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ORIGINAL ARTICLE

Long-Term Results after Percutaneous Closure of Atrial Septal Defect: Cardiac Remodeling and Quality of Life

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ABSTRACT

Background: Atrial septal defect (ASD) represents a common congenital heart malformation, cause of right ventricle (RV) volume overload, pulmonary hypertension, atrial arrhythmias, and paradoxical emboli. Percutaneous closure represents the treatment of choice for ASD. However, it is still difficult to associate symptoms to the success of ASD treatment. **Objective:** To investigate any possible correlation between transthoracic echocardiography (TTE) findings and patients' symptoms after ASD treatment. **Materials and Methods:** Thirty patients (mean age 49 ± 17 years; 10 younger ≤40 years and 20 > 40 years) underwent percutaneous closure of ASD type ostium secundum. Every patient underwent clinical examination, electrocardiogram (ECG) and TTE before procedure and at 1, 6, and 12 months after procedure and a multichoice questionnaire to collect patients' symptoms and complain severity. **Statistical analysis:** Continuous variables were summarized by means and standard deviation. Estimates of occurrence of events were expressed as percentages. Comparison between mean follow-ups was achieved using paired t-test sample. **Results:** At end of follow-up, TTE showed a decrease of RV dimensions (34.4 vs 37.5 mm preclosure; $P = 0.01$), pulmonary artery systolic pressure (PAPs 28.4 vs 39.5 mmHg; $P = 0.00003$), atrial dimensions (51 vs 56 mm; $P = 0.085$), and of right myocardial performance index (MPI; 0.39 vs 0.42; $P = 0.05$). PAPs was significantly reduced in group more than 40-years-old ($P = 0.00004$), while the reduction was not significant in the less or equal than 40 years of age ($P = 0.08$) group because the baseline value was significantly lower. Many patients after procedure complained headache, insomnia, palpitations, fatigue, and dyspnea; but no cardiac morphological abnormalities related to symptoms were found. **Conclusions:** Our data showed a great improvement in symptoms and positive cardiac remodeling after closure of ASD, more effective in elderly patients compared to younger patients. The symptoms are not correlated with the principal disease or procedure.

Key Words: Atrial septal defect, transthoracic echocardiography

INTRODUCTION

Atrial septal defect (ASD) represents a common congenital heart malformation comprising 5-10% of all congenital heart diseases (CHD)[1] and often diagnosed in adult age.[2] The ASD can be cause of right ventricle (RV) volume overload, pulmonary hypertension, atrial arrhythmias, and paradoxical emboli in later life.[3]

Nowadays, percutaneous closure represents in many centers the treatment of choice for ASD, because of its safety, effectiveness, and low complication rate. This has been reported in several studies on follow-up looking at short-, mid-, and long-term safety and effectiveness of percutaneous closure of ASD. These findings have been confirmed even with the usage of various kinds of devices and in different patients' age group.[4-7] Some studies have even demonstrated a significant functional improvement of ASD in patients with mild (RV) dilatation and lower systolic pulmonary arterial pressure (SPAP).[8]

Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) are used to investigate ASD as well as to follow-up it.[9]

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It is still difficult to associate symptoms to the success of ASD treatment. We aim to investigate any possible correlation between echocardiography findings and patients' symptoms in order to help clinicians to make a precise differential diagnosis among a variety of clinical scenarios, when patient comes symptomatic for follow-up after ASD treatment.

MATERIALS AND METHODS

The study population consists of 30 patients (mean age 49 ± 17 years, 16 female) who underwent percutaneous closure of ASD from August 2008 to August 2011 in the Cardiology Department of the Ferrarotto University Hospital in Catania. The most frequent indication for ASD closure was: RV dilatation (43%) and pulmonary hypertension (50%). On the basis of TEE assessment and screening for transcatheter closure we included: ASD morphology and excluded any additional lesions such as an anomalous pulmonary venous connection and a significant left-to-right shunt (signs of RV volume overload) irrespective of the presence of symptoms.

In our sample 10 patients were younger than 40 years (mean 29.6 ± 7.3 years) and 20 older than 40 years (mean 58.4 ± 11 years). All patients had an ASD type ostium secundum.

