Original Article

Transcatheter Closure of Secundum Atrial Septal Defects: Results in Patients with Large and Extreme Defects

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Background: **Transcatheter closure of moderate sized atrial septal defects (ASD) has been demonstrated to be safe and effective. However, the feasibility of transcatheter closure of very large defects is less clear, particularly when an aortic rim of septal tissue is absent.**

Methods: **The study included patients referred for transcatheter ASD closure with maximal ASD diameter ≥20 mm at pre-procedural transoesophageal echocardiography. Patients were grouped according to presence of moderately large (20–29 mm), very large (30–39 mm), or extremely large (≥40 mm) ASD size. Procedural success was defined by successful device deployment and absence of complications.**

Results: **Forty-two patients (median age 40 years, range 12–85 years, 76% female) were included in the study. The mean maximal ASD diameter was 29.0 ± 7.4 mm. Twenty-three patients had moderately large ASDs (23.0 ± 2.8 mm); 13 had very large ASDs (33.1 ± 2.9 mm) and six had extremely large ASDs (41.3 ± 1.6 mm). The aortic rim was absent in 22 patients, and present in 20 patients (4.7 ± 2.9 mm). Transcatheter defect closure was successful in 36 of 42 patients (86%). Procedural success was 100% in the moderately large ASD group, 92% in the very large group but only 17% (one out of six) in the extremely large group. If patients with ASD ≥40 mm were excluded ($n = 6$), the overall success rate was 97%. A single complication (device dislodgement) occurred in a patient with a 42 mm defect and a deficient postero-inferior rim. The presence or absence of an aortic rim of septum did not influence procedural success.**

Conclusion: **The vast majority (97%) of large ASDs in the range 20–39 mm can be successfully closed percutaneously with a low or zero complication rate. However, procedural success is poor when attempting closure of extreme defects (≥40 mm), regardless of whether an aortic rim of septal tissue or present or absent.**

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Keywords. Atrial septal defect; Transcatheter closure; Structural heart disease; Congenital heart disease; Percutaneous intervention

Introduction

Secundum atrial septal defects (ASD) have been closed percutaneously using a transcatheter approach for nearly 40 years [1]. Although surgical and transcatheter closure success rates are comparable, the transcatheter approach, where feasible is now the preferred technique as it is associated with shorter hospitalisation and lower morbidity [2–4]. Previous studies have demonstrated that transcatheter closure of moderate sized ASDs is safe and effective [5,6]. However, the feasibility of a transcatheter approach for very large defects (>30 mm diameter) is less clear, particularly when a rim of septal tissue at the aortic root is absent and when the postero-inferior rim is deficient (<5 mm). Whilst the European and Canadian congenital heart disease guidelines recommend transcatheter closure for ASDs measuring less than 38 mm diameter, US guidelines do not specify a maximal ASD size that is suitable for transcatheter closure [7–9]. Indeed few studies have compared success rates and safety for transcatheter closure of moderately large, very large and extremely large ASDs on an intention to treat basis. We therefore report results from a series of patients with moderately large (20–29 mm), very large (30–39 mm) and extremely large (≥40 mm) ASDs who underwent attempted transcatheter closure at a single interventional cardiology centre.

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Methods

Patients

The study population consisted of 42 consecutive patients referred to a single large interventional cardiology service for transcatheter closure of a single large ASD, defined as maximal ASD diameter of ≥20 mm but <40 mm on the pre-procedural transoesophageal echocardiogram (TOE). All study patients had demonstrated right heart dilatation and colour Doppler evidence of left to right inter-atrial shunting on pre-procedural transthoracic echocardiography (TTