Assessment of right atrial and right ventricular size in children after percutaneous closure of secundum atrial septal defect
with Amplatzer Septal Occluder.

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Abstract

Introduction: The aim of this study was to evaluate right atrial (RA) and right ventricular (RV) size in children after percutaneous closure of secundum atrial septal defect using Amplatzer device.

Patients and methods: The study group consisted of 42 children, aged 4.5 to 18.5 years. The following measurements (indexed to body surface area) were performed using 2D echocardiography: the longitudinal, transverse axis and area of RA; RV inflow dimensions at one-third and halfway between the tricuspid annulus and the apex (in the apical 4-chamber view) and short axis and M-mode RV diastolic dimensions. All measurements were obtained during the first 24 hours, 1, 3, and 12 months after the procedure, and then annually over 4 years follow-up and compared with the values obtained from the control groups.

Results: A significant decrease in all RA and RV values was observed after 24 hours. RV transverse dimension normalized after one month, the RA longitudinal axis and area and the RV inflow dimensions after three months, and the RA transverse axis and M-mode RV diastolic dimension after two years but the ratio of transverse to longitudinal RA axis remained significantly higher.

Conclusions: 1. Right atrial and right ventricular measurements decrease rapidly during the first 24 hours, and most of them normalize within a three-month period. 2. M-mode RV ventricular diastolic dimension do not capture the real RV changes. 3. The Amplatzer device closure of ASD influences the RA geometry which is reflected by the higher transverse to longitudinal RA axis ratio.

Keywords: atrial septal defect, Amplatzer, children.

Introduction

Secundum atrial septal defect (ASD II) is one of the most common cardiac defects, accounting for approximately 6% to 10% of all congenital cardiac anomalies in children. Right ventricular and right atrial volume overload are well known consequences of unclosed ASD II. Persisting shunt, resulting in right atrial dilatation may lead to symptomatic cardiac arrhythmias [1]. Marked progress in interventional cardiology has led to the development of a non-surgical method for ASD II closure [2, 3]. The ASD- Amplatzer device has been used since 1995. After multicenter clinical trials, the device was approved by the United States Food and Drug Administration (FDA) in 2002 for use in children and adults.

The aim of this study was to assess right atrial (RA) and right ventricular (RV) size in children after percutaneous closure of ASD II.

Methods

The study group consisted of 42 children treated with percutaneous closure of ASD II. The children ranged in age from 4.5 to 18.5 years (mean: 11.7 years) and ranged in weight from 16 kg to 97.5 kg (mean: 42.7 kg). The patients' heights ranged from 106 cm to 176 cm (mean: 145.8 cm), and their body surface area (BSA) ranged from 0.69 m2 to 1.87 m2 (mean: 1.3 m2).

Transcatheter, two-dimensional echocardiography (Acuson-Aspen system with 2.5 - 4 MHz probe) was used for ASD II diagnosis, preliminary qualification for the procedure, and RA and RV measurements. In the apical 4-chamber view, the following RA parameters were determined [8, 9]:

1. RAD1 - the longitudinal RA axis measured from the level of the tricuspid valve annulus to the opposite upper RA wall
2. RAD2 - the transverse RA axis measured perpendicular to the longitudinal axis in its mid-length
3. RAD3 - measurement of the RA surface area planimetrically determined
4. RAD4 - measurement of the RA transverse diameter in the apical 4-chamber view
5. RAD5 - measurement of the RA transverse diameter in the parasternal short-axis view
6. RAD6 - measurement of the RA transverse diameter in the parasternal long-axis view
7. RAD7 - measurement of the RA transverse diameter in the parasternal long-axis view
8. RAD8 - measurement of the RA transverse diameter in the parasternal long-axis view
9. RAD9 - measurement of the RA transverse diameter in the parasternal long-axis view
10. RAD10 - measurement of the RA transverse diameter in the parasternal long-axis view

Each measurement was obtained at end-systole of the ventricles, as recommended by Weyman [9], and averaged from three consecutive cardiac cycles. The ratio of transverse to longitudinal axis (RAD2 / RAD1) was also calculated.

To account for the complexity of RV geometry, the estimation of the size of the geometry, as recommended by Ercole et al. [10] was based on measurements obtained from two-dimensional echocardiography and M-mode examination.