Ten out of 30 (34%) procedures were performed in general anesthesia with oral intubation and TEE guidance, while 20 out of 30 (67%) were carried out using local balloon sizing of ASD. All percutaneous closure procedures were carried out with Amplatzer septal occluder (ASO) device. The median ASO size was of 27.3 ± 6.2 mm.

Every patient underwent clinical examination, ECG, and TTE before procedure (at baseline) and at 1, 6, and after 12 months of the procedure.

A complete TTE included: M-mode, two-dimensional (2D), continuous-wave, pulsed-wave, color Doppler echocardiography, and tissue Doppler velocity imaging (TDI) and it were performed in accordance to the international guidelines.[10-12] The investigation aimed to rule out RV, left ventricle (LV), mitral valve (MV), and tricuspid valve (TV) structure and function, to assess prosthesis positioning in interatrial septum and also the presence of residual shunting.

In the apical four-chamber view were evaluated: RV diastolic (RVD) size by taking the transverse diameter, right atrial volume (RAV), tricuspid annular plane systolic excursion (TAPSE), SPAP estimated from the tricuspid regurgitate velocity and inferior cava vein diameter and its respiratory excursion, and LVEF and left atrial volume (LAV). Using pulsed-wave (PW) were evaluated early diastole (E) and atrial (A) filling velocities at mitral (MV) and tricuspid valve (TV): MV_E, MV_A, TV_E, TV_A, respectively and ratio MV_E/A, TV_E/A. Tissue Doppler was applied in the PW-Doppler mode (PW-TDI) at the lateral sides of the mitral and tricuspid annulus and evaluated early and late diastolic myocardial velocities (E' and A' wave, respectively), the ratio between E and E' (E/E' ratio) and the myocardial performance index (MPI).

Grey scale images were obtained using second-harmonic imaging. All the examinations were recorded in digital imaging. Off-line analysis of standard echocardiographic variables was performed with the use of dedicated software (Echo PAC BT09; GE Healthcare, Fairfield, Connecticut). Three consecutive beats were measured and average for each measurement was also included.

We used also a multichoice questionnaire (with six possible answers) to collect patients' symptoms and complain severity.

Moreover, an ECG-Holter was performed on every patient who reported palpitations.

Statistical analysis

Continuous variables were summarized by means and standard deviation. Estimates of occurrence of events were expressed as percentages (or hazard ratio with 95% confidence interval). Comparison between mean follow-ups was achieved using paired *t*-test sample. A *P*-value < 0.05 was considered statistically significant.

RESULTS

Clinical findings: Baseline

Our 30 patients (mean age 49 ± 17 years) were followed-up prospectively and had a medium follow-up time of 28 ± 16 months (range 3-51 months). All clinical characteristics have been summarized in Table 1. All patients were in sinus rhythm and no supraventricular or ventricular arrhythmias were reported before study. Nobody reported history of cardiovascular accident. The median procedure time was of 45 ± 8 min. No moderate or severe residual shunt was observed in all cases at the end of procedure. There were no episodes of acute erosion of the atrial wall or of the aorta as well as there were not peripheral or cerebral thrombus-embolic events. No major ventricular arrhythmias were observed and no major vascular complications. There were no deaths during the procedure.

Clinical findings: Follow up

Follow-up using the multichoice questionnaire, reported five different symptoms, fatigue, dyspnea, insomnia, headache, palpitations, and the frequency of the use of medical. Symptoms more often present were insomnia and palpitations [Figure 1].

All symptoms observed at 1, 6, and 12 months follow-up have been summarized in Table 2.

At 6 month follow-up, in ≤40 years group there was not modification of New York Heart Association (NYHA) class, instead there was an improvement of physical ability in one patient of >40 years group without a modification of NYHA class. At 12-month follow-up, the ≤40 group (20%) patient reported physical ability improvement, in >40 years group 3 (15%) patient passed from NYHA class II to NYHA class I.

