# Improvement in cardiac structure and functions early after transcatheter closure of secundum atrial septal defect in children and adolescents

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**We sought to assess the effects of transcatheter closure of atrial septal defect (ASD) on right and left ventricular form and functions, as well as atrial volumes and pulmonary venous flows. We enrolled 25 patients (mean age: 9.02) prospectively who underwent successful transcatheter closure of secundum ASD. We performed transthoracic echocardiography, including two-dimensional, pulsed wave Doppler, M-mode echocardiography, and tissue Doppler imaging before the procedure and 1 day, 1 month, 3 months and 6 months after the procedure. Serum brain natriuretic peptide (BNP) levels were measured prior to the procedure, and 1 day, 1 month, and 3 months thereafter. Mitral inflow early diastolic wave increased significantly, while isovolumetric relaxation time and deceleration time did not change during the follow-up. The E/E'was also increased significantly during follow-up. After the closure, right ventricular size and right atrial volume reduced, while left ventricular size increased significantly. There was a statistically significant improvement in left and right ventricular Tei indices. Pulmonary vein systolic velocity and the ratio of systolic to diastolic wave decreased, while atrial reversal wave (ARW) velocity increased immediately after the procedure. Although the concentration of BNP was increased on the first day after the procedure, its levels reduced and had reached the pre-procedure values at 1 month of follow-up. In the study, a significant improvement in the right and left ventricular functions was detected after transcatheter closure of secundum ASD in the short-term follow-up. In addition, we found a significant reduction in right heart sizes with corresponding global functional improvement in the right ventricle after the procedure.**

***Key words: diastolic functions, Tei index, filling pressure, cardiac chambers, pulmonary venous flow.***

Secundum atrial septal defect (ASD) accounts for 6–10% of all forms of congenital heart diseases. It is two times more frequent in females than males[1-5]. Interatrial communications in the region of the fossa ovalis usually represent a true secundum ASD, which can be closed conveniently with the transcatheter technique. A chronic left-to-right shunt via the interatrial communication causes a volume overload on the right-sided cardiac structures and results in dilation of the right atrium, right ventricle and pulmonary artery. Furthermore, left ventricular function may deteriorate during the disease course since left ventricular geometry changes in subjects with right ventricular overload that denominated as ventricular interdependence[6-8]. Previous reports have suggested that right ventricular volume overload might improve

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dramatically and left ventricular volume expand markedly early after transcatheter closure of the secundum ASD[8,9]. A post-closure adjustment may take longer in adults compared with the pediatric population[10]. Since adverse ventricular interaction or interdependence exists in patients with ASD, simple measurements of left ventricular function using M-mode echocardiography may not be representative of systolic or diastolic properties. A noninvasive Doppler-derived index, the Tei index or myocardial performance index, is easily reproducible, independent of heart rate and age, and incorporates both systolic and diastolic ventricular performance[11]. Recently, the tissue Doppler-derived Tei index has also been shown to correlate well with pulsed wave Doppler-derived Tei index[12]. Tissue Doppler imaging is a promising method to permit the analysis of regional myocardial and annular diastolic velocities[13]. Recent observations suggest that early diastolic velocity of the mitral annulus behaves as a preload independent index of left ventricular diastolic function[13-15]. We conducted this prospective study to determine the changes in right and left ventricular functions, atrial and ventricular structures and pulmonary vein flows in the acute phase after transcatheter closure of secundum ASD and in the short-term follow-up period using two-dimensional, M-mode, pulsed wave, and tissue Doppler echocardiographic parameters as well as brain natriuretic peptide (BNP) levels.

## Material and Methods

### *Patient Population*

A total of 25 patients - 14 girls and 11 boys – with a mean age of 9.02±3.13 years with secundum ASD underwent transcatheter closure at İzmir Dr. Behçet Uz Children's Hospital, Division of Pediatric Cardiology, between June 2009 and March 2010. Transthoracic echocardiography was used for the diagnosis of the secundum ASD. At least one week before the closure, anatomy of the defect and interatrial septum were examined in detail with transesophageal echocardiography (TEE). As a result of TEE, 28 patients were considered for transcatheter closure. The procedure was performed successfully in 25 patients, while the device could not be implemented in the remaining three patients. The inclusion criteria were the presence of secundum-type ASD with a left-to-right shunt and an increased right ventricular volume overload (pulmonary-to-systemic blood flow(Qp/Qs) ratio greater than 1.5 or presence of right ventricular dilation). The exclusion criteria were Qp/Qs ratio less than 1.5, other types of ASD, pulmonary vascular resistance exceeding 8 Wood units, and inferior and superior rims smaller than 5 mm. The protocol was approved by İzmir Dr. Behçet Uz Children's Hospital Ethics Committee, and informed consent from parents was provided prior to participation in the study.

### *Devices*

Transcatheter closure of the ASD was performed using Amplatzer septal occluder (AGA Medical, Golden Valley, MN) in 10 patients, Solysafe septal occluder (Swissimplant AG, Solothurn, Switzerland) in 14 patients and BioSTAR septal implant (NMT Medical, Boston, MA) in 1 patient. Amplatzer devices have a nitinol-braided skeleton with a thrombogenic effect provided by polyester Dacron fibers made up of double discs, which are described in detail elsewhere[16]. The Solysafe septal occluder began to be used for transcatheter ASD closure in 2007[17]. This device was constructed of a double-patch self-centering occluder system. The two foldable polyester patches were mounted between eight metal wires made of Phynox, a cobalt-based alloy. The device could be stretched, and thus implanted, via a short 10 French introducer sheath from the femoral vein - no long implantation sheath was needed - and is commonly available in five different sizes (15, 20, 25, 30, and 35 mm). Only the first three sizes (15, 20 and 25 mm) were used for ASD closure in this study population. The requisite device sizes for defect sizes of 4–12 mm, 13–17 mm, and 18–22 mm were the 15 mm, 20 mm, and 25 mm devices, respectively[17]. The exact implantation procedure has been described previously[17-19]. Unfortunately, the manufacturer (Swissimplant AG, Switzerland) was immediately informed and alerted to wire fracture problems related to the device in August 2010. Immediately thereafter, the implantation, marketing, selling, and distribution of Solysafe septal occluder were stopped. No patient experienced wire fracture in our series during the follow-up. BioSTAR septal implant (NMT Medical, Boston, MA) is the first device incorporating a bioabsorbable material for the treatment of secundum ASD[20]. It is only recommended for transcatheter closure of patent foramen ovale and small ASDs. This device is composed of an acellular porcine intestinal collagen layer matrix attached with a MP35N STARFlex, double-umbrella framework[20]. BioSTAR has a self-centering mechanism that consists of nitinol microsprings connected between the left and right atrial umbrellas[21]. Details of the implantation procedure have been described before[21].

*Echocardiographic Examination*

Transthoracic echocardiography was performed using 3- and 7-MHz transducers with Vivid-3 (GE Healthcare, Milwaukee, WI) echocardiography device before as well as 1 day, 1 month, 3 months, and 6 months after device implantation. The TEE evaluation was performed in the cardiac catheterization laboratory with the patient under deep sedation using a Vivid 3 echocardiography device and a pulsed wave 9-MHz transducer. Complete two-dimensional, M-mode, pulsed-wave, color-flow, and tissue Doppler echocardiography were performed for every follow-up examination. Images were stored digitally and then analyzed off-line following each study. The left ventricular ejection fraction (EF), left ventricular fractional shortening (FS), left ventricular end-diastolic diameter (LVEDd), left ventricular end-systolic diameter (LVESd), and posterior wall thickness of the left ventricle were obtained by M-mode echocardiography. In addition to M-mode echocardiography, the right ventricular diameter at the end diastole at three levels were measured in the apical four-chamber view due to the crescent shape of the right ventricle, as in the following: (1) maximal long-axis dimension, defined as the distance between the right ventricle apex and the midpoint of the tricuspid annulus, (2) short-axis dimension (inlet), defined as the maximal dimension beneath the tricuspid annulus, and (3) tricuspid annular dimension[22]. Maximal preatrial–systolic left atrial volume was determined using the equation for a prolate ellipsoid method as described previously[23]. For right atrial volume measurements, because parasternal long-axis determination of the right atrium width was unavailable, the modified equation was used[24].

