidism, lung disease were not independent predictors of severe PAH at baseline.

Univariate analysis showed the independent predictors of severe PAH prior to device closure in OS ASD patients were baseline PVR, baseline PVR/SVR ratio, pulmonary artery systolic/ aorta systolic pressure ratio, and on multivariate analysis, the variables were baseline PVR, baseline PVR/SVR ratio, pulmonary artery systolic/ aorta systolic pressure ratio.

The predominant symptom was dyspnoea, followed by palpitations which is consistent with previous studies(13,16)

Percutaneous device closure in a selected group of patients with ostium secundum ASD associated with moderate or severe pulmonary arterial hypertension can be done successfully with favorable outcomes. This study had a procedural success rate of 100%. There was only one

incidence of immediate device embolization, which was successfully snared, and a bigger size device was deployed successfully.

Change in pulmonary artery pressures at follow up:

There was a significant fall in pulmonary artery systolic pressures after device closure in ASD patients with moderate or severe PAH at early, intermediate and long-term follow-up. This decrease in pulmonary artery pressures is consistent with findings seen in other studies.(13,16,17,35,44)

Univariate analysis showed Baseline PVR, Baseline PASP/AO systolic pressure ratio , Baseline Resistance Ratio(PVR/SVR ratio), Use of pulmonary vasodilators were independent predictors of normalisation of PASP on long-term follow-up. The age at device closure and the defect size were not independent predictors of normalisation of PASP on long-term follow-up.

The mean of (PASP) pulmonary artery systolic pressures as estimated by 2D echocardiography at long-term follow-up in ASD moderate PAH group was 37.29 ± 10.63 lower than that in ASD severe PAH group was 45.42 ± 11.57 with a statistically significant difference.

In the **whole study cohort**, about 60% (46/77) of the patients had normalization of pulmonary artery systolic pressures as estimated by 2D echocardiography at long-term follow-up, which is consistent with a previous study(13). 7.7% (6/77) patients had pulmonary artery systolic pressures ≥ 60 mm Hg at long-term follow-up. The remaining 32.4% (25/77) patients had PA systolic pressures in the mild to moderate PAH range.

In **ASD moderate PAH group**, at long term follow up 78% (40/51) of patients had normalization of pulmonary artery systolic pressures as estimated by 2D echocardiography, 13.7% (7/51) had PA systolic pressures in mild to moderate PAH range, 7.8% (4/51) of patients had worsened PA systolic pressures to severe PAH range, whereas in **ASD severe PAH group** 23.4% (6/26) of patients had normalization of pulmonary artery systolic pressures, 69.2% (18/26) of patients had a

decrease in PA systolic pressures into mild to moderate PAH range. 7.7% (2/26%) continued to have a persistently severe degree of PAH.

There was a statistically significant difference between ASD moderate PAH group and ASD severe PAH with respect to normalization of (PASP) pulmonary artery systolic pressures as estimated by 2D echocardiography at long-term follow-up. However, on long-term follow-up in ASD severe PAH group, 71.4% (20/ 26) of patients had PASP dropped (estimated by 2D echo) to mild pulmonary hypertension level, which was statistically significant when compared to their baseline. These results are similar to the recent studies(13,46) which showed that normalization of (PASP) pulmonary artery systolic pressures (<40 mm Hg) as estimated by 2D echocardiography at long-term follow-up was seen in most of the patients mild or moderate PAH after atrial septal device closure but normalization of (PASP) pulmonary artery systolic pressures is $\leq 25\%$ in patients with ASD severe pulmonary hypertension (baseline PASP >60 mm Hg).

In the whole study cohort, among the six patients who had pulmonary artery systolic pressures ≥ 60 mm Hg at long-term follow-up, two patients belonged to ASD severe PAH group, and their PVR at baseline was more than 6 WU. The remaining four patients had worsened pulmonary artery pressures on long term follow up, belonged to ASD moderate PAH group at baseline; among these four, two patients had other associated contributory factors for PAH (uncontrolled chronic bronchial asthma in one, in another pulmonary artery pressures worsened after chronic asthmatic pregnancy & delivery. However, there was no evidence of pulmonary thromboembolism, but the underlying autoimmune disease was suspected as antinuclear antibody (ANA) test was positive. The third patient had borderline operability (PVR between 3-5 WU) with PVR of 4.7 WU and PASP of 60 mm Hg at baseline cardiac catheterization and was not on any pulmonary vasodilator medications.

In this study, ROC curve analysis showed that baseline pulmonary artery systolic pressure measured by cardiac catheterisation prior to device closure [AUC= 0.849, 95% Confidence Interval: 0.762 to 0.935, P value <0.001] was able to predict the persistence of pulmonary hypertension at long

term follow-up, with ≥ 50.5 mm Hg as the optimal cut-off having 96.77% sensitivity and 65.22% specificity. In another study by Wang et al.(40) it was shown by ROC analysis that, if the baseline RVSP > 46 mm Hg, the normalization of pulmonary artery pressures is less likely at long term follow-up period of 84 ± 45 months.

In this study, ROC curve analysis showed that baseline pulmonary artery mean pressure measured by cardiac catheterisation prior to device closure [AUC= 0.792, 95% Confidence Interval: 0.685 to 0.900, P value <0.001] was able to predict the persistence of pulmonary hypertension at long term follow-up, with ≥ 34.5 mm Hg as the optimal cut-off having 77.42% sensitivity and 76.09% specificity. In another study by Wang et al.(40) it was shown by ROC analysis that the baseline mean pulmonary artery pressure > 42 mm Hg was the best cut-off for the predicting the persistence of pulmonary hypertension at long term follow-up period of 84 ± 45 months.

In this study, ROC curve analysis showed that baseline pulmonary vascular resistance (PVR) measured by cardiac catheterisation prior to device closure [AUC= 0.765, 95% Confidence Interval: 0.655 to 0.874, P value <0.001] was able to predict the persistence of pulmonary hypertension at long term follow-up, with ≥ 2.81 WU as the optimal cut-off having 74.19% sensitivity and 76.09% specificity. In another study by Wang et al.(40) **PVRI (pulmonary vascular resistance INDEX)** was used instead of PVR and it was shown by ROC analysis that the baseline **pulmonary vascular resistance index** > 5.69 WU.m² was the best cut-off for the predicting the persistence of pulmonary hypertension at long term follow-up period of 84 ± 45 months.

In this study, ROC analysis showed that **baseline pulmonary vascular resistance (PVR)** measured by cardiac catheterisation prior to device closure [AUC= 0.730, 95% Confidence Interval: 0.554 to 0.907]. was able to predict **the persistence of severe pulmonary hypertension at long term follow-up, with ≥ 4.15 WU as the optimal cut-off** having 66.6% sensitivity and 76.06 % specificity.

NYHA functional class:

The functional class of the patients improved after device closure on early follow-up, and the improvement was sustained at intermediate and long-term follow-up. Only two patients had worsening functional class. The improvement in NYHA class has been reported in multiple older studies.(13,16,17,35,40,45) Our study also confirmed the same. After device closure, the reduction in right ventricular volume overload and improvement in left ventricular diastolic function could be the reason for the improvement in NYHA class.

Prevalence of atrial fibrillation:

All patients who had atrial fibrillation were more than 40 years of age at the time of device closure. This is consistent with the previous studies, which showed that the prevalence of atrial fibrillation is uncommon in less than 40 years of age; the incidence increases with an increase in age.(25,26,28)

In the whole study cohort, Atrial fibrillation (AF) was seen in 10.1 % (9/89) of patients at baseline, in 11.2% (10/89) of patients at early follow-up, 8.1% (7/86) of patients at intermediate follow up, in 13% (10/77) of patients at long term follow up. New-onset AF was seen in (2/77) 2.6% of patients. One patient had new-onset atrial bigeminy.

In ASD moderate PAH group, 9.8% (6/61) of patients had AF at baseline. Two patients with AF at baseline reverted to sinus rhythm after treatment; however, recurrence of AF was seen in one of them at further follow-up visits. Two patients in group 1 had new-onset AF on early follow up which got reverted to sinus rhythm after treatment.