Frequencies of symptoms during follow-up

During the 1st month there was an increase of insomnia in 22 patients (45%), at 6 months 23 patients (77%) reported insomnia only after 12 months on the other hand there was a decrease with 14 patients with insomnia. No significant different are present into ≤40 years of age group and >40 years old group at 1, 6, and 12 months or between sex.

Palpitations and headache

Palpitations was the other symptom often reported and present every patient was monitored with ECG-Holter. Nobody of them had a significant ECG. No significant different were present between patients less than ≤40 years of age and >40 years of age at 1, 6, and 12 months. On the contrary, at 1 month all female patients reported at least one case of palpitations vs 56% of male. During all controls female patients reported the presence of short-term palpitations [Figure 2].

Headache was reported from in 60% of women younger than 40 years and in 70% of women older than 40 years of age during the 1st month. At 6 months we had 70% of women younger than 40 years of age and 75% of women older than 40 years of age. At 12 months, 70% in women younger than 40 years of age and 80% of women older than 40 years of age. All female in both groups complained of headache at baseline and it was present in 28% at 1 month, 42% at 6 months, and 50% at 12 months.

Fatigue and dyspnea

Fatigue were the more often symptom reported from the group of women older than 40 years of age, during 1st month 70% of over 40 year refer fatigue and 90% dyspnea at least 1 day during previously month against 10% of fatigue and the 20% of dyspnea in the patients younger than 40 year. At 6 months, fatigue was reported from 70%, but only one complained of fatigue to daily routine of >40 group.

TABLE 1: Clinical characteristics of study population

Characteristics	*N*/mean ± SD	(%)
Age	49 ± 17	-
Male	14	(47)
Prior cardiovascular diseases	5	(17)
Diabetes	6	(20)
Hypertension	9	(30)
Dyslipidemia	8	(27)
Smoker	7	(23)
NYHA		
I	26	87
II	4	13
III-IV	0	0

NYHA = New York Heart Association

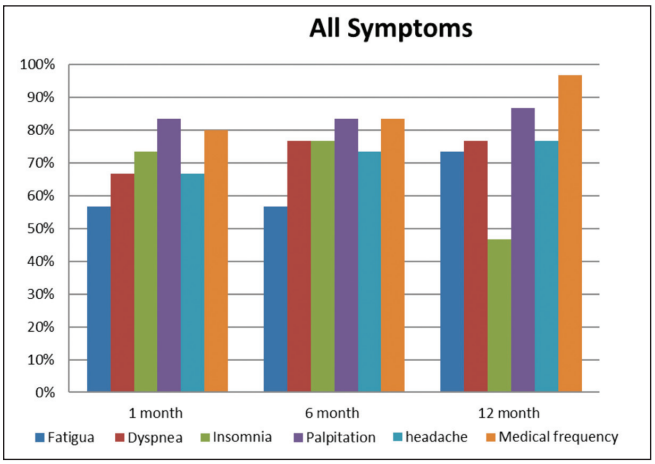

Figure 1: Frequency of all different symptoms reported at 1, 6, and 12 months after septal closure

TABLE 2: Symptoms observed at 1, 6, and 12 months follow-up

	Baseline		1 month		6 months		12 months	
Symptoms	*Absent*	*Present*	*Absent*	*Present*	*Absent*	*Present*	*Absent*	*Present*
Fatigue	20 (67%)	10 (33%)	13 (47%)	17 (53%)	13 (47%)	17 (53%)	8 (27%)	22 (63%)
Headache	10 (33%)	20 (67%)	10 (33%)	20 (67%)	8 (27%)	22 (63%)	7 (23%)	23 (77%)
Dyspnea	23 (77%)	7 (23%)	10 (33%)	20 (67%)	7 (23%)	23 (77%)	7 (23%)	23 (77%)
Insomnia	25 (83%)	5 (17%)	8 (27%)	22 (73%)	7 (23%)	23 (77%)	16 (53%)	14 (57%)
Palpitation	5 (17%)	25 (83%)	5 (17%)	25 (83%)	5 (17%)	25 (83%)	4 (13%)	26 (87%)

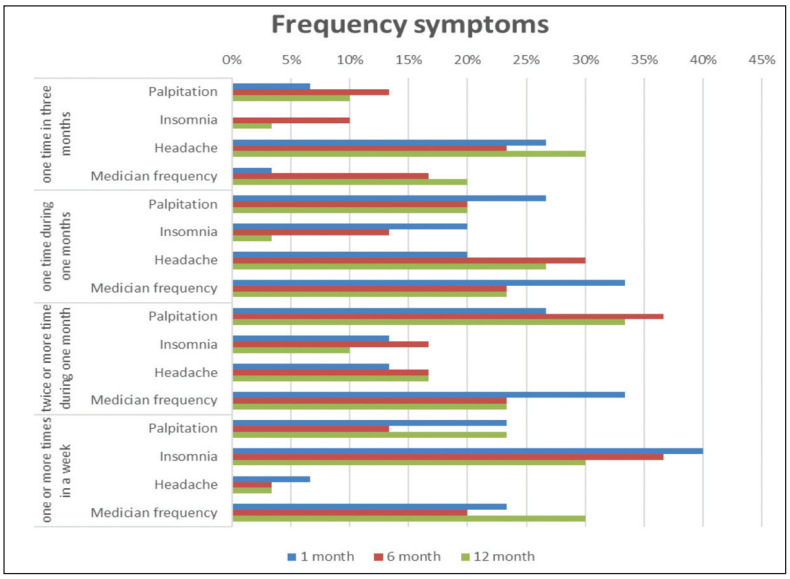

Figure 2: Presence and frequency of palpitation, insomnia, headache, and medicine frequency reported at 1, 6, and 12 months after septal closure

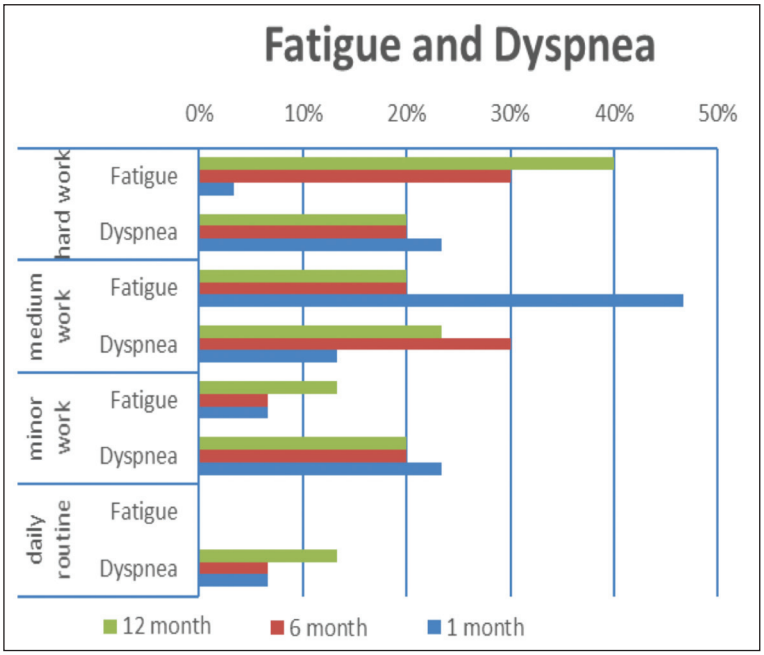

Figure 3: Frequency and intensity of fatigue and dyspnea reported at 1, 6, and 12 months after septal closure

Moreover, 10 patients (33%) were under or equal to 40 years old and on the contrary 20 patients (67%) were above 40-years-old. Patients under 40 years old were all in NYHA class I after closure and only 2/10 of patients reported physical ability improvement [Figure 3].

In the second group, we had 20 patients over 40-years-old and of those four (13%) patients were in NYHA class II after ASD closure among these 3/4 improved to class NYHA class I, seven of 16 patients were in NYHA class I reported a subjective improvement of their physical ability in daily routine.

Transthoracic echocardiography

Baseline

All basal echocardiographic data and the degree of severity of shunt have been summarized in Table 3.

At the baseline the examination of the right heart with TTE showed a median RV end-diastolic diameter (RVEDD) of

37.5 ± 5 mm with a medium TAPSE of 23.1 ± 4.7 a SPAP of 39.5 ± 7.1 mmHg, right atrium diastolic size (RAD) of 56 ± 7.1 mm, and RV_MPI = 0.4 ± 0.05.

The left chambers evaluation showed a median LV end-diastolic diameter (LVEDD) of 42 ± 3.4 mm and the left atrium diastolic size (LAD) was 59.6 ± 12.1 mm. Median LVEF was 60.2 ± 3.9%. Doppler examination showed tricuspid regurgitation (TR) in 24 (80%) patients and it was trivial in 17 (71%) patients, moderate in six (25%), and severe in one (4%), and mitral regurgitation (MR) in 12 patients (40%): Trivial 92%, moderate 8%, and aortic regurgitation (AR) in four (13%) and they were all trivial.

During all follow-up no shunt residual and no thrombi on device were observed.

One month after procedure

Follow-up did not highlight any concerns. Median RVEDD of 36.7 ± 5 mm (P = 0.55) with a TAPSE of 29.1 ± 4.5 (P = 0.97), a SPAP of 37.1 ± 7.0 mmHg (P = 0.34), RAD of 54.8 ± 7.0 mm (P = 0.66), and RV_MPI of 0.42 ± 0.05. The left chambers evaluation showed LVEDD of 42.5 ± 3.9 mm (P = 0.61), LAD was 58.5 ± 11.9 mm (P = 0.8), and LVEF was 60.2 ± 3.9% (P = 0.98). TR in 24 (80%) patients and it was trivial in 17 (71%) patients, moderate in six (25%), and severe in one (4%). Moreover, MR in 12 patients (40%) (11 trivial 92%, one moderate 8%) and AR in four (13%) and they were all trivial.

Six months after procedure

Right chambers analysis showed a median RVEDD of 35.5 ± 4.7 mm (P = 0.13) with a medium TAPSE of 23.4 ± 4.0 mm (P = 0.84), a SPAP of 31.5±6.7 mmHg (P = 0.01), RAD of 53.6 ± 6.5 mm (P = 0.37), and RV_MPI of 0.41 ± 0.04 (P = 0.18). The left chambers evaluation showed a median LVEDD of 44.3 ± 3.9 mm (P = 0.02), LAD was 57.2 ± 10.7 mm (P = 0.8), and LVEF was 60 ± 4.4% (P = 0.84). TR in 24 (80%) patients and it was trivial in 19 (79%) patients, moderate in five (21%), and nobody with severe. Moreover, MR in 13 patients (43%) all trivial and AR in four (13%) and they were all trivial.

12 months after procedure

There was significant reductions in RVEDD (34.4 ± 4.2 mm; P = 0.01), RAD (51 ± 6.0 mm; P = 0.085), RV_MPI (0.39 ± 0.04; P = 0.05), and SPAP (28.4 ± 6.4 mmHg; P = 0.00003). There was also significant improvement of LVEDD, while staying within the normal range (46.4 ± 4.3 mm; P = 0.0006); LAD reduced but its reduction did not reach the statistical significance (P = 0.3).

There was not a new onset of MR or AR and instead our data showed a median improvement of mitral valve regurgitation when MR was present at baseline.

Additionally, we divided our pattern related to the age (≤40-years-old or >40-years-old) and we compared the follow-up after 12 months from the closure to baseline values [Table 4].

TABLE 3: Echocardiographic data at 1, 6, and 12 months follow-up and degree of severity of shunt

