Influence of Percutaneous Occlusion of Atrial Septal Defect on Left Atrial Function Evaluated Using 2D Speckle Tracking Echocardiography

Kazutaka Suzuki, MD, Taichi Kato, MD, Satoshi Koyama, MD, Tsutomu Shinohara, MD, Sachiko Inukai, MD, Jun Sato, MD, Hidenori Yamamoto, MD, Daisuke Omori, MD, Shuichiro Yoshida, MD, Sho Takeda, MD, Hiroshi Nishikawa, MD, Naoki Ohashi, MD, Hajime Sakurai, MD and Shinji Saitoh, MD

Summary

Percutaneous occlusion of atrial septal defect (ASD) has recently become a standard therapeutic strategy, but little is known about left atrial (LA) function thereafter. The present study aimed to determine LA function in 43 children with ASD and 13 controls based on LA strain measured by two-dimensional echocardiographic speckle tracking (2DE-ST). Among these children, 12 underwent surgery (ASD-S), 31 had device closure (ASD-D), and 13 were included as controls. LA strain was significantly decreased after ASD-D but was not significantly altered after ASD-S, indicating that percutaneous occlusion of an ASD might decrease LA function. Furthermore, the size of the ASD device negatively correlated with LA strain. These results imply that ASD occlusion devices negatively influence LA function and might be important when deciding therapeutic strategies for ASD. LA strain measured by 2DE-ST should become a good indicator of LA function after ASD treatment in children.

Key words: Strain, Left atrial reservoir function, Left atrial conduit function, Left atrial booster pump function

Atrial septal defect (ASD) with a left-to-right shunt is the most prevalent congenital heart disease. Patients with ASD develop right heart failure, atrial arrhythmias, and eventually pulmonary hypertension if a significant right heart volume load persists. Since the risk of developing atrial fibrillation due to ASD without treatment increases with age, ASD should be treated before patients reach the age of 40 years. Surgical outcomes have been very good for patients with ASD. Less invasive percutaneous occlusion using a specific device has recently been introduced as an alternative to surgery. The outcomes of percutaneous occlusion and surgery are comparable, and percutaneous occlusion has become more popular for ASD closure.

Although ventricular functions or volumes after percutaneous occlusion of ASD have been studied, information about the effects of percutaneous occlusion on atrial performance is limited. Several methods have been developed to measure atrial function, including left atrial (LA) strain, indicating LA reservoir, conduit, and booster pump function. Representative methods of evaluating strain on echocardiographic Doppler images (TDI) of tissues have the disadvantages of angle dependence and poor reproducibility and the potential for compromised evaluative accuracy. A method that is independent of angle is needed to accurately measure strain.

Two-dimensional echocardiographic speckle tracking (2DE-ST) is a novel, noninvasive way to resolve the issue of angle dependence. It systemically evaluates local or global myocardial movement, speed, and function by automatically tracking specific myocardial speckles. Atrial function has recently been analyzed using this method, but it has not been applied to assessing LA function among patients with ASD.

The present study aimed to determine the effects of surgical or percutaneous occlusion of ASD on LA function in children using 2DE-ST.

Methods

Patients: We retrospectively investigated data from 59 children (28 males and 31 females, median age 8.0 years; IQR, 6.5-11.0 years) with ASD or Kawasaki disease who were admitted to Chukyo Hospital between April 2015 and 2018. The study was approved by the institutional review board of Nagoya City University Graduate School of Medical Sciences. Written informed consent was obtained from all participants or their legal guardians.

Address for correspondence: Kazutaka Suzuki, MD, Department of Pediatrics and Neonatology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan. E-mail: suzuki.k@med.nagoya-cu.ac.jp

Received for publication April 3, 2019. Revised and accepted October 1, 2019. Released in advance online on J-STAGE January 17, 2020.

All rights reserved by the International Heart Journal Association.
and August 2017. Three patients were excluded because of poor image quality. We therefore enrolled 56 patients in this study. Twelve had been treated by surgical repair of ASD (ASD-S), 31 had ASD device closure (ASD-D), and 13 with Kawasaki disease who were in the convalescence phase without coronary lesions served as controls. All had secundum ASD, and patients with abnormalities affecting hemodynamics such as complications requiring other treatments, pulmonary hypertension, atrioventricular valve regurgitation, and arrhythmia were excluded. All patients in the ASD-S group had undergone direct ASD closure. An AMPLATZER™ septal occluder (AGA Medical Corporation, Plymouth, MN, USA) was inserted into all patients in the ASD-D group. This group was subclassified according to the size of the ASD device (mm) inserted per body surface area (BSA; m²) as small (< 15 mm²; n = 10), medium (≥ 15-20 mm²; n = 10), or large (≥ 20 mm²; n = 11).

