

## ORIGINAL ARTICLE

# Transcatheter Closure of Secundum Atrial Septal Defect Using the Amplatzer Device: Single Center Experience in 140 Patients

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## ABSTRACT

**BACKGROUND:** Transcatheter closure of secundum atrial septal defect (ASD) is nowadays widely practiced and has replaced surgical ASD closure in many centers. Improvements in design have made the closure devices retrievable, and reduction in the size of the introduction systems allows interventional treatment even in young patients. In this paper we present our experience with the Amplatzer septal occluder device in patients with ASD.

**PATIENTS AND METHODS:** Between October 2002 and February 2006, 206 consecutive patients with a significant ASD, demonstrated by initial transthoracic echocardiography (TTE), were considered for transcatheter closure with the Amplatzer septal occluder. A total of 156 patients underwent cardiac catheterization, and 140 patients had successful transcatheter ASD closure. Routine examination before catheterization included a standard ECG, a chest x ray, blood tests and TTE. The initial TTE showed the location of the ASD, its septal rim, and its diameter and also helped to measure the length of the interatrial septum in the four-chamber view. These measurements were used to assess the feasibility of transcatheter closure with the Amplatzer device. The "stretched" diameter of the ASD, determined by a balloon sizing catheter, was used to select the diameter of the waist of the device. The size of the selected device was 1 to 2 mm larger than the stretched diameter of the defect. Transesophageal echocardiography was used to monitor the implantation procedure.

**RESULTS:** The Amplatzer device was finally employed in 140 patients for percutaneous closure of ASD. The age of patients ranged between 5.3 and 70 years, median 21.9 years. Procedure time ranged between 25 and 240 minutes, median 60 minutes; fluoroscopy time ranged between 3.5 and 45 minutes, median 12 minutes. The size of the selected device ranged between 6-40 mm. Two devices were implanted in two patients. Serious procedure related complications (embolization and perforation of the left atrial wall) occurred in two cases. At follow up (10 days to 3.4 years, median 2.3 years) complete closure was documented in 97% of this patient group. Unrecognized during implantation, but detected after release, small additional defect with trivial residual shunt was documented in 4 patients. A young critically ill patient, cyanotic due to right-to-left shunt, with complex congenital heart disease developed a brain abscess three months after implantation.

**CONCLUSION:** Percutaneous ASD closure with use of the Amplatzer device in this cohort of 140 patients was highly successful with a low complication rate.

**KEY WORDS:** atrial septal defect; patent foramen ovale; device closure; interatrial shunt

## ABBREVIATIONS AND ACRONYMS

ASD: atrial septal defect

TEE: transesophageal echocardiography;

TTE: transthoracic echocardiography

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## INTRODUCTION

The first nonoperative closure of atrial secundum defect (ASD) was performed by Noel L. Mills and Terry D. King in a 17-year old female patient on April 8, 1975<sup>1,2</sup>. In the following years (1983) Rashkind developed a Clamshell device<sup>3</sup>. There was little interest in this clinical field and the trials with the “Clamshell Device” had been discontinued because of arm fractures. From the late 1980s until the mid 1990s E. B. Sideris (“Buttoned Device”)<sup>4</sup> and Babic<sup>5</sup> (“ASDOS”)<sup>5-7</sup> kept the ideas of King & Mills alive while G.S. Das developed the first self-centering device (“Angel Wings”)<sup>5-7</sup>. Clinical trials with ASDOS and Angel Wings have stopped because of complicated technology and risk of perforation. Since the pioneering works of King & Mills marked improvements in devices and delivery systems have been achieved.

Device ASD closure is now widely practiced and has replaced surgical ASD closure in many centers. Improvements in design have made the devices retrievable, and reduction in the size of the introduction systems allows interventional treatment even in young patients. Different types of device are in widespread use, and new devices are being introduced. While the patch type occlusion device—represented by the CardioSeal, or its modification, the StarFlex<sup>8,9</sup> occluder (NMT Medical) and the Helex-device<sup>7</sup> (Gore) mimics surgery by placing a patch over the ASD, the self centering Amplatzer septal occluder<sup>6,8</sup>, (AGA Medical Corporation) offers a different approach by stenting the interatrial communication. This unique technique makes it possible to close even up to 40 mm large defects, while the inability to close such large defects remains a limitation of the patch type devices.

Since the first clinical trials with the Amplatzer septal occluder in 1995 and 1997, there have been many reports of excellent early follow up results after ASD closure with the Amplatzer occluder<sup>6-12</sup>. We now report our own clinical experience and short-midterm results with this device in patients who have presented with ASDs in our center.

## PATIENTS - METHODS

Between October 2002 and February 2006, 206 consecutive patients with a significant ASD, demonstrated by initial transthoracic echocardiography (TTE), were considered for transcatheter closure with the Amplatzer septal occluder. A total of 156 patients underwent cardiac catheterization, and 140 patients had successful transcatheter ASD closure with the Amplatzer device.

Routine examination before catheterization included a standard ECG, a chest x ray, blood tests and TTE (Figure 3A). Magnetic resonance imaging (MRI) (Figure 3B), transesophageal echocardiography (TEE), Valsalva maneuver and

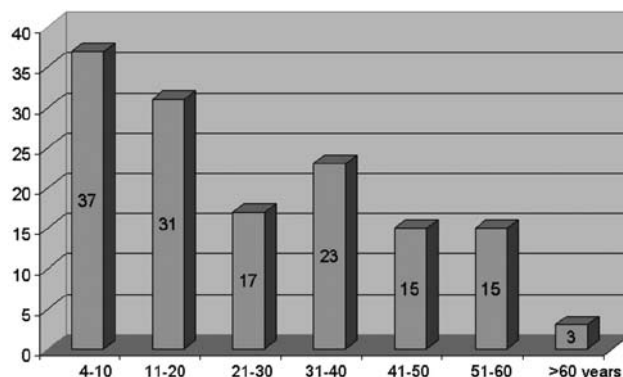


FIGURE 1. Patient age distribution.

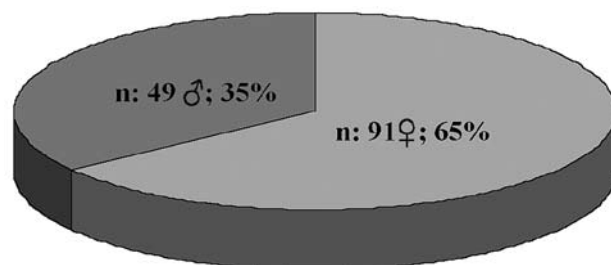


FIGURE 2. Gender distribution: 49 were male (35%) and 91 female (65%).



FIGURE 3. The ASD as depicted by TTE (A), and MRI (B) in two candidates for interventional therapy. Volume overload-large right atrium and ventricle, central ASD with adequate rims.

contrast injections were performed in selected cases.

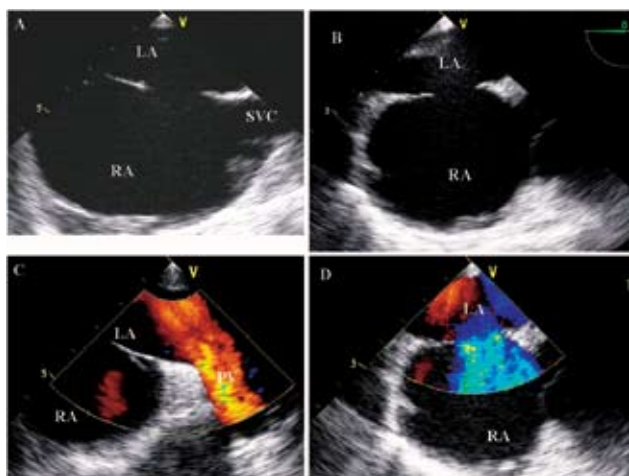
We followed the manufacturer’s recommendation for echocardiographic exclusion criteria if the patient presented in TTE or TEE a distance of less than 5 mm from the rim of the defect to the atrioventricular valves, the coronary sinus, or the right upper pulmonary vein. After ASD closure the patients remained in the hospital for one night, and received heparin (partial thromboplastin time  $\geq 50$ -60 seconds) for 14-18 hours, followed by aspirin 2-3 mg/kg/d or and clopidogrel 75 mg/d for six months. In the stroke group and in cases with coagulation disorders warfarin or acenocoumarol were given

for six to twelve months. Before discharge an ECG, a biplane chest x ray, and a TTE examination were performed. Follow up examinations including ECG were scheduled at 1, 3, 12, 24, and 48 months after the procedure. The 3 and 12 month follow-up examination also included a 24 hour Holter ECG recording. In order to study the right ventricular-remodeling, MRI studies were performed in 32 patient 3-12 months before and after transcatheter closure.

