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ARTICLE

Predictors of Spontaneous Closure of Isolated Secundum Atrial Septal Defect in Children: A Longitudinal Study

Andreas Hanslik, MD[a], Ulrich Pospisil[b], Ulrike Salzer-Muhar, MD[a], Susanne Greber-Platzer, MD[a], Christoph Male, MD, MSc[a]

[a]Division of Pediatric Cardiology, Department of Pediatric and Adolescent Medicine, Medical University of Vienna, Vienna, Austria; [b]School of Psychology, University of Vienna, Vienna, Austria

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ABSTRACT

OBJECTIVES. The goals were to assess the frequency of spontaneous closure of isolated secundum atrial septal defect in children and to identify predictors of spontaneous atrial septal defect closure.

METHODS. A retrospective cohort study was performed in a tertiary care pediatric cardiology center. Consecutive patients (n = 200) diagnosed as having isolated atrial septal defects (no multiple or fenestrated atrial septal defects, no additional congenital heart disease, and no syndromes) were monitored for >6 months with serial 2-dimensional echocardiography, according to a standardized protocol.

RESULTS. The median age at diagnosis was 5 months (minimum: 0 months; maximum: 13.9 years). The atrial septal defect diameter at diagnosis was 4 to 5 mm in 40% of cases, 6 to 7 mm in 28% of cases, 8 to 10 mm in 21% of cases, and >10 mm in 11% of cases. The median age at the final follow-up evaluation was 4.5 years (range: 6.8 months to 16.2 years). Thirty-four percent of atrial septal defects showed spontaneous closure, and 28% decreased to a diameter of ≤3 mm. Logistic regression analysis revealed atrial septal defect diameter and age at diagnosis as independent predictors of spontaneous closure or regression to ≤3-mm defect size. Of atrial septal defects with a diameter of 4 to 5 mm at diagnosis, 56% showed spontaneous closure, 30% regressed to a diameter of ≤3 mm, and none required surgical closure. Of atrial septal defects with a diameter of >10 mm at diagnosis, none closed spontaneously, whereas 77% required surgical or device closure. Gender and observation time were not associated with spontaneous atrial septal defect closure or regression to ≤3 mm.

CONCLUSIONS. In the present study population of children with atrial septal defects, 62% showed spontaneous closure (34%) or regression to ≤3 mm (28%). Initial atrial septal defect diameter was the main predictor of spontaneous closure.

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Key Words
atrial septal defect, congenital heart disease, spontaneous closure, natural course

Abbreviations
ASD—atrial septal defect
BSA—body surface area
OR—odds ratio
CI—confidence interval

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Address correspondence to Christoph Male, MD, MSc, Division of Pediatric Cardiology, Department of Pediatric and Adolescent Medicine, Medical University of Vienna, Währinger Gürtel 18-20, 1090 Vienna, Austria. E-mail: christoph.male@meduniwien.ac.at

ATRIAL SEPTAL DEFECT (ASD) is among the most common types of congenital heart disease, with ostium secundum ASD representing the majority of cases.[1,2] Surgical closure is regarded as the standard method for ASD closure.[3] For asymptomatic or mildly symptomatic children with right ventricular volume overload, defects are usually closed electively at an age of 4 to 6 years.[3] In the past decade, device closure has been used increasingly as an alternative to conventional surgery and may even have surpassed surgical closure in numbers. Device closure has satisfying closure rates and low complication rates, which are comparable to those of surgery.[4–9] Although transcatheter closure has been performed successfully even for young children, the optimal age for elective device closure has not been established.[5,10–12] Some authors suggest elective ASD closure as soon as the diagnosis has been made.[12] However, early intervention may forestall possible spontaneous closure. Therefore, knowledge regarding the natural course of ASDs is important.