In ASD severe PAH group, 10.7% (3/28) of patients had AF at baseline. In group 2, one patient with AF at baseline developed a complete heart block on follow-up and underwent permanent pacemaker insertion. Two patients had new-onset AF in this group.

The prevalence of atrial fibrillation in the whole study cohort was lower compared to other similar studies.(13,16) This difference could be due to the lower mean of age of the present study population compared to other similar studies.

Previous studies (25,26) have shown the incidence of AF increases with an increase in severity of the PAH; however, in the present study, there was no significant difference in the prevalence of atrial fibrillation between the ASD moderate PAH group and severe ASD PAH group. In another study(16), there was a decrease in the prevalence of AF at long-term follow-up compared to baseline and was attributed to the corresponding reduction in the PA pressures at long-term follow-up. Such observation was not seen in the present study, probably because the proportion of patients with AF is less in the present study.

Major Adverse Cardiac and Cerebrovascular Events (MACCE) and mortality at long term follow up:

Five MACCE events (5/89, 5.6%) occurred in the study cohort on long-term follow-up (mean 76.9 months), which were three deaths, one Myocardial infarction, one heart failure hospitalization. Causes of death were massive GI bleed with refractory shock and acute kidney injury due to oral anticoagulation for AF in one patient, stroke in one patient.

Use of pulmonary vasodilators:

In the whole study cohort, 10/ 89 patients (11.2%) were patients at baseline, 8/89 (9%) at early follow-up, 9/86 (10.6%), at intermediate follow up and (9/77) 11.7% at long-term follow up were using pulmonary vasodilators. Univariate analysis showed that the use of pulmonary vasodilators was independent predictor of normalisation of PASP on long-term follow-up.

The pulmonary vasodilators were stopped after device closure in three patients. One patient using pulmonary vasodilators at baseline had lost for long-term follow-up. Three patients were newly started on pulmonary vasodilators on follow-up due to worsening severity of pulmonary

artery hypertension. The pulmonary vasodilator commonly used was sildenafil. One patient used tadalafil. One patient used combination treatment (sildenafil with ambrisentan) at baseline. At the same time, two patients used combination treatment (sildenafil with ambrisentan) at long-term follow-up.

On long term follow up, four patients in the moderate PAH group had an increase in PASP to severe PAH level, three of them were started on pulmonary vasodilators (Two patients had contributory factors for pulmonary hypertension, which were poorly controlled chronic asthma in one patient, another patient with chronic asthma had worsening PA pressures at follow up after delivery with suspected autoimmune disease (Antinuclear antibodies positive). The third patient, who was newly started on pulmonary vasodilators at early follow-up, did not come for further follow-ups.

Other variables:

The right ventricular internal diameter in diastole (RVIDD) reduced significantly from baseline to early follow up which is consistent with other studies(17,35) that have shown right ventricular remodelling with improvement in RV dimensions post-ASD device closure

The severity of tricuspid regurgitation reduced on long term follow up due to right ventricular remodelling, which is similar to a previous study(17,35)

There was no incidence of device migration, device erosion, infective endocarditis at long-term follow-up in the study cohort.

LIMITATIONS

1. This is a retrospective observational study, and it focussed mainly on the pattern of change in pulmonary artery systolic pressures in OS ASD patients with moderate or severe pulmonary hypertension.
2. Pulmonary vasodilators were not uniformly used in all patients with $PVR > 5$ wood units or $PASP > 60$ mm Hg, or $PA\ mean > 40$). If they were used with a uniform protocol, more patients from ASD severe PAH group might have had a further reduction of pulmonary artery pressures.
3. As it was a retrospective study, there was no uniform protocol for using the fenestrated device.
4. The dimensions of the right ventricle in apical four-chamber view were not taken, the measurement of RV internal diameter in diastole in parasternal long-axis view was done, other dimensions in apical four-chamber were not taken, and also another parameter of right ventricular function like RV fractional area change was not assessed in all patients.
5. All patients did not come for long-term follow-up. (86.5% (77/89) patients had long-term follow-up.)
6. The follow-up assessment of pulmonary artery pressures was done by 2D echocardiography only, not cardiac catheterization. However, the baseline pulmonary artery pressures estimated by 2D echocardiography and measured by cardiac catheterization had a good correlation, and also cardiac catheterization at follow-up only to measure pulmonary artery pressures is not the standard/ appropriate indication.

CONCLUSIONS

Transcatheter device closure in selected ostium secundum patients with moderate PAH or severe PAH with suitable anatomy and favorable hemodynamic study can be done successfully and has very good outcomes. There is a significant improvement in pulmonary artery pressures at early follow-up with further improvement at intermediate and long-term follow-ups. The normalization of pulmonary artery pressures was not seen in all the patients. At the long-term follow-up, the proportion of patients with normal pulmonary artery pressures is significantly higher in ASD moderate PAH group compared to ASD severe PAH group. However, the majority of patients in the ASD severe PAH group had pulmonary artery pressures decreasing to mild pulmonary hypertension level. There can be a risk of worsening pulmonary artery pressures in a small fraction of patients, especially if associated with any contributory risk factors for pulmonary hypertension. The use of pulmonary vasodilators in the presence of severe PAH after device closure would be beneficial and will further reduce the pulmonary artery pressures.

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APPENDIX 1 : INSTITUTIONAL ETHIC COMMITTEE APPROVAL



श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
Thiruvananthapuram - 695 011, Kerala, India
(An Institute of National Importance under Govt. of India)

Grams : Chitramet, Phone : +91-471-2443152, Fax : +91-471-2550728 / 2446433, E-mail : sct@sctimst.ac.in, Website : www.sctimst.ac.in

Institutional Ethics Committee

(IEC Regn No. ECR/189/Inst/KL/2013/RR-21)

SCT/IEC/1708/AUGUST/ 2021

20.10.2021

Dr. Gurajala Venkatesh

PDF, Paediatric Cardiology

Department of Cardiology

SCTIMST, Thiruvananthapuram

Dear Dr. Gurajala Venkatesh,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "LONG TERM OUTCOMES OF TRANSCATHETER DEVICE CLOSURE OF OSTIUM SECUNDUM ATRIAL SEPTAL DEFECT WITH MODERATE AND SEVERE PULMONARY HYPERTENSION (IEC/1708)" on 18th August, 2021.

The following members of the Ethics Committee were present at the meeting held on 18th August, 2021 at Residences and Offices of IEC Members via Video Conference

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Prof. C.C. Kartha	MBBS,MD	Male	Basic Medical Scientist (Chairman)	No
2.	Dr. Kala Kesavan P	MBBS,MD	Female	Basic Medical Scientist	No
3.	Smt. Sathi Nair	MA (English Literature)	Female	Lay Person	No
4.	Dr. Pradeep S	MBBS, MD	Male	Basic Medical Scientist	No
5.	Dr. Achuth Sankar S. Nair	Ph.D (i.Engineering ii.Music)	Male	Social Scientist	No
6.	Dr. Rejnish Kumar	MBBS,MD ,DNB	Male	Clinician	No
7.	Adv. N Anand	BAL, L.LB	Male	Legal Expert	No
8.	Adv. Priya Kaimal	LLM, MBL	Female	Legal Expert	No
9.	Dr. Harikrishna Varma P. R	Ph.D (Materials Sciences)	Male	Medical Technology	Yes
10.	Dr. Manikandan.S	MBBS,MD,PDCC	Male	Clinician	Yes
11.	Dr. Narayanan Namboodiri. K K	MBBS,MD,DM	Male	Clinician	Yes
12.	Dr. Biju Soman	MBBS,MD, DPH, MSc, DLSHTM	Male	Basic Medical Scientist	Yes
13.	Dr. Srinivas G	PhD	Male	Basic Medical Scientist (Member Secretary)	Yes

Page 1 of 2

The following documents were reviewed:

Original submission

1. Covering letter addressed to the Chairperson, IEC, SCTIMST dated 20.05.2021
2. TAC Application Form
3. Dean's signature form
4. IEC Application Form
5. Study proposal
6. CV of PI and Co-PIs
7. Letter addressed to the Technical Advisory Committee regarding the consent waiver form
8. Declaration Form
9. Proforma
10. TCMC Registration Form