Echocardiographic evaluation: One experienced cardiologist conducted all transthoracic echocardiographic assessments during the study using an IE-33 echo system (Philips North America LLC, Andover, MA, USA) before and after ASD treatment. Patients in the ASD-S group were examined one day before surgery and one day before discharge, and those in the ASD-D group were examined one day before and one day after intervention. Parasternal, apical, and subcostal images were acquired using a 5- or 8-MHz transducer.

We calculated ASD size and left ventricular (LV)-TEI index, and pulmonary venous flow were obtained from pulse Doppler images. The velocity of LV inflow and outflow was recorded on pulse Doppler images. E′ was measured at the septal and lateral mitral annulus velocities on images acquired in the apical four-chamber view. The ratio of mitral peak velocity of early filling (E) to early diastolic mitral annular velocity (E′) was measured to estimate LV filling pressure. Pulmonary venous return velocities were measured from the apical four-chamber view by sampling the right upper pulmonary vein.

Measurement of LA strain using 2DE-ST: Two pediatric cardiologists who were blinded to demographic data measured LA strain by 2D speckle tracking using QLAB version 10.7 software (aDMQ; Philips North America) in apical four-chamber views of images that were acquired at a frame rate of > 50 Hz. This software was originally devised to measure LV strain, but we applied it to measure LA strain as described.23 Using this method, we evaluated speckle tracking in patients with ASD.23,24 After one cardiac cycle was selected, we selected the septal and lateral corners of the mitral annulus and the LA roof in the systolic frame. The QLAB software automatically provided seven tracking regions on the LA wall and calculated the longitudinal strain (LS) using speckle tracking. Unsatisfactory tracking of the LA endocardium was manually adjusted. The LA walls were segmented into seven parts: the intra-atrial septum (IAS) of LA into three parts, the free wall (FW) of LA into three parts, and the roof of the LA into one part (Figure). We could not accurately calculate strain on the IAS due to the lack of a septal wall. Therefore, we calculated only LS of the FW as the average strain in three segments of the FW and did not include LS of IAS or global longitudinal strain.23 We calculated the average of the peak LS of FW during the systolic phase (LSs-FW) in three segments, which indicated LA reservoir function. LS of FW during the early diastolic phase (LSe-FW) indicated LA conduit function. We calculated LS of FW during the late diastolic phase (LSa-FW), which indicates LA booster pump function, as the difference between LSs and LSe strain (Figure).14-16)

Statistical analysis: All data were statistically analyzed using the JMP software (SAS Institute, Cary, NC, USA). Data are presented as medians (IQR 25-75%). Differences among ASD-S, ASD-D, and controls were assessed using nonparametric Kruskal-Wallis tests. Significant differences between two unpaired groups were assessed using nonparametric Steel-Dwass tests. Significant differences among the three groups classified by ASD device size were assessed using Kruskal-Wallis and Steel-Dwass tests. Correlations between ASD device size and LA strain were assessed using Spearman’s rank correlation test. We considered values with P < 0.05 as being statistically significant. Inter- and intra-observer variability was assessed using Bland-Altman plots.

Informed consent: The Ethics Committee of the Nagoya City University Graduate School of Medical Sciences waived the need for informed consent due to the retrospective observational nature of the present study. The Ethics Committee at the Nagoya City University Graduate School of Medical Sciences and the Japan Community
Let drugs were given to the ASD-D group for six months, and some patients in the ASD-S group received low-dose diuretics. Echocardiographic findings showed that LV contraction and dilation did not significantly differ among the ASD-D, ASD-S, and control groups. Atrial function assessed using 2DE-ST also did not significantly differ. The ASD was significantly larger in the ASD-S group than the ASD-D group because percutaneous occlusion was indicated for patients with an intact atrial septum margin and some patients in the ASD-S group received low-dose diuretics. Echocardiographic findings showed that LV contraction and dilation did not significantly differ among the ASD-D, ASD-S, and control groups. Atrial function assessed using 2DE-ST also did not significantly differ. The ASD was significantly larger in the ASD-S group than the ASD-D group because percutaneous occlusion was indicated for patients with an intact atrial septum margin and a relatively small ASD.

