Effect of Patient Age at Surgical Intervention on Long-Term Right Ventricular Performance in Atrial Septal Defect

A Pulsed Wave Tissue Doppler Echocardiography Study

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SUMMARY

Controversy exists about the influence of patient age on the benefit of surgery in atrial septal defect (ASD). Tissue Doppler echocardiography (TDE) when applied to atrioventricular annuli provides variables reliably reflecting the performance of the corresponding ventricle. We sought to investigate the effect of timing of surgery on biventricular functions by comparing the conventional echocardiography variables and TDE profiles of right and left atrioventricular annuli in patients treated at various ages. Conventional echocardiography and TDE analysis of mitral and tricuspid annuli were performed in 20 controls and 61 patients who underwent surgical ASD closure 2.8 ± 2.5 years before the study. Standard parameters included were right and left-sided dimensions, estimated pulmonary artery pressure, ejection fraction, and tricuspid annular motion amplitude. TDE variables were systolic, early and late diastolic peak velocities at tricuspid lateral-and mitral-annulus at lateral and septal corners. Two subsets of patients who underwent surgery before (group 1, n = 20) and after 25 years (group 2, n = 41) formed our subgroups. Peak systolic TDE velocity and tricuspid annular motion amplitude had the lowest value in group 2 (P < 0.01 and <0.02, respectively). Late diastolic TDE velocity was significantly lower in group 2 compared to group 1 (P < 0.05). Increased right ventricular and atrial dimensions (P < 0.001 for both) and the estimated pulmonary artery pressure (P < 0.03) were the conventional measurements discriminating group 2 from group 1. The TDE profile of the mitral annulus was similar between the groups. These results suggest that delayed ASD closure is a relatively less effective procedure to restore secondary right ventricular dysfunction, as demonstrated by significantly different TDE measurements reflecting right ventricular longitudinal contraction and relaxation. (Jpn Heart J 2004; 45: 265-273)

Key words: Atrial septal defect, Right ventricle, Tissue Doppler echocardiography

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Atrial septal defect (ASD) is among the most commonly encountered congenital heart diseases in adults. Patients with ASD may suffer early complications such as pulmonary hypertension, arrhythmias, and decreased functional capacity, or may remain asymptomatic for a long time. Although early closure of the defect is advised in order to prevent pulmonary hypertension, controversy exists about the need for surgery in elderly patients in whom ASD is diagnosed incidentally.

The volume overload caused by ASD results in the enlargement of right-sided chambers and right ventricular dysfunction. The recovery of these changes after surgical closure may exhibit case by case variation.

The limitations of standard echocardiography are most pronounced in the assessment of right ventricular function because of its complex geometry, the unsatisfactory images of its endocardial motion, and wall thickening. Tissue Doppler echocardiography (TDE) is a promising ultrasonographic modality that extends the echocardiographic interrogation to quantitatively measure the systolic and diastolic velocities of a selected region of interest with high temporal and spatial resolution. Following many studies applying TDE in disease states affecting the left heart, some recent investigations have utilized this technique in the assessment of right ventricular functions.

The present study was designed to investigate the effect of timing of surgery on heart chambers and biventricular functions by comparing the conventional echocardiography variables and TDE profiles of right and left atrioventricular annuli in patients treated at various ages and healthy subjects.

Methods

Sixty-one consecutive patients (mean age 36 ± 15, 23 males) who were followed-up in our outpatient clinic after undergoing surgical ASD closure were enrolled in the study. All of these patients who were retrospectively evaluated 2.8 ± 2.5 years after the operation were diagnosed as having ostium secundum type atrial septal defect before surgery. The functional status (NYHA class), ECGs, and echocardiography findings including the ratio of pulmonary to systemic blood flow (Qp/Qs) before the interventions were obtained from their files. Twenty age- and sex-matched healthy individuals (mean age 35 ± 12, 8 males) with no history of any cardiac or systemic illness served as controls. All subjects were informed about the investigational nature of the study.