Revised submission

1. Covering letter addressed to the Chairperson, IEC, SCTIMST dated 13.09.2021
2. SRC comments and responses
3. Study proposal
4. IEC Application Form
5. Dean's signature form
6. Proforma
7. Patient Information Sheet English and Malayalam
8. Consent Form English and Malayalam
9. Study Assent Form English and Malayalam
10. Paternal consent form for patients in English and Malayalam
11. CV of PI and Co-PIs
12. TCMC Registration Form

IEC Decision

The IEC approved the conduct of the study in the present form

Remarks:

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,



G. Srinivas
Member Secretary, IEC



APPENDIX 2: DATA COLLECTION PROFORMA

PROFORMA

Subject ID No:

Name:

Age:

Sex:

Weight:

Height:

BSA:

BMI

Symptoms and duration

NYHA class

size of the ASD:

Any additional ASD

arrhythmias

other risk factors for PAH

ECG

Chest X ray:

echo parameters at base line

RV function

RA/RV volume overload

TR

PASP

Mean PA pressure

LV function

MR

use of cardiac medications:

- pulmonary vasodilators before device closure or at baseline
- any other medications

Cardiac catheterization:

Parameter	baseline	Post AVT (acute vasoreactivity test)
Pressures		
AORTA		
RA		
RV		
PA		
LA		
calculations		
Qp/Qs		
PVR		

SVR		
PVRI		
SVR		
PVR/SVR ratio		

ASD DEVICE CLOSURE PROCEDURAL CHARACTERISTICS:

- Size of the device:
- Fenestration of device done or not:
- Any complications
- Any Device migration

FOLLOW-UP: data at followup

- NYHA functional class
- **echo parameters at follow up**

RV function

- TAPSE

- RV FAC

RVIDd

TR

RVSP

Mean PA pressure

LV function

MR

Status of fenestration shunt if fenestrated device was used

- Arrhythmias
- Use of pulmonary vasodilators at follow up
- Any other cardiac medications.
- MACCE (cardiac events, heart failure hospitalisation, stroke)
- Device migration
- Device erosion
- Infective endocarditis
- Any mortality

APPENDIX 3: CONSENT FORM- ENGLISH

SREE CHITRA THIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY,
TRIVANDRUM
DEPARTMENT OF CARDIOLOGY

PATIENT INFORMATION SHEET

Study Title: “ Long term outcomes of transcatheter device closure of ostium secundum Atrial Septal Defect with moderate and severe pulmonary hypertension”.

Name of the Investigators:

Dr. Gurajala Venkatesh, Dr. K.M. Krishnamoorthy, Dr. Deepa Sasi Kumar
Dr. Arun Gopalakrishnan, Dr. Hari Krishnan. K.N

Dear Subject,

We welcome you and thank you for your interest in this research project titled “ **Long term outcomes of transcatheter device closure of ostium secundum Atrial Septal Defect with moderate and severe pulmonary hypertension**”. Before you participate in this study, it is important for you to understand why this research is being carried out. This form will provide you all the relevant details of this research. It will explain the nature, the purpose, the benefits, the risks, the discomforts, the precautions and the information about how this project will be carried out. It is important that you read and understand the contents of the form carefully. This form may contain certain scientific terms and hence, if you have any doubts or if you want more information, you are free to ask the study personnel or the contact person mentioned below before you give your consent and also at any time during the entire course of the project.

What is the Study about?

To assess pulmonary artery pressures and right ventricular function, in post atrial septal defect device closure in patients by 2D echocardiography.

If you take part what will you have to do?

You need to tell us about symptoms of your disease, allow us to collect your data (History, Clinical and ECHO reports) from electronic medical records. You need to undergo ECG and 2D ECHO during your regular followup.

How long does it take?

During your OPD visit assessment will take 15 minutes & ECG and 2D ECHO will take 15 to 30 minutes.

Will you have to pay for above tests?

These tests are part of your routine care and amount paid for the tests would be the amount decided by hospital as for all general patients at that time.

Is there any risk or benefit for this study?

There are no risks involved in the study, echocardiography is safe non-invasive procedure. If on evaluation any reports are abnormal you will receive treatment according to the standard operating procedure of the hospital for which you have to pay for the hospital and this is not part of the study.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment.

What happens after the study is over?

2D Echo report will be available for your use and it will be stored in EMR in your Hospital I.D.

Will participants be compensated for participation in this study?

You will not be paid for participation in the study.

Will your personal details be kept confidential?

The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study.

If you have any further questions, please ask Dr. Gurajala Venkatesh, Post Doctoral Fellow in Paediatric cardiology, Department of Cardiology, SCTIMST (Tel: 8884633567) or email: drgvn7@gmail.com or drgvn7@sctimst.ac.in

For any clarifications regarding the study's ethics clearance you may contact the Member Secretary of the SCTIMST-IEC. The phone number is: 91-471-2524-234 and the email id is iec.mem.sec@sctimst.ac.in

SREE CHITRA THIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY,
TRIVANDRUM
DEPARTMENT OF CARDIOLOGY

CONSENT FORM FOR ADULT PATIENTS (FOR AGE ≥ 18 YRS)

Study Title: “Long term outcomes of transcatheter device closure of ostium secundum Atrial Septal Defect with moderate and severe pulmonary hypertension”

Participant's name: _____ Age: ____ Y ____ M; Sex: M /
F
I (Name of Participant/ Parent / Guardian) _____
aged (in years) _____ son/daughter of

(Please tick boxes).

☐ I Declare that I have read the above information provided to me regarding the study: : “ **Long term outcomes of transcatheter device closure of ostium secundum Atrial Septal Defect with moderate and severe pulmonary hypertension**” and have clarified any doubts that I had.

☐ I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights.

☐ I understand that the study staff and institutional ethics committee members may not need my permission to look at my health records even if I withdraw from the trial. I agree to this access.

☐ I understand that my identity may not be revealed in any information released to third parties or published.

☐ I voluntarily agree to take part in this study.

☐ I received a copy of this signed consent form.

Name:

Signature:

Date:

Name & Signature of witness:

Relation to participant

Date:

=====

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any benefits and risk that may reasonably be expected to occur. I

further certify that I encouraged the participant to ask questions and that all questions asked were answered.

Name and Signature of Person obtaining consent:

Dr. Gurajala Venkatesh

Fellow in Paediatric cardiology (PDF),

Dept. of Cardiology, SCTIMST.

Date:



SREE CHITRA THIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY,
TRIVANDRUM
DEPARTMENT OF CARDIOLOGY

STUDY ASSENT FORM (for age group :13-17 YEARS)

Study Title: “ Long term outcomes of transcatheter device closure of ostium secundum Atrial Septal Defect with moderate and severe pulmonary hypertension”

Participant’s name:

Date of Birth / Age (in years):

I _____,
FATHER/MOTHER/LEGAL GUARDIAN of _____ (Please tick
boxes).

☐ I Declare that I have read the above information provide to me regarding the study “ **Long term outcomes of transcatheter device closure of ostium secundum Atrial Septal Defect with moderate and severe pulmonary hypertension**”and have clarified any doubts that I had.

☐ I also understand that the participation of my child in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights.

☐ I understand that the study staff and institutional ethics committee members may be not need my permission to look at my child’s health records even if I withdraw consent from the study. I agree to this access.

☐ I understand that my child’s identity may be not be revealed in any information released to third parties or published.

☐ I voluntarily agree for my child to take part in this study.

☐ I received a copy of this signed consent form.

Name:

Signature:

Date:

Signature of witness:

Name of witness:

Date:

FOR PARTICIPANT

I, _____ (Name of participant) _____(Hosp No)_____(Age)

☐ I Declare that I have read the above information provide to me regarding the study “ **Long term outcomes of transcatheter device closure of ostium secundum Atrial Septal Defect with moderate and severe pulmonary hypertension**”and have clarified any doubts that I had.

☐ I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment my legal rights.

☐ I understand that the study staff and institutional ethics committee members may be not need permission to look at my health records even if I withdraw consent from the study. I agree to this

☐ I understand that my identity may be not be revealed in any information released to third party published.

☐ I voluntarily agree to take part in this study.

☐ I received a copy of this signed consent form.