1. RVDD1 - measurement of the RV inflow dimension assessed in the apical 4-chamber view at one-third the distance from the tricuspid annulus to the apex
2. RVDD2 - measurement of the median RV dimension assessed in the apical 4-chamber view halfway between the tricuspid annulus and the apex
3. RVDD3 - measurement of the RV transverse dimension assessed in the parasternal short-axis view
4. RVDD4 - measurement of the RV end-diastolic dimension assessed in M-mode echocardiography from the parasternal long-axis view

The mean of the measurements from three cardiac cycles was taken at end-diastole.

The follow-up TTE examinations were carried out at 24 hours, 1, 3 and 12 months, and then annually for 4 years after the procedure.

The control groups consisted of healthy children matched for age, body weight, height and body surface area with the
Table 1
The values of RA and RV measurements in control groups

|         | K  | K-1 | K-2 | K-3 | K-4 |
|---------|----|-----|-----|-----|-----|
|         | N=40 | N=40 | N=13 | N=8 | N=13 |
| RAD1/BSA (mm/m²) | 28.7±7.0 | 27.7±5.5 | 27.5±5.1 | 27.5±3.8 | 26.7±4.6 |
| RAD2/BSA (mm/m²) | 25.1±6.1 | 24.0±5.3 | 24.2±5.3 | 23.3±3.7 | 23.0±4.4 |
| RAA/BSA (cm²/m²)  | 8.6±1.6 | 8.5±1.5 | 8.0±1.1 | 8.0±1.5 | 8.5±1.5 |
| RVD1/BSA (mm/m²)  | 27.7±6.1 | 26.7±5.4 | 26.4±4.8 | 26.3±3.1 | 25.7±4.2 |
| RVD2/BSA (mm/m²)  | 22.9±5.1 | 21.5±4.6 | 21.2±4.1 | 21.3±2.8 | 20.8±4.1 |
| RVD3/BSA (mm/m²)  | 19.3±5.1 | 17.7±4.2 | 18.1±4.1 | 17.8±2.6 | 17.0±3.7 |
| RVD4/BSA (mm/m²)  | 14.4±3.5 | 13.6±2.9 | 13.8±2.6 | 13.1±2.0 | 12.9±2.2 |

RAD - right atrial dimension
RAA - right atrial area
RVD - right ventricular dimension
BSA - body surface area

Table 2
Mean values of RA measurements before and after ASD II closure with results of statistic analysis

| RA measurements | Time after ASD II closure |
|-----------------|---------------------------|
|                 | ASD II | 24 hours | 1 month | 3 months | 1 year | 2 years | 3 years | 4 years |
|                 | N=40   | N=40     | N=40    | N=40     | N=40   | N=13    | N=8     | N=13    |
| RAD1/BSA (mm/m²) | 32.7±7.6* | 30.6±7.0* | 30.3±6.6* | 29.0±6.5 | 28.8±5.9 | 28.9±5.4 | 27.4±3.1 | 26.6±2.9 |
| p1<0.0001 | NS | p3<0.0001 | NS | NS |
| RAD2/BSA (mm/m²) | 29.5±7.6* | 27.8±7.1* | 27.4±7.1* | 27.0±6.8* | 26.2±6.0* | 26.3±5.7 | 24.8±3.7 | 24.5±3.1 |
| p1<0.0001 | NS | NS | p4<0.05 | NS |
| RAA/BSA (cm²/m²) | 10.27±1.9* | 9.2±1.9 | 9.0±1.7 | 8.7±1.7 | 8.7±1.5 | 8.5±1.4 | 8.2±1.0 | 8.9±1.3 |
| p1<0.0001 | p2<0.05 | p3<0.05 | NS | NS |

* difference statistically significant compared with control group, p<0.05
p1 - before the procedure versus 24 hours after the procedure.
p2 - 24 hours versus 1 month following defect closure.
p3 - 1 month versus 3 months following defect closure.
p4 - 3 months versus 1 year following defect closure.
NS - differences not significant, p>0.05

The results of measurements in the study group obtained before the procedure and 24 hours, 1 month, and 3 months after the procedure were compared with those of control K. The data obtained from the study group at one, two, three, and four years after the procedure were compared with controls, K-1, K-2, K-3, K-4, respectively. For characteristics of the control groups see Table 1.

One patient was excluded from statistical analysis due to concomitant significant valvular pulmonary artery stenosis, and another patient was excluded for non-compliance reasons.

Statistical analysis was performed with the statistical software package SPSS/PC+. Following confirmation with the Shapiro - Wilk test of normal distribution of continuous variables, the statistics of location and dispersion were described, including mean values, standard deviation and (in case of significant dispersion) standard error of the mean (relative losses - differences in measurements in initial and remote phases).

