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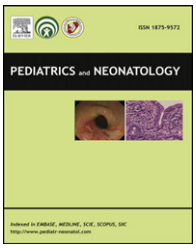

ORIGINAL ARTICLE

Cardiac Troponin I Release After Transcatheter Atrial Septal Defect Closure Correlated With the Ratio of the Occluder Size to Body Surface Area

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Key Words
atrial septal defects;
cardiac troponin I;
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Background: Cardiac troponin I (cTnI) is a very specific and sensitive marker of myocardial injury. The degree of myocardial injury associated with transcatheter atrial septal defect (ASD) closure in children is unknown.
Methods: In a longitudinal study on children with ASD, cTnI serum concentrations were measured after transcatheter ASD closure. Implantation success, complications, and latest patient follow-up were described.
Results: We inserted 73 Amplatzer septal occluders in 73 patients. Of these, we excluded two patients in whom the device embolized to the right ventricle the day after deployment. The median age was 4.5 years (range, 1.1—18.0) with 20 boys and 51 girls (male:female ratio, 1:2.6). The mean ASD size was 17 ± 7 mm, and device size ranged from 7 mm to 38 mm. The Amplatzer size/body surface area ratio was validated by demonstrating positive correlation with cTnI elevation. In children who had a successful attempt, 30 samples had a cTnI value higher than 1.0 μg/L l at 6 hours after procedure. Six patients had a significant release of cTnI greater than normal limits (mean level of 1.51 ± 0.26 μg/L).

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Conclusion: In our study, transcatheter ASD closure induced minor myocardial lesion, the extent of which depended on the ratio of the occluder size to body surface area ($p < 0.05$) but not on the patient's weight or preprocedural left ventricular ejection fraction.
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1. Introduction

The Amplatzer septal occluder (ASO) (AGA Medical, Plymouth, MN, USA) has been proved to be a safe system for the occlusion of secundum atrial septal defect (ASD), and its high success rate has led to its widespread use. Interventional ASD occlusion produces much lower myocardial damage than does surgical ASD closure. However, little is known about myocardial lesions after occluder implantation in patients, especially the relationship between occluder size and the patient's age, body weight, and body surface area (BSA).

Cardiac troponin I (cTnI) is a sensitive and specific marker for myocardial damage.[1–3] When compared with adult studies, pediatric patients seem to be at a higher risk for myocardial injury from interventional cardiac catheterization.[4] Catheter manipulation can also result in usually transient but sometimes permanent damage to valvular apparatus or to the conduction of the right or left bundle branches because of mechanical trauma. cTnI increase is generally used for the diagnosis of myocardial infarction, and its concentration is increased after cardiac surgery. The aim of this study was to evaluate the feasibility and efficacy of percutaneous ASD closure in young children.

2. Materials and Methods

2.1. Study population

Between October 2004 and November 2008, ASD closure with the ASO (AGA Medical, Plymouth, MN, USA) was attempted in 73 children at our institution. Of these, we excluded two patients in whom the device embolized to the right ventricle the day after deployment. Seventy-one patients were included in a prospective protocol of ASD transcatheter closure. The median age was 4.5 years (range, 1.1–18.0), with 20 boys and 51 girls (male:female ratio, 1:2.6). Each patient had to have a parent or legal guardian capable of giving informed consent in accordance with the Helsinki Declaration.

2.2. Device

A sizing balloon catheter was introduced over an extra-stiff guide wire positioned in the left upper pulmonary vein to measure the balloon-stretched diameter. Interatrial communications were assessed by transesophageal echocardiography (TEE) with reference to size, position in the interatrial septum, proximity to surrounding structures, and adequacy of septal rim. The device was delivered through an 8–12F kink-resistant Teflon long delivery sheath.

2.3. Technique

In all patients, implantation of an ASO was carried out under general anesthesia. Heparin (50 mg/kg) was used as an anticoagulant for surgical procedures, and the operation usually required 45–90 minutes. All of them followed a common protocol designed by Amplatz. Detailed assessment of the size and morphology of the ASD was performed by TEE with a multiplanar probe. The ASD was sized with a sizing balloon catheter and a precalibrated sizing template. The stretched diameter of the ASD was defined as the diameter of a balloon that could be withdrawn across the ASD with mild resistance and slight deformity.

Both fluoroscopy and TEE guidance were used throughout the sizing procedure to verify proper positioning of the sizing balloon catheter. Device selection was based on and matched to the stretched diameter of the ASD. The selected ASD device was 1 mm or 2 mm larger than the stretched diameter. The selected ASO device was attached to the delivery wire by the screw mechanism and was loaded by withdrawal into the loader by traction on the delivery wire.

Once the device was successfully deployed across the ASD, its position and stability were assessed by fluoroscopy and TEE. Its position was deemed optimal if the device was stable and did not obstruct the right pulmonary veins, coronary sinus, caval veins, or the mitral valve. Any residual shunt was documented using color flow Doppler on TEE. The ASO device was then released by rotating anticlockwise the delivery wire.