Signature of participant:

Date:

Signature of witness

Name of witness:

Date:

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

Name and Signature of Person obtaining consent:

Dr. Gurajala Venkatesh
Fellow in Paediatric cardiology (PDF),
Dept. of Cardiology, SCTIMST.

Date:

**SREE CHITRA THIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY,
TRIVANDRUM
DEPARTMENT OF CARDIOLOGY
PARENTAL CONSENT FORM FOR PATIENTS (≤ 12 yrs)**

Study Title: "Long term outcomes of transcatheter device closure of ostium secundum Atrial Septal Defect with moderate and severe pulmonary hypertension"

Participant's name:

Date of Birth / Age (in years):

I _____,
FATHER/MOTHER/LEGAL GUARDIAN of _____ (Please tick
boxes).

☐ I Declare that I have read the above information provide to me regarding the study "**Long term outcomes of transcatheter device closure of ostium secundum Atrial Septal Defect with moderate and severe pulmonary hypertension**" and have clarified any doubts that I had.

☐ I also understand that the participation of my child in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights.

☐ I understand that the study staff and institutional ethics committee members may be not need my permission to look at my child's health records even if I withdraw consent from the study. I agree to this access.

☐ I understand that my child's identity may be not be revealed in any information released to third parties or published.

☐ I voluntarily agree for my child to take part in this study.

☐ I received a copy of this signed consent form.

Name:

Signature of witness:

Signature:

Name of witness:

Date:

Date:

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

Name and Signature of Person obtaining consent:

Dr. Gurajala Venkatesh
Fellow in Paediatric cardiology (PDF),
Dept. of Cardiology, SCTIMST.

Date:

For any technical clarifications, please contact Dr. Mala Ramanathan, Member Secretary, IEC, SCTIMST and Professor, AMCHSS, SCTIMST (Email: iec.mem.sec@sctimst.ac.in, Phone no. 0471-2524234)



APPENDIX 4: CONSENT FORM- MALAYALAM

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസസ് ആന്റ് ടെക്നോളജി,

(SCTIMST) തിരുവനന്തപുരം-695011

കാർഡിയോളജി ഡിപ്പാർട്ട്മെന്റ്

രോഗിക്കുള്ള കാര്യവിവരണപത്രം

പഠനശീർഷകം

സാമാന്യമോ തീവ്രമോ ആയ പരീക്ഷണ രീതികളിലൂടെയും സാധാരണ ജനങ്ങളുടെയും സഹകരണത്തോടെയും സാധ്യമാകുന്നതാണ്. അതിനായി സാധ്യമായ എല്ലാ മാർഗ്ഗങ്ങളും സ്വീകരിക്കേണ്ടതാണ്.

ഗവേഷകരുടെ പേര്

ഡോ. ഗുർജാല വെങ്കിടേഷ്, ഡോ. കെ. എം. കൃഷ്ണമൂർത്തി, ഡോ. ദീപ ശശികുമാർ, ഡോ. അരുൺ ഗോപാലകൃഷ്ണൻ, ഡോ. ഹരി കൃഷ്ണൻ കെ. എൻ

പ്രിയ സുഹൃത്തേ,

സാമാന്യരോട് തീവ്രമോ ആയ പശ്ചാത്താപം രക്താതിസമ്മർദ്ദമുള്ള ഓസ്റ്റിയോ സൈക്ലൈറ്റിക് ഓസ്റ്റിയോ സൈക്ലൈറ്റിക് തകരാർ കത്തിറ്റിനുള്ളിലൂടെ ഉപകരണപരമായിട്ട് അടയ്ക്കുന്നതിന്റെ ദീർഘകാല നേട്ടം എന്ന പഠനത്തിൽ പങ്കെടുക്കാൻ താല്പര്യം എന്തെങ്കിലും ക്ലിനിക്കിനു.

ഈ പഠനത്തിൽ പങ്കെടുക്കുവാൻ സമ്മതിക്കുന്നതിനുമുമ്പ് ഈ ഗവേഷണം എന്തിനാണ് നടത്തുന്നതെന്ന് താങ്കൾ അറിയേണ്ടതുണ്ട്. ഈ പത്രിക അറിയേണ്ടുന്ന പ്രസക്തമായ എല്ലാ വിവരങ്ങളും നൽകുന്നു. പഠനത്തിന്റെ സമഗ്രം, ഉദ്ദേശം, നേട്ടങ്ങൾ, അപായങ്ങൾ, അസാധനതകൾ, മുൻകരുതലുകൾ എന്നെല്ലാമുണ്ട് ഈ പദ്ധതി നടപ്പിലാക്കുന്നത് മുതലായ വിവരങ്ങൾ ഈ കാര്യവിവരണപത്രം നൽകും. ഈ പത്രികയിലെ ഉള്ളടക്കം ശ്രദ്ധയോടെ വായിക്കുകയും മനസ്സിലാക്കുകയും ചെയ്യണം. സമ്മതം നൽകുന്നതിനുമുമ്പോ പഠനകാലയളവിലെപ്പോഴും താങ്കൾക്കെന്തെങ്കിലും ചോദ്യങ്ങളുണ്ടെങ്കിൽ അവ വിശദീകരിച്ചുതരുവാൻ ഗവേഷകനോടോ ബന്ധപ്പെടാൻ താങ്കൾക്ക് പേര് നൽകിയിരിക്കുന്നയാളോടോ ചോദിക്കാൻ താങ്കൾക്ക് സാധിക്കുമുണ്ട്.

ഈ പഠനം എന്തിനാണ്?

ഭരണികളിലെ എടിയൽ സെപ്റ്റൽ തകരാർ ഉപകരണമുപയോഗിച്ച് അടച്ചതിനുശേഷമുള്ള പരമനറി മഹാധമനിയുടെ മർദ്ദങ്ങളും വലത് വെൻട്രിക്കിൾ പ്രവർത്തനവും 2ഡി എക്കോകാർഡിയോഗ്രഫി ഉപയോഗിച്ച് വിലയിരുത്തുന്നതിനുവേണ്ടി.

താങ്കൾ പങ്കെടുക്കുകയാണെങ്കിൽ എന്തുചെയ്യണം?

താങ്കളുടെ രോഗത്തിന്റെ ലക്ഷണങ്ങൾ ഞങ്ങളോട് പറയുകയും താങ്കളുടെ വിവരങ്ങൾ (രോഗചരിത്രം, ക്ലിനിക്കൽ, എക്കോ പരിശോധനകളുടെ റിപ്പോർട്ടുകൾ) മെഡിക്കൽ രേഖകളിൽ നിന്നും ശേഖരിക്കാൻ അനുവദിക്കുകയും വേണം. താങ്കൾ ഇസിജിയും 2ഡി എക്കോയും ചെയ്യേണ്ടതാവശ്യമാണ്.

ഇതിനെത്ര സമയമെടുക്കും?

താങ്കളുടെ ഓഫീസി സന്ദർശനസമയത്ത് വിലയിരുത്തലിന് 15 മിനിട്ടും. ഇസിജി, 2ഡി എക്കോ എന്നിവയ്ക്ക് 15 മുതൽ 30 മിനിട്ടും വേണ്ടിവരും.

പരിശോധനകൾക്ക് താങ്കൾ പണം നൽകുന്നു?

ഈ പരിശോധനകളിൽ താങ്കളുടെ തുടർഭീകിസയുടെ ഭാഗമാണ്, ആ സമയത്ത് ആശുപത്രി തീരുമാനിക്കുന്ന, സാധാരണ രോഗികൾ നൽകേണ്ടുന്ന പണം നൽകണം.

ഈ പഠനത്തിൽ എന്തെങ്കിലും അപായമോ നേട്ടമോ ഉണ്ടോ?

ഈ പഠനത്തിൽ അപായങ്ങളൊന്നുമില്ല. ശരീരത്തിൽ പ്രവേശിക്കാതെയുള്ള സൂക്ഷ്മമായ പരിശോധനയാണ് എക്കോ കാർഡിയോഗ്രാഫി. വിലയിരുത്തൽ നടത്തുന്ന റിപ്പോർട്ടുകളിൽ എന്തെങ്കിലും അസാധാരണതാമുണ്ടെങ്കിൽ ആശുപത്രിയിലെ അംഗീകൃത നടപടിക്രമപ്രകാരമുള്ള ചികിത്സ താങ്കൾക്ക് ലഭിക്കും, അതിന്റെ ചിലവ് താങ്കൾ വഹിക്കണം, ആയത് പഠനത്തിന്റെ ഭാഗമല്ല.