The natural course and frequency of spontaneous closure of ASDs have been assessed in a number of studies, but results are divergent, with closure rates ranging from 4% to 87%.[13–19] These differences may be explained by varying selections of study populations with respect to ASD sizes or patient ages. In early reports, ASDs were diagnosed through cardiac catheterization; therefore, those study populations are hardly comparable to those in more-recent studies with echocardiographic diagnosis.[13,20] In one of the latter studies, Radzik et al[15] reported a very high rate of spontaneous closure (87%) but concentrated on ASDs in neonates and infants and included mainly small defects and persistent foramina ovalia. Similarly, Brassard et al[16] described the natural course of defects of <6-mm diameter. In contrast, a study by McMahon et al[18] including children and adults, one third with small defects (3–5 mm), reported spontaneous closure for only 4% of patients. A recent study by Saxena et al[19] with a relatively small population of 52 infants reported spontaneous closure for 29%. The objectives of the present study were to assess the frequency of spontaneous ASD closure, in a representative pediatric cohort, and to identify predictors of spontaneous ASD closure.

METHODS

Design and Setting

The study was a retrospective cohort study of consecutive children diagnosed as having isolated ASDs at a tertiary care pediatric cardiology center. Patients were monitored longitudinally with 2-dimensional echocardiography, according to a standardized protocol. The study protocol was approved by the local ethics committee (ethics committee of the Medical University of Vienna).

Patients

All patients with isolated secundum ASDs (no primum or sinus venosus ASDs, no multiple or fenestrated ASDs, no additional cardiac malformations, and no syndromes), with diameters of ≥4 mm, that were diagnosed between January 1993 and April 2003 at the Division of Pediatric Cardiology, Medical University of Vienna, were included in the study. The secundum type of ASD was defined by the typical location of defects within the fossa ovalis. Any defect with a diameter of <4 mm was considered a persistent foramen ovale and therefore was not included in the study. The cutoff value of <4 mm was chosen in accordance with earlier studies of the natural course of ASDs, to distinguish persistent foramen ovale from ASD.[14–18] An exclusion criterion was an observation time of <6 months.

Medical records and 2-dimensional echocardiographic data for all patients were reviewed. Demographic and clinical variables recorded were age at diagnosis, gender, weight, body surface area (BSA), surgery, device closure, and age at final follow-up assessment. Serial echocardiography (Vivid S; GE Vingmed, Horten, Norway) was performed according to a standardized examination protocol, including complete evaluation with 2-dimensional, M-mode, and color-coded Doppler echocardiography (parasternal long- and short-axis views, apical 4-chamber view, subcostal 4-chamber view, subcostal short-axis view, and suprasternal view), and data were transferred into a database at the time of examination. Echocardiographic evaluations were performed by a total of 4 examiners. The ASD diameter was measured several times in both subcostal views (short- and long-axis views), and the largest diameter during the cardiac cycle was used. Only measurements from 2-dimensional echocardiograms were used, to avoid the risk of overestimating the ASD diameter in color Doppler images. Other echocardiographic parameters (eg, dimensions of the right atrium or ventricle) were not used for the study because these measurements are not well standardized.

For the purpose of describing the distribution of ASD sizes at the time of diagnosis in the study population, patients were divided into groups on the basis of ASD diameters (4–5 mm, 6–7 mm, 8–10 mm, or >10 mm). Groups of ASD diameters were defined similarly as in previous studies, to allow comparison of results.[14–18] The scientific basis for this grouping mainly involved practical clinical considerations. Smaller ranges were selected for smaller ASD diameters at diagnosis for better differentiation, whereas wider ranges were considered appropriate for larger ASD diameters at diagnosis. Actual ASD diameters were mathematically rounded to millimeter values.

Patients were monitored until spontaneous ASD closure occurred or defects reached a size of ≤3 mm, after which patients were not monitored systematically. For all patients with ASD diameters of ≥4 mm at the end of

the study period, the residual ASD diameter at the latest follow-up evaluation was recorded.

Study Outcomes

The primary outcome was the residual ASD diameter at the time of the final follow-up evaluation. Outcome categories were classified as (1) spontaneous ASD closure, (2) defect size of ≤3 mm, (3) residual ASD size of ≥4 mm, or (4) surgical or device closure. A secondary outcome parameter was change in ASD size over time (ie, regression rate or growth rate, calculated as the final ASD diameter minus the initial diameter, divided by observation time).

