ORIGINAL ARTICLE

The effect of transcatheter atrial septal defect closure on the left heart function in pediatric patients

Çocuklarda transkateter atriyal septal defekt kapatılmasının sol kalp fonksiyonları üzerine etkisi

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ABSTRACT

Objective: The aim of this study was to use tissue Doppler imaging to evaluate the left atrial systolic and the left ventricular (LV) diastolic function as well as the left atrial ejection force in children who underwent transcatheter closure of a secundum atrial septal defect (ASD).

Methods: Tissue Doppler measurements of the left atrial ejection force, the mitral valve, and left atrial volume were performed before the ASD closure procedure, and on the 1st day, 10th day, and 1st and 3rd months after the procedure in 56 patients and in 28 healthy controls.

Results: There was a significant decrease in the septal and lateral a' velocities on the first day ($p<0.05$). There was a statistically significant increase in the septal e'/a' parameters at the third month compared with the initial measurements. The left atrial ejection force was lower in patients with an ASD than in the healthy group (10.69±4.94 kdyn, 12.31±4.05 kdyn, respectively), but there was no significant difference ($p=0.053$). The left atrial ejection force was significantly greater in the patient group 3 months after the procedure, and there was no significant difference compared with the control group.

Conclusion: Improvement in the LV diastolic and left atrial systolic functions was observed in children who underwent transcatheter closure of an ASD. There was no negative effect related to the devices used.

ÖZET

Amaç: Transkateter atriyal septal defekt (ASD) kapatılan çocuklarda sol atriyal ejeksiyon force (LAEF) ve doku Doppler ölçümleri ile sol atriyal sistolik fonksiyonları ve sol ventriküler diyastolik fonksiyonları değerlendirdik.

Yöntemler: Transkateter ASD kapatılan 56 çocukta kapatma öncesi, ertesi gün, onuncu gün, birinci ay ve üçüncü aylarda LAEF, mitral kapak doku Doppler ve sol atriyal volüm hesaplamaları yapıldı. Hastaların ASD kapatma öncesi değerleri sağlıklı yaş ve cinsiyet uyumlu 28 kontrol ile karşılaştırıldı.

Bulgular: Hasta grubunun izleminde, mitral A ve septal e' velositesinde anlamlı düşme ve sonrasında artış saptandı ($p<0.05$). Septal ve lateral a' değerlerinde anlamlı düşme saptandı ($p<0.05$). Septal e'/a' değerlerinde başlangıca göre 3. ayda anlamlı artma saptandı. LAEF hasta grubunda ortalama 10.69±4.94 kilodyne, sağlıklı grupta 12.31±4.05 kilodyne ile daha yüksek bulundu, istatistiksel anlamlı fark bulunmadı ($p=0.053$). Ortalama LAEF değerleri işlem öncesi ortalama 10.68±3.87, ertesi gün 9.57±3.25, 10. gün 9.57±3.93, 1. ay 9.41±3.44, 3. ay 12.93±4.59 kilodyne bulundu. İşlem öncesine göre 3. ayda anlamlı artış saptandı ve sağlıklı grup ile anlamlı fark bulunmadı.

Sonuç: Transkateter ASD kapatılması ile sol atriyum sistolik ve sol ventrikül diyastolik fonksiyonlarında olumlu yönde etkilenme izlenmiştir. Cihazın mekanik olumsuz etkisi görülmemektedir.

Atrial septal defect (ASD) represents 8% to 10% of all congenital heart defects in children.[1] Transcatheter ASD closure is a safe and effective alternative to surgical closure methods, and has become the primary choice of treatment in cases of secundum ASD.

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In adults with an ASD, left ventricular (LV) diastolic function can deteriorate due to right ventricular dilatation.[2,3] The small number of studies of children that have evaluated LV diastolic function have reported diverse results, including an increase, decrease, or no change in tissue Doppler velocities.[4–8] Early improvement in LV diastolic properties has been reported in patients who have undergone transcatheter ASD closure.[9]

Left atrial ejection force was first proposed by Manning et al.[10] as a noninvasive method to evaluate left atrial systolic function. Left atrial ejection force has also been reported as a possible early, noninvasive indicator of LV diastolic dysfunction.[11] It has been found to be increased in asphyxiated newborns, noncompaction cardiomyopathy, hypertrophic cardiomyopathy, hypertensive patients with LV hypertrophy, and in patients with autoimmune diseases.[12–16]

The objective of this study was to evaluate left atrial systolic and LV diastolic function by assessing left atrial ejection force, left atrial volume, and mitral valve tissue Doppler measurements in children who underwent a transcatheter ASD closure procedure.