പഠനമാരംഭിച്ചശേഷം താങ്കൾക്ക് പിൻമാറാനാകുമോ?

പഠനത്തിലെ താങ്കളുടെ പങ്കാളിത്തം സ്വമേധയാ ഉള്ളതും പങ്കെടുക്കുന്നതിൽ നിന്നും അനുവാദം പിൻവലിക്കാൻ താങ്കൾക്ക് സ്വാതന്ത്ര്യമുള്ളതുമാണ്. അങ്ങനെ ചെയ്യുന്നതുകൊണ്ട് താങ്കളുടെ പതിവ് ചികിത്സയെ ഒരു വിധത്തിലും ബാധിക്കില്ല.

പഠനം പൂർത്തിയായശേഷം എന്തുണ്ടാകും?

താങ്കളുടെ ഉപയോഗത്തിനായി 2ഡി എക്കോ റിപ്പോർട്ട് ലഭ്യമാകും, അത് താങ്കളുടെ ആശുപത്രി ഐഡിയിൽ ഇഎംആറിൽ സൂക്ഷിക്കും.

ഈ പഠനത്തിൽ പങ്കെടുക്കുന്നവർക്ക് പ്രതിഫലം ലഭിക്കുമോ?

ഈ പഠനത്തിൽ പങ്കെടുക്കുന്നതിന് പ്രതിഫലം നൽകില്ല.

താങ്കളുടെ വ്യക്തിവിവരങ്ങൾ രഹസ്യമായിരിക്കുമോ?

പഠനഫലങ്ങൾ പ്രസിദ്ധീകരണത്തിനോ പ്രദർശനത്തിനോ ഉപയോഗിക്കും. പക്ഷേ താങ്കളുടെ വ്യക്തിവിവരങ്ങൾ രഹസ്യമായി സൂക്ഷിക്കും, പഠനഫലങ്ങളുടെ പ്രസിദ്ധീകരണത്തിലോ പ്രദർശനത്തിലോ ഉപയോഗിക്കില്ല. എന്നിരുന്നാലും താങ്കൾ പഠനത്തിൽ പങ്കെടുക്കാൻ തീരുമാനിച്ചാൽ വീണ്ടുമുള്ള താങ്കളുടെ സമ്മതം കൂടാതെ താങ്കളുടെ ചികിത്സാരേഖകൾ ഈ പഠനവുമായി ബന്ധപ്പെട്ട ഗവേഷകർ അവലോകനം ചെയ്തേക്കാം.

താങ്കൾക്ക് കൂടുതലായി എന്തെങ്കിലും ചോദ്യങ്ങളുണ്ടെങ്കിൽ ദയവായി ബന്ധപ്പെടുക

പ്രധാന ഗവേഷകന്റെ പേര്. ഡോ ഗുർജാലാ വെങ്കിടേഷ്, പോസ്റ്റ് ഡോക്ടറൽ ഫെല്ലോ, പീഡിയാട്രിക് കാർഡിയോളജി, (ഫോൺ: 8884633567), ഇമെയിൽ drgvn7@gmail.com അല്ലെങ്കിൽ, drgvn7@sctimst.ac.in

മേൽവിലാസവും ബന്ധപ്പെടാനുള്ള വിവരങ്ങളും

പോസ്റ്റ് ഡോക്ടറൽ ഫെല്ലോ, പീഡിയാട്രിക് കാർഡിയോളജി, കാർഡിയോളജി ഡിപ്പാർട്ട്മെന്റ്,

ബന്ധപ്പെടാനുള്ള ഫോൺ നമ്പർ: +91-8884633567

പ്രധാന ഗവേഷകന്റെ ഒപ്പ്

തീയതി

പഠനത്തിന്റെ നൈതിക അനുവാദസംബന്ധമായ ബന്ധപ്പെട്ട വിശദീകരണങ്ങൾക്ക് ബന്ധപ്പെടുക: ഡോ. ശ്രീനിവാസ് ജി, മെമ്പർ സെക്രട്ടറി എത്തിക്സ് കമ്മിറ്റി SCTIMST, (ഫോൺ. 0471-2524689 ഇമെയിൽ. iec.mem.sec@sctimst.ac.in).

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസസ് ആൻ്റ് ടെക്നോളജി,
(SCTIMST) തിരുവനന്തപുരം-695011

കാർഡിയോളജി ഡിപ്പാർട്ട്മെൻ്റ്

മുതിർന്ന രോഗികളുടെ (≥ 18 വയസ്സ്) സമ്മതപത്രം

ഞാൻ.....(പങ്കെടുക്കുന്നയാളുടെ പേര്)
.....(ആശുപത്രി നമ്പർ)വയസ്സ്.....

(ദയവായി കോളങ്ങൾ അടയാളപ്പെടുത്തുക)

മുകളിൽ പറഞ്ഞ സാമാന്യമോ തീവ്രമോ ആയ പശ്ചാത്താപരഹിതമായ ഒരു ഓസ്റ്റിയോ സൈക്കിൾ ഓഫ് എക്സൈസ് സെപ്റ്റൽ തകരാർ കത്തിടുന്നതിനുള്ള ഉപകരണമുപയോഗിച്ച് അടയ്ക്കുന്നതിൻ്റെ ദീർഘകാല നേട്ടം എന്ന പഠന സംബന്ധമായ പങ്കെടുക്കുന്നവർക്കുള്ള കാര്യവിവരണപത്രം വായിച്ചതായി ഞാൻ സമ്മതിക്കുന്നു. ചോദ്യങ്ങൾ ചോദിക്കാൻ എനിക്ക് അവസരം ലഭിച്ചു. []

എൻ്റെ പങ്കാളിത്തം സ്വമേധയായാണെന്നും, കാരണമൊന്നും നൽകാതെയും എൻ്റെ വൈദ്യപരിചരണത്തെ ബാധിക്കാതെയും ഏതു സമയത്തും എനിക്ക് പിൻമാറ്റാൻ സ്വാതന്ത്ര്യമുണ്ടെന്നും മനസ്സിലാക്കുന്നു. []

രോഗചരിത്രം മറ്റ് ക്ലിനിക്കൽ വിശദാംശങ്ങൾ, ചിത്രീകരണ വിശദാംശങ്ങൾ (കാർഡിയാക് എംആർഐ) ഞാൻ വിധേയമാകുന്ന തുടർചികിത്സയിലെ ക്ലിനിക്കലും റേഡിയോളജിക്കലുമായ രോഗ സംബന്ധമായ വിവരങ്ങളും ചികിത്സയും എന്നിവയിലെ ചില വിവരങ്ങൾ ഗവേഷകർ ഉപയോഗിക്കുമെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. []

ഗവേഷണത്തിൻ്റെ ഭാഗമായി അധികചിലവോ, അധികം മരുന്നോ ഉണ്ടാകില്ലെന്നും അധികം അപായസാധ്യതയില്ലെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. []

ഞാൻ പഠനത്തിൽനിന്നും പിൻമാറിയാലും പഠനം നടത്തുന്നവർക്കും നൈതീകകമ്മിറ്റിക്കും എൻ്റെ കൂട്ടിയുടെ ആരോഗ്യരേഖകൾ പരിശോധിക്കാൻ എൻ്റെ സമ്മതം ആവശ്യമില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു, അതിന് ഞാൻ സമ്മതിക്കുന്നു. []

പഠനഫലമായി ശേഖരിച്ച വിവരങ്ങൾ പ്രസിദ്ധീകരിക്കുമ്പോഴോ മൂന്നാം കക്ഷികൾക്ക് നൽകുമ്പോഴോ എന്നെ യെ തിരിച്ചറിയാനിടയാകുന്നതൊന്നും വെളിപ്പെടുത്തുകയില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു. []

മുകളിൽ പറഞ്ഞ പഠനത്തിൽ പങ്കെടുക്കാൻ സ്വമേധയാ ഞാൻ സമ്മതിക്കുന്നു. []

സമ്മതപത്രത്തിൻ്റെ ഒപ്പിട്ട ഒരു പ്രതി എനിക്ക് ലഭിച്ചു. []

പേര്

ഒപ്പ്

തിയതി

സാക്ഷിയുടെ പേര്

ഒപ്പ്

തീയതി

സമ്മതപത്രം വാങ്ങുന്നയാളുടെ പ്രസ്താവന

മെഡിക്കൽ റിസർച്ച് പ്രോജക്ടിനാവശ്യമായ സമ്മതപത്രത്തിനു വേണ്ടുന്ന എല്ലാ ഘടകങ്ങളും തൃപ്തികരമായി നിർവഹിച്ചിരിക്കുന്നുവെന്ന് ഞാൻ ബോധ്യപ്പെടുത്തുന്നു. പഠനപങ്കാളിയുമായി ഗവേഷണ പദ്ധതിയെപ്പറ്റി സാങ്കേതികേതര പദങ്ങളുപയോഗിച്ച് എല്ലാ വിവരങ്ങളെപ്പറ്റിയും ചർച്ച നടത്തുകയും പ്രതീക്ഷിക്കാവുന്ന അപകട സാധ്യതകളും പാർശ്വഫലങ്ങളും വിശദീകരിക്കുകയും ചെയ്തു. പങ്കാളിയെചോദ്യങ്ങൾ ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും എല്ലാ ചോദ്യങ്ങൾക്കും ഉത്തരം നൽകുകയും ചെയ്തു എന്നും ഞാൻ സാക്ഷ്യപ്പെടുത്തുന്നു.

സമ്മതം വാങ്ങുന്നയാളുടെ പേര്

ഒപ്പ്

തീയതി

പ്രധാന ഗവേഷകന്റെ പേര്

ഡോ ഗുർജാലാ വെങ്കിടേഷ്, പോസ്റ്റ് ഡോക്ടറൽ ഫെല്ലോ, പീഡിയാട്രിക് കാർഡിയോളജി, (ഫോൺ: 8884633567), ഇമെയിൽ drgvn7@gmail.com അല്ലെങ്കിൽ, drgvn7@sctimst.ac.in

പ്രധാന ഗവേഷകന്റെ ഒപ്പ്

ഗവേഷണത്തിന്റെ നൈതിക അനുവാദത്തെപ്പറ്റി താങ്കൾക്ക് ചോദ്യങ്ങൾ, ഉണ്ടെങ്കിൽ ദയവായി ബന്ധപ്പെടുക:

ഡോ. ശ്രീനിവാസ് ജി, മെമ്പർ സെക്രട്ടറി, ഇൻസ്റ്റിറ്റ്യൂഷണൽ എത്തിക്സ് കമ്മിറ്റി

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസസ് ആന്റ് ടെക്നോളജി

ഫോൺ 0471- 2524689, ഇമെയിൽ: iec.mem.sec@sctimst.ac.in

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസസ് ആന്റ് ടെക്നോളജി,
(SCTIMST) തിരുവനന്തപുരം-695011

കാർഡിയോളജി ഡിപ്പാർട്ട്മെന്റ്

പഠനത്തിനുള്ള അനുവാദപത്രം (13 മുതൽ 17 വയസ്സ് പ്രായമുള്ളവരുടെ)

പഠനശീർഷകം

സാമാന്യമോ തീവ്രമോ ആയ പൾസസ് രക്താതിസമ്മർദ്ദമുള്ള ഓസ്ട്രിയൻ സെക്കൻഡറി എഡ്യൂക്കേഷൻ സെന്റർ തകരാർ കത്തിറ്റിനുള്ളിലൂടെ ഉപകരണമുപയോഗിച്ച് അടയ്ക്കുന്നതിന്റെ ദീർഘകാല നേട്ടം.

പങ്കെടുക്കുന്നയാളുടെ പേര് ജനനതീയതി/വയസ്സ് (വർഷത്തിൽ)

ഞാൻ..... അച്ഛൻ/അമ്മ/നിയമപരമായ രക്ഷകർത്താവ്
.....

(ദയവായി കോളങ്ങൾ അടയാളപ്പെടുത്തുക)

മുകളിൽ പറഞ്ഞ സാമാന്യമോ തീവ്രമോ ആയ പൾസസ് രക്താതിസമ്മർദ്ദമുള്ള ഓസ്ട്രിയൻ സെക്കൻഡറി എഡ്യൂക്കേഷൻ സെന്റർ തകരാർ കത്തിറ്റിനുള്ളിലൂടെ ഉപകരണമുപയോഗിച്ച് അടയ്ക്കുന്നതിന്റെ ദീർഘകാല നേട്ടം എന്ന പഠന സംബന്ധമായ പങ്കെടുക്കുന്നവർക്കുള്ള കാര്യവിവരണപത്രം വായിച്ചതായി ഞാൻ സമ്മതിക്കുന്നു. ചോദ്യങ്ങൾ ചോദിക്കാൻ എനിക്ക് അവസരം ലഭിച്ചു. []

എന്റെ കുട്ടിയുടെ പങ്കാളിത്തം സ്വമേധയായാണെന്നും, കാരണമൊന്നും നൽകാതെയും എന്റെ കുട്ടിയുടെ വൈദ്യപരിചരണത്തെ ബാധിക്കാതെയും ഏതു സമയത്തും എനിക്ക് പിൻമാറാൻ സ്വാതന്ത്ര്യമുണ്ടെന്നും മനസ്സിലാക്കുന്നു. []

രോഗചരിത്രം മറ്റ് ക്ലിനിക്കൽ വിശദാംശങ്ങൾ, ചിത്രീകരണ വിശദാംശങ്ങൾ (കാർഡിയാക് എംആർഐ) എന്റെ കുട്ടി വിധേയമാകുന്ന തുടർചികിത്സയിലെ ക്ലിനിക്കലും റേഡിയോളജിക്കലുമായ രോഗ സംബന്ധമായ വിവരങ്ങളും ചികിത്സയും എന്നിവയിലെ ചില വിവരങ്ങൾ ഗവേഷകർ ഉപയോഗിക്കുമെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. []

ഗവേഷണത്തിന്റെ ഭാഗമായി അധികചിലവോ, അധികം മരുന്നോ ഉണ്ടാകില്ലെന്നും അധികം അപായസാധ്യതയില്ലെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. []

എന്റെ കുട്ടി പഠനത്തിൽനിന്നും പിൻമാറിയാലും പഠനം നടത്തുന്നവർക്കും നൈതീകകമ്മിറ്റിക്കും എന്റെ കുട്ടിയുടെ ആരോഗ്യരേഖകൾ പരിശോധിക്കാൻ എന്റെ സമ്മതം ആവശ്യമില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു, അതിന് ഞാൻ സമ്മതിക്കുന്നു. []

പഠനഫലമായി ശേഖരിച്ച വിവരങ്ങൾ പ്രസിദ്ധീകരിക്കുമ്പോഴോ മൂന്നാം കക്ഷികൾക്ക് നൽകുമ്പോഴോ എന്റെ കുട്ടിയെ തിരിച്ചറിയാനടയ്ക്കുന്നതൊന്നും വെളിപ്പെടുത്തുകയില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു. []

മുകളിൽ പറഞ്ഞ പഠനത്തിൽ പങ്കെടുക്കാൻ സ്വമേധയാ ഞാൻ സമ്മതിക്കുന്നു. []

സമ്മതപത്രത്തിന്റെ ഒപ്പിട്ട ഒരു പ്രതി എനിക്ക് ലഭിച്ചു. []

പേര്

ഒപ്പ്

തീയതി

സാക്ഷിയുടെ പേര്

ഒപ്പ്

തീയതി

സമ്മതപത്രം വാങ്ങുന്നയാളുടെ പ്രസ്താവന

മെഡിക്കൽ റിസർച്ച് പ്രോജക്ടിനാവശ്യമായ സമ്മതപത്രത്തിനു വേണ്ടുന്ന എല്ലാ ഘടകങ്ങളും തൃപ്തികരമായി നിർവഹിച്ചിരിക്കുന്നുവെന്ന് ഞാൻ ബോധ്യപ്പെടുത്തുന്നു. പഠനപങ്കാളിയുമായി ഗവേഷണ പദ്ധതിയെപ്പറ്റി സാങ്കേതികേതര പദങ്ങളുപയോഗിച്ച് എല്ലാ വിവരങ്ങളെപ്പറ്റിയും ചർച്ച നടത്തുകയും പ്രതീക്ഷിക്കാവുന്ന അപകട സാധ്യതകളും പാർശ്വഫലങ്ങളും വിശദീകരിക്കുകയും ചെയ്തു. പങ്കാളിയെചോദ്യങ്ങൾ ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും എല്ലാ ചോദ്യങ്ങൾക്കും ഉത്തരം നൽകുകയും ചെയ്തു എന്നും ഞാൻ സാക്ഷ്യപ്പെടുത്തുന്നു.

സമ്മതം വാങ്ങുന്നയാളുടെ പേര്

ഒപ്പ്

തീയതി

പ്രധാന ഗവേഷകന്റെ പേര്

ഡോ ഗുർജാലാ വെങ്കിടേഷ്, പോസ്റ്റ് ഡോക്ടറൽ ഫെല്ലോ, പീഡിയാട്രിക് കാർഡിയോളജി, (ഫോൺ: 8884633567), ഇമെയിൽ drgvn7@gmail.com അല്ലെങ്കിൽ, drgvn7@sctimst.ac.in

പ്രധാന ഗവേഷകന്റെ ഒപ്പ്

ഗവേഷണത്തിന്റെ നൈതിക അനുവാദത്തെപ്പറ്റി താങ്കൾക്ക് ചോദ്യങ്ങൾ, ഉണ്ടെങ്കിൽ ദയവായി ബന്ധപ്പെടുക:

ഡോ. ശ്രീനിവാസ് ജി, മെമ്പർ സെക്രട്ടറി, ഇൻസ്റ്റിറ്റ്യൂഷണൽ എത്തിക്സ് കമ്മിറ്റി
ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസസ് ആന്റ് ടെക്നോളജി

ഫോൺ 0471- 2524689, ഇമെയിൽ: iec.mem.sec@sctimst.ac.in

പങ്കെടുക്കുന്നയാൾ

ഞാൻ.....(പങ്കെടുക്കുന്നയാളുടെ പേര്)

.....(ആശുപത്രി നമ്പർ)വയസ്സ്.....

(ദയവായി കോളങ്ങൾ അടയാളപ്പെടുത്തുക)

മുകളിൽ പറഞ്ഞ സാമാന്യമോ തീവ്രമോ ആയ പശ്ചാത്താപരഹിതമായ രക്താതിസമ്മർദ്ദമുള്ള ഓസ്റ്റിയോ സെക്കണ്ട്രിയം എട്രിയൽ സെപ്റ്റൽ തകരാർ കത്തിറ്റിനുള്ളിലൂടെ ഉപകരണമുപയോഗിച്ച് അടയ്ക്കുന്നതിന്റെ ദീർഘകാല നേട്ടം എന്ന പഠന സംബന്ധമായ പങ്കെടുക്കുന്നവർക്കുള്ള

കാര്യവിവരണപത്രം വായിച്ചതായി ഞാൻ സമ്മതിക്കുന്നു. ചോദ്യങ്ങൾ ചോദിക്കാൻ എനിക്ക് അവസരം ലഭിച്ചു []

എന്റെപങ്കാളിത്തം സ്വമേധയായാണെന്നും, കാരണമൊന്നും നൽകാതെയും എന്റെ വൈദ്യപരിചരണത്തെ ബാധിക്കാതെയും ഏതു സമയത്തും എനിക്ക് പിൻമാറാൻ സ്വാതന്ത്ര്യമുണ്ടെന്നും മനസ്സിലാക്കുന്നു. []

രോഗചരിത്രം മറ്റ് ക്ലിനിക്കൽ വിശദാംശങ്ങൾ, ചിത്രീകരണ വിശദാംശങ്ങൾ (കാർഡിയാക് എംആർഐ) ഞാൻ വിധേയമാകുന്ന തുടർചികിത്സയിലെ ക്ലിനിക്കലും റേഡിയോളജിക്കലുമായ രോഗ സംബന്ധമായ വിവരങ്ങളും ചികിത്സയും എന്നിവയിലെ ചില വിവരങ്ങൾ ഗവേഷകർ ഉപയോഗിക്കുമെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. []

ഗവേഷണത്തിന്റെ ഭാഗമായി അധികചിലവോ, അധികം മരുന്നോ ഉണ്ടാകില്ലെന്നും അധികം അപായസാധ്യതയില്ലെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. []

ഞാൻ പഠനത്തിൽനിന്നും പിൻമാറിയാലും പഠനം നടത്തുന്നവർക്കും നൈതീകകമ്മിറ്റിക്കും എന്റെ കൂട്ടിയുടെ ആരോഗ്യരേഖകൾ പരിശോധിക്കാൻ എന്റെ സമ്മതം ആവശ്യമില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു, അതിന് ഞാൻ സമ്മതിക്കുന്നു. []

പഠനഫലമായി ശേഖരിച്ച വിവരങ്ങൾ പ്രസിദ്ധീകരിക്കുമ്പോഴോ മൂന്നാം കക്ഷികൾക്ക് നൽകുമ്പോഴോ എന്നെ യെ തിരിച്ചറിയാനിടയാകുന്നതൊന്നും വെളിപ്പെടുത്തുകയില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു. []

മുകളിൽ പറഞ്ഞ പഠനത്തിൽ പങ്കെടുക്കാൻ സ്വമേധയാ ഞാൻ സമ്മതിക്കുന്നു. []

സമ്മതപത്രത്തിന്റെ ഒപ്പിട്ട ഒരു പ്രതി എനിക്ക് ലഭിച്ചു. []

പേര്

ഒപ്പ്

തീയതി

സാക്ഷിയുടെ പേര്

ഒപ്പ്

തീയതി

സമ്മതപത്രം വാങ്ങുന്നയാളുടെ പ്രസ്താവന

മെഡിക്കൽ റിസർച്ച് പ്രോജക്ടിനാവശ്യമായ സമ്മതപത്രത്തിനു വേണ്ടുന്ന എല്ലാ ഘടകങ്ങളും തൃപ്തികരമായി നിർവഹിച്ചിരിക്കുന്നുവെന്ന് ഞാൻ ബോധ്യപ്പെടുത്തുന്നു. പഠനപങ്കാളിയുമായി ഗവേഷണ പദ്ധതിയെപ്പറ്റി സാങ്കേതികേതര പദങ്ങളുപയോഗിച്ച് എല്ലാ വിവരങ്ങളെപ്പറ്റിയും ചർച്ച നടത്തുകയും പ്രതീക്ഷിക്കാവുന്ന അപകട സാധ്യതകളും പാർശ്വഫലങ്ങളും വിശദീകരിക്കുകയും ചെയ്തു. പങ്കാളിയെചോദ്യങ്ങൾ ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും എല്ലാ ചോദ്യങ്ങൾക്കും ഉത്തരം നൽകുകയും ചെയ്തു എന്നും ഞാൻ സാക്ഷ്യപ്പെടുത്തുന്നു.

സമ്മതം വാങ്ങുന്നയാളുടെ പേര്

ഒപ്പ്

തീയതി

പ്രധാന ഗവേഷകന്റെ പേര്

ഡോ ഗുർജാലാ വെങ്കിടേഷ്, പോസ്റ്റ് ഡോക്ടറൽ ഫെല്ലോ, പീഡിയാട്രിക് കാർഡിയോളജി, (ഫോൺ: 8884633567), ഇമെയിൽ drgvn7@gmail.com അല്ലെങ്കിൽ, drgvn7@sctimst.ac.in

പ്രധാന ഗവേഷകന്റെ ഒപ്പ്

ഗവേഷണത്തിന്റെ നൈതിക അനുവാദത്തെപ്പറ്റി താങ്കൾക്ക് ചോദ്യങ്ങൾ, ഉണ്ടെങ്കിൽ ദയവായി ബന്ധപ്പെടുക:

ഡോ. ശ്രീനിവാസ് ജി, മെമ്പർ സെക്രട്ടറി, ഇൻസ്റ്റിറ്റ്യൂഷണൽ എത്തിക്സ് കമ്മിറ്റി

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസസ് ആന്റ് ടെക്നോളജി

ഫോൺ 0471- 2524689, ഇമെയിൽ: iec.mem.sec@sctimst.ac.in

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസ് ആന്റ് ടെക്നോളജി,
(SCTIMST) തിരുവനന്തപുരം-695011

കാർഡിയോളജി ഡിപ്പാർട്ട്മെന്റ്

പഠനത്തിനുള്ള രക്ഷകർത്താക്കളുടെ (<12 വയസ്സ്) അനുവാദപത്രം

പഠനശീർഷകം

സാമാന്യമോ തീവ്രമോ ആയ പശ്ചാത്താപ രക്താതിസമ്മർദ്ദമുള്ള ഓസ്റ്റിയം സെക്കണ്ട്രിയം എട്രിയൽ സെപ്റ്റൽ തകരാർ കത്തിറ്ററിനുള്ളിലൂടെ ഉപകരണമുപയോഗിച്ച് അടയ്ക്കുന്നതിന്റെ ദീർഘകാല നേട്ടം.

ഞാൻ..... അച്ഛൻ/അമ്മ/നിയമപരമായ രക്ഷകർത്താവ്
.....

(ദയവായി കോളങ്ങൾ അടയാളപ്പെടുത്തുക)

മുകളിൽ പറഞ്ഞ സാമാന്യമോ തീവ്രമോ ആയ പശ്ചാത്താപ രക്താതിസമ്മർദ്ദമുള്ള ഓസ്റ്റിയം സെക്കണ്ട്രിയം എട്രിയൽ സെപ്റ്റൽ തകരാർ കത്തിറ്ററിനുള്ളിലൂടെ ഉപകരണമുപയോഗിച്ച് അടയ്ക്കുന്നതിന്റെ ദീർഘകാല നേട്ടം എന്ന പഠന സംബന്ധമായ പങ്കെടുക്കുന്നവർക്കുള്ള കാര്യവിവരണപത്രം വായിച്ചതായി ഞാൻ സമ്മതിക്കുന്നു. ചോദ്യങ്ങൾ ചോദിക്കാൻ എനിക്ക് അവസരം ലഭിച്ചു. []

എന്റെ കുട്ടിയുടെ പങ്കാളിത്തം സ്വമേധയായാണെന്നും, കാരണമൊന്നും നൽകാതെയും എന്റെ കുട്ടിയുടെ വൈദ്യപരിചരണത്തെ ബാധിക്കാതെയും ഏതു സമയത്തും എനിക്ക് പിൻമാറാൻ സാതന്ത്ര്യമുണ്ടെന്നും മനസ്സിലാക്കുന്നു. []

രോഗചരിത്രം മറ്റ് ക്ലിനിക്കൽ വിശദാംശങ്ങൾ, ചിത്രീകരണ വിശദാംശങ്ങൾ (കാർഡിയാക് എംആർഐ) എന്റെ കുട്ടി വിധേയമാകുന്ന തുടർചികിത്സയിലെ ക്ലിനിക്കലും റേഡിയോളജിക്കലുമായ രോഗ സംബന്ധമായ വിവരങ്ങളും ചികിത്സയും എന്നിവയിലെ ചില വിവരങ്ങൾ ഗവേഷകർ ഉപയോഗിക്കുമെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. []

ഗവേഷണത്തിന്റെ ഭാഗമായി അധികചിലവോ, അധികം മരുന്നോ ഉണ്ടാകില്ലെന്നും അധികം അപായസാധ്യതയില്ലെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. []

എന്റെ കുട്ടി പഠനത്തിൽനിന്നും പിൻമാറിയാലും പഠനം നടത്തുന്നവർക്കും നൈതീകകമ്മിറ്റിക്കും എന്റെ കുട്ടിയുടെ ആരോഗ്യരേഖകൾ പരിശോധിക്കാൻ എന്റെ സമ്മതം ആവശ്യമില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു, അതിന് ഞാൻ സമ്മതിക്കുന്നു. []

പഠനഫലമായി ശേഖരിച്ച വിവരങ്ങൾ പ്രസിദ്ധീകരിക്കുമ്പോഴോ മൂന്നാം കക്ഷികൾക്ക് നൽകുമ്പോഴോ എന്റെ കുട്ടിയെ തിരിച്ചറിയാനിടയാകുന്നതൊന്നും വെളിപ്പെടുത്തുകയില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു. []

മുകളിൽ പറഞ്ഞ പഠനത്തിൽ പങ്കെടുക്കാൻ സ്വമേധയാ ഞാൻ സമ്മതിക്കുന്നു. []

സമ്മതപത്രത്തിന്റെ ഒപ്പിട്ട ഒരു പ്രതി എനിക്ക് ലഭിച്ചു. []

പേര്

ഒപ്പ്

തിയതി

സാക്ഷിയുടെ പേര്

ഒപ്പ്

തിയതി

സമ്മതപത്രം വാങ്ങുന്നയാളുടെ പ്രസ്താവന

മെഡിക്കൽ റിസർച്ച് പ്രോജക്ടിനാവശ്യമായ സമ്മതപത്രത്തിനു വേണ്ടുന്ന എല്ലാ ഘടകങ്ങളും തൃപ്തികരമായി നിർവ്വഹിച്ചിരിക്കുന്നുവെന്ന് ഞാൻ ബോധ്യപ്പെടുത്തുന്നു. പഠനപങ്കാളിയുമായി ഗവേഷണ പദ്ധതിയെപ്പറ്റി സാങ്കേതികേതര പദങ്ങളുപയോഗിച്ച് എല്ലാ വിവരങ്ങളെപ്പറ്റിയും ചർച്ച നടത്തുകയും പ്രതീക്ഷിക്കാവുന്ന അപകട സാധ്യതകളും പാർശ്വഫലങ്ങളും വിശദീകരിക്കുകയും ചെയ്തു. പങ്കാളിയെചോദ്യങ്ങൾ ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും എല്ലാ ചോദ്യങ്ങൾക്കും ഉത്തരം നൽകുകയും ചെയ്തു എന്നും ഞാൻ സാക്ഷ്യപ്പെടുത്തുന്നു.

സമ്മതം വാങ്ങുന്നയാളുടെ പേര്

ഒപ്പ്

തീയതി

പ്രധാന ഗവേഷകന്റെ പേര്

ഡോ. ഗുർജാലാ വെങ്കിടേഷ്, പോസ്റ്റ് ഡോക്ടറൽ ഫെല്ലോ, പീഡിയാട്രിക് കാർഡിയോളജി, (ഫോൺ:

8884633567), ഇമെയിൽ drgvn7@gmail.com അല്ലെങ്കിൽ, drgvn7@sctimst.ac.in

പ്രധാന ഗവേഷകന്റെ ഒപ്പ്

ഗവേഷണത്തിന്റെ നൈതീക അനുവാദത്തെപ്പറ്റി താങ്കൾക്ക് ചോദ്യങ്ങൾ, ഉണ്ടെങ്കിൽ ദയവായി ബന്ധപ്പെടുക:

ഡോ. ശ്രീനിവാസ് ജി, മെമ്പർ സെക്രട്ടറി, ഇൻസ്റ്റിറ്റ്യൂഷണൽ എത്തിക്സ് കമ്മിറ്റി

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസസ് ആന്റ് ടെക്നോളജി

ഫോൺ 0471- 2524689, ഇമെയിൽ: iec.mem.sec@sctimst.ac.in

APPENDIX 5: PLAGIARISM CHECK



Report: Dr. GURAJALA VENKATESH thesis Long term outcomes of transcatheter device clos...

Dr. GURAJALA VENKATESH thesis Long term outcomes of transcatheter device closure of ostium Secundum Atrial Septal Defect w

by harsh pandey

General metrics

81,734	13,316	1037	53 min 15 sec	1 hr 42 min
characters	words	sentences	reading time	speaking time

Score

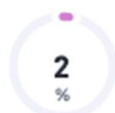


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Issues left	Critical	Advanced

Plagiarism



33
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