Differences in the mean of more than two consecutive measurements were tested with repetitive analysis of variance, using the previous result as contrast. For paired variables in the control groups and the study group (age, body

study group.

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Table 3
RA transverse to longitudinal axis ratio in children before and after ASD II closure and in control groups

| RAD2/RAD1 ratio | Study Group | Control Group | Follow-up | p |
|------------------|-------------|---------------|-----------|---|
|                  | ASD II      | after ASD II closure |          |    |
|                  | N=40        | 24 hours | 1 month | 3 months | 1 year | 2 years | 3 years | 4 years |
|                  | 0.9±0.07    | 0.9±0.07 | 0.9±0.07 | 0.9±0.06 | 0.9±0.07 | 0.9±0.06 | 0.9±0.06 | 0.92±0.04 |
|                  | 0.87±0.06   | 0.87±0.06 | 0.87±0.06 | 0.87±0.06 | 0.87±0.06 | 0.85±0.08 | 0.86±0.09 |
| p                | p<0.05      | p<0.05 | p<0.05 | p<0.05 | NS | p<0.05 | p<0.05 |

Table 4
Mean values of RV measurements before and after ASD II closure with results of statistic analysis

| RA measurements | Time after ASD II closure | p |
|-----------------|---------------------------|---|
|                 | ASD II | 24 hours | 1 month | 3 months | 1 year | 2 years | 3 years | 4 years |
|                 | N=40   | N=40    | N=40    | N=40    | N=40   | N=13    | N=8     | N=13    |
| RVD1/BSA (mm/m2) | 32.1±8.1 | 30.1±7.3 | 29.1±7.2 | 27.9±7.2 | 26.6±6.0 | 27.9±6.0 | 26.3±3.7 | 25.6±3.1 |
| p                | p<0.0001 | p2<0.0001 | p3<0.0001 | p4<0.01 | NS | p<0.0001 | p<0.05 | NS |
| RVD2/BSA (mm/m2) | 26.1±6.7 | 24.6±6.3 | 23.9±5.8 | 22.8±5.8 | 21.0±4.7 | 22.4±4.6 | 21.0±3.1 | 20.6±2.7 |
| p                | p<0.0001 | p2<0.01 | p3<0.0001 | p4<0.05 | NS | p<0.0001 | p<0.05 | NS |
| RVD3/BSA (mm/m2) | 22.0±4.7 | 20.4±5.1 | 19.4±4.6 | 18.9±4.7 | 17.7±3.6 | 17.5±4.0 | 17.0±3.1 | 16.1±2.2 |
| p                | p<0.0001 | p2<0.0001 | p3<0.05 | p4<0.05 | NS | p<0.0001 | p<0.05 | NS |
| RVD4/BSA (mm/m2) | 19.5±4.7 | 17.9±4.5 | 16.5±3.9 | 15.5±3.3 | 14.6±3.3 | 13.8±2.6 | 13.1±2.0 | 12.9±2.2 |
| p                | p<0.0001 | p2<0.0001 | p3<0.0001 | p4<0.01 | NS | p<0.0001 | p<0.05 | NS |

Results

Single Amplatz occluders were used in all patients, with diameters ranging from 11 mm to 30 mm and a mean diameter of 17.5 mm±4.5 mm. The Student’s T-test for related groups was used. A value of p<0.05 was considered to be statistically significant. All tests were performed two-tailed.

Indexed RA measurements

Table 2 presents the mean values of RA indexed measurements before the procedure and after percutaneous closure of the defect and the results of statistical analysis. Before the procedure, all RA measurements were significantly higher in the study group than in the control group. Twenty-four hours following defect closure, the mean values of all assessed parameters decreased significantly as compared to the pre-procedure values; at one month, further significant reduction was observed only for RAA/BSA. The values of RAD1/BSA and RAD2/BSA remained significantly higher than in the control group at 24 hours and 1 month after ASD closure.

At three months, further significant reduction occurred for RAD1/BSA and RAA/BSA mean values but not for RAD2/BSA which significantly decreased after one year but still remained higher compared to K-L controls. Mean values of indexed RA measurements after two, three and four years did not differ significantly between each time point nor as compared to respective control groups (p>0.05). RA transverse/longitudinal axis ratio (RAD2) was determined before and after the procedure, in both the study group and the control group were presented in Table 3. There were no differences in the mean RAD2/RAD1 values measured in the study group before and after the procedure. Following defect closure in children these values remained higher than in controls. This difference was statistically significant (p<0.05) for all time points, except at two years following the procedure when it almost reached significance (p=0.07).