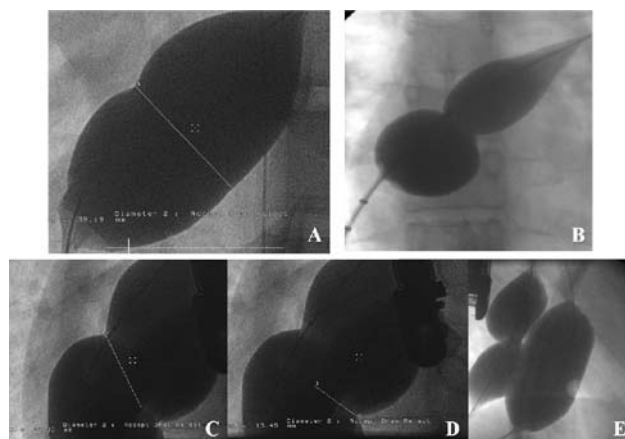
The initial TTE (Figure 4) showed the location of the ASD, its septal rim, and its diameter and also enabled us to measure the length of the interatrial septum in the four chamber view. These measurements were used to assess the feasibility of transcatheter closure with the Amplatzer septal occluder. The Amplatzer septal occluder is a self expanding, self centering, and repositionable double disc device constructed of a mesh of 72 nitinol wires. A 3-4 mm short cylindrical waist connects the two round discs. Basically, the Amplatzer septal occluder stretches and stents the ASD. Thus the diameter of the waist has to correspond to the so called “stretched” diameter of the ASD, determined by a balloon sizing catheter. Additionally, polyester fibers are sewn into the device promoting thrombosis and complete defect occlusion. Twenty seven different sizes with waist diameters from 4-40 mm are available. For devices between 4-10 mm, the left atrial disc is 12 mm larger than the waist and the right atrial disc is 8 mm larger. For bigger devices the left atrial disc is either 14 mm larger than the waist (waist

diameter 11-30 mm) or 16 mm larger than the waist (waist diameter 32-40 mm).

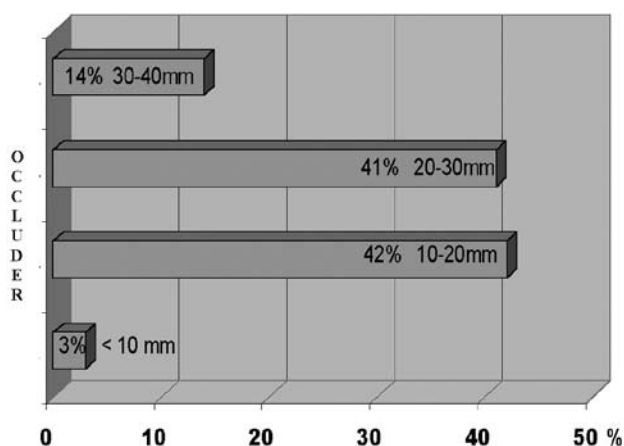
For transvenous implantation of the Amplatzer occluder, the manufacturer provides a loader, a delivery cable, and a 6-12 French long sheath. Before loading the device into the long sheath it is connected to the delivery cable by a microscrew fixed to the right atrial disc. In the catheterization laboratory a biplane transesophageal echocardiogram (TEE) was done under general anesthesia (in all except one) to evaluate the size and location of the defect and its margins. Vascular access was obtained from the femoral vein, and heparin (100 IU/kg max 9000 IU, ACT  $\geq$ 250), and antibiotics (cefazolin) were given; two cases with coagulation disorders received danaparoid sodium (Orgaran). After making a complete haemodynamic evaluation, an anomalous pulmonary vein connection was excluded by angiocardiography in the pulmonary artery. The “stretched” diameter of the ASD (Figure 5A, 5B and 5C, 5D, 5E: 2 defects, 2 balloons) was measured using a Numed or Amplatzer sizing balloon. A device with a waist diameter similar to, or in large defects up to 2 mm bigger than, the stretched ASD diameter was chosen. After introducing the long sheath over the exchange guide wire into the left upper pulmonary vein, the device was inserted and deployed under fluoroscopic and TEE guidance, as described in previous publications. A secure and stable position of the occluder within the defect was checked by a push-pull maneuver (Minnesota wiggle). The device and adjacent structures were then examined by TEE to ensure that there was no encroachment of the device on the atrioventricular valves or the right pulmonary veins. After releasing the device from the cable by unscrewing it (Figure 7), a final TEE examination was undertaken to demonstrate the position of the device and any residual shunting (Figure 8).



