“The Effect of Atrial Septal Defect Closure on Cardiac Volumetric Changes in Adults, Transcatheter Versus Surgical Closure, and the Outcome of Tricuspid Regurgitation, a Pilot Cmr Study”

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Abstract

Background

Closure of an atrial septal defect (ASD) reduces right heart volumes by eliminating shunting while improving left ventricle (LV) filling and function due to ventricular interdependence, thereby improving symptoms. Furthermore, studies on atrial volume changes following ASD closure are paucity. Functional tricuspid regurgitation (TR) is frequently seen in adult patients with ASD as a consequence of right ventricle (RV) dilatation. Cardiac magnetic resonance (CMR) is widely accepted as the gold standard method for measuring cardiac volume and mass.

Objective

We aimed at studying the cardiac volumetric changes preclosure and 6 months after transcatheter and surgical closure, as well as fate of TR, using CMR analysis.

Methods

We prospectively enrolled 30 adult patients with isolated secundum ASD who were referred for ASD closure. CMR evaluates the right and left atrial volumes, as well as the ventricular end diastolic and end systolic volume indexes (EDVI and ESVI), function, the mass index, and tricuspid regurgitant fraction.

Results

RV volumes decreased in both groups when compared to baseline (P value 0.001), with the device group experiencing more reduction in volumes and improvement in RV function after closure (P 0.001). In each group, the absolute value of RV mass decreased significantly from the baseline (P value (0.001)), but with no difference between groups (P value 0.31). Improvement in functional TR occurred in both groups.

LVEDVI increased significantly in both groups (P values 0.001 and 0.005, respectively), with a significant improvement in the LV mass index (P value = 0.01) and a non-significant difference in LVESVI. Only device closure resulted in an improvement in LV function (63.53 ± 3.85 versus 67.13 ± 4.34, P value =0.01). There was a significant reduction in right atrial (RA) volume (P value = 0.5), with a trend to decrease in left atrial (LA) volume but it was insignificant, with no difference between groups.

Conclusion

Our findings revealed that both procedures resulted in normalization of ventricular volume and reduction of RA volumes, with only the device group showing improvement in ventricular function. Functional TR improved after closure with either a device or a surgical approach.

Background

ASD is the most common congenital heart disease diagnosed in adults [1]. Long-term exposure causes chronic right heart volume overload, which results in RV dilatation and, as a result, pulmonary hypertension and right heart failure due to increased pulmonary flow [2]. Following the elimination of the shunt, ASD closure causes mechanical reverse remodeling [3]. Transcatheter ASD closure has proven to be a cost-effective alternative to secundum ASD closure, avoiding the complications of surgical closure [4]. Functional TR is a common but frequently overlooked condition in clinical practice [5]. Functional TR occurs frequently in adult patients with ASD due to prolonged volume or pressure overload from a long-standing left to right interatrial shunt [6]. CMR is used to precisely quantify shunts, ventricular volumes, and function due to its multiplanar imaging capabilities [7].

Aim:

We aimed at studying the cardiac volumetric changes preclosure and 6 months after transcatheter and surgical closure, as well as fate of TR, using CMR analysis.

Methods

Our institutional and local review boards approved this study, and all patients enrolled in it provided written informed consent. 30 patients with isolated secundum ASD were included in the study, 15 of whom had successful transcatheter ASD device closure and 15 had surgical closure. CMR was performed on all patients prior to and 6 months after the ASD closure.

Patients with secundum ASD, RV volume overload, and/or a QP/QS ratio greater than 1.5 were included in the study. Patients with secundum ASD and associated coronary artery disease, patients with pulmonary vascular resistance (PVR) > 5woods units, and patients with anomalous pulmonary venous return were excluded.

Patients who had evidence of elevated pulmonary artery pressure or whose non-invasive pulmonary artery pressure assessment was inconclusive underwent an invasive haemodynamic study as well as pulmonary vascular resistance assessment.

Transthoracic (TTE) or transoesophageal (TEE) echocardiography:

TTE and TEE were used to evaluate the size of the ASD, its rims, and to rule out any anomalous pulmonary venous drainage [8].

The mean pulmonary artery pressure (mPAP) and right ventricular systolic pressure (RVSP) were calculated using the modified Bernoli equation after applying a continuous wave doppler to the regurgitation jet after it had been properly aligned [9].

Cardiac magnetic resonance assessment:

All CMR studies were conducted with subjects lying supine, head first. Scanning was performed with ECG gating during the end-expiratory breath-holding phase on a 1.5 Tesla MRI scanner (Ingenia Philips).

ECG gated sequences of Steady-State Precession (SSFP) were obtained retrospectively (image matrix 256 x150, field of view 380 mm, repetition time 52.05 ms, echo time 1.74 ms, and flip angle 70°) [10].

• Volumetric measurement:

The ventricular image set consisted of a stack of cine SSFP images acquired in a short axis view from the mitral valve level to the left ventricular apex with 8 to 12 slice thickness, and measurements were indexed to the patient's body surface area (BSA) [11].

