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*Original Article*

# A comparison between the early and mid-term results of surgical as opposed to percutaneous closure of defects in the oval fossa in children aged less than 6 years

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**Abstract** *Objectives:* To compare surgical as opposed to percutaneous interventional closure of isolated atrial septal defects in the oval fossa in terms of hospital stay, efficacy, and complications, and to study the respective role of the two techniques in current practice. *Methods:* Between January 1998 and April 2004, 126 out of 1210 patients treated at our institution for closure of an isolated defect in the oval fossa were aged less than 6 years. The mean age of these 126 patients at procedure was 4.2 plus or minus 1 year. The ratio of females to males was 74 to 52. *Results:* Of the patients, 62% were treated successfully using a percutaneous approach. The groups treated surgically or percutaneously did not differ for age, gender, or indications for treatment. No deaths occurred. The rates of total and major complications were higher in the group undergoing surgical closure, at 34% versus 9%, p less than 0.0001, and 10.5% versus 1%, p equal to 0.01, respectively. Embolisation of the device requiring subsequent surgery occurred in 1% of patients. The stay in hospital was shorter in those closed percutaneously, at 3.2 plus or minus 0.9 days versus 6.8 plus or minus 2.8 days, p equal to 0.0001. During a mean follow-up of 3.4 plus or minus 1.9 years, no major complications occurred in either group, and symptoms improved significantly in both groups. Additional sequels occurred in 2 patients who had major complications subsequent to surgical closure. *Conclusions:* Even in young children, it is both feasible and safe to close defects in the oval fossa percutaneously. Compared to surgical closure, the transcatheter approach allows a shorter stay in hospital, and has a lower rate of complications. Early and mid-term follow-up has confirmed the safety and efficacy of both techniques.

Keywords: Interventional cardiology; congenital heart disease; secundum atrial septal defect

DEFECTS WITHIN THE OVAL FOSSA, SO-CALLED "secundum" defects, account for up to one-tenth of congenital cardiac malformations encountered at birth.[1] It is generally agreed that such defects associated with significant left-to-right shunting, and either symptoms or significant cardiomegaly, should be electively closed. Surgical closure gives good early post-operative and long-term results,[2–5] and surgical repair has been proven to be superior to medical treatment in middle-aged and elderly patients.[6,7] In the last decade, however, another therapeutic option has become available, namely percutaneous insertion of devices.[8–15]

As is the case for surgery, percutaneous closure in our Institution is performed electively at 4 to 5 years of age.[16] Comparisons between the two methods have previously been published in heterogeneous series of patients, but as far as we know, there are no data concerning young children. The aim of this study, therefore, was to study the impact of techniques of closure in current day practice, comparing the results, complications, and follow-up of closure performed by surgery or by transcatheter insertion of devices in a population of 126 consecutive children younger than 6 years.

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## Materials and methods

Between January 1998 and April 2004, 1210 patients were referred to our institution for assessment and management of isolated defects within the oval fossa, or secundum atrial septal defects. From among these subjects we prospectively collected data from 126 patients aged under 6 years. Of these patients, 75 were female, and the overall group had a mean age of 4.3 plus or minus 1.1 year, with a range from 5 months to 5.8 years.

Patients were assessed by standard echocardiography, with all undergoing a complete transthoracic examination. Parents gave their informed, written consent to the procedure. Any necessary approval was secured from the review board of the Hospital.

### *Criterions for inclusion, and indications for closure*

Criterions for closure were the identification of an isolated defect within the oval fossa permitting a ratio of pulmonary to systemic flows of more than 1.5 to 1, and/or signs of right ventricular volume overload.

We also closed defects in the oval fossa in some children as preventive treatment prior to liver transplantation. We excluded from the study patients with

- Defects in the oval fossa associated with complex congenital cardiac malformations
- Defects associated with partial anomalous pulmonary venous drainage
- Patency of the oval foramen and a history of stroke or transient ischaemic attack
- Defects associated with severe mitral and/or tricuspid regurgitation.

The indications were "routine" closure, closure in patients with frequent respiratory infections and/or failure to thrive, and closure of patent oval foramens, or small defects, in patients requiring liver transplantation.

Frequent respiratory infections were defined as more than 6 events per year.[17] Failure to thrive was defined according to Hamil et al.[18] Subjects requiring liver transplantation underwent closure because of the potential right-to-left shunt during transplantation.

### *Choice of the method of closure*

The defects were closed surgically in all subjects excluded from the percutaneous approach.