Standard echocardiography: Transthoracic echocardiography recordings were obtained from parasternal, apical, and subcostal windows using a GE-Vingmed System V equipped with 1.5 - 3.7 MHz multifrequency phase array sector transducers. Conventional M-mode, two-dimensional, pulsed wave, and color Dop-
pler images were acquired with simultaneous ECG tracings. Left and right ventricular systolic and diastolic dimensions and left and right atrial dimensions were measured according to the recommendations of The American Society of Echocardiography. Left ventricular ejection fraction was calculated with the Teichholz formula. Transmitral Doppler spectra were recorded, and the early (E) and late-diastolic velocity (A) and E-deceleration time were measured with previously described methods. Right ventricular systolic performance was determined with the total magnitude of tricuspid annular plane systolic excursion that was recorded from the apical four chamber window with the M-mode cursor positioned through the lateral angle of the tricuspid valve annulus.

The presence of residual shunt was investigated with color Doppler. Pre- and postoperative pulmonary artery systolic pressures were estimated using the Doppler spectra of the tricuspid regurgitation that was graded from mild to severe.

**Tissue Doppler analyses:** Guided by the apical four-chamber view, left and right ventricular base-to-apex dynamics were determined by recording pulsed wave TDE samplings that were obtained by placing three 0.5 cm sample volumes at the septal and lateral corners of the mitral annulus, and at the lateral corner of the tricuspid leaflet. The lowest possible Nyquist limits were selected in order to obtain high frequency low amplitude annular velocities. The first systolic velocity reflecting isovolumic contraction was ignored, and the peak systolic velocity (TAn S) and early (TAn E) and late diastolic (TAn A) velocities were recorded. To minimize the respiratory variations, patients were asked to avoid deep inspiration, and the spectra were recorded during 30 seconds of shallow breathing. The average value of 3 consecutive cycles was calculated for the peak velocities.

Off-line analysis of all echocardiographic variables was performed using an Echopac program (ver. 6.2) within the echocardiography equipment.

**Statistical analysis:** Data are expressed as the mean ± SD. Continuous variables within and between groups were compared with paired Student's t test and ANOVA test, respectively. Categorical variables were compared using the chi-square test. The improvement in functional NYHA classes of two groups was compared by repeated measurement analysis. Significance was set at a P value < 0.05. A SPSS 10.0 computer program was used for the statistical computations.

To test the intra- and interobserver variability, the measurements of peak annular Doppler velocities of 20 samplings randomly selected by two observers (S.C and B.D.) and the same observer at different times were determined by linear regression analysis and percent SEE. The correlation coefficients and percent SEE of two sets of measurements were r = 0.99, 5.3% for intraobserver and r = 0.97, 6.7% for interobserver determinations.
RESULTS

Table I presents a comparison of pre- and postoperative levels of the functional status and conventional echocardiography parameters of the study patients. In all patients the surgical intervention resulted in a significant improvement of their functional NYHA class ($P < 0.0001$). The ECG recordings of 61 ASD patients demonstrated that 52, 9, and 19 patients had sinus rhythm, atrial fibrillation, and a complete right bundle branch block pattern, respectively, which did not differ after ASD closure.

The influence of surgery upon the conventional echocardiography parameters right ventricular and atrial dimensions ($P < 0.01$ and $< 0.0001$, respectively), and the estimated pulmonary artery systolic pressure ($P < 0.02$) was decreased. Left ventricular systolic and diastolic diameters showed no significant differences after ASD closure (Table I).

**Subgroup analysis:** Based on their age at the time of ASD closure, two subsets of our ASD patients who underwent surgery before (group 1, $n = 20$) and after 25 years (group 2, $n = 41$) formed two subgroups of the patient population. First, the pre- and postoperative echocardiography parameters were compared within each group. In group 1, ASD closure resulted in a slight increase in left ventricular diastolic dimension, and decreases in right atrial diameter and estimated pulmonary artery pressure (Table II). On the other hand, group 2 demonstrated an enlargement in left-sided chambers, a considerable decrease in estimated systolic pulmonary artery pressure, but no significant differences between the pre- and postoperative right-sided dimensions (Table III).