The ventricular volumes were examined on a slice-by-slice basis, with the endocardial and epicardial borders manually contoured. The Simpson's method was used to calculate volumes [12].The trabeculations and papillary muscles were included in the ventricular volume [13].

• Main pulmonary artery (MPA)area

To obtain a cross-section of the MPA, an oblique cine acquisition was located immediately distal to its Sino-tubular junction [14].

• Atrial measurement

RA measurements: The biplane area-length method was used to calculate the maximum volume of the RA in the 4 -chamber and right 2-chamber SSFP image views (during ventricular systole and was defined as last cine image before opening of the tricuspid valve). The atrial appendage was included, but the cava veins were not [15].

LA measurements: The LA maximal volume was measured using bi-plane area-length manually drawn endocardial contours in 2- and 4-ch SSPS cine images, with the left atrial appendage and pulmonary veins excluded, at the end of the systolic phase of the left ventricle before the mitral valve opened [15].

• Shunt fraction assessment (QP/QS)

Using phase contrast MRI sequences, the cardiac output (CO) is calculated. Usually, the contrast phase (PC) sequence is planned in the PA trunk and aortic root. Two orthogonal locating planes were used for adequate cut plane planning [16].

• TR severity assessment:

We calculated TR severity using CMR by measuring the regurgitant fraction[17].The tricuspid regurgitant fraction is calculated by dividing the tricuspid regurgitant volume (RVol) by the right ventricle stroke volume (RV SV) and multiplying the result by 100[18]. RVol was calculated as total RV SV minus forward SV across the pulmonary valve, with forward SV measured by pulmonic valve PC imaging (in the absence of significant PR) [17]. The severity of regurgitation was graded as (i.e., a regurgitant fraction of ≤ 15% for mild TR; 16–25% for moderate TR; 26–48% for moderately severe; and > 48% for severe TR)[17] .

Tricuspid annular diameter (TAD) was calculated as the maximum diameter of the tricuspid annulus in four chamber cine gradient echo sequences[19].

Atrial septal defect closure:

Patients with defects that were not suitable for transcatheter closure (due to inadequate rims) underwent surgical closure using the patch technique.

When the rims were adequate, percutaneous transcatheter ASD closure was performed under general anaesthesia with fluoroscopic and TEE guidance. In every case, heparin (100 IU/kg) was administered. To avoid oversizing, the diameter of the defect was measured with a 24- or 34-mm sizing balloon (AGA Medical Corp). The Amplatzer septal occluder (ASO) device was used for the procedure, and its sizes ranged from (11–38 mm).

Statistical Analysis:

SPSS was used to collect and analyse data (Statistical Package for Social Science, version 25, IBM, and Armonk, New York). Continuous data was expressed as mean, whereas nominal data was expressed as frequency and percentage.

The Chi2 test was used to compare nominal data from different groups, and the Mann Whitney test was used to compare continuous data from both groups. The Wilcoxon test was used to compare baseline and follow-up data from the same group. The percentage of change between baseline and follow up data was calculated using the following equation: percentage of change = ((follow up-baseline data)/baseline 142 data)) * 100. The level of confidence was kept at 95%, and thus the P value was considered significant if < 0.05.

Results

Demographic and clinical data of the study groups:

In both groups, the majority of patients (66.7 %) were females under the age of 40. The mean age of patients underwent device closure was 33.73 ± 13.06 years while mean age of those underwent surgical closure was 35.33 ± 15.18 years with insignificant difference between both groups (*P* = 0.75), Table 1.

Table 1
demographic date of studied patients:

	Group 1 (Device closure) (n = 15)	Group 2 (Surgical closure) (n = 15)	*P* value
Age (years)	33.73 ± 13.06	35.33 ± 15.18	0.75
Sex Female Male	10 (66.7%) 5 (33.3%)	10 (66.7%) 5 (33.3%)	0.65
BMI (Kg/m^2)	24.78 ± 2.94	24.44 ± 4.02	0.79
Heart rate (bpm)	92 ± 10.14	93 ± 9.59	0.78
Data expressed as frequency (percentage), mean (SD). *P* value was significant if < 0.05.			

Thirteen (86.7%) and twelve (80%) patients with baseline New York Heart Association (NYHA) class II underwent device and surgical closure, respectively, and the majority of patients in both groups had NYHA class I after closure. There were no significant differences in HR or BMI between the two groups.

TTE measures:

Both groups showed a significant reduction in mPAP after closure, with the device group showing a greater reduction than the surgical group (18.13 ± 7.21 vs. 23.93 ± 6.63(mmHg)); P = 0.03, Table 2.