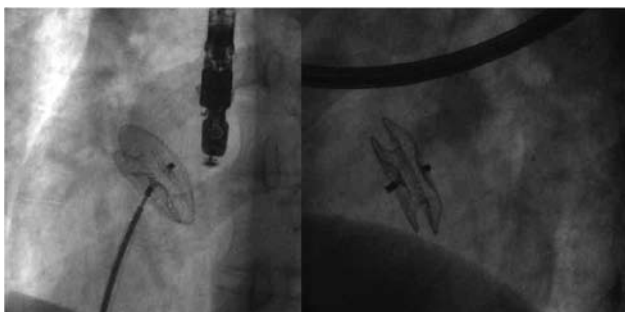
**FIGURE 4.** TEE with the location of the ASD, its septal rim, and its diameter. The ASD and the rims must be exactly measured. Only patients with a distance of more than 5 mm (rim) of the defect to the superior vena cava, atrioventricular valves, the coronary sinus, or the right upper lobe pulmonary vein are candidates for interventional treatment. Device closure of inferior and anterior defects with rims <5 mm or oversized devices could compromise the mitral valve or obstruct the SVC, IVC or the pulmonary vein. ASD= atrial septal defect; IVC= inferior vena cava; SVC= superior vena cava.



**FIGURE 5.** ASD sizing procedure: The waist of the balloons, A: 39 mm and B: 10mm respectively, clearly indicates the “stretched” diameter of the atrial septal defects. C, D, E: 11-year-old patient with two large defects. The waists of the balloons are 16 mm and 26 mm respectively.



**FIGURE 6.** Occluder diameter: 55% of patients with an ASD were closed with large devices of 20-40 mm, 42% with devices 10-20 mm and only 3% with devices <10 mm.