METHODS

A total of 56 patients who underwent transcatheter ASD closure and 28 controls were initially included in the study. The control group consisted of age- and gender-matched children without cardiac pathologies who underwent echocardiography due to nonspecific chest pain or an innocent murmur. Patients with accompanying arrhythmia, hypertension, cardiomyopathy, or significant mitral valve insufficiency, as well as those with additional systemic diseases, were excluded from the study. Patients who missed any follow-ups throughout the duration of the study were also excluded. Prior to the procedure, the height, weight, body mass index, and blood pressure of all of the patients were measured and recorded. In addition, an electrocardiogram was performed prior to the procedure and at all follow-ups. Echocardiographic examination was performed 24 hours before the procedure, after 24 hours, and then repeated 10 days, 1 month, and 3 months after the procedure. Two researchers performed the echocardiography using a 3 MHz transducer (Vivid S6, GE Healthcare Inc., Chicago, IL, USA). The mitral annulus and apical velocity were measured in the 4-chamber view. Peak E and A velocities were calculated by averaging 3 consecutive measurements in the apical 4-chamber view at the level of the mitral valve (Fig. 1a, b). Left atrial ejection force was calculated using the formula 0.5 x P x mitral valve area x peak A velocity2. Mitral valve area was calculated using the mitral annulus measurements determined in the apical 4-chamber view and the formula π x mitral annulus 2/4.[2] The left atrial volume was measured using the Simpson's model at the end of the systole in the apical 4-chamber view. M-mode measurements were performed in the parasternal short-axis and long-axis view to determine the LV ejection fraction and fractional shortening, Three consecutive tissue Doppler measurements of mitral septal and lateral junction points were averaged.

Abbreviations:

ASD *Atrial septal defect*
LV *Left ventricular*

The Kolmogorov-Smirnov test was used to determine whether the continuous variables were normally distributed. The Student's t-test was used to compare 2 independent groups with normally distributed variables, while the Mann-Whitney U test was used for

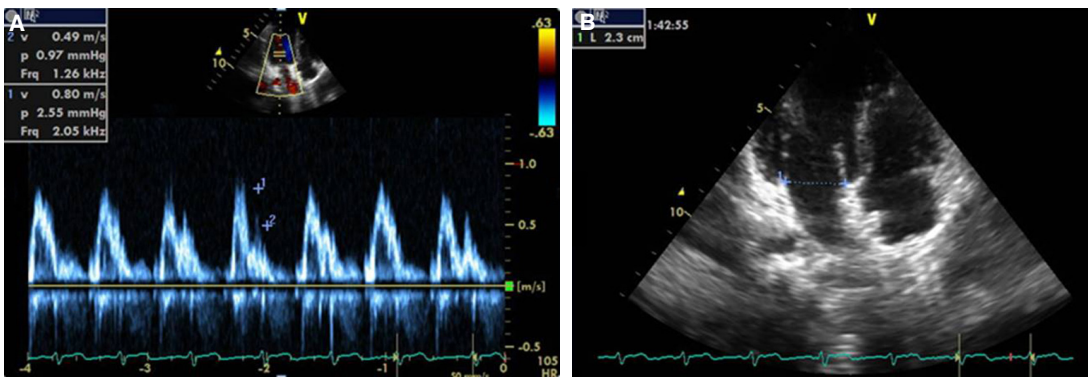

Figure 1. **(A, B)** Mitral valve velocity and mitral valve annulus diameter measurement in the 4-chamber view.

non-normally distributed variables. Relationships between categorical variables were assessed with a chi-square test. Repeated analysis of variance was used to test the change over time of more than 2 repeated quantitative measurements. The mean±SD was used as the descriptive statistic format for quantitative variables, and number and percent values were used for categorical variables. The statistical analysis was performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA) and $p<0.05$ was considered statistically significant.

This study was performed in accordance with the ethical standards of the institutional and/or national research committee. Informed consent was obtained from all of the participants involved in the study.

RESULTS

The study included 56 patients, of whom 33 (58.9%) were female and 23 (41.1%) were male. The patients' baseline variables were compared with 28 healthy controls who were matched for age and gender. The mean age was 7.25±3.81 years, the mean weight was 25.40±14.61 kg, the mean height was 119±23 cm, the mean systolic blood pressure was 95.8±9.2 mmHg, and the mean heart rate was 106±17 bpm. No significant difference was found between the patient and control groups in terms of age, gender, height, weight, or body mass index. All of the patients were in sinus rhythm before the procedure and during the follow-up. The average Qp/Qs shunt ratio was 1.90±0.55. The mean diameter of the closure device was 16 cm (range: 8–32 cm). An Amplatzer (St. Jude Medical, Inc., St. Paul, MN, USA) device was used in 31% of the patients, a Lifetech Ceraflex (Lifetech Scientific (Shenzhen), Shenzhen, China) in 31% of the patients, and an Occlutech Figulla Flex II (Occlutech AB, Helsingborg, Sweden) was used in 38.1% of the patients. No significant difference was determined between the patient and control groups in terms of LV ejection fraction, fractional shortening, or mitral valve E, A velocity. However, the left atrial volume was found to be significantly lower in the patient group ($p=0.02$). There were significant differences in the septal a', lateral e', and lateral a' tissue Doppler measurements ($p<0.05$). Moreover, the mitral annular diameter and mitral annulus area were significantly lower in the patient group than in the control group ($p<0.05$). Although the left atrial ejection force was lower in the patient group when compared with the control group, it was insignificant ($p=0.053$). The mean left atrial ejection force in the patient group was 10.69±4.94 kdyn, while in the healthy group it was higher, with a mean of 12.31±4.05 kdyn. A comparison of demographic characteristics and echocardiographic measurements of the patient and control groups is presented in Table 1. A comparison of basal level echocardiographic measurements of the patient and control groups is shown in Table 2.

Since patients with missed follow-ups were excluded from the study, a total of 42 patients with complete repeated measurements were evaluated progressively. The values of the patient groups are shown in Table 3.

The left atrial ejection force was calculated based on the previously mentioned formula. The mean left atrial ejection force before the procedure was 10.68±3.87 kdyn, 9.57±3.25 kdyn on the next day, 9.57±3.93 kdyn after 10 days, 9.41±3.44 kdyn at 1 month, and

Table 1. Demographic data of patients and controls

	Patient group (n=56)			Healthy group (n=28)			*p*
	n	%	Mean±SD	n	%	Mean±SD	
Age (years)			7.25±3.81			8.37±3.22	0.185
Sex							
Female	33	58.9		12	42.9		0.164
Male	23	41.1		16	57.1		
Height (cm)			120±23			129±20	0.074
Weight (kg)			25.4±14.6			29.1±10.4	0.243
Body mass index (kg/m^2)			16.4±2.6			16.7±2.2	0.644

Table 2. Comparison of basal levels of echocardiographic measurements of the patient and control groups

	Patient group (n=56)	Healthy group (n=28)	*p*
Left ventricular ejection fration (%)	72.75±6.59	73.89±5.78	0.438
Left ventricular fractional shortening (%)	39.14±5.70	40.32±5.19	0.361
Mitral E velocity (m/s)	1.06±0.19	1.04±0.15	0.584
Mitral A velocity (m/s)	0.70±0.15	0.68±0.11	0.665
Mitral E/A	1.55±0.24	1.53±0.19	0.652
Mitral valve annulus (cm)	2.29±0.42	2.50±0.38	0.019*
Mitral valve area (cm^2)	4.27±1.51	05.01±1.52	0.016*
Septal e' (m/s)	0.134±0.03	0.147±0.07	0.254
Septal a' (m/s)	0.106±0.04	0.072±0.02	0.001*
Septal e'/a'	1.39±0.52	2.14±1.06	0.001*
Septal s (m/s)	0.086±0.02	0.079±0.01	0.100
Lateral e' (m/s)	0.143±0.04	0.172±0.09	0.042*
Lateral a'(m/s)	0.094±0.04	0.074±0.01	0.015*
Lateral e'/a'	1.74±0.75	2.38±1.15	0.003*
Lateral s (m/s)	0.087±0.02	0.088±0.02	0.882
Left atrial volume (mL)	17.27±8.27	21.21±7.72	0.020*
Left atrial ejection fraction (kydn)	10.69±4.94	12.31±4.05	0.053
Qp/Qs	1.90±0.55		