Table 2
PAP and shunt fraction (QP/QS) in both groups:

	Device closure (n = 15)	Surgical closure (n = 15)	*P* value
PAP (mmHg)	27.93 ± 5.18	30.67 ± 5.30	0.16
Baseline	18.13 ± 7.21	23.93 ± 6.63	0.03
Post-closure	2.03 ± 0.25	2.23 ± 0.40	0.11
QP/QS ratio	0.95 ± 0.13	1.04 ± 0.09	0.04
Before closure			
After closure			
Data expressed as frequency (percentage), mean (SD). *P* value was significant if < 0.05.			
PAP: pulmonary artery pressure, QP\QS: shunt fraction			

CMR measures:

There were no significant differences in the baseline QP/QS ratio between the two groups; shunt fraction was significantly reduced in both groups, but significantly lower in patients who underwent device closure (0.95 ± 0.13 vs. 1.04 ± 0.09; $P = 0.04$), Table 2.

RVEDVI and RVESVI showed significant changes from baseline measurements after ASD closure in both groups. When the two groups were compared, there was a significant difference, with the transcatheter arm showing more reduction (P value 0.05), Table 3.

Table 3
Parameters of PA, RV and LV in comparison among two groups:

	Group 1 (Device closure) (n = 15)	Group 2 (surgical closure) (n = 15)	P value
PA maximum area (mm)	10.22 ± 1.52	10.96 ± 4.01	0.51
Before closure	7.90 ± 1.62	7.88 ± 2.62	0.98
After closure	(-) 22.76 ± 10.96	(-) 27 ± 9.55	0.26
Percentage of change	133.33 ± 25.26	152.33 ± 52.36	0.21
RV-EDV (ml/mm^2)	87.10 ± 14.08	106.60 ± 31.21	0.03
Before closure	(-) 32.60 ± 13.55	(-) 27.20 ± 15.07	0.31
After closure			
Percentage of change			
RV-ESV (ml)	51.63 ± 11.31	69.20 ± 33.81	0.06
Before closure	35.52 ± 8.24	50.67 ± 23.90	0.02
After closure	(-) 29.33 ± 15.37	(-) 21.86 ± 23.99	0.31
Percentage of change			
RV function (%)	56.93 ± 4.38	56.33 ± 8.72	0.81
Before closure	60.67 ± 5.12	52.73 ± 8.62	< 0.001
After closure	6.64 ± 5.85	(-) 6.22 ± 3.19	< 0.001
Percentage of change			
RV mass (mm)	37.53 ± 5.02	39.35 ± 8.71	0.48
Before closure	29.78 ± 5.46	32.29 ± 7.82	0.31
After closure	(-) 20.38 ± 10.80	(-) 16.63 ± 14.91	0.43
Percentage of change			
LV-EDV (ml/mm^2)	**77.20 ± 12.23**	**72.40 ± 16.19**	**0.36**
Before closure	**83.42 ± 11.65**	**80.30 ± 18.03**	**0.57**
After closure	**8.64 ± 7.80**	**11.17 ± 9.83**	**0.44**
Percentage of change			

Data expressed mean (SD). *P* value was significant if < 0.05. PA: Pulmonary artery, RV: right ventricle; EDV: end-diastolic volume; ESV: end-systolic volume, LV: Left ventricle.

	Group 1 (Device closure) (n = 15)	Group 2 (surgical closure) (n = 15)	P value
LV-ESV (ml)	26.79 ± 5.29	27.05 ± 7.94	0.91
Before closure	28.28 ± 5.02	30.70 ± 8.52	0.35
After closure	3.01 ± 1.94	5.70 ± 2.34	0.06
Percentage of change			
LV function (%)	63.53 ± 3.85	62.86 ± 5.55	0.70
Before closure	67.13 ± 4.34	62 ± 6.18	0.01
After closure	5.66 ± 2.37	(-) 1.30 ± 1.01	< 0.001
Percentage of change			
LV mass (mm)	42.86 ± 7.02	45.46 ± 9.59	0.40
Before closure	45.50 ± 7.20	49.48 ± 10.93	0.24
After closure	6.39 ± 5.15	9.87 ± 6.91	0.38
Percentage of change			

Data expressed mean (SD). *P* value was significant if < 0.05. PA: Pulmonary artery, RV: right ventricle; EDV: end-diastolic volume; ESV: end-systolic volume, LV: Left ventricle.

Table 4
Parameters of atrium among studied patients-based type of closure

	Device closure (n = 15)	Surgical closure (n = 15)	*P* value
RA maximum area (mm)	74.53 ± 23.98	81.90 ± 30.07	0.46
Before closure	46.88 ± 12.77	55.38 ± 18.03	0.14
After closure	(-) 34.38 ± 17.47	(-) 30.15 ± 17.11	0.50
Percentage of change	99.23 ± 24.20	90.13 ± 33.81	0.40
LA maximum area (mm)	92.33 ± 25.51	82.30 ± 29.72	0.33
Before closure	(-) 6.27 ± 7.61	(-) 7.69 ± 4.48	0.73
After closure			
Percentage of change			

Data expressed mean (SD). *P* value was significant if < 0.05. RA: right atrium, LA : left atrium

The absolute value of RV mass indexed decreased significantly in each group from the baseline (P = 0.001), but the difference between the two groups was statistically insignificant (P value 0.31). RV function only improved after device closure, in contrast to surgical closure, which resulted in function reduction, Table 3 .