We evaluated all parameters stated above in all patients regardless of which device was applied.

*Standard Doppler Flows and Tei Index*

Mitral and tricuspid inflow patterns were recorded from the apical four-chamber view with the pulsed wave Doppler. A sample volume was positioned at the tips of the leaflets. Early (E) and late (A) transmitral inflow velocities, the ratio of early-to-late peak velocities (E/A), and mitral deceleration time (DT) were obtained. Thereafter, the cursor was positioned midway between the left ventricular outflow and the mitral inflow to record the isovolumetric relaxation time (IVRT). The left and right ventricular outflow velocity patterns were recorded from the apical long-axis view and parasternal short-axis view, respectively. Tei index was calculated as the sum of isovolumetric contraction time and IVRT divided by ejection time from at least three cardiac cycles as described previously[11]. Pulmonary venous flow velocity was recorded from the apical four-chamber view, placing a sample volume 1 cm into the right upper pulmonary vein. Peak systolic (S), diastolic (D), and atrial reversal wave (ARW) velocities were obtained from the pulmonary vein records.

*Tissue Doppler Imaging*

Myocardial diastolic properties were assessed using tissue Doppler imaging. Tissue Doppler measurements were performed in the apical four-chamber view. A sample volume was placed at the lateral and septal corner of the mitral annulus and lateral corner of the tricuspid annulus for measurements of the peak early (E’) and late diastolic (A’) annular velocities and peak systolic (S’) myocardial

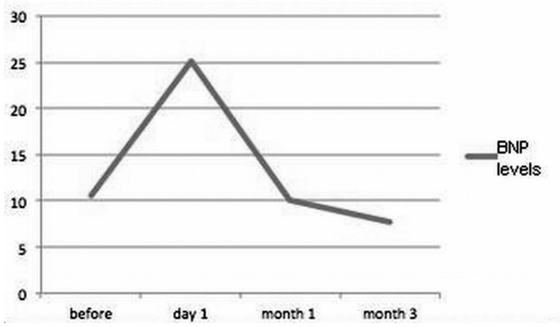


**Fig. 1.** Change in BNP levels before and after closure.

**Table I.** Baseline Clinical and Angiographic Data of the Patients

| | mean±SD | range |
|---|---|---|
| Age (year) | 9.02±3.13 | (5-18) |
| Weight (kg) | 32.36±17.78 | (11-80) |
| Body surface area (m$^2$) | 1.04±0.36 | (0.55-1.91) |
| Defect size (by TTE) cm | 12.24±5.25 | (6-26) |
| Defect size (by TEE) cm | 12.60±5.22 | (6-25) |
| Angiographic data | | |
| Procedure time (minute) | 53.00±17.97 | (30-110) |
| Scopy time (minute) | 15.67±8.43 | (7.3-42) |
| RAP (mmHg) | 7.92±2.18 | (5-13) |
| LAP (mmHg) | 8.08±1.73 | (5-12) |
| RVSP (mmHg) | 31.32±8.73 | (17-62) |
| mPAP (mmHg) | 15.04±4.16 | (8-29) |
| Qp/Qs | 2.00±0.29 | (1.67-2.70) |
| Post-RAP (mmHg) | 5.83±1.89 | (4-9) |
| Post-RVSP (mmHg) | 23.56±5.92 | (11-37) |

LAP: Left atrial pressure. mPAP: Mean pulmonary artery pressure. Qp/Qs: Ratio of pulmonary-to-systemic flow. RAP: Right atrial pressure. RVSP: Right ventricular systolic pressure. TEE: Transesophageal echocardiography. TTE: Transthoracic echocardiography.

tissue velocities. Thereafter, the right and left ventricular Tei indices were derived as described previously[14,15]. The ratio of early transmitral inflow velocity divided by the early diastolic mitral annular velocity (E/E’) was also included as an indicator of diastolic dysfunction.

*BNP Levels*

Serum BNP levels are often used to obtain information about myocardial function both in children and adults[25,26]. In this study, BNP levels were measured from blood taken into EDTA-containing tubes using Triage MeterPlus device (Biocide, San Diego, CA) before the transcatheter closure, and at 1 day, 1 month and 3 months afterwards consecutively.

## Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) 17.0 statistical software package program (SPSS for Windows, Chicago, IL) was used to perform all statistical calculations. Continuous variables were expressed as the mean value ± standard deviation. Echocardiographic data were evaluated before and after transcatheter closure using the paired t-test. Statistical significance was considered as a p value less than 0.05. We performed a reproducibility study in 10 randomly selected patients. Inter- and intra-observer variability were assessed using the intraclass correlation coefficient.

## Results

Transcatheter closure of ASD was performed in 25 patients successfully, achieving a complete occlusion 1 day after the procedure in 24 patients. The baseline clinical and angiographic data are presented in Table I. All patients had a single device implanted. Solysafe septal occluders were used in 14 patients: 6 patients (type 15), 6 patients (type 20) and 2 patients (type 25). Amplatzer devices were implanted in 10 patients, and average device size was 19.6 ±5.98 mm (range: 13-30 mm). We also

**Table II.** Comparison of Atrial Volumes and Ventricular Diameters Before and After the Procedure

| | Before | Day 1 | Month 1 | Month 3 | Month 6 |
|---|---|---|---|---|---|
| Right atrial volume (ml) | 20.68±6.77 | 16.95±5.12* | 15.38±4.19* | 14.71±4.28* | 14.00±4.30* |
| Left atrial volume (ml) | 15.99±5.41 | 15.69±5.27 | 15.74±4.90 | 15.63±4.96 | 16.38±4.94 |
| Left ventricular end diastolic diameter (cm) | 3.57±0.56 | 3.63±0.53 | 3.75±0.57* | 3.83±0.56* | 3.87±0.59* |
| Left ventricular end systolic diameter (cm) | 2.27±0.42 | 2.27±0.43 | 2.30±0.42 | 2.32±0.42 | 2.31±0.46 |
| Right ventricle tricuspid annular diameter (cm) | 2.60±0.52 | 2.21±0.34* | 2.21±0.33* | 2.03±0.30* | 1.96±0.39* |
| Right ventricle short-axis diameter (cm) | 3.02±0.52 | 2.63±0.40* | 2.59±0.33* | 2.36±0.36* | 2.28±0.40* |
| Right ventricle long-axis diameter (cm) | 4.58±0.68 | 4.64±0.60 | 4.46±0.71 | 4.35±0.66* | 4.21±0.72* |
| Right ventricular end diastolic diameter (cm) | 2.55±0.45 | 2.23±0.39* | 2.10±0.34* | 1.93±0.31* | 1.81±0.31* |
| RVEDd/LVEDd | 0.72±0.13 | 0.63±0.12* | 0.57±0.09* | 0.51±0.08* | 0.47±0.09* |
| EF (%) | 65.28±7.28 | 68.61±2.63* | 70.24±4.14* | 71.12±4.07* | 72.16±3.42* |
| FS (%) | 37.16±6.82 | 37.32±2.56 | 39.36±3.59 | 39.40±3.46 | 40.40±3.28* |

Cm: Centimeter. EF: Ejection fraction. FS: Fractional shortening. LVEDd: Left ventricular end diastolic diameter. ml: Milliliter. RVEDd: Right ventricular end diastolic diameter.
*Statistically significant from pre-procedure.

used the no. 23 BioSTAR device in 1 patient.

*Echocardiographic Variables*

Transcatheter ASD closure resulted in significant changes in cardiac chambers with a reduction of the left-to-right shunt. Right atrial volumes were statistically significantly decreased, while left atrial volumes did not change significantly over a six-month follow-up (Table II). Right ventricular size was reduced and left ventricular size increased significantly. However, right ventricle long-axis diameter showed a delayed decrease compared with other right ventricle diameters (Table II). The global ventricular remodelling resulted in a significant decrease in the ratio of right ventricular end-diastolic diameter divided by the LVEDd (RVEDd/LVEDd) with an increase of the EF from 65% to 72% ($p<0.05$) during the follow-up.

*Pulsed Wave and Tissue Doppler Measurements*

The trends of echocardiographic variables before, on day 1, and at 1 month, 3 months and 6 months after transcatheter ASD closure are shown in Table III. Mitral E wave and the ratio of E/A waves were gradually increased ($p<0.05$), while IVRT and DT did not change during the follow-up ($p>0.05$). The Tei indices measured by both pulsed wave and tissue Doppler were abnormally high before the closure. After the closure, Tei indices were markedly decreased ($p<0.05$) (Table III). The pulmonary venous ARW had been identified in 14 patients before the procedure and in all patients at 1 month after the procedure. Pulmonary venous peak S velocity and the S/D ratio gradually decreased; peak D velocity, peak atrial reverse velocity and ARW duration markedly increased after the closure. The E/E'ratio showed an increase 1 month after the closure ($p<0.05$). Among the myocardial tissue velocities measured by tissue Doppler, few parameters had significant changes in the follow-up compared to the initial examination. The ratio of early diastolic wave divided by late diastolic wave (E'/A') of the mitral septal annulus and the E' velocity of the tricuspid lateral annulus showed an increase 6 months after the closure.

*BNP Levels*

The serial changes in BNP levels before and after ASD closure are presented in Figure 1. Plasma concentrations of BNP also increased significantly 24 hours after closure (25.06±0.69 pg/ml) when compared to pre-procedure values (10.57±5.95 pg/ml) ($p<0.001$). One month

**Table III.** Comparison of Left and Right Ventricular Functions and Pulmonary Flows Before and During Follow-Up After Procedure

| | Before | Day 1 | Month 1 | Month 3 | Month 6 |
|---|---|---|---|---|---|
| Mitral E wave | 82.88±9.65 | 89.60±7.60* | 93.28±7.20* | 97.60±10.15* | 99.72±11.05* |
| E/A ratio | 1.29±0.14 | 1.43±0.12* | 1.42±0.19* | 1.49±0.17* | 1.51±0.12* |
| E/E' ratio | 6.19±0.93 | 6.40±0.96* | 6.71±1.11* | 6.69±1.14* | 6.82±1.01* |
| IVRT | 75.32±15.64 | 72.48±7.41 | 72.12±10.22 | 74.48±11.31 | 77.92±7.73 |
| DT | 151.16±33.72 | 159.80±22.66 | 159.68±19.25 | 157.00±24.98 | 163.64±19.85 |
| Left ventricular Tei (by pulsed wave) | 0.46±0.08 | 0.43±0.07 | 0.42±0.08 | 0.36±0.05* | 0.34±0.05* |
| Right ventricular Tei (by pulsed wave) | 0.34±0.057 | 0.37±0.06 | 0.32±0.06* | 0.28±0.06** | 0.27±0.03 |
| Left ventricular Tei (by tissue Doppler) | 0.43±0.07 | 0.42±0.08 | 0.39±0.07* | 0.35±0.06* | 0.33±0.05* |
| Right ventricular Tei (by tissue Doppler) | 0.36±0.07 | 0.38±0.08 | 0.33±0.06 | 0.29±0.05* | 0.26±0.04* |
| Pulmonary venous S wave | 64.23±7.66 | 59.96±10.29* | 56.28±6.88* | 54.16±5.74* | 51.88±6.75* |
| Pulmonary venous D wave | 56.18±7.04 | 58.44±10.03 | 60.08±8.37* | 61.00±6.89* | 59.20±6.50* |
| Pulmonary venous S/D ratio | 1.14±0.10 | 1.03±0.11* | 0.94±0.12* | 0.90±0.11* | 0.89±0.13* |
| Pulmonary venous ARW | 16.79±3.82 | 20.10±4.00* | 26.21±4.15* | 29.00±3.97* | 29.84±4.37* |
| Pulmonary venous atrial reversal duration | 45.79±5.56 | 50.90±7.43* | 57.29±10.93* | 64.12±9.31* | 67.00±8.86* |

ARW: Atrial reversal wave. DT: Deceleration time. E/A: Ratio of mitral early to late inflow wave velocity. E/E': Ratio of early transmitral inflow velocity divided by the early diastolic mitral annular velocity. IVRT: Isovolumetric relaxation time. S/D: Ratio of systolic to diastolic wave of pulmonary vein.
*Statistically significant from pre-procedure.

after the procedure, BNP levels had returned to initial levels (mean value: 10.15±6.7 pg/ml) and continued to decline at 3 months after the closure (mean value: 7.63±8.23 pg/ml).

Inter-Observer and Intra-Observer Variability

Mean values for all variables were calculated according to two investigators. Interclass correlation coefficients for inter-observer variability for left ventricular Tei index, right ventricular Tei index, IVRT, DT, pulmonary vein S wave, left atrial volume, right atrial volume, LVEDd, FS, RVEDd, and the ratio of E/E' velocity were 0.862, 0.762, 0.934, 0.955, 0.988, 0.982, 0.982, 0.992, 0.988, 0.928, and 0.937, respectively. The means of measurements due to interclass correlation coefficients were found more reliable for all variables.

To document intra-observer variability, repeat measurements were done in randomly selected patients. Interclass correlation coefficients for intra-observer variability for left ventricular Tei index, right ventricular Tei index, IVRT, DT, pulmonary vein S wave, left atrial volume, right atrial volume, LVEDd, FS, RVEDd, and the ratio of E/E' velocity were 0.885, 0.759, 0.965, 0.948, 0.989, 0.987, 0.993, 0.993, 0.951, 0.957, and 0.973, respectively. The means of measurements due to interclass correlation coefficients were found more reliable for all variables.

## Discussion

Currently, transcatheter closure is considered the primary treatment of secundum ASDs. Right ventricular and right atrial dilatation due to chronic volume load is an expected result of the secundum ASD. However, impairment of the left ventricle has been reported to occur as a result of interaction between the ventricles over time. Right ventricular dimensions were reported to reduce significantly within 1-3 days after the procedure[9,27]. In the present study, right ventricular diameters, except the longitudinal diameter, started to decline 24 hours after the transcatheter closure and continued to decrease during the six months of follow-up. This is in accordance with previous publications, which demonstrated that diameters of the right heart had normalized six months after the procedure[9,28]. Santoro et al.[29] showed in 2004 right ventricular diameters including inlet started to decrease significantly 24 hours after the procedure. Pascotto et al.[8] also reported that right ventricular changes were seen earlier at the infundibular septum rather than the inlet. They explained that this different time course of ventricular geometric remodelling might be due to a different shape of these regions or a different orientation of their myocardial layers. However, in this study, right ventricular long-axis diameter decreased around 3 months after the procedure, while decreases in other right ventricular diameters were detected from the first day of the ASD closure. Myocardial fibrin arrangements and distinct remodelling potentiality of these right ventricular regions may have had a role in this different time course of remodelling. This study also demonstrates a significant reduction in right atrial volume as early as 24 hours following device closure of the ASD, while left atrial volume did not change significantly. Presumably, early reduction in right heart size is secondary to removal of the left-to-right shunt, with a reduction of the preload[30]. The increase in LVEDd after closure seen in this study is similar to results reported in other studies[9,31-35]. Giardini et al.[36] reported similar results that included an increase in the LVEDd and left ventricular EF and no change in the LVESd. Furthermore, decreased left ventricular systolic performance associated with right ventricular volume overload has been well described in previous reports[6,7]. In the present study, left ventricular EF started to increase 1 day after the procedure. Interventricular septal motion toward the left ventricular cavity takes place during the end-diastole and is reported to cause a reduction in the EF of the left ventricle in right ventricular volume overload[6,37]. Adverse ventricular interdependence associated with right ventricular volume overload was previously described as “Bernheim effect”, in which the interventricular septum bulges into the left ventricular cavity and leads to impairment of left ventricular filling.[6,38] Hence, improvement in left ventricular form and function seen in patients after closure can be explained by improvement in left ventricular filling.

In this study, mitral early diastolic inflow velocity and the ratio of early to late peak diastolic velocities were significantly increased, while IVRT and DT did not change during the follow-up at 6 months. This may be due to reduced preload resulting from shunting through the ASD at baseline, but probably not to the diastolic dysfunction of the left ventricle, since no other indices of diastolic function such as IVRT and DT had changed[39]. Recent observations suggest that mitral annular early diastolic velocity measured by tissue Doppler imaging is available as a preload independent index of left ventricular relaxation[40,41]. Consistent with these reports, we did not obtain any significant changes in terms of mitral annular diastolic velocity and the ratio of early to late diastolic mitral lateral annulus velocity in the 6 months of follow-up. In contrast, Schroh et al.[42] also suggested that both the mitral annular and septal early diastolic wave and the ratio of E/E’ velocity could be influenced by the left ventricular preload reduction in patients with secundum ASD. The study of Schroh et al.[42] is not a follow–up study; they only compared the patients who did and did not have ASD. Furthermore, in their study, mean diameters of ASDs were not reported. Possibly, one can propose that the amount of the right-to-left shunt through the ASD or the degree of ventricular relaxation may determine whether preload can influence E’ wave or not. We think that long- term follow-up of these patients may provide more satisfactory results. However, the ratio of E/E’ velocity was significantly increased during the follow-up in our patients. Gomez et al.[43] also reported that this ratio was increased significantly immediately after transcatheter closure. This ratio is relatively simple to obtain and conceptually has the potential for providing a reasonable estimate of filling pressures throughout a wide range of relaxation abnormalities[44]. However, the E/E’ ratio could be influenced by the left ventricular preload reduction as a result of the interatrial shunting[42]. It is well known that the pulmonary vein flow pattern changes in patients with diastolic dysfunction. Because a part of the pulmonary venous flow passes to the right atrium via the ASD, pulmonary venous flow changes do not seem like an outcome of the left ventricular diastolic function[42]. Pulmonary venous diastolic wave amplitude is usually higher than systolic wave amplitude in normal children and adolescents; thus, the ratio of S/D less than 1 is indicative of diastolic predominance[42,45,46]. At baseline, the mean S/D ratio was established as greater than 1 in the current study. We found significant changes in pulmonary venous flow pattern after the closure with a decrease in S/D ratio being under 1. Pulsed wave Doppler examination was reported to show systolic flow disturbance beginning midway through systole and continuing almost up to the wave of atrial contraction in the ASD, resulting in a systolic predominance and S/D ratio greater than 142. In addition, increased right ventricular systolic function due to the volume overload secondary to the atrial shunting could be responsible for the change in the pulmonary venous flow pattern, by suctioning not only the systemic venous return, but also the left atrial flow and pulmonary veins through the ASD[42]. The diminished ARW in our patients at baseline probably suggests that a preferential blood flow exists during atrial systole through the low-resistance ASD at the expense of retrograde flow into the pulmonary veins[47]. Doppler-derived left and right ventricular Tei indices were significantly decreased during follow-up in this study. Ding et al.[15] also reported that the increase in right ventricular Tei index was primarily due to prolongation of right ventricular IVRT in a wide age range (6 to 63 years) of the patient population. They suggested that long-standing volume overload may have a more pronounced negative effect on diastolic function than on systolic function[15]. In the present study, right ventricular Tei indices by both pulsed wave and tissue Doppler were determined to increase clinically 24 hours after the closure, and then they also decreased significantly during follow-up. The unloading of the right ventricle may cause a decrease in right ventricular function immediately after the procedure. Values that were measured in this study increased 24 hours after closure[48,49]. This phenomenon might also be related to myocardial compliance of the right ventricle[10]. We found that left ventricular Tei indices measured by both pulsed and tissue Doppler were significantly decreased during the follow-up. This improvement may be due to the restoration of LV compression10 and the increase in left ventricular filling. Studies in the adult population have reported that device closure of ASD was associated with an improvement in the left ventricular Tei index[10,33]. Previous studies have shown that plasma BNP and N-terminal pro-BNP levels are hemodynamic indicators of left ventricular function[26,50]. We showed that BNP levels were increased 24 hours after closure with a return to pre-procedure values 1 month after closure. Weber et al.[51] also reported that an increase in N-terminal pro-BNP was associated with an increase in left ventricular dimensions in an adult population. Muta et al.[52] also reported the mechanism for the transient elevation in plasma BNP levels after closure may reflect both an increase in left ventricular volumes and an elevation of left ventricular end-diastolic pressure, despite a regression of the right ventricular volume overload. In accordance with Muta et al.[52], our data are similar, indicating that the major source of the BNP synthesis is the left ventricular myocardium. Schoen et al.[26] reported that N-terminal pro-BNP is a parameter that correlates with right ventricular dilatation, pulmonary pressure and the amount of interatrial shunting in volume overload of the right heart. They also speculated that N-terminal pro-BNP levels might be used to differentiate in whom to perform ASD closure. However, further studies, especially in the pediatric population, are necessary to evaluate BNP levels as a marker of right ventricular impairment.

*Limitations*

This study has some limitations. First, the right ventricular inflow and outflow velocities and durations were measured in different cardiac cycles to obtain the Tei index. However, we found similar values with tissue Doppler imaging, which is a reliable technique for Tei index. Second, the number of patients may be small to demonstrate persistent changes in cardiac functions. Finally, our data were obtained over a six-month period only, so longer follow-up is mandatory to elucidate further changes in ventricular physiology.

In conclusion, in pediatric patients undergoing transcatheter closure of secundum ASD, we found a significant reduction in right heart sizes, even on the first day after the procedure, and global functional improvement in the right ventricle in the follow-up. Left ventricular

Tei indices that measured by pulsed wave and tissue Doppler imaging were improved 3 months and 1 month, respectively, after the procedure. However, the right ventricular Tei indices measured by both methods were increased 24 hours after closure but started to decrease at 1 month after the procedure. This phenomenon can be explained by increased right ventricular compliance. Since IVRT and DT did not change significantly, change in the transmitral E wave and elevation in the ratio of E/E' velocity in the follow-up as a reflection of increased left ventricular preload are not due to diastolic dysfunction. We showed that BNP levels increased significantly 24 hours after closure compared to pre-procedure values. However, 1 month after closure, BNP levels had returned to initial pre-procedure levels. Notably, a different time course of remodelling was found between the long-axis diameter and transverse diameters of the right ventricle. A significant increase in left ventricular size and EF might be responsible for the clinical improvement after closure. Finally, our data suggested that right and left ventricular form and function improve following transcatheter closure in children and adolescents.

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