Statistical Analyses

Statistical analyses were performed with SPSS software (version 12.0; SPSS, Chicago, IL). Continuous variables are summarized as medians (minimum and maximum) and categorical data as percentages. The Mann-Whitney test was used for comparisons of ASD diameters between age groups. The χ^2 test and Fisher's exact test were used for comparisons of proportions between groups of ASD sizes. Logistic regression analysis was used to identify predictors of (1) spontaneous ASD closure, (2) the combination of spontaneous ASD closure and regression to ≤3 mm, or (3) the probability of surgical/device closure (dependent variables). Independent variables entered into the regression models were ASD diameter at diagnosis, age at diagnosis, BSA, gender, and observation time. Effects are reported as odds ratios (ORs) and 95% confidence intervals (CIs). *P* values of <.05 were considered significant.

RESULTS

Patient Demographic Characteristics

A population of 250 consecutive children fulfilled the inclusion criteria. Fifty patients were excluded because they were monitored for <6 months. The median age at diagnosis of the 50 excluded patients was 2.6 years (range: 0.1 month to 13.9 years). Forty of these patients with defects of >10 mm showed clinical signs of heart failure and required surgical or device closure of their ASDs shortly after diagnosis. Of the remaining 10 patients, 1 experienced spontaneous ASD closure, 6 experienced regression of their defects to ≤3 mm within 6 months, and 3 patients still had larger defects but did not reach the minimal observation time.

The study cohort consisted of 200 patients, who were studied longitudinally. There were 133 girls and 67 boys (ratio: 2:1). The median age at diagnosis was 5 months (range: 0 months to 13.9 years), with 74% of patients (n = 147) having their ASDs diagnosed within the first 1 year of life. The median weight at diagnosis was 6.3 kg (range: 1.3–67 kg), and the median BSA at diagnosis was 0.3 m^2 (range: 0.13–1.67 m^2).

At the time of diagnosis, 40% of patients (n = 81) had an ASD diameter of 4 to 5 mm, 28% (n = 56) an ASD diameter of 6 to 7 mm, 21% (n = 41) an ASD diameter of 8 to 10 mm, and 11% (n = 22) an ASD diameter of >10 mm. There was a significant association between ASD diameter at diagnosis and age at diagnosis, with children <1 year of age, on average, having smaller defects (median diameter: 6 mm; range: 4–15 mm), compared with older children (median diameter: 8 mm; range: 4–23 mm; $P < .001$). This finding is likely attributable to the fact that echocardiography is frequently performed for infants for various indications, leading to incidental detection of small ASDs. A second explanation could be that some ASDs grow with age.

Natural Course of ASDs

The overall observation time was 3.5 years (range: 6 months to 9.4 years). The median age at the final follow-up evaluation was 4.5 years (range: 6.8 months to 16.2 years). At the final follow-up assessment, 34% of defects (n = 67) showed spontaneous closure, and 28% of defects (n = 55) had decreased to a defect diameter of ≤3 mm. In total, 62% of defects (n = 122) showed regression to ≤3 mm. Twenty-one percent of ASDs (n = 42) still had a diameter of ≥4 mm. Eighteen percent of patients (n = 36) required surgical or device closure. Indications for ASD closure were a combination of clinical signs (eg, failure to thrive or frequent respiratory infections) and echocardiographic signs (right ventricular volume overload) of heart failure. Median ages at final follow-up assessments and median observation times for patients in these outcome categories are shown in Table 1.

Seventy-seven percent of defects (n = 153) decreased in size, with a regression rate of −1.2 mm/year (range: −0.13 to −11.9 mm/year). Five percent of defects (n = 11) remained similar in size. Eighteen percent (n = 36) of defects increased in size, with a growth rate of 1.0 mm/year (range: 0.1–11.7 mm/year).

TABLE 1 **Natural Course of ASD**

ASD Outcome Category	Proportion, % (*n*)	Age at Final Follow-Up Evaluation, Median (Minimum; Maximum)	Observation Time, Median (Minimum; Maximum)
Spontaneous closure	34 (67)	4.2 y (7 mo; 16.3 y)	3.8 y (6 mo; 9.0 y)
Regression to ≤3 mm	28 (55)	4.5 y (7 mo; 10.2 y)	3.8 y (7 mo; 8.2 y)
Residual ASD of ≥4 mm	21 (42)	5.3 y (9 mo; 11.8 y)	3.2 y (9 mo; 9.4 y)
Surgical or device closure	18 (36)	4.7 y (1.1 y; 13.3 y)	2.1 y (6 mo; 7.2 y)