LVEDVI and LV mass index increased significantly after closure in both groups, but there were no significant changes in LVESVI, and LV function only improved in the device group, Table 3.

In our study, there was a reduction in MPA maximal area after ASD closure, with a statistically insignificant difference between groups, Table 3.

Both groups experienced a significant reduction in RA volumes 6 months after ASD closure. There was a trend toward reduction in LA volumes following ASD closure, but it did not reach statistical significance in either group. With no difference between both groups, Table 5.

Table 5
Characteristics of TR among patients based on type of closure:

	Device closure (n = 15)	Surgical closure (n = 15)	*P* value
TR regurgitant volume (ml)	26.40 ± 20.77	28.20 ± 16.56	0.79
Baseline	16.13 ± 13.07	18.53 ± 16.73	0.66
Post-closure	22.30 ± 16.50	20.46 ± 14.04	0.74
TR regurgitant fraction (%)	17.20 ± 13.45	19 ± 12.29	0.70
Baseline	(-) 19.18 ± 9.28	(-) 18.89 ± 11.01	0.12
Post-closure	7 (46.7%)	7 (46.7%)	0.81
Percentage of change	6 (40%)	7 (56.7%)	0.63
Class	2 (13.3%)	1 (6.7%)	
Baseline	9 (60%)	7 (46.7%)	
Mild	2 (13.3%)	4 (26.7%)	
Moderate/severe	4 (26.7%)	4 (26.7%)	
Severe			
Post-closure			
Mild			
Moderate			
Moderate/severe			

Data expressed as frequency (percentage), mean (SD). *P* value was significant if < 0.05. TR: tricuspid regurgitation

Functional TR was reduced after percutaneous and surgical ASD closure, with no statistically significant difference between groups, but the percentage of change was greater in the device group than the surgically closed one ((-) 19.18 ± 9.28 in device vs (-) 18.89 ± 11.01 in surgery). Persistence TR after closure was discovered in 40% of the ASD-device group and 53.4% of the ASD-surgical group, Table 5 .

To identify potential clinical and CMR predictors of remodeling, univariate and multivariate logistic regression analyses were performed. TR regurgitant fraction, RA SV, LA SV, LA maximal area, and QP/QS are the predictors of remodeling using univariate logistic regression.

Discussion

In a prospective study, we included 30 adult patients who were age, gender, and BSA matched to compare the mid-term outcomes of cardiac volumetric changes following transcatheter and surgical ASD closure, as well as the fate of TR.

We found that mean PAP decreased in all patients after ASD closure in comparison to baseline measurements, with more reduction among patients underwent device closure .This in agree with findings of Michael et al. [20] who reported that after ASD closure, all patients experienced a decrease in pulmonary artery pressure, which was at least partially due to a decrease in transpulmonary flow.

CMR has been shown to be both reliable and reproducible in terms of volumetric quantitative assessment for both the atria and ventricle, as well as tricuspid regurgitation assessment [21]. It is also considered safe following cardiac implants [22].

Both the ASD device and surgical closure resulted in a reduction in RV volumes in our cohort. Transcatheter ASD closure resulted in more reverse remodelling in the indexed RVEDV and RVESV measurements when compared to the surgical arm, as shown in Fig. 2.

This agreed with Castaldi et al.[23] who showed either surgical or percutaneous closure of ASD has a similar efficacy on the volume normalization of the right chamber, but this was a long-term follow-up study. Contrary to the findings of Pascotto et al.[24] who reported that surgical repair failed to completely reverse right chamber overload, these findings have been attributed to functional anomalies related to cardiopulmonary bypass or to cardiac geometric changes caused by pericardial opening, Fig. 3.

When compared to baseline parameters in both groups, the RV mass index decreased significantly while the LV mass index increased. Schoen et al [25]. demonstrated that RV mass regressed at 6 months follow-up, but this was not significant when compared to baseline MRI measurements, due to the fact that in their study, the moderator band and trabeculations were included in the mass but excluded from the RV volume [26]. No study reported effect of surgery in RV mass post-surgical closure. In terms of indexed LV mass Karen et al.[27] reported that, contrary to our findings, mass was not significantly different from age-matched controls before or after ASD closure.

Only in the device group did our research find a statistically significant improvement in RV and LV function, this in disagree with Berger et al. [28] who showed early normalization of RVEF, regardless of whether this was achieved surgically or by transcatheter closure, which is the only study that reported this, the reason for divergent results regarding RV performance after ASD closure is the limited accuracy of two dimensional echocardiography in quantifying RV parameters [29]. In agreement with our findings Omid et al. [30] found an increase in LV end diastolic volumes with no changes in LV end systolic volumes with an increase in LV stroke volume and function after ASD device closure, Fig. 4.