	Baseline	1 month	6 months	12 months	
	Mean value ± SD	Mean value ± SD	Mean value ± SD	Mean value ± SD	*P*-value
Right ventricle					
RVEDD mm	37.5±5.0	36.7±5.0	35.5±4.7	34.4±4.2	0.01
TAPSE mm	23.1±4.7	29.1±4.5	23.4±4.0	23.7±3.5	0.7
SPAP mmHg	39.5±7.1	37.1±7.0	31.5±6.7	28.4±6.4	0.00003
RAD mm	56±7.1	54.8±7.0	53.6±6.5	51±6.0	0.085
RV_MPI	0.42±0.05	0.42±0.05	0.41±0.04	0.39±0.04	0.05
TV_E/A	1.49±0.1	1.51±0.2	1.54±0.4	1.56±0.6	0.8
E/E'	3.9±1.8	3.8±1.7	3.7±1.8	3.5±1.9	0.87
Left ventricle					
LVEDD mm	42.0±3.4	42.5±3.9	44.3±3.9	46.4±4.3	0.0006
LAD mm	59.6±12.1	58.5±11.9	57.2±10.7	55.4±9.5	0.37
LVEF %	60.2±3.9	60.2±3.9	60±4.4	59.9±5.4	0.81
MV_E/A	1.53±0.9	1.51±1.0	1.50±0.9	1.60±1.0	0.83
E/E'	6.7±0.9	6.6±0.9	6.1±1.4	5.9±2.0	0.03
Degree of severity of shunt (n pts)	Mild 3 Moderate 20 Severe 7	None	None	None	None

SD = Standard deviation; SPAP = systolic pulmonary arterial pressure; TAPSE = tricuspid annular plane systolic excursion; RVEDD = right ventricle end-diastolic diameter; RAD = right atrium diastolic size; RV_MPI = right ventricle myocardial performance index; LVEDD = left ventricle end-diastolic diameter; LAD = left atrium diastolic size

TABLE 4: Echocardiographic data divided for age group: data at 12 months from the closure compared to baseline values

	Group ≤ 40 (age 29 ± 7.3 years)			Group > 40 (58 ± 11 years)		
Echo values	**Baseline**	**12 months**	***P*-values**	**Baseline**	**12 months**	***P*-values**
LAVi ml/m²	39 ± 7.8	40±8.2	0.81	48.7±6.1	48.5±10	0.96
RAVi ml/m²	44.8±4	41.4±4.6	0.11	46.2±6.2	43.3±3.7	0.28
SPAP mmHg	35.1±6.6	28±2.8	0.08	41.2±6.4	28.4±6.5	0.00004
TAPSE mm	25.2±5.5	26.5±2.2	0.64	21.3±3.4	22.1±3.1	0.63
RVEDD mm	38.2±2.8	34.6±3.3	0.02	37.5±5.7	34.3±4.7	0.06
RV_MPI	0.42±0.04	0.39±0.04	0.2	0.42±0.06	0.38±0.04	0.15

LAVi = LA volume normalized for body surface area; RAVi = RA volumes normalized for body surface area; SPAP = systolic pulmonary arterial pressure; TAPSE = tricuspid annular plane systolic excursion; RVEDD = right ventricle end-diastolic diameter; RV_MPI = right ventricle myocardial performance index

Ten patients (33%) were under or equal to 40-years-old and conversely 20 patients (67%) were above 40-years-old. Patients under 40-years-old were everybody in NYHA class I, after closure only a minimal part of patients (two of 10) reported an improvement of physical ability. In this group, heart modification assessed by echocardiography, showed, compared to baseline, a nonsignificant reduction of SPAP (35.1 ± 6.6 to 28 ± 2.8 mmHg, $P = 0.08$), RVEDD (38.25 ± 2.28 to 34.6 ± 3.3 mm, $P = 0.02$), RV_MPI (0.43 ± 0.04 to 0.39 ± 0.04, $P = 0.2$), and of LA and RA volumes normalized for body surface area (LAVi and RAVi, respectively).

In the second group done by 20 patients over 40-years-old, four (13%) patients were in NYHA class II, after ASD closure three of four passed to class NYHA class I, seven of 16 patients were in NYHA class I reported a subjective improvement of their physical ability to daily routine. In this group, heart modification assessed by echocardiography showed, when compared to baseline, a more significant reduction of SPAP (41.2 ± 6.5 to 28.4 ± 6.5 mmHg, $P = 0.00004$), RVEDD (37.52 ± 5.7 to 34.35 ± 4.71 mm, $P = 0.06$), RAVi (46.2 ± 6.2 to 43.3 ± 3.7 mm, $P = 0.28$), and RV_MPI (0.42 ± 0.04 to 0.38 ± 0.04, $P = 0.04$).