Predictors of Spontaneous ASD Closure

There was a strong association between ASD diameter at diagnosis and the frequency of spontaneous ASD closure (Fig 1). Fifty-six percent of defects ($n = 45$) with a diameter at diagnosis of 4 to 5 mm showed spontaneous closure, and 30% ($n = 24$) regressed to a diameter of ≤3 mm. No patient with an initial defect diameter of 4 to 5 mm required surgical closure. Of patients with ASD diameters at diagnosis of >10 mm, none experienced spontaneous ASD closure, whereas 77% ($n = 17$) required surgical or device closure. Frequencies of spontaneous closure ($P < .001$) and frequencies of surgical/device closure ($P < .001$) differed significantly between groups with different ASD diameters at diagnosis.

Figure 2 shows ASD diameter change rates according to ASD size at diagnosis. Eighty-nine percent of defects with a diameter at diagnosis of 4 to 5 mm showed regression in size, 6% showed no change, and 5% increased in size. Thirty-six percent of defects with a diameter at diagnosis of >10 mm showed regression, 18% showed no change, and 46% increased in size.

Age at diagnosis was also associated with the incidence of spontaneous ASD closure. Children <1 year of age at ASD diagnosis experienced spontaneous ASD closure in 39% of cases, whereas children >1 year of age experienced spontaneous ASD closure in 19% of cases ($P = .008$). Age at diagnosis was also associated significantly with the probability of requiring surgical/device closure. Children <1 year of age at diagnosis required eventual ASD closure in 11% of cases, whereas children >1 year of age required closure in 38% of cases ($P < .001$). However, this finding might be explained by the association between age and ASD diameter at diagnosis.

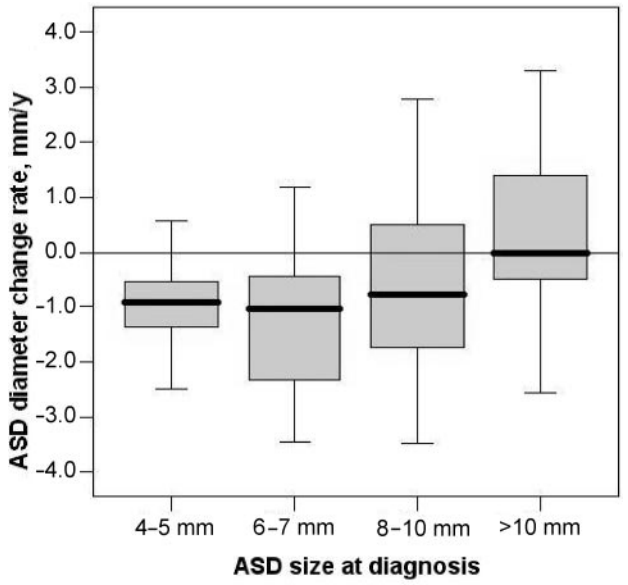

FIGURE 2
ASD diameter change rates according to ASD size at diagnosis. The box plot represents the distribution of ASD diameter change rates according to ASD size at diagnosis. Solid lines indicate median values; boxes, 25th and 75th percentile values; whiskers, 1.5 times interquartile ranges.

Logistic regression analysis was performed to assess simultaneously the effect of several potential predictors of the natural course of ASD. Diameter of ASD at diagnosis, age at diagnosis, BSA, gender, and observation

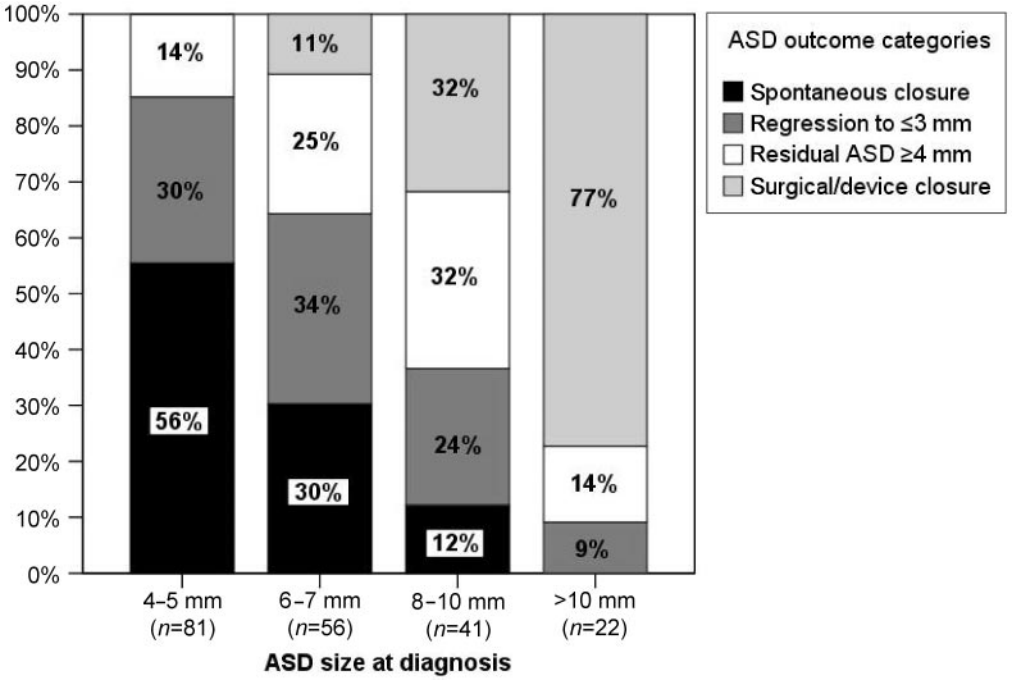

FIGURE 1
Natural course of ASDs according to ASD size at diagnosis. The bars represent the proportions of ASD outcome categories for each ASD diameter group at diagnosis.

time were used as independent variables and spontaneous closure, the combination of spontaneous closure and regression to ≤3 mm, and surgical/device closure as dependent variables. With spontaneous closure as the dependent variable, the model showed ASD diameter at diagnosis as the only significant predictor (OR: 2.0; 95% CI: 1.5–2.5; $P < .001$). Smaller defects were more likely to close spontaneously. With the combination of spontaneous closure and regression to ≤3 mm as the dependent variable, ASD diameter at diagnosis was the main predictor (OR: 1.7; 95% CI: 1.4–2.0; $P < 0001$), but age at diagnosis also had an independent effect (OR: 1.2; 95% CI: 1.0–1.4; $P < .037$). These results indicate that, independent of ASD size, younger age at ASD diagnosis was associated with a higher probability of spontaneous ASD closure. Gender, BSA, and observation time were not associated significantly with spontaneous ASD closure or regression to ≤3 mm. With surgical/device closure as the dependent variable, logistic regression analysis found ASD diameter at diagnosis to be a significant predictor (OR: 1.9; 95% CI: 1.5–2.3; $P < .001$). Age at diagnosis, BSA, gender, and observation time were not associated significantly with the probability of surgical/device closure. Therefore, the finding of more-frequent requirements for surgical closure among children >1 year of age at diagnosis is explained by the association between age at diagnosis and ASD diameter at diagnosis.

DISCUSSION

Knowledge regarding the natural course of secundum ASD is important in considering the optimal timing of elective ASD closure. Results of previous studies differed widely, with reported spontaneous closure rates ranging from 4% to 87%.[15,18] These differences may be explained by varying selections of study populations. The present study was performed with a representative sample of children with ASDs. The study population consisted of 200 consecutive children diagnosed as having isolated ASDs in a defined time period of the past 10 years. Therefore, the present study population represents current pediatric cardiology care. The proportions of small and moderate-sized defects were in accordance with the distribution of ASD sizes reported in 1999 by Helgason and Jonsdottir[17] for the entire population of Iceland. In addition, the female/male ratio of 2:1 was similar to previous reports.[2,17] The predominance of small and moderate-sized defects is explained by the frequent use of echocardiography for infants for various indications, for example, in NICUs and for the evaluation of heart murmurs. Echocardiography may result in early discovery of small defects in infants that otherwise might not have been diagnosed at all. There was a positive correlation of ASD size with age at diagnosis. This correlation is probably explained by the fact that, in older children, small defects have already closed spontaneously, leaving mainly large defects to be detected.