With the closure of ASD Both procedures result in a decrease in RA volume with no difference between groups. RA volume overload had a strong correlation ($P = 0.0001$, $r = 0.7$) to preclosure shunt fraction, the greater the shunt fraction, the larger was the RA volume, with weak correlation between volume overload preclosure and magnitude of remodeling of RA this in disagree with Fang et al.[31] who found in their study that 57% of the patients had persistent RA enlargement that was independently related to excessive preclosure RA dilation rather than the presence of functional tricuspid regurgitation or pulmonary arterial hypertension, who used Fick's principle to calculate shunt fraction and 2D echo to measure RV volumes. In agreement with Karen et al.[27], our cohort observed a trend for LA volume reduction after shunt removal and improved LV filling. However, it was insignificant and similar in both groups.

In the current study, functional TR was reduced after percutaneous and surgical ASD closure. The percentage of change in tricuspid regurgitant fraction correlated significantly positively with a moderate degree of agreement to the percentage of change in RVSP, but there was no significant correlation with tricuspid annulus diameter after ASD closure. This was consistent with the findings of Toyono et al.[32] who discovered that the only factor associated with TR jet area after ASD closure was pulmonary artery systolic pressure prior to ASD closure.

Univariate analysis was in agree with Pascotto et al. [33] who reported a striking correlation between preprocedural cardiac overload and its reduction after shunt disappearance, regardless of the volume overload extent, and partially disagree with Thilén et al.[34] who documented that Sex, age, size of the defect, QP/QS, RV area prior to closure did not significantly influence the potential to normalize RV area 1 year post-closure.

In our study, we found that baseline QP/QS has 86.5 % sensitivity and 63 % specificity for predicting remodeling after ASD closure, with an overall accuracy of 80 % at a cut-off point of > 1.9. This consistent with findings of Stephensen et al.[35], who reported that the change in RVEDV had a strong correlation with shunt size prior to ASD closure ,Fig. 1.

Limitations and Recommendations

- We require multicenter experience rather than single-center experience.
- A small sample size in our study was used due to financial constraints
- Instead of focusing on a single age group, we should look at different age groups to see how the passage of time affects remodeling.

Conclusion

- Both transcatheter and surgical ASD closure resulted in ventricular and atrial mechanical reverse remodeling, with the device group having better ventricular reverse remodeling.
- Percutaneous ASD closure is not only less invasive than open-heart surgery, but it also improves RV function.
- Secondary TR appeared to be resolved with RV volume restoration and RVSP reduction rather than tricuspid annulus diameter reduction in any group.

Abbreviations

ASD: atrial septal defect, ECG: electrocardiogram, CMR: cardiac magnetic resonance, RA: Right atrium, LV: left ventricle, RV: right ventricle, LA: left atrial, EDV: end diastolic volume, end systolic volume (RVESV), TR: tricuspid regurgitation, PAH: pulmonary arterial hypertension, PVR: pulmonary vascular resistance, mPAP: mean pulmonary artery pressure , RVSP: right ventricular systolic pressure , BSA: body surface area, TEE: transesophageal echocardiography, SSFP : Steady-State Precession , TTE : Transthoracic echocardiography , MPA : Main pulmonary artery , CO: cardiac output , PC: contrast phase , RVol : tricuspid regurgitant volume , SV: stroke volume , TAD :Tricuspid annular diameter , NYHA : New York Heart Association , ASO : Amplatzer septal occluder

Declarations

Ethics approval and consent to participate:

This study was approved by the ethics committee of Assiut university; Institutional review board (IRB), (independent ethics committee) (IEC); Project Approval Number: CA-19-9635

An informed written consent was obtained from all the participant's legal guardians. The study has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

Consent for publication: not applicable

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"all authors have read and approved the manuscript"

AM has contributed in the Conceptualization, methodology, Data Curation, software, validation, formal analysis, investigation, resource, Writing - Original Draft, Writing - Review & Editing, Visualization, Supervision, Project administration

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“all authors have read and approved the manuscript”