Indexed RV measurements

The mean values of indexed RV measurements obtained before and after percutaneous closure of the defect and the statistical interpretation of the results are summarized in Table 4. Before the procedure all RV indexed measurements in the study group were significantly higher than in the control groups. Twenty-four hours following defect closure, the mean values of all RV indexed parameters decreased significantly...
as compared to pre-procedure values, but RVD1/BSA, RVD2/BSA and RVD4/BSA remained significantly higher than controls. No significant difference was demonstrated for RVD3/BSA. Further significant reduction of all assessed RV parameters was also observed at one month, three months and one year following the procedure. Values of RVD4/BSA measured in the study group after one month, three months and one year of follow-up still remained larger than the values measured in the control group. The mean values of all RV measurements after two, three and four years did not differ between each time point nor as compared to respective control groups (p>0.05).

Discussion

Percutaneous closure of secundum atrial septal defect was made possible by the rapid development of interventional cardiology techniques. There are reports of many groups of patients, adult and children who have been treated with the Amplatz device [11-19].

Right atrial and right ventricular enlargement is a well-known consequence of uncorrected secundum atrial septal defect, and some published data focus on the persistence of RV enlargement after successful surgical repair as well as after transcatheter closure [20-24].

Our point of interest was to assess the speed of normalization of RA and RV size in children following percutaneous closure with Amplatz device.

In the study group, complete closure of the defect was observed in 90% of the children immediately after the procedure and in 95% of the children after one year. This finding was similar to published results [15, 16, 20].

Changes in indexed RA measurements demonstrated a significant decrease in the longitudinal and transverse axis during the first 24 hours after procedure. The longitudinal axis as well as the right atrial surface area reached the mean value observed in controls after three months, whereas the transverse axis decreased more slowly and reached the control levels at two years after the procedure.

The results of a study by Kort et al. [25], performed on 18 patients with ages ranging from 1 to 69 years, are close to those obtained in our study in terms of the parameter values obtained 24 hours post-procedure. The cited authors reported a marked decrease of indexed RA surface area during this time; however, the indexed RA surface area did not normalize during the subsequent two-years of follow-up, while in our study it normalized after three months of follow-up. According to these authors, the decrease in the RA surface area, was inversely related to the pre-closure age of the patient. The persistence of an increased RA surface area could be attributed to a relatively high proportion of older patients with ASD II, in whom normalization of RA surface area is slower.

Our study demonstrated that the RA transverse axis decreased more slowly than the longitudinal axis, which may reflect the change in RA geometry caused by the Amplatzer device closure of ASD. The argument for this observation is the persistence of the increased ratio of RAD2/RAD1 (from 0.90 to 0.99) in patients during the four-years of follow-up compared to healthy children (from 0.85 to 0.88). It is possible that the Amplatzer septal occluder may influence RA geometry by stiffening interatrial septum, and this change may be reflected by a persisting increase in transverse RA axis.

The role of a possible high geometric profile of the Amplatz occluder was reported by Vogel et al. [17] based on their observations after ASD closure in children younger than two years of age.

In the studied children, all indexed RV measurements significantly decreased during the first 24 hours after defect closure. During further follow-up all the parameters of RV assessed in the two-dimensional study reached control levels during the first three months, whereas RVD4/BSA assessed in M-mode examination did not normalize until two years after defect closure. The results obtained by Eerola et al. [27] shows also persistence of increased right ventricular M-mode dimension more than 1 year but the hemodynamic improvement still is faster in children treated percutaneously than surgically.

Kort et al. [25] reported normalization of indexed RV volume (RV volume/BSA) in children two years after ASD II closure with Amplatz device. It seems that due to the complexity of the RV geometry, in our opinion, the M-mode dimension alone do not capture the real ongoing changes in RV size after percutaneous closure of ASD and adding two-dimensional measurements could better reflect the ongoing changes. Also the use of three-dimensional echocardiography could be beneficial not only for assessment of RA but also for assessment of RV geometry [26].

Conclusions

1. The right atrial and right ventricular measurements decrease rapidly during the first 24 hours, and most of them normalize within a three-months period.
2. M-mode RV ventricular diastolic dimension do not capture the real RV changes.
3. The Amplatzer device closure of ASD influences the RA geometry which is reflected by the higher transverse to longitudinal RA axis ratio.
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