The majority (77%) of ASDs in the present study showed regression in size, and 34% of ASDs showed spontaneous closure. This finding of frequent regression is in contrast to the results of McMahon et al,[18] who reported increasing defects in 66% of cases and regression in only 14%. Twenty-eight percent of ASDs showed regression to a residual defect size of ≤3 mm. Defects of ≤3-mm diameter, corresponding to a patent foramen ovale, were not monitored systematically any longer. However, persistent foramen ovale has been implicated in cryptogenic stroke and decompression sickness (and device closure has been suggested for adults).[21,22] Therefore, echocardiographic follow-up monitoring during adolescence may be advisable for patients with residual defects of ≤3 mm.

The percentage (21%) of residual ASDs with a size of ≥4 mm is an overestimation, because some of these patients had relatively short observation periods and additional regression of defects may be expected. Therefore, additional follow-up monitoring of this group of patients is required.

Eighteen percent of study patients ($n = 36$) required surgical or device closure of their ASDs. This proportion increased to 32% of all patients (76 of 240 patients) who presented with ASDs if the 40 excluded patients who underwent ASD closure shortly after diagnosis were added. The latter percentage (32%) of children requiring surgical or device closure is in accordance with the results of Helgason and Jonsdottir[17] (34%). Indications for closure were a combination of clinical and echocardiographic signs of heart failure.

The ASD diameter at diagnosis was the main predictor of the natural course of ASDs in children. First, the ASD diameter at diagnosis was the main predictor of spontaneous closure, with smaller defects having a higher probability of spontaneous closure. Spontaneous closure rates of 56% for defects with an initial diameter of 4 to 5 mm and 34% for defects with an initial diameter of 6 to 7 mm were similar to closure rates reported by Radzik et al[15] and Helgason and Jonsdottir.[17] However, the present results are different from those of a study that observed only 10% spontaneous closure for ASDs with a diameter of 3 to 5 mm.[18] In the present study, there was a 12% rate of spontaneous closure for patients with initial ASD diameters of 8 to 10 mm, which indicates that spontaneous closure is possible even for larger defects. Second, the ASD diameter at diagnosis predicted the probability of eventual requirement of surgical or device closure. None of the patients with an initial ASD diameter of 4 to 5 mm required closure, whereas 77% of patients with an ASD diameter at diagnosis of >10 mm underwent surgical or device closure.

The age at ASD diagnosis was also associated, independent of ASD size, with the probability of spontaneous closure or regression to ≤3 mm. This finding is consistent with the results of Cockerham et al[13] and Mody.[20]

Apparently, the higher growth potential of the flap valve of the atrial septum in younger children increases the likelihood of ASD regression.

The median age at spontaneous ASD closure was 4.2 years, and the 75th percentile was at 5.8 years. Therefore, the optimal timing for elective device closure for young children with 8- to 10-mm defects must be considered carefully. Our results provide evidence supporting current recommendations that elective closure (surgical or device) for asymptomatic children should not be performed before the age of 5 to 6 years.[3] With this approach, elective closure would not forestall spontaneous closure of ASDs.

The present study has some limitations. First, the retrospective identification of study patients introduced the potential for selection bias, although every effort was made to include consecutive patients. Because patients were monitored with a standardized protocol and echocardiographic data were stored in a database at the time of examination, observation bias was minimized. Second, the study did not investigate whether other echocardiographic measurements (eg, dimensions of the right ventricle) were associated with the natural course of ASDs, because such data were not collected in a standardized manner.

CONCLUSIONS

The present study of a representative sample of children with isolated ASDs demonstrates a high frequency (62%) of spontaneous closure or regression to ≤3 mm. ASD diameter at diagnosis and age at diagnosis allow prediction of the probabilities of spontaneous closure and of surgical or device closure. On the basis of this information, parents can be informed about the prognosis for their child's disease. Considerations regarding the timing of elective closure for clinically asymptomatic children must take into account the high probability of spontaneous closure.