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Figures

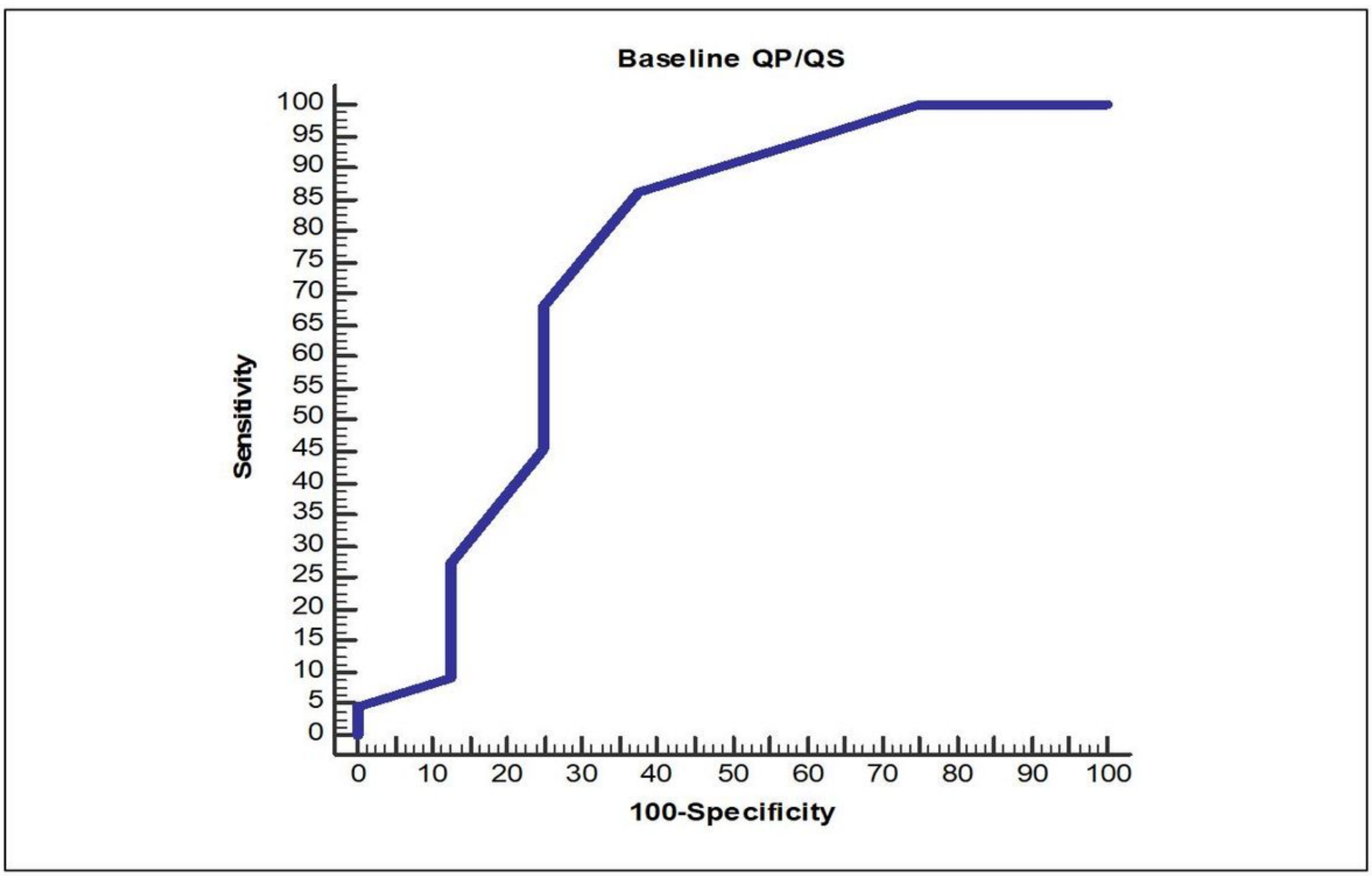

Figure 1

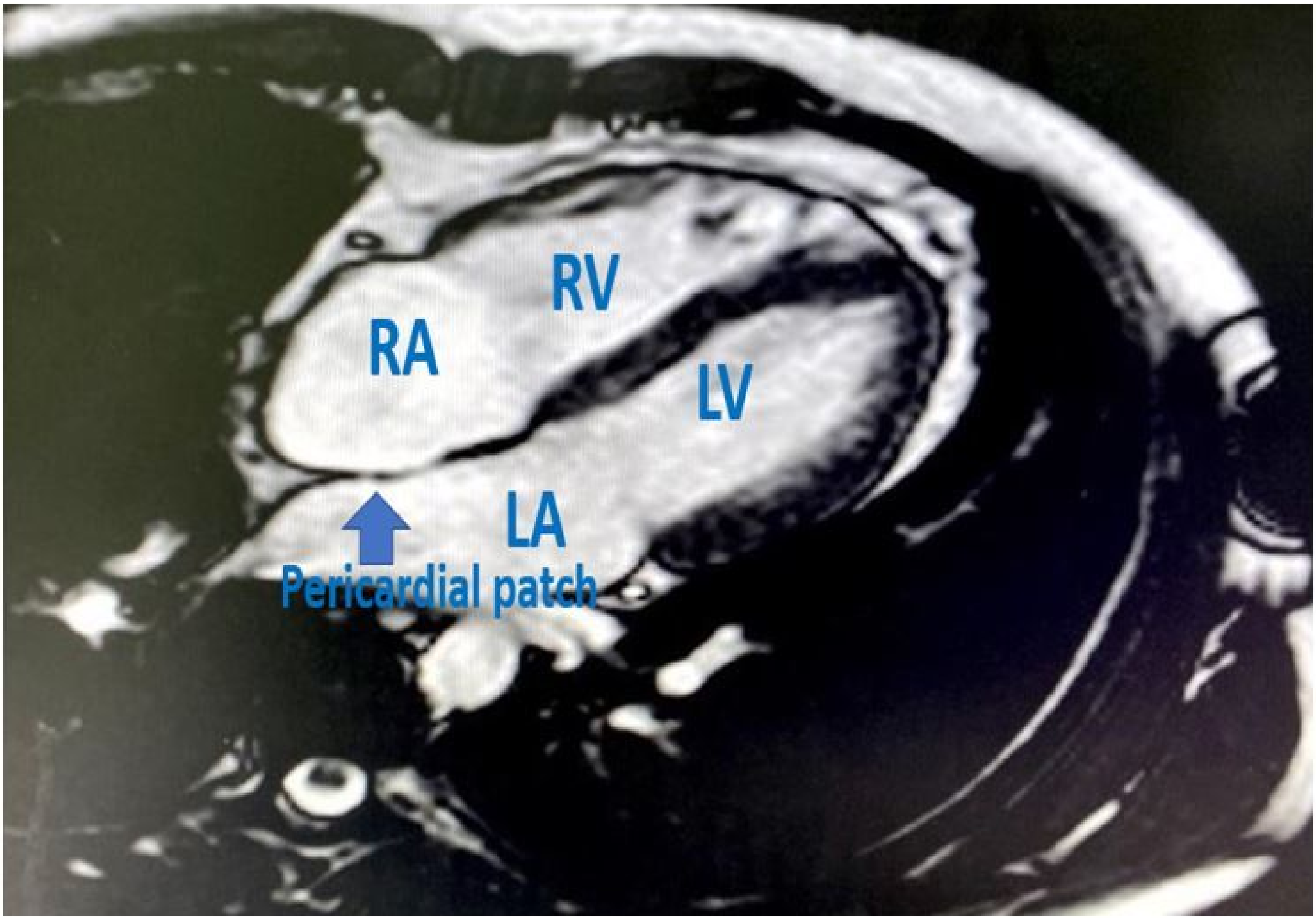

Figure 2

Cine SSFP 4 chamber MRI view in surgically closed case by conventional method with revolution of RA and RV volumes .RA; right atrium, RV; right ventricle, LA; left atrium, LV; left ventricle.