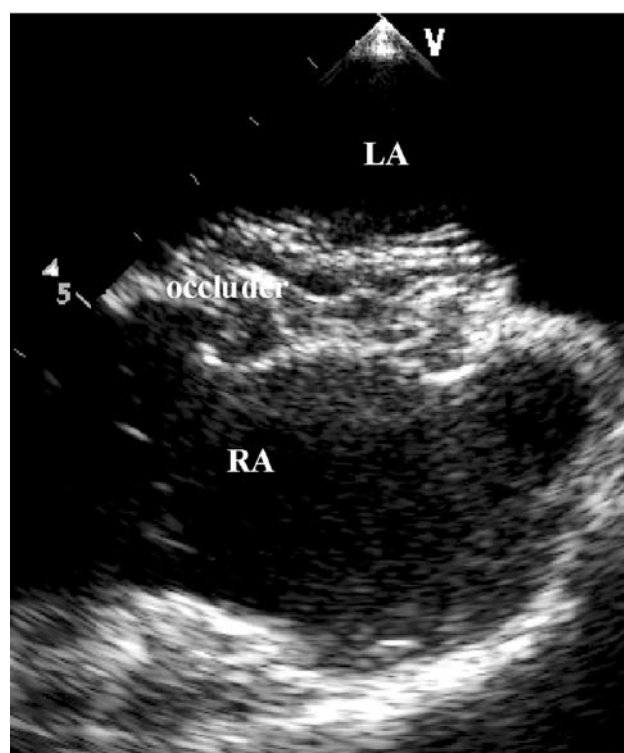


**FIGURE 7.** Lateral view of an implanted Amplatzer septal occluder (16 mm) during and directly after implantation.

## RESULTS

Between October 2002 and February 2006, 156 patients underwent cardiac catheterization, and 140 patients had successful transcatheter ASD closure with the Amplatzer device. Their ages ranged from 5.3 to 70 years (median 21.9 years), 49, 35%, were male, 91, 65% female (Figure 1 and 2 for age and gender distribution). The majority (85%) of the patient group showed a simple, single centrally located fossa ovalis ASD on echocardiographic examination, while 15% of the cases had multiple or fenestrated defects, an additional septal aneurysm, inferior extension of the defect towards the atrioventricular valves or coronary sinus. Nine patients suffered from stroke. One patient had a significant residual ASD after previous CardioSeal implantation, two devices were implanted in two patients, one during the same session.

On TEE, the maximum defect diameter varied between 4-38 mm, while the balloon stretched diameter (Figure 5) varied between 6.5-40 mm. Implanted devices had a waist



**FIGURE 8.** TEE after implantation. The device was inserted and deployed under fluoroscopic and TEE guidance. Occluder and adjacent structures were then examined to ensure that there was no encroachment on the atrioventricular valves or the right pulmonary veins.

diameter similar to or slightly larger than the stretched diameter implanted, ranging between 6-40 mm (Figure 6). The procedure time varied between 45-175 minutes (median 60 minutes) and the fluoroscopy time between 3.5-65 minutes (median 12 minutes), with a tendency to shorter procedural and screening times after the initial learning curve. In 55% of the patients with an ASD, large devices of 20-40 mm were employed and devices <10 mm were used in only 4 patient. Two 40 mm devices were implanted.

Nine of 10 patients with multiple or fenestrated defects were treated with a single device, while in one patient two devices were implanted simultaneously through separate delivery systems. Defects with an additional septal aneurysm were successfully closed by catching the aneurysm during the process of configuring the right atrial disc (or using the cribriform occluder in two cases), resulting in a firm compression of the aneurysm towards the atrial septum.

At the time of cardiac catheterization, nine patients were excluded after TEE examination, as follows: inferior-posterior defects and no rim near the orifice of the inferior caval vein, defects that were very near the coronary sinus, large defect that was near the-entrance of the superior caval vein, with only a small rim towards the right pulmonary veins, two symptomatic



children had a defect diameter of more than 36 mm on TEE and interatrial septum length of only 46 mm.

Seven further patients were excluded after initial angiography, hemodynamic evaluation, balloon sizing of the defect, or trial of device placement. Three of these showed drainage of the right pulmonary veins into the superior cava vein. One symptomatic adult had additional coronary disease. After balloon sizing four patients were excluded; three of these had large inferior-posterior defects with a stretched diameter of between 26 mm and more than 36 mm and an insufficient margin towards the inferior caval vein. Despite repeated trials, device placement failed in three cases because of insufficient inferior margins (1) or large defects with a floppy septum (2).

On color flow Doppler, residual shunting – including foaming through the wire mesh of the device – was seen in about 80% of cases directly after implantation. By the time of discharge, 24 hours after ASD closure, the rate of residual leakage had decreased to 15%. During further follow up examinations (10 days to 3.4 years, median 2.3 years) the complete closure rate has reached 97-98%. A trivial residual shunt is still present in 4 patients. 2/4 patients had unrecognized small additional defects during initial TTE and implantation. The third and fourth patient of this subgroup had small defects near the superior and inferior vena cava respectively.

After transcatheter closure of the interatrial communication in adults a reduction of migraine or headache was observed. In this small group of patients (retrospectively analyzed) migraine disappeared completely in 60%, while 40% described improvement in symptoms.