Table 3. Comparison of variables before and after transcatheter atrial septal defect closure

	Pre-closure	1 day	10 days	1 month	3 months	*p*
Mitral E (m/s)	1.08±0.18	1.05±0.19	1.02±0.17	1.04±0.16	1.06±0.15	0.296
Mitral A (m/s)	0.70±0.15	0.63±0.14	0.62±0.11	0.62±0.09	0.69±0.12	0.001*
Mitral E/A	1.56±0.26	1.67±0.27	1.68±0.33	1.70±0.24	1.55±0.29	0.014*
Left ventricular ejection fration (%)	73±7	72±6	72±6	72±5	73±5	0.717
Left ventricular fractional shortening (%)	39±6	38±5	38±5	38±5	38±4	0.765
Mitral valve area (cm^2)	2.28±0.40	2.38±0.41	2.44±0.44	2.42±0.41	2.55±0.41	0.001*
Septal e' (m/s)	0.14±0.04	0.11±0.03	0.11±0.03	0.11±0.02	0.12±0.03	0.001*
Septal a' (m/s)	0.10±0.04	0.07±0.02	0.07±0.02	0.08±0.02	0.07±0.02	0.001*
Septal e'/a'	1.39±0.08	1.51±0.05	1.54±0.06	1.54±0.06	1.77±0.01	0.001*
Septal s (m/s)	0.08±0.01	0.08±0.01	0.07±0.01	0.08±0.01	0.07±0.01	0.001*
Lateral e' (m/s)	0.14±0.04	0.14±0.03	0.14±0.04	0.14±0.03	0.15±0.04	0.13
Lateral a' (m/s)	0.09±0.04	0.07±0.02	0.07±0.02	0.08±0.02	0.08±0.02	0.001*
Lateral e'/a'	1.75±0.81	1.88±0.42	1.93±0.50	1.98±0.44	2.03±0.66	0.37
Lateral s (m/s)	0.09±0.02	0.08±0.02	0.08±0.02	0.08±0.02	0.08±0.02	0.027*
Left atrial volume (mL)	17.42±8.79	15.62±8.39	15.81±8.30	16.88±9.24	18.09±8.62	0.001*
Left atrial ejection fraction (kdyn)	10.68±3.88	9.58±3.26	9.57±3.93	9.42±3.44	12.93±4.59	0.001*

12.93±4.59 kdyn 3 months after the procedure. There was a significant increase in left atrial ejection force at 3 months when compared with the pre-procedure values. There was no significant difference between the control group and the patient group in the left atrial ejection force in 3 months of follow-up.

DISCUSSION

In this study, we evaluated left heart function using M-mode tissue Doppler assessment of left atrial volume and left atrial ejection force in children who underwent a transcatheter ASD closure. Previous studies have reported an increase in the right ventricle tissue Doppler velocity in early periods following the closure of the ASD.[17] The number of studies that have assessed function of the LV and left atrium is limited.

Left atrial function has been evaluated in many diseases and poor function is associated with mortality and morbidity. It has been found to be associated with an increase in the size of the left atrium, LV diastolic dysfunction, development of atrial fibrillation, cardiac mortality, and stroke.[11] In our study, a significant increase from the baseline was observed at the 3-month follow-up in the left atrial volume. Low basal left atrial volume may have been associated with decreased diastolic filling of the left atrium because of a left-right shunt. A decrease after closure suggests that the LV diastolic filling improves or has not yet recovered left atrial volume in the early period. The device may also have an effect on left atrium volume measurement. Studies have shown that left atrial volume increased, decreased, or did not change following a transcatheter ASD closure in adults.[3,7,18] It has been reported that in children who underwent transcatheter ASD closure, left atrial volume did not change, while that of both the right ventricle and right atrium was significantly reduced and the LV significantly increased.[19]

In this study, lateral e' and septal and lateral a' values were higher in the patient group before the procedure and supported diastolic involvement. These parameters decreased during the follow-up period. There was no significant difference between the control and patient groups at the third month. This suggests that early diastolic impairment can occur in children and that it may improve after the ASD closure. Giardini et al.[6] determined a significant increase in the e', a' and s velocities in tissue Doppler measurements taken immediately after the transcatheter ASD closure procedure of 15 children. Although the e' and s velocities were lower in the patient group when compared with the control group before the procedure, there was no significant difference between the groups after treatment. Acute improvement of LV preload and early diastolic function following a transcatheter ASD closure in children has been reported.[5] We also obtained similar results. Yılmazer et al.[19] reported an increase in mitral E/A, E/e', and e'/a' ratios at 6 months of follow-up of children who underwent a transcatheter ASD closure. They associated these findings with restoration of LV compression and increased LV filling. Moreover, they suggested that it was a reflection of preload increase, rather than LV diastolic dysfunction. Gomez et al.[8] examined 18 patients with a wide age range and determined that mitral E increased, E/e' increased significantly, and tissue Doppler measurements did not change in the early period immediately after closure of the ASD. They indicated that a healthy myocardium reabsorbed increased volume with normal relaxation and compliance. Similarly, in our study, there was no significant change in E and e' velocities in the early period. There was a significant decrease at the first month control examination and values increased again at the third month. In this regard, different studies have reported varied results. Studies that have evaluated LV diastolic function have reported both a decrease and no change in the mitral E/A ratio and variable tissue Doppler e' velocity.[2] All of these different results may be related to dissimilar patient groups, follow-up periods, or small patient groups.

Manning et al.[10] reported low post-procedure left atrial ejection force in patients who underwent cardioversion due to atrial fibrillation; however, these parameters had improved significantly in patients who remained in sinus rhythm at the 3-month follow-up. Other studies that have evaluated left atrial systolic function have reported similar results.[20,21] In addi-

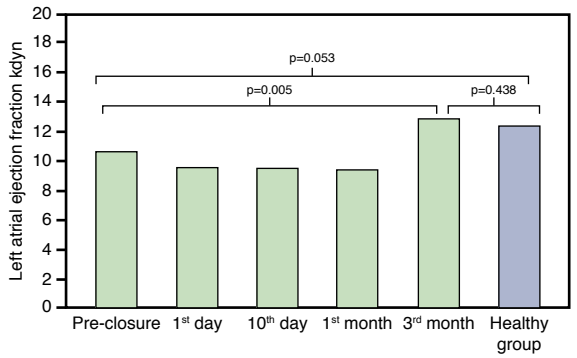

Figure 2. A comparison of progressive left atrial ejection fraction values in patients who underwent transcatheter atrial septal defect closure and the control group.

tion, there is research that has reported increased left atrial ejection force in patients with LV dysfunction.[12–16,18,22] In our study, the left atrial ejection force was lower before the ASD closure in the patient group when compared with the control group, but this difference was not significant. Moreover, the left atrial ejection force continued to decrease until the 1-month follow-up after the closure procedure, but once again, this decrease was not significant. However, the left atrial ejection force had increased significantly at the 3-month follow-up and there was no significant difference in comparison with the control group (Fig. 2). The initial decrease might be due to right ventricular dilatation, which may be associated with improvement of LV diastolic filling. The increase seen in the follow-up was assessed in relation to the improvement of left atrial systolic function. No device-associated negative effect was observed in left atrial systolic function.

Study limitations

In our study, the primary aim was to evaluate LV diastolic and left atrial systolic function with left atrial systolic force and mitral valve tissue Doppler measurements. The power of the study could be increased by using methods such as pulmonary venous Doppler, atrial strain, and mitral annular plane systolic excursion. Evaluation of the right ventricle and right atrium could also be useful.

Conclusion

In this study, the findings of prospective tissue Doppler evaluations and left atrial ejection force assessments were suggestive of early period diastolic impairment in children. Three months after the ASD closure, possible signs of right ventricular dilatation had declined and the shunt directed the blood that passed to right ventricle toward the LV. In the patient group, left atrial ejection force, which is a noninvasive indicator of left atrial systolic function, showed a significant increase during follow-up and was at similar levels to those of the control group. The ASD closure positively affected left atrial function and no negative mechanical device effects were observed in the systolic function of the left atrium.

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Keywords: Left atrial ejection force; left atrial volume; secundum atrial septal defect; tissue Doppler; transcatheter closure.

Anahtar sözcükler: Sol atrial ejeksiyon force; sol atrial volüm; sekundum atrial septal defekt; doku Doppler; transkateter ASD kapama.