### *Criterions for exclusion for percutaneous closure*

A percutaneous approach was considered inappropriate if the defect was deemed to be too close to the superior or inferior caval veins, the pulmonary veins, the atrioventricular valves, or the coronary sinus. A rim of less than 7 millimetres between the defect and these structures was considered a contraindication to percutaneous closure, Percutaneous closure was also ruled out if the defect was considered too large. To assess the latter situation, if we considered using an Amplatzer septal occluder, we added 12 to 14 millimetres to the echocardiographically measured diameter of the defect, these dimensions representing the diameter of the rim around the central retention skirt of the Amplatzer septal occluder, 12 millimetres in devices up to 20 millimetres, and 14 millimetres in larger devices. When the value obtained was more than the length of the atrial septum measured in the four chamber view on transthoracic or transoesophageal echocardiography, we referred the patient for surgery. If we contemplated using a CardioSEAL/StarFLEX or a Helex device for closure, we used a ratio of defect to device of 1.8. When this value was more than the length of the atrial septum, the patient was again referred for surgery.

### *Techniques for closure*

The surgical approach was performed as previously described.[19,20] The size of the defect within the oval fossa was measured manually by the surgeon. The percutaneous procedure was undertaken under general anaesthesia with fluoroscopic and transoesophageal echocardiographic control with a multiplane transesophageal probe interfaced with a Vingmed 800 machine (Vingmed Sound, Horten, Norway). In babies who needed liver transplantation we used only transthoracic echocardiography, using a 5-mega Hertz ultrasound probe, because of the risk of oesophageal varices associated with liver failure. The procedure was undertaken under heavy sedation with fluoroscopic control.

The right heart was catheterised according to standard procedures, and the ratios of pulmonary to systemic flows and pulmonary to systemic vascular resistances, along with the angiographic and stretched diameters of the defect, were measured in a standard way.

We used 3 different devices, the CardioSEAL/StarFLEX® (Nitinol Medical Technical Incorporated, Boston, Massachusetts), the Amplatzer® Septal Occluder (AGA Medical Corporation, Golden Valley, MN), and the Helex device (W.L. Gore and Associates, Flagstaff, AZ). The features and techniques of delivering these devices have been previously described.[11,13,15]

### *Outcomes studied*

To assess the success of the procedures, we studied mortality, complications, length of stay in hospital, and the presence of any residual shunt.

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*Definitions of complications*

Complications were classified as minor, major, and death, calculating such problems on the basis of the intention-to-treat.

*Minor complications.* We defined a complication as minor if it could be completely treated by drugs, and produced no haemodynamic abnormalities. Such complications included transient arrhythmias, or arrhythmias interrupted by drugs, mild pericardial effusion, mild pneumothorax, mild anaemia, fever, anaemia requiring blood transfusion, and groin haematoma.

*Major complications.* We defined a complication as major if it gave haemodynamic instability, and/or needed immediate invasive treatment. In those treated surgically, these complications were heart failure, pericardial or pleural effusion requiring surgical drainage, pneumothorax, cardiac tamponade, arrhythmias needing immediate external cardioversion, and severe formation of thrombus on the atriotomy treated by heparin.

Major complications in the group treated percutaneously were embolisation or malposition of the device needing surgical retrieval and surgical closure of the atrial septal defect, vascular injury of the femoral vessels requiring surgical repair, pericardial effusion with or without cardiac tamponade due to perforation of the left atrial and aortic wall by the device, as well as all the complications described for the group treated surgically.

*Stay in hospital*

This was defined as the period of time from procedure until discharge from the hospital, including the days of admission and discharge.

*Residual shunt*

A residual shunt was considered to be present if colour-Doppler flow mapping showed a left-to-right shunt across the interatrial septum. It was defined as trivial if the width of the clour jet was less than 1 millimetre, small with a jet of 1 to 2 millimetres, moderate when the jet measured from 2 to 4 millimetres, or large in the presence of a jet wider then 4 millimetres.

*Protocol for follow-up*

All patients underwent clinical examination, electrocardiography, chest X-rays and transthoracic echocardiography before discharge, at 1, 6, and 12 months after the procedure, and yearly thereafter. Antiaggregation daily therapy with aspirin, 5 milligrams per kilogram, was prescribed for 6 months in those patients treated with transcatheter closure.