There were 3 major procedure related complications at our institution. The first was an embolization in a patient with small inferior rim directly after release. In this case the device embolized just above the mitral valve. Although the child was stable and asymptomatic device transcatheter retrieval was not attempted. The device was retrieved surgically and the ASD closed by patch. The second procedure related complication was a perforation of the left atrial posterior wall with the extra stiff madrain which led to 5 mm pericardial effusion. The procedure was stopped; there were no sequelae of this event. A significant event occurred 3 months after a successful and uneventful closure of a fenestrated Fontan with an Amplatzer occluder in a young cyanotic patient with complex congenital heart disease. This 8-year old girl developed fever and headache. Computed tomography showed a brain abscess. On TTE no unusual finding, thrombus formation or residual shunt were seen. After operation and antibiotic therapy for 4 weeks, patient's symptoms completely resolved without any neurological sequelae (this event confirms our recommendation of life long observation after device implantation).

Relevant cardiac dysrhythmias associated with transcatheter closure occurred in one case. A 38-year old man developed recurrent atrial flutter three months after uncomplicated ASD closure with a 36 mm occluder. In this patient long term main-

tenance of sinus rhythm was achieved first with propafenone. Six months later the patient decided to stop his medication. Recurrent atrial flutter led us to plan and perform ablation of the right circuit. It was not necessary to study the left atrial wall or the pulmonary vein region. No patient complained about amaurosis fugax or blurred vision after the procedure. No other early or late complications such as pericardial effusion, compromise of intracardiac structures, late device embolization, cerebral embolism or endocarditis-occurred during follow up.

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## DISCUSSION

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The ease of implantation and the superior success rate of ASD closure<sup>12</sup> with the Amplatzer septal occluder has led to the widespread employment of transcatheter occlusion of ASD and has replaced routine surgical closure in many centers<sup>8,10,12</sup>. There is no doubt that this success rate is a result of the design of the Amplatzer occluder, which is completely different from the patch type systems. The most important aspect is that the device's waist between the left and right retention discs is a stent, resulting in self-centering within the defect. Thus, the Amplatzer occluder requires only a small rim around the defect for firm cross clamping by the retention discs. The unique design, using a nitinol mesh, overcomes many of the limitations of other ASD occlusion devices. Although large delivery systems up to 12 French are necessary, the Amplatzer septal occluder is retrievable without damaging the device, the device is self-centering, and occluders large enough to close defects of up to 40 mm in diameter are available. Other devices can only close defects of up to 20 mm diameter, which excludes many patients with larger defects.

TTE and TEE have proved to be very important tools for the exact anatomical delineation of the defect within the atrial septum<sup>9,11-13</sup>. As it is difficult to examine defects in older patients using TTE, inspection of the exact nature of the septal rim near other cardiac structures like the atrioventricular valves, the right pulmonary veins, or the inferior caval vein must be carried out with TEE before catheterization. Defects near the entrance of the inferior caval vein, should easily be identified by TTE in the pediatric age group.

The manufacturer's recommended exclusion criterion is an ASD with a rim to the atrioventricular valves of less than 5 mm<sup>6,8,10,11</sup>. Device closure of these inferior and anterior defects could compromise the mitral valve. None of our patients with a rim of <6 mm developed mitral regurgitation. Similarly, the device can obstruct the orifice of the right pulmonary veins in rare cases with a more superior and posterior defect location; this did not happen in our patients<sup>8,11</sup>. The possibility of the retention discs impinging on sensitive structures is particularly pertinent when dealing with small children or using large or oversized devices<sup>8,11,12</sup>. An additional consideration is the

length of the interatrial septum, which should be sufficient to accommodate the device<sup>13</sup>.

TEE is also very important to ensure the correct positioning of the device before and after its release<sup>8,11,13</sup>. This is critical in the closure of large defects because the left atrial retention disc in bigger devices is relatively small in relation to the waist diameter. Because of this, its cranial portion tends to slip through the defect, and this may result in early or even late embolization of the device<sup>13,14</sup>. Furthermore, TEE is useful in directing the catheter through the largest communication in cases of multiple ASDs, and helps to reduce the screening time significantly<sup>8,12,13</sup>. It has even been suggested that ASD closure with the Amplatzer occluder can be carried out under TEE guidance alone<sup>13,15</sup>.

Cobra head malformation of the Amplatzer septal occluder is sometimes difficult to overcome and may prolong the procedure<sup>8,15</sup>. While it occurred more often in the past with the first generation of Amplatzer devices, it still may happen, particularly if there is not enough space for the configuration of the left or right atrial disc within the left or right atrium in a small patient. This can cause twisting of the occluder during deployment owing to the leading edge of the device catching on the atrial free wall or the appendage.