**Results**

Baseline characteristics of patients, outcomes, and echocardiographic parameters: Table I shows the demographic data and echocardiographic parameters before undergoing treatment for ASD. The ASD was closed without post-procedural complications in all patients in the device closure (ASD-D) and surgery (ASD-S) groups. Antiplatelet drugs were given to the ASD-D group for six months, and some patients in the ASD-S group received low-dose diuretics. Echocardiographic findings showed that LV contraction and dilation did not significantly differ among the ASD-S, ASD-D, and control groups. Atrial function assessed using 2DE-ST also did not significantly differ. The ASD was significantly larger in the ASD-S group than the ASD-D group because percutaneous occlusion was indicated for patients with an intact atrial septum margin and a relatively small ASD.

**LA function after ASD treatment:** Table II shows the echocardiographic findings after ASD treatment. Speckle tracking showed that LS of the FW significantly decreased.
in the ASD-D group. Mean pre- and post-procedural differences in strain were significantly high in the ASD-D group (Table III).

The ASD-D group was subclassified depending on having a small, medium, or large device. We compared the strain among the three groups before and after treatment (Table IV). The ASD device size negatively correlated with LSs and LSe of FW (Table V). Mean pre- and post-procedural differences in strain were significantly high in the ASD-D group. We found negative correlations between the size of ASD devices and LA strain. To our knowledge, this is the first study to use novel speckle tracking to compare the effects of catheter and surgical approaches on LA function in children with ASD and evaluate the correlation between device size and LA function.

We found that LSs, LSe, and LSa of FW were significantly decreased after ASD occlusion in the ASD-D group. A decrease in LSs of FW indicated an impaired atrium reservoir function in the ASD-D compared with ASD-S and control groups. The atrium reservoir function during the LV systolic phase was compromised by the device causing an extended disturbance, which led to a decrease in LA compliance. Since LV contraction and dilation were preserved, decreased LA reservoir function was affected by LA compliance rather than LV function. Decreased LSe of FW reflects impaired atrial conduit function. The atrium conduit function during the early diastolic LV filling phase is compromised due to resistance to the device. Decreases in LSa of FW reflect the impaired function of the atrial booster pump that becomes compromised by disturbed contraction caused by the device, which results in decreased LA contractility. A previous study reported that reduced atrial function is a risk factor for the development of atrial fibrillation. After ASD treatment, decreased LA strain might cause atrial arrhythmia, which would require long-term follow-up. Giovannini, et al. found that LA strain determined using TDI was significantly decreased in the ASD-S group compared with a large device, compared with a small device after treatment (Table IV). The ASD device size negatively correlated with LSs and LSe of FW (Table V).

**Discussion**

We used speckle tracking to assess LA dysfunction that was not evident after percutaneous occlusion of an ASD. We found negative correlations between the size of ASD devices and LA strain. To our knowledge, this is the first study to use novel speckle tracking to compare the effects of catheter and surgical approaches on LA function in children with ASD and evaluate the correlation between device size and LA function.

| Table III. Comparison of Left Atrial Strain Before and After Procedures in ASD-D Group |
|-----------------|-----------------|-----------------|-----------------|
|                  | Before procedure | After procedure | Mean difference 95% CI | P      |
| LSs-FW (%)       | 43 (34-46)       | 28 (19.8-31) *  | −14.43 (−17.88 to −10.99) | < 0.0001 |
| LSe-FW (%)       | 32.3 (24.6-39.6) | 21.7 (17.5-27.6) * | −11.43 (−14.55 to −8.30) | < 0.0001 |
| LSa-FW (%)       | 6 (4-11.15)      | 5.2 (1.9-7.7) *  | −3.54 (−5.63 to −1.44) | 0.0020  |

Data are expressed as medians and interquartile ranges. ФW indicates free wall; and LS, longitudinal strain. *Significant difference between before and after procedure.