*Statistical analysis*

Data are expressed as a frequency or percentage for the nominal variables, as the median for the ordinal variables, and as the mean with standard deviation for continuous variables. We also calculated 95% confidence intervals. Differences between groups were tested by a two-tailed t-test or Wilcoxon's rank-sum test as appropriate. Nominal variables were compared using the chi-squared test or Fisher's exact test as appropriate.

Chi squared for r $\times$ 2 contingency tables was used to study the change in frequency of successful percutaneous closure in children treated during the period of the study. When a significant result was obtained, the method of portioning contingency tables[21] was used to find where the significant differences were located. All tests were two-sided. A p-value of greater than 0.05 was considered statistically significant.

## Results

*General characteristics* (Table 1)

We performed surgical closure in 38 patients (30%) based only on the transthoracic echocardiographic findings. In 8 subjects (6.5%), we took them to the catheterisation laboratory, but then referred them for surgery after transoesophageal echocardiography and balloon sizing of the defect.

Percutaneous closure was planned, therefore, for 80 patients (62.7%), and was achieved in all of them but one (0.8%), the latter due to embolisation of the device. The diameter of the defect was larger in those referred for surgery. Most of the patients in both groups were treated electively, and were aged more than 4 years. There were no differences in indications for closure between the two groups. We treated 10 subjects before they were 2 years old, achieving percutaneous closure in 7, of whom six were prior to liver transplantation. The indication for closure in the seventh subject treated percutaneously, and in the three patients requiring surgical closure, was failure to thrive.

In patients aged between 2 and 4 years, 55% were treated because of symptoms. In older subjects aged more than 4 years, symptoms were present in 8%.

*Results of the procedures*

*Surgical group.* A total of 47 subjects were treated surgically. Of these, 38 (83%) were referred for surgery after transthoracic echocardiography, while 9 more patients were treated surgically after a study in

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Table 1. General characteristics.

| | Surgical group | Percutaneous group | p |
|---|---|---|---|
| Number | 38 | 88 | |
| Age | 4 ± 1.2 | 4.5 ± 0.8 | Not significant |
| Weight | 14 ± 3 | 15 ± 4 | Not significant |
| Gender (female/male) | 23/15 | 51/37 | Not significant |
| Strial septal defect diameter | 19 ± 7 | 17 ± 5 | 0.04 |
| Indications for closure | | | |
| Pre-liver transplantation | 0 | 6 (7%) | |
| Symptomatic pts | 9 (24 %) | 17 (19%) | Not significant |
| Elective | 29 (76%) | 65 (74%) | |
| Age groups | | | |
| <2 yrs | 3 (3 symptomatic) | 7 (6 pre-liver tx; symptomatic 1) | |
| 2–4 yrs | 10 (5 symptomatic) | 17 (10 symptomatic) | |
| 4–6 yrs | 25 (1 symptomatic) | 64 (6 symptomatic) | |

the catheterization laboratory. We used 2 approaches, median sternotomy in 45 subjects, and minister-notomy in 2. The defect was closed either by direct suture in 19 patients, or by insertion of pericardial or Dacron patches in 28 patients. The mean time required for bypass was 29.5 plus or minus 8 minutes, with a range from 18 to 56 minutes, and the mean period of aortic cross-clamping was 14.3 plus or minus 5.5 minutes, with a range from zero to 28 minutes.

*Percutaneous group* (Table 2). We sent 88 subjects to the catheterisation laboratory with the intention to close the defect percutaneously. We excluded 8 after transoesophageal echocardiography and balloon sizing because of an insufficient rim in 5 cases, in all these the deficit being of the posterior-inferior rim, and too large a stretched diameter in 3 patients. We implanted a device in 80 patients, and only one embolized, needing subsequent cardiac surgery.

There were no differences in the ratio of pulmonary to systemic flows or pulmonary pressures between the nine subjects referred for surgery after assessment in the catheterisation laboratory, and those patients in whom the defect was successfully closed percutaneously.

Multiple defects were found in eight subjects. A single device was used to close these defects in 3 patients, while simultaneous placement of 2 devices was needed in 5 patients. An aneurysm of the inter-arial septum was treated in 3 patients. In one subject, it was associated with multiple defects in the floor of the fossa, while in 2 patients it was associated with a single defect.