### Table I. Comparison of Pre- and Postoperative Functional Class and Standard Echocardiography Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>FC</td>
<td>2.7 ± 0.7</td>
<td>1.1 ± 0.3</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>LVDD (cm)</td>
<td>4.6 ± 0.5</td>
<td>4.7 ± 0.5</td>
<td>NS</td>
</tr>
<tr>
<td>LVSD (cm)</td>
<td>2.8 ± 0.6</td>
<td>2.9 ± 0.5</td>
<td>NS</td>
</tr>
<tr>
<td>EF (%)</td>
<td>66 ± 10</td>
<td>68 ± 8</td>
<td>NS</td>
</tr>
<tr>
<td>RA (cm)</td>
<td>4.6 ± 0.9</td>
<td>3.6 ± 0.8</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>RVDD (cm)</td>
<td>4.6 ± 0.6</td>
<td>4 ± 0.5</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>PAP (mmHg)</td>
<td>40 ± 15</td>
<td>29 ± 10</td>
<td>&lt; 0.02</td>
</tr>
</tbody>
</table>

FC = functional class according to New York Heart Association; LVDD = left ventricular diastolic diameter; LVSD = left ventricular systolic diameter; EF = ejection fraction; RA = right atrial diameter; RVDD = right ventricular diastolic diameter; PAP = estimated pulmonary artery pressure; NS = not significant.
A comparison of the demographic features and echocardiography variables between the controls and the postoperative status of the two subgroups are presented in Table IV. Before the operation, the functional NYHA classes of group 1 patients were class III in 68%, class II in 28%, and class I in 4%; all 20 patients in this group improved to class I with ASD closure. In group 2, 9.6%, 9.6%, 67.3%, and 13.5% were in class I, II, III, and IV, respectively, before surgery. In this group, no patient remained in class III or IV; 71% and 29% were in class I and II, respectively, after the intervention. Repeated measurement analysis revealed that all improvements in both groups were statistically significant ($P < 0.05$).

Conventional echocardiography demonstrated that the ejection fractions were comparable in the two groups and controls after the operation. However, the left ventricular systolic and diastolic dimensions were higher in group 2 (Table IV). The right ventricular and atrial dimensions were similar in group 1 and the controls, but were significantly higher in group 2 (Table IV).
Tissue Doppler echocardiography examination revealed the systolic and diastolic velocities of both septal and lateral mitral annulus corners demonstrated no statistically significant difference between the two patient groups. On the other hand, tricuspid annular peak systolic TDE velocity was significantly lower in group 2 compared to group 1 and the controls. Late diastolic TDE velocity was significantly lower in both groups than the controls. However, the lowest late diastolic TDE velocities were measured in group 2. The three groups were similar with respect to their peak early diastolic TDE velocities (Table IV). The M-mode determined magnitude of tricuspid annular motion was significantly lower in group 2 compared to group 1 and the controls. We reanalyzed all patients according to their preoperative NYHA functional classes in order to assess the effect of preop severity of the illness on right ventricular function. No significant differences were found when the systolic and diastolic tricuspid velocities of class I-II patients \( (n = 17) \) were compared with class III-IV \( (n = 44) \) patients \( (8.9 \pm 2.4 \text{ vs} \)
8.6 ± 2.5, 9.3 ± 3 vs 9.6 ± 3.8, and 7.7 ± 3.6 vs 8.2 ± 3.3 for TAn S, TAn E, and TAn A, respectively, \( P > 0.05 \) for all).

**DISCUSSION**

Consistent with previous observations, our results suggested the benefit of surgical ASD closure by demonstrating a considerable decrease in righ-sided dimensions, a small increment in left ventricular size, decrease in the estimated pulmonary artery pressure, and an improvement in NYHA functional status. Tissue Doppler echocardiography applied to the left and right atrioventricular annuli revealed that patients who were operated on before age 25 had superior right ventricular performance as shown by significantly higher systolic and lower late-diastolic longitudinal TDE velocities of tricuspid annulus. Comparison of our subgroups additionally revealed that this group had significantly lower right atrial and ventricular dimensions, and higher tricuspid annular motion amplitude at the time the echocardiography was performed. No significant difference was observed between left ventricular TDE parameters. In addition, comparison of tricuspid annulus velocities of patients who were classified according to preoperative functional classes revealed no significant difference. Therefore, the operation timing rather than the severity of disease at operation seems to determine right ventricle function at a late period.

The effect of patient age at the time of ASD closure has been a subject of some previous investigations. Murphy, et al suggested that the prognosis of patients operated on before age 25 had a comparable survival expectancy to that of healthy individuals.\(^9\) Pearlman, et al reported that RV enlargement persists after surgical closure in 23\% of patients; and those subjects had usually been operated on after age 25.\(^{10}\) The larger right-sided dimensions and higher levels of pulmonary artery pressure we observed in our group 2 are consistent with those observations suggesting the importance of timing of intervention. Supporting these findings, about one third of our patients in group 2 showed no satisfactory improvement in their functional NYHA status. All these findings could be explained by the irreversible nature of pulmonary vascular and also right ventricular - myocardial morphological alterations due to long-standing volume- and pressure overload in patients who were operated on after age 25.

TDE is an evolving noninvasive tool complementing conventional echocardiography in the assessment of left ventricular systolic and diastolic functions in various clinical conditions. Quantitative analysis of mitral annular dynamics with the use of TDE has been reported to provide reliable measurements that satisfactorily correlate with the gold standard indexes of global systolic and diastolic per-
formance in disease states.\textsuperscript{11-13} Tissue Doppler interrogation of the tricuspid annulus was validated as a method for evaluating RV functions in several recent studies. Peak systolic and late diastolic tricuspid annular velocities were demonstrated to have a positive and negative correlation with the ejection fraction and right atrial pressure, respectively.\textsuperscript{14,15} In our study, these two velocities were significantly higher in patients treated before age 25, emphasizing relatively more preserved systolic and diastolic RV performances in this group. In group 2 patients with the largest right atria, the late diastolic TDE velocity was the lowest, possibly reflecting an extremely severe form of diastolic dysfunction accompanied by the loss of atrial activity.

Another finding of our subgroup comparison was the significantly decreased tricuspid annular motion amplitude in group 2. Considering the previous observations suggesting that the annular motion amplitude reflects both the systolic and diastolic function of the corresponding ventricle, this finding could be interpreted to have supported the decreased RV performance in group 2 as demonstrated by the TDE analysis.\textsuperscript{16-18}

\textbf{Study limitations:} The main limitation of the present study is the retrospective nature of the work, and thus the absence of tissue Doppler parameters before the surgical interventions. Although the influence of surgery on tricuspid annulus dynamics in children with ASD was recently reported by Hanseus, \textit{et al} \textsuperscript{19}, that study interpreted early findings after the surgery; it would be of particular interest to compare before- and late-after measurements of tricuspid annular TDE spectra.

The use of M-mode and TDE at the apical echocardiographic windows allows measurement of long axis RV dynamics. An independent radionuclide RV study would have allowed the comparison of more objective measurements of RV functions between the groups. Right heart catheterization would also provide more reliable measurements, but this approach could not have been justified due to ethical reasons. Finally, the study shares the known limitations of pulsed wave TDE, which is affected by the angle of the Doppler beam and heart displacement.\textsuperscript{20} Due to a tethering effect from the adjacent tissues, even if the right ventricular function is quite good, the annulus velocity (and M-mode determined annulus motion) may be low because of the postoperative pericardial adhesion. However this effect seems minor in the present study because there was still a significant difference between both postsurgical groups.

\textbf{Conclusion:} The results of both standard echocardiography and TDE analysis performed 2.8 ± 2.5 years after ASD closure underline the difference in right-sided dimensions and right ventricular performance between patients treated before and after age 25. The findings emphasize the advantages of an early intervention in patients suffering ASD.
REFERENCES