| Table IV. Comparison of Echocardiographic Parameters Among Small, Medium, and Large Devices |
|-----------------|-----------------|-----------------|-----------------|
|                  | Small           | Medium          | Large           | P      |
|                  | 10              | 10              | 11              |        |
| Device/BSA       | 9.42 (8.95-13.66) | 18.5 (17-19.16) | 23.1 (20.6-25.3) | < 0.0001 |
| LSs-FW (%)       | 43 (35.5-49.5)  | 36 (33-44.5)    | 40 (28-46)      | 0.3443  |
| LSe-FW (%)       | 35.7 (24.8-42.2) | 30.6 (26.1-37.3) | 29.7 (22.6-41.5) | 0.6771  |
| LSa-FW (%)       | 9.7 (4.45-14.2) | 5.3 (2.6-14.3)  | 5.2 (3.3-10.8)  | 0.4346  |

Data are expressed as medians and interquartile ranges. FW indicates free wall; and LS, longitudinal strain. *Significant difference between small and large devices.

| Table V. Correlation Between ASD Device Size and LA Strain |
|-----------------|-----------------|-----------------|-----------------|
|                  | Before procedure | After procedure |                 |
| Parameter       | ρ               | P               | ρ               | P        |
| LSs-FW          | −0.2465         | 0.1892          | −0.5176         | 0.0034   |
| LSe-FW          | −0.1502         | 0.4283          | −0.5809         | 0.0012   |
| LSa-FW          | −0.1878         | 0.3203          | −0.0047         | 0.9812   |

FW indicates free wall; and LS, longitudinal strain.
with the control and ASD-D groups. This might have been due in part to the angle dependence and poor reproducibility of TDI. Another report has suggested that color Doppler myocardial imaging cannot significantly discriminate an ASD device from the normal atrial wall. Color Doppler myocardial imaging is not appropriate for accurate evaluation of LA function.

Regional strain was also significantly decreased after ASD closure in the ASD-D group. Insertion of the ASD device reduced the LS of FW, whereas FW was not directly obstructed by the ASD device. Anatomically, the atrial walls consist of circumferential and longitudinal muscular bundles. Therefore, the large device used to close the ASD might have initially disrupted these bundles in the IAS directly, followed by the subsequent disruption of the free wall of the left atrium. Furthermore, LSs-FW and LSs-FW were decreased more by a larger device in the ASD-D group. In fact, the size of the ASD device negatively correlated with the LA reservoir and conduit function. These data suggest that careful follow-up of LA function might be needed for patients with larger devices. A previous study found no significant correlation between device size and atrial function between a patent foramen ovale and ASD.

Our results differed from these, in part, because we measured the atrium strain using 2DE-ST, whereas the previous study measured using TDI.

We confirmed that the traditional parameters of atrial function, transmural velocities of late wave (MV-A), ratios of systolic to diastolic pulmonary venous flow (PVF), and PVF of atrial reversal flow did not significantly decrease after ASD closure in both the ASD-D and ASD-S groups. The evaluation of mitral Doppler flow and mitral annular motion suggested that atrial stiffness increased after device placement. However, these parameters did not directly reflect atrial functions. Contrary to these traditional parameters, our results showed that strain determined by speckle tracking could identify small changes in LA dysfunction.

This study had some limitations. Firstly, two-dimensional analysis of atrial strain from the apical four-chamber view might not have assessed the function of the entire atrium. Regardless of LA morphology, the assessment of LA function was too difficult, and a 3DE method of assessing LA strain has not been established. Secondly, we evaluated a short-term endpoint after ASD treatment, so an accurate long-term prognosis in this cohort cannot be elucidated by this study design. However, a previous study that evaluated LA strain immediately and six months after ASD closure found no difference. Although validation is needed, LA performance in the short and long terms might correlate.

In conclusion, analyzing LA strain using 2DE speckle tracking allowed simple and valuable assessment of the LA reservoir, conduit, and booster pump function of ASD after treatment. We showed that LA function was decreased after ASD occlusion in the ASD-D group compared with the ASD-S group. Furthermore, LA reservoir and conduit function negatively correlated with device size. These findings warrant further investigation of the relationship between long-term atrial function and complications after ASD treatment, which would facilitate more appropriate decisions regarding treatment strategies.

Acknowledgments

We thank Satoshi Osaga for assistance with statistical processing.

Disclosure

Conflicts of interest: The authors have no conflicts of interest to declare.

References

14. Vianna-Pinton R, Moreno CA, Baxter CM, Lee KS, Tsang TS, Appleton CP. Two-dimensional speckle-tracking echocardiography of the left atrium: feasibility and regional contraction and