Table 2. Procedural data of patients treated percutaneously.

| | |
|---|---|
| Number | 88 |
| Pulmonary to systemic flow ratio (Qp/Qs) | 2 ± 0.5 |
| Systolic pulmonary artery pressure (millimetres of mercury) | 25 ± 8 |
| Mean pulmonary artery pressure (millimetres of mercury) | 16 ± 6 |
| Devices used | |
| Helex | 4 |
| Amplatzer | 65 |
| CardioSEAL/STARflex | 10 |
| Fluoroscopic time (minutes) | 12.2 ± 7 (range 3–50) |
| Procedure time (minutes) | 70 ± 30 (range 40–180) |

## *Complications* (Table 3)

*No deaths occurred in either group*. The rate of total complications was higher in the surgical group (34% versus 9%; p less than 0.001) as was the rate of major problems (10.5% versus 1%; p less than 0.001).

*Surgical group.* A 4-year-old girl experienced hemiplegia due to an embolic event. A thrombus formed 3 days post-operatively on the left side of the interatrial patch and embolised on the fourth post-operative day, causing an ischaemic stroke. A 3-year-old girl developed heart failure after cardiopulmonary bypass in the immediate post-operative period and had residual chronic heart failure that persisted during the follow-up. A 3-year-old boy experienced pericardial tamponade 5 days after surgery, which needed immediate drainage. Finally, a 4-year-old girl had severe bilateral pleural effusion that caused haemodynamic and respiratory instability and necessitated immediate drainage.

*Percutaneous group.* The most severe complication was embolisation of the device, requiring surgical retrieval and subsequent closure of the defect. This complication occurred early in our experience in a 4-year-old girl with a defect having a stretched diameter of 20 millimetres. She also had a deficient aortic rim and a floppy posterior rim. A 22 Amplatzer septal occluder was implanted, but embolised immediately into the right pulmonary artery. The patient was sent for surgical closure, which was achieved

Table 3. Complications in the two groups.

| | Surgical group | Percutaneous group |
|---|---|---|
| Major complications | 4 pts (10.5%) | 1 pt (1%) |
| Embolisation | / | 1 |
| Hemiplegia | 1 | / |
| Left ventricular dysfunction | 1 | / |
| Pericardial tamponade | 1 | / |
| Pleural effusion needing surgical drainage | 1 | / |
| Other complications | 9 pts (23.5%) | 5 pts (8%) |
| Blood transfusion | 1 | / |
| Fever | 2 | 2 |
| Bronchitis | 1 | 1 |
| Femoral vein thrombosis | 1 | / |
| Pericardial effusion needing therapy | 4 | / |
| Transient atrial fibrillation | / | 1 |
| Mild retropharyngeal bleeding | / | 1 |
| Total complications | 13 pts (34%) | 6 pts (9%) |

successfully and uneventfully. Transient atrial fibrillation occurred in a 4-year-old boy treated with a 14-millimetre Amplatzer septal occluder. In one subject, a boy aged 4.8 years, mild retropharyngeal bleeding occurred due to oro-tracheal intubation. In 2 subjects, there was transient fever. Finally, 3 out of 9 patients sent to surgery after transcatheter evaluation had mild problems, bronchitis in one, and pericardial effusion needing medical treatment in two.

*Stay in hospital.* Patients treated percutaneously spent a significantly shorter time in hospital than did patients treated surgically, at 1.2 plus or minus 0.5 days versus 4.8 plus or minus 2.5 days, p equal to 0.0001.

*Residual shunt.* In the surgical group, a trivial to small residual leak was observed in 2.8% of patients. Among all the patients closed percutaneously, 70 (88%) achieved total occlusion at implantation. At discharge, the total rate of occlusion had risen to 94%. In all other subjects, the residual shunt was defined as small to trivial. Echocardiography at the follow-ups at 1 and 6 months showed total occlusion in 98%, and all were found to be closed at 12 and 24 months follow-up.

*Follow-up.* The mean duration of follow-up was 3.5 plus or minus 1.8 years, with a range from 0.5 to 6 years in the group closed surgically, and 3.3 plus or minus 2 years, with a range from 0.5 to 6 years in those undergoing percutaneous closure. Neither death nor complication occurred during the follow-up.

In 2 patients who underwent surgery, post-pericardiotomy syndrome occurred, which was treated by anti-inflammatory drugs. The patient with severe left ventricular dysfunction soon after surgery developed dilated cardiomyopathy, which was well tolerated with drug treatment. Finally, the subject who experienced the neurological problem has neurological sequels. In both groups, patients with failure to thrive had complete recovery of growth, from below the 5th percentile to between the 25–50th percentile after one year of follow-up. Subjects with frequent respiratory infections had no significant recurrences.