2.4. Sampling and assays

The cTnI levels were measured with the Architect STAT Troponin I assay (Abbott Diagnostic Division, Abbott Park, IL, USA). The assay has a minimum detectable concentration of <0.01 μg/L, and the cutoff level (the 99th percentile value of a reference population) for positivity is 0.032 μg/L.[5] The area under the curve (AUC), representative of the total release of cTnI in 1 mL (cTnI-AUC) was calculated.[6] CTnI concentrations were measured in serial venous blood samples at three time intervals: before, immediately after the intervention, and 6 hours later. If the cTnI level is higher than 1.0 μg/L, another blood sample is taken every 6 hours until the cTnI level is less than 0.2 μg/L.

To identify cTnI rise after ASD closure and to determine its prognostic significance, we correlated the overall cTnI release with the patient's age, body weight, BSA, dimensions of the device, and ratio of device diameter to BSA. The procedure time and the number of attempts of deployment were not amenable to intervention. The study was approved by the local research ethics committee. Written informed consent had to be obtained from parents or the legal guardian before each medical intervention.

We divided the patients into two groups. The first group had serum cTnI levels $<0.4\ \mu g/L$ from the time of defect closure to latest follow-up, whereas the second group, with cTnI levels greater than the reference level ($\geq 0.4\ \mu g/L$), were assessed for evidence of subclinical myocardial injury at baseline using serial echocardiography and followed for 6 months. The increase in cTnI $>0.4\ \mu g/L$ was chosen arbitrarily as a cutoff for myocardial injury before all collection of data.[7,8] All data were then compared between these two groups.

2.5. Statistics

Data were expressed as mean $\pm$ standard deviation as appropriate, whereas Chi-square tests were used for categorical variables. Independent two-sample *t* test was used to test the difference between groups. Pearson's correlation coefficient was used to determine the degree of correlation of myocardial damage with the ratio of the occluder size to BSA. Tests of whether coefficients differed significantly from zero were conducted at the 5% significance level (two tailed). All the statistical analyses were performed using SPSS version 16.0 for Windows (SPSS Inc., Chicago, IL, USA).

3. Results

None of the patients had cTnI elevation before the procedure, but 52 of the patients had cTnI elevation greater than the WHO criterion for myocardial cell damage ($>0.4\ \mu g/L$) within 12 hours after the procedure.[9]

3.1. Implantation success

We reported our experience using the ASO for defects ranging from 7 mm to 38 mm in 73 patients. The mean ASD size was 17 ± 7 mm, and transcatheter closure was successful in 71 of 72 patients (97.3%). However, six patients had a significant release of cTnI greater than the normal limits (mean level of $1.51 \pm 0.26\ \mu g/L$), and peak serum levels of cTnI were reached within 6 hours after the procedure. A high Amplatzer size/BSA ratio is thought to be one of the contributing factors for elevated cTnI. Significant ST-T elevation (>0.1 mV in peripheral leads) was not observed on electrocardiogram. No renal function impairment was noted in these patients.

The clinical characteristics of the patients when divided into two groups according to the threshold value of cTnI are presented in Table 1. Univariate analysis showed age, body height, Amplatzer size, and Amplatzer size/BSA ratio to be contributing factors for elevated cTnI. Multivariate logistic regression analysis showed that age, body height, and Amplatzer size did not independently predict the elevated cTnI levels. The only significant contributory factor was the Amplatzer size/BSA ratio. The correlation between the Amplatzer size/BSA ratio and the degree of myocardial injury detected by cTnI is shown in Figure 1.

3.2. Complications and follow-up

Two patients had a device embolized into the right ventricle (surgical removal and closure of the ASD). There were no cases of suspected or proven device erosion. In one patient, atrial premature contractions (APCs) were noted 1 week after the procedure and resolved after 3 weeks of corticosteroid treatment. The size of ASO device implanted was 38 mm, but the postoperative cTnI level was not impressively elevated 4 hours after the procedure

Table 1 Clinical characteristics of the patients according to the values of cTnI at 12 hours after percutaneous atrial septal defect closure.

Variable	cTnI $<0.4\ \mu g/L$ ($n = 21$)	cTnI $\geq 0.4\ \mu g/L$ ($n = 50$)	*p*
Age (y)	8.81 ± 5.55	5.88 ± 4.68	0.026
Sex			
Male	7 (35.0)	13 (65.0)	0.531
Female	14 (27.5)	37 (72.5)	0.531
Body height (cm)	125.93 ± 28.87	107.22 ± 20.33	0.019
Body weight (kg)	30.77 ± 17.83	23.18 ± 17.50	0.102
BSA (m^2)	0.97 ± 0.40	0.79 ± 0.37	0.086
Preprocedural LVEF	75.52 ± 5.32	74.34 ± 5.53	0.408
Amplatzer size	14.24 ± 6.09	18.26 ± 7.18	0.028
Amplatzer size/BSA	17.29 ± 12.47	24.91 ± 8.28	0.003[a]

Data are presented as *n* (%) or mean $\pm$ standard deviation.
[a] Statistically significant associations after multivariate logistic regression analysis.
BSA = body surface area; cTnI = cardiac troponin I; LVEF = left ventricular ejection fraction.