A point of criticism of the Amplatzer septal occluder is that it sometimes appears bulky after implantation. This may be the case if, owing to inaccurate balloon sizing, a device with too large a stent is implanted. "Mushrooming" of the retention discs can then occur<sup>15</sup>. This is more likely when the stent is compressed so that the waist measured on fluoroscopy is more than 4 mm smaller than the nominal diameter of the stent<sup>8,11-13,15</sup>. Inaccurate balloon sizing is now rare owing to the introduction of new static sizing balloons; overestimation of the defects mushrooming has become rare. Inaccurate sizing of the ASD is not the only cause of malformation of the implanted occluder; it could also happen if the diameter of the retention discs exceeds the length of the interatrial septum<sup>11,14</sup>. To avoid such a deformation and any potential obstruction of cardiac structures, this experience led us to be making an initial assessment of the interatrial septal length from the four chamber view on TTE as an important body weight dependent variable. In cases of large ASDs the septal length should not be exceeded by the diameter of the left disc occluder. In addition to echocardiographic follow up studies, 32 patients also had an MRI study, which showed no evidence of any device related obstruction. From this limited experience, we conclude that MRI, in addition to echocardiography, will allow non-invasive follow up examination and probably has the potential to replace x ray for ASD closure in the future<sup>16</sup>. In the future this method may be used also as an indicator of endothelialization of the device and it could be interpreted as a potential advantage that protects the integrity of the occluder<sup>8,16</sup>.

The high percentage of previously reported residual leaks, which were up to 53% with the first generation of patch type

devices has improved over the years but is still 20% at one year after the procedure, as reported recently in the multicenter experience using CardioSeal and StarFlex devices<sup>13,15</sup>. With the Amplatzer occluder we observed a complete occlusion rate of 97-99% during follow up, with only 4 patients still showing a trivial shunt on color flow Doppler. Though these residual leaks are trivial, it seems of interest that with one exception they occurred only in patients who had an additional ASD or defects with an additional septal aneurysm.

Whether or not one should use general anesthesia for specific interventional procedures may be a question of economics for some institutions or simply a question of the availability of anesthetic coverage<sup>6,8,9,11,15</sup>. On the other hand, unlike adult patients, a child will not tolerate the TEE probe without heavy sedation (for example, with propofol or ketamine) and continued spontaneous breathing, which may carry a risk of air embolism through the long sheath, owing to the negative intrathoracic pressure. In order to avoid irreversible myocardial or cerebral damage or even death after air embolism to the left heart, we now perform all interventional ASD closures under general anesthesia with mechanical ventilation.

Until now, we have seen only one patient who developed arrhythmias after ASD closure with the Amplatzer occluder. In the case of a 38-year-old man with atrial flutter, development of the arrhythmia seemed to be the result of long standing right atrial volume overload and dilatation rather than being device related. In our patient group sudden onset of complete atrioventricular block did not occur.

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## CONCLUSIONS

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Transcatheter closure of atrial septal defects has become a routine procedure in many countries of the world. It spares many patients cardiac surgery and has proven efficacy in long-term studies. Device improvements have resulted in a continuous reduction of complications and of residual shunt frequency. Although lifelong observation is required, this single center experience with the Amplatzer septal occluder shows good closure results for the majority of the ASD patients.

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## ΕΠΙΣΗΜΑΝΣΗ

Η αναφορά των εικόνων στο κείμενο ξεκινά από την εικόνα 3 και η αναφορά των εικόνων 1, 2 και 6 είναι μετά την αναφορά της εικόνας 8.

Μήπως θα 'πρεπε να αλλάξουμε την αρίθμηση των εικόνων και στις λεζάντες και στο κείμενο και να είναι τοποθετημένες οι εικόνες σύμφωνα με την αναφορά τους κείμενο;

Δηλαδή η αναφορά της εικόνας 3 στο κείμενο να γίνει 1 και η λεζάντα της εικόνας 3 να γίνει επίσης 1 κ.λπ.

Ευχαριστώ.