DISCUSSION

The natural history of ASD is characterized by chronic RV volume overload that leads to right chambers enlargement, dysfunction, and finally to chronic heart failure. Thus, closure of ASD leads to symptom's improvement and anatomical, geometrical, and functional improvement of right heart chambers.[8,9,13,14] A number of studies have shown feasibility, safety, and a low complications rate in percutaneous ASD closure interventions and short- and long-term follow-up have also confirmed these data.[4,7]

In our series, these findings are fully confirmed as in our patients all devices were effectively implanted and we did not have any device embolization, erosions of atrial wall, or of the aorta and/or major vascular complications. We had only three (10%) minimal self-limiting bleeding episodes from the femoral vein puncture site.

Echocardiography has been extensively used to assess right heart chambers' morphology and function in ASD. We agreed with the literature as we found a decrease of RVEDD (34.4 mm 12 months after closure vs 37.5 mm preclosure, mean reduction = 3.4 mm; $P = 0.01$), SPAP (28.4 vs 39.5 mmHg, mean reduction = 11.1 mmHg; $P = 0.00003$), and RAD (51 vs 56 mm, mean reduction = 5 mm, $P = 0.085$); as a result of the reduction of right chambers volume overload.

On the other hand, we have not noticed a significant modification of the left chambers morphology and function, in fact there was not a significant modification in LVEF and a slight increase of LVEDD was also noticed (46.4 mm 12 months after closure vs 42 mm preclosure, mean increase +4.4 mm; $P = 0.0006$). The LVEDD increase could occur after ASD closure due to the higher chamber volume load status that is not associated to a pressure increase, as evidenced by the values constantly normal of mitral flow (MV_E/A), LAD, and E/E' [Table 4]. However, this is an increase within the normal range for our study population and no patients had left ventricular dilation.

All these data highlighted that ASD principally affects right heart chambers. The echocardiographic study of right heart chambers has several issues due to the asymmetric, "crescent" shape of the RV; so it is not easy to assess RV volume and ejection fraction by 2D and M-mode classic evaluation. Using 3D echocardiography can overtake this limitation and this has been demonstrated by several authors.[9,15]

In agreement with the literature, in our series we have found a marked reduction of RV_MPI at follow-up (0.42 baseline vs 0.39 after 12 months after ASD closure; $P = 0.05$), which confirmed the effectiveness of ASD closure and how this procedure can improve RV function.

MPI is a reproducible index that could be easily calculated by standard Doppler evaluation, as it is independent from cardiac frequency and from RV geometry. It has been extensively evaluated in patients with ASD to assess the global (systolic and diastolic) RV function. For all these reasons in our study we have decided to include MPI assessment and to review RV function.

It is worthwhile mentioning that the parameters evaluated in the two different groups (≤40-years-old and >40 years group) did not change significantly a part for reduction of PAPS more of >40 years group than ≤40 years group. The RV MPI index improvement is more evident in older patients group, even though our data were not statistically significant and therefore more studies with a larger sample size would be useful to confirm our findings.

Many patients after procedure complained of different symptoms. Headache, insomnia, palpitations, fatigue, and dyspnea are the most frequent symptoms reported on our sample and after echographic examination we could not find any cardiac morphological abnormalities related to patients' symptoms, but our overall impression is that their symptoms are not correlated with the principal disease or procedure. We can conclude that their symptoms are psychogenic in nature.

CONCLUSIONS

Our echocardiographic data showed a positive right cardiac remodeling very early after percutaneous closure of a large ASD in RV morphology and function, but the symptoms are not correlated with the principal disease or procedure. Moreover, we can conclude that improvement in symptoms and in RV morphology and function is more effective in elderly patients when compared to younger patients, probably due to a short time when remodeling can occur in young women and also for an early diagnosis in the same patients. Our results suggest that percutaneous ASD closure may be deferred until later in life in suitable young patients, perhaps wait until adolescence when growth has progressed.

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