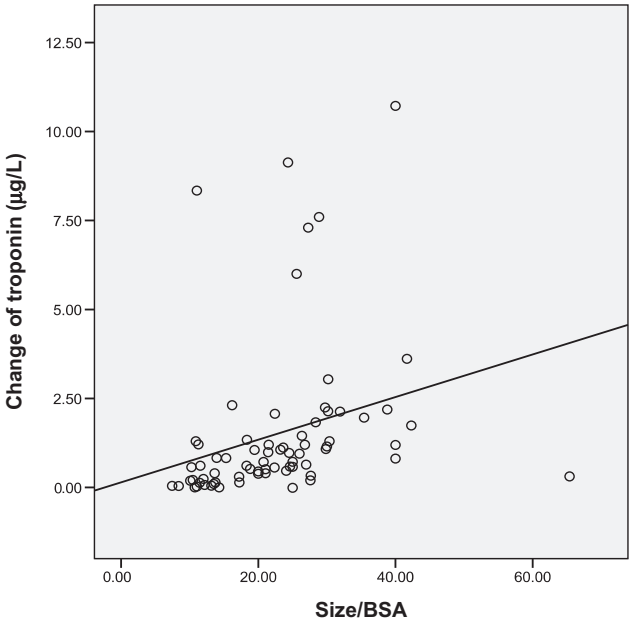

Figure 1 Correlation of myocardial damage with the ratio of the occluder size to BSA. Overall cardiac troponin I release after myocardial damage by interventional atrial septal defect closure is shown versus the ratio of the occluder size to BSA. Linear regression: $R = 0.276$, $p = 0.02$. Each point represents data of an individual patient. BSA = body surface area.

(0.577 μg/L). Local irritation of the conducting system caused by device compression was strongly suspected, which consequently might induce APC. Corticosteroids were used to reduce inflammation and swelling. Complete occlusion occurred in all patients during the follow-up period.

4. Discussion

After the initial report of successful nonsurgical transcatheter closure of ASD,[10] various devices for transcatheter closure of ASD were introduced and are currently being evaluated. It is well known that cardiac surgery leads to a transient increase in cTnI serum concentration.[11] Interventional ASD occlusion produces much lower myocardial damage than does surgical ASD closure.[12] High implantation and closure rates using transcatheter ASO in children avoid the need for cardiac surgery.[13] However, a temporary rise of the cTnI concentration was also observed after occluder implantation, and this increase was more pronounced in children than adults.[14] After interventional ASD occlusion, increased cTnI levels for several hours indicate some transient, reversible myocardial membrane instability because of the device.[15] Most pediatric interventional catheterization procedures are associated with myocardial damage as detected by cTnI elevation. Conversely, most diagnostic procedures are associated with no detectable myocardial injury.[4] Furthermore, the patients with APCs after ASD occlusion, which are closely associated with an inflammatory focus, may respond to large doses of corticosteroids.[16]

CTnI is a very specific and sensitive marker of myocardial injury.[17,18] A significant increase of cTnI levels after ASD closure has been reported.[10] Some reports suggest that the child's myocardium is more susceptible to trauma than that of adults, based on higher cTnI-AUC after surgery at a younger age.[6] Our results show an increase in myocardial injury with the size of the Amplatzer device. Its size, in turn, is defined by the ratio of the occluder size to BSA. In our study, the intraoperative TEE showed mere nonspecific findings.

Transcatheter closure of ASD has become a substantial alternative to surgical therapy with regard to economic costs, medical outcome, avoidance of unnecessary blood transfusions, and prevention of the complications of extracorporal circulation.[2,19] Even in pediatric patients, there is some evidence that bypass surgery could be related to a worse neuropsychological outcome in the follow-up.[20] In our study, transcatheter ASD closure was considered safer than surgical closure. Transcatheter closure of ASD may result in reversible myocardial damage, the extent of which depends on the ratio of the occluder size to BSA but is irrespective of the patient's body weight. In fact, the absence of skin scars, a shortening of the hospital stay, and avoidance of admission to the intensive care unit are more appreciated by patients and parents.

In experienced hands and highly specialized centers, transcatheter ASD closure provides excellent results and fewer complications, and the patients spend a shorter time in hospital. Obtaining the measurements of cTnI in the peri- or postprocedural period seems to be of clinical significance in identifying high-risk patients. More studies are needed to further clarify the exact role of postprocedural troponin measurement in cardiovascular risk prediction.

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