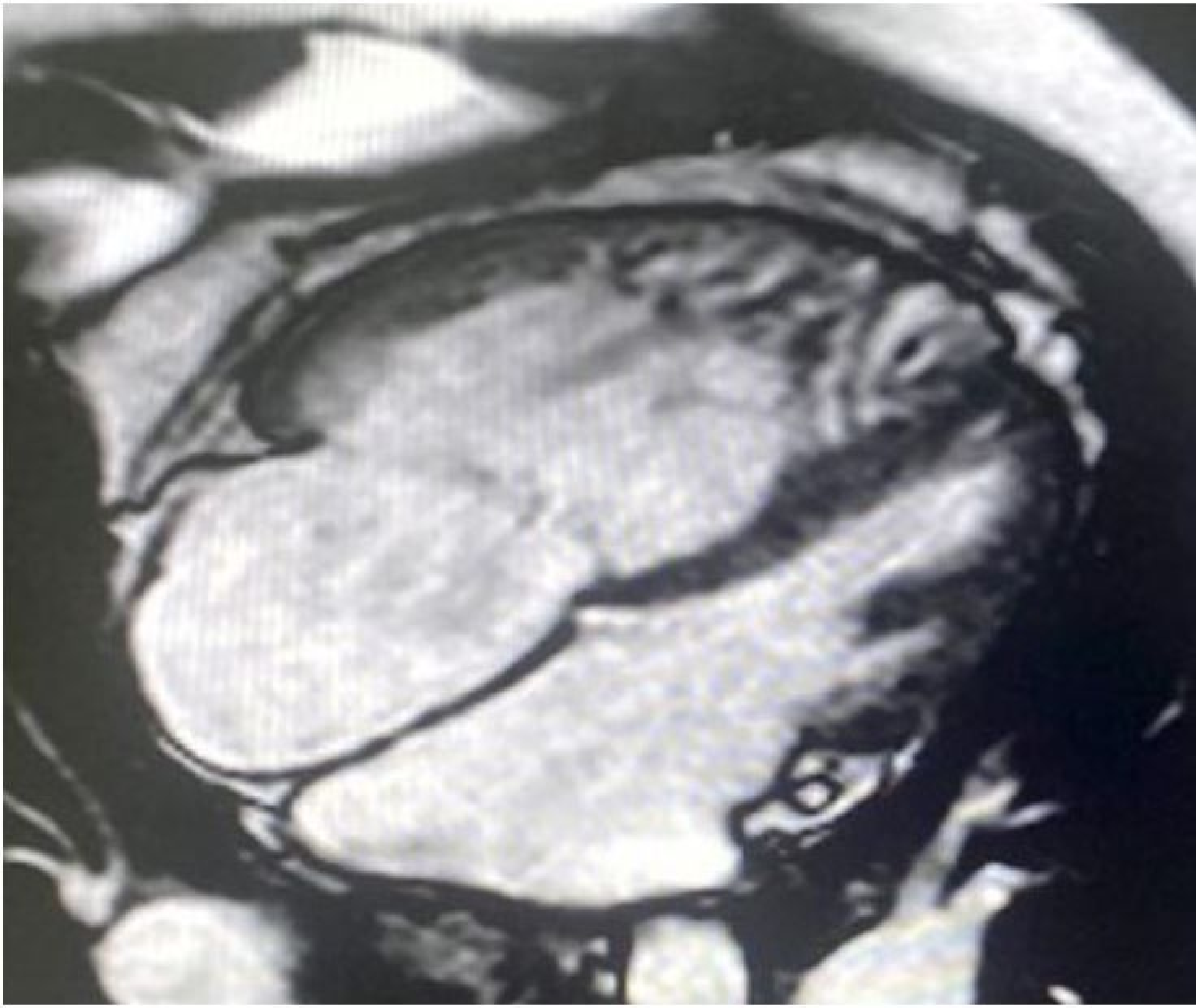

Figure 3

Cine SSFP 4 chamber MRI view in surgically closed case by conventional method with persistently dilated RA and RV volumes .

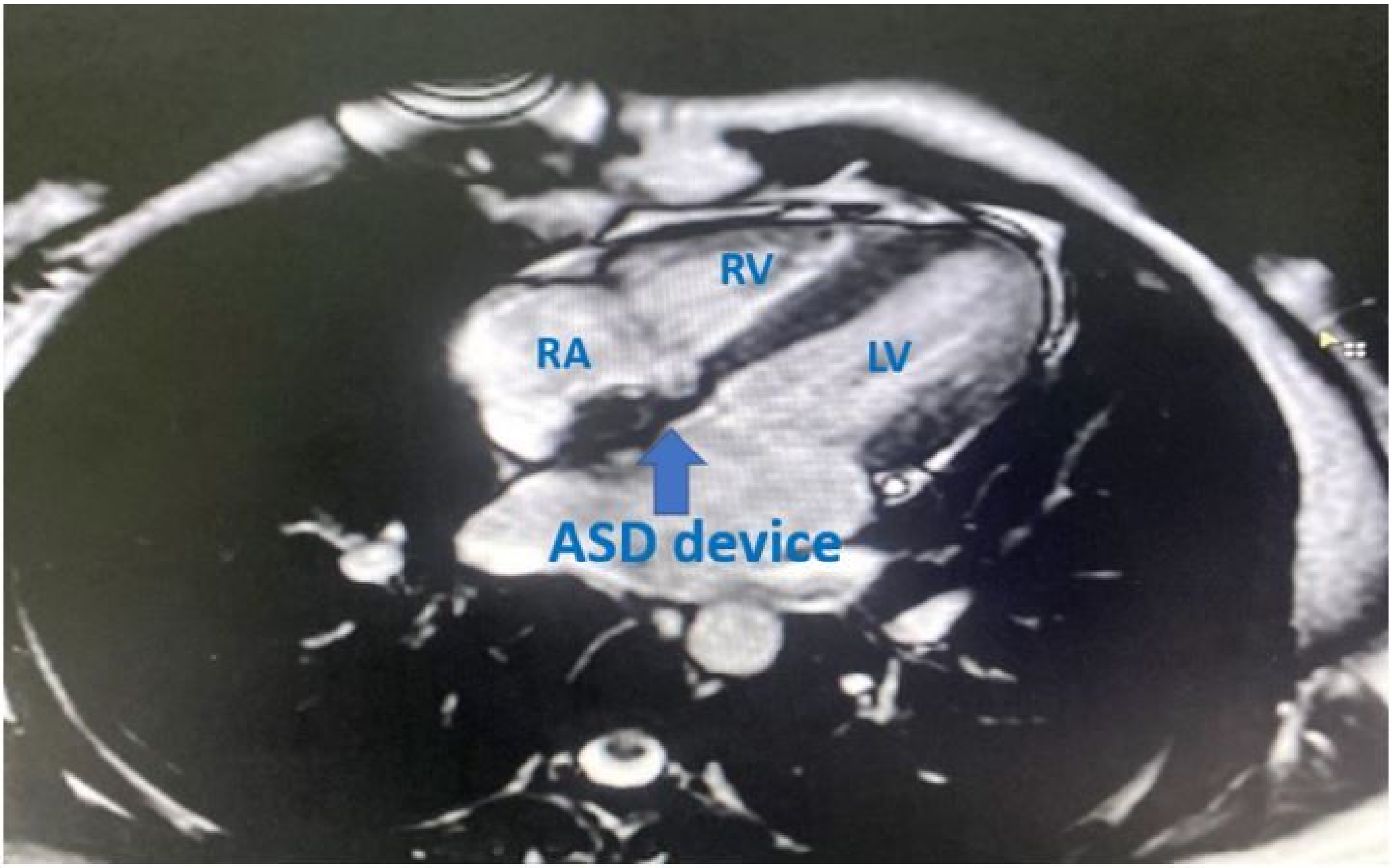

Figure 4

Cine SSFP 4 chamber MRI view in transcatheter closed case by ASO. RA; right atrium, RV; right ventricle, LA; left atrium, LV; left ventricle.