REFERENCES

1. Dickinson DF, Arnold R, Wilkinson JL. Congenital heart disease among 160 480 liveborn children in Liverpool 1960 to 1969: implications of surgical treatment. *Br Heart J.* 1981;46:55–62
2. Rigby ML. Atrial septal defect. In: Gatzoulis MA, Webb GP, Daubeney PEF, eds. *Diagnosis and Management of Adult Congenital Heart Disease*. Edinburgh, Scotland: Churchill Livingston; 2003:163–178
3. Kirklin JW, Barrat-Boyes BG. *Cardiac Surgery*. 3rd ed. Edinburgh, Scotland: Churchill Livingstone; 2003:16
4. Fischer G, Stieh J, Uebing A, et al. Experience with transcatheter closure of secundum atrial septal defects using the Amplatzer septal occluder: a single centre study in 236 consecutive patients. *Heart.* 2003;89:199–204
5. Butera G, De Rosa G, Chessa M, et al. Transcatheter closure of atrial septal defect in young children: results and follow-up. *J Am Coll Cardiol.* 2003;42:241–245
6. Du ZD, Hijazi ZM, Kleinmann CS, et al. Comparison between transcatheter and surgical closure of secundum atrial septal defect in children and adults. *J Am Coll Cardiol.* 2002;39:1836–1844
7. Cowley CG, Lloyd TR, Bove EL, et al. Comparison of results of closure of secundum atrial septal defect by surgery versus Amplatzer septal occluder. *Am J Cardiol.* 2001;88:589–591
8. Thomson JD, Aburawi EH, Watterson KG, et al. Surgical and transcatheter (Amplatzer) closure of atrial septal defect: a prospective comparison of results and cost. *Heart.* 2002;87:466–469
9. Berger F, Vogel M, Alexi-Meskishvili V, et al. Comparison of results and complications of surgical and Amplatzer device closure of atrial septal defects. *J Thorac Cardiovasc Surg.* 1999;118:674–678
10. Formigari R, Di Donato RM, Mazzera E, et al. Minimally invasive or interventional repair of atrial septal defects in children: experience in 171 cases and comparison with conventional strategies. *J Am Coll Cardiol.* 2001;37:1707–1712
11. Vogel M, Berger F, Dähnert I, et al. Treatment of atrial septal defects in symptomatic children aged less than 2 years of age using the Amplatzer septal occluder. *Cardiol Young.* 2000;10:534–537
12. Bjornstad PG, Holmstrom H, Smevik B, et al. Transcatheter closure of atrial septal defects in the oval fossa: is the method applicable in small children? *Cardiol Young.* 2002;12:352–356
13. Cockerham JT, Martin TC, Gutierrez FR, et al. Spontaneous closure of secundum atrial septal defect in infants and young children. *Am J Cardiol.* 1983;52:1267–1271
14. Ghisla RP, Hannon DW, Meyer RA, et al. Spontaneous closure of isolated secundum atrial septal defects in infants: an echocardiographic study. *Am Heart J.* 1985;109:1327–1333
15. Radzik D, Davignon A, van Doesburg N, et al. Predictive factors for spontaneous closure of atrial septal defects diagnosed in the first 3 months of life. *J Am Coll Cardiol.* 1993;22:851–853
16. Brassard M, Fouron JC, van Doesburg NH, et al. Outcome of children with atrial septal defect considered too small for surgical closure. *Am J Cardiol.* 1999;83:1552–1555
17. Helgason H, Jonsdottir G. Spontaneous closure of atrial septal defects. *Pediatr Cardiol.* 1999;20:195–199
18. McMahon CJ, Feltes TF, Bricker JT, et al. Natural history of growth of secundum atrial septal defects and implications for transcatheter closure. *Heart.* 2002;87:256–259
19. Saxena A, Divekar A, Soni NR. Natural history of secundum atrial septal defect revisited in the era of transcatheter closure. *Indian Heart J.* 2005;57:35–38
20. Mody MR. Serial hemodynamic observations in secundum atrial septal defect with special reference to spontaneous closure. *Am J Cardiol.* 1973;32:978–981
21. Landzberg MJ, Khairy P. Indications for the closure of patent foramen ovale. *Heart.* 2004;90:219–224
22. Braun M, Fassbender D, Schön SP, et al. Transcatheter closure of patent foramen ovale in patients with cerebral ischemia. *J Am Coll Cardiol.* 2002;39:2019–2025

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