*Study period and change in successful percutaneous treatment.* During the period of the study, the number of patients treated percutaneously increased significantly ($\chi^2$ equal to 35.9; p equal to 0.00003). The percentage of subjects treated percutaneously in 1998 was significantly lower than the percentages in 2000, 2001, 2002, 2003 and 2004 (42% versus 61% (p equal to 0.001), versus 65% (p equal to 0.001), versus 75% (p equal to 0.001), versus 70% (p equal to 0.001), versus 64% (p equal to 0.01), respectively). The percentage of children treated in 1999 was significantly lower than the percentages in 2001, 2002, 2003 and 2004 (47% versus 65% (p equal to 0.01), versus 75% (p equal to 0.001), versus 70% (p equal to 0.001), versus 64% (p equal to 0.02), respectively).

## Discussion

Surgery for closure of defects within the oval fossa is usually performed electively at 4 to 5 years of age.[19,20] This is because defects up to 8 millimetres may close spontaneously in children as old as 2 to 3 years of age.[21,22] In our study, most of our patients were treated electively when they were older than 3 years. We treated children aged less than 3 years only when they were symptomatic, as occurred in 26 patients, or prior to liver transplantation in 6 patients.

In a previous publication, we showed that percutaneous closure could be performed safely and successfully in a series of 48 very young children.[16] Surgery, nonetheless, is generally regarded as the gold standard in this age group. In this study we aimed to investigate the impact of techniques of closure in current day practice, comparing results and complications between the two methods of closure in young children.

In this analysis, we show that, in current practice in a tertiary referral centre, up to seven-tenths of children aged less than 6 years may be treated successfully using the percutaneous approach. During the period of study, the rate of subjects treated percutaneously increased significantly, from just over two-fifths in 1998 to three-quarters in 2004.

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Most of these young children were treated electively, and there were no differences in indications, age, and gender between the two groups. The diameter of the defects was larger in the patients treated surgically, but there were no differences in the ratio of pulmonary to systemic flows or pulmonary pressures between patients who underwent successful closure and those who had a complete haemodynamic study but were then sent to surgery. Furthermore, no difference in clinical state was found in patients in the two groups. There are some doubts, however, about the comparability of balloon sizing in a beating heart and the measurements made by the surgeon of an atrial septal defect during cardiopulmonary bypass.

There are few reports comparing results and complications between surgery and device closure in children and these data are not restricted to very young children. Hughes et al.[23] compared 19 children aged from 0.9 to 17 years treated surgically and 43 subjects treated by percutaneous insertion of a device. They showed no differences in rates of complication, but hospital stay was shorter and pain score significantly lower in the group treated percutaneously.

Formigari et al.[24] studied early post-operative results in 172 children with a median age of 5.8 years treated by either surgery or implantation of a device. They found that the overall rate of complications was higher in those closed surgically, at around 12%, than in the group in which transcatheter closure was used, the comparable figure being 3.8%. When they studied the rate of clinically relevant complications, however, they found no differences.

Bialkowski et al.[25] compared 44 children treated surgically to 40 patients treated by percutaneous implantation of an Amplatzer device. Ages ranged from 2 to 17 years. The rate of closure was similar in both groups. Rates of complication rate, stay in hospital, and need for blood products were significantly higher in those closed surgically.

In our current study, no patients died in either group. The rate of total complications was significantly higher in those closed surgically. Embolisation of a device necessitating surgery occurred in only one patient. Hospital stay was also longer in the surgical group. A percutaneous approach was successfully used to manage complex anatomies in 10 subjects. During a mean follow-up of about 3 years only 2 patients had post-pericardiotomy syndrome during the first month after surgical closure. Of the subjects who experienced major complications, however, 2 had long-term sequels. No complications occurred, and patients with failure to thrive had complete recovery of growth.

Our study does have several limitations. First, it was not a randomised trial, which limits the possibility of comparing the two strategies. True randomization of these two strategies of management, however, is not easily feasible. In an era in which parents of children in Western countries are aware of therapeutic options, a randomized trial of closure of defects in the oval fossa would be hard to accept. Furthermore, the true superiority of randomized controlled trials over well-designed observational studies has been questioned.[26,27] Finally, although the technique of percutaneous closure appears to be safer than surgical procedures, we do not know whether the devices are safe during a very long follow-up, and very rarely, life-threatening complications may occur.[28] In contrast, the long-term safety and efficacy of surgery are well known.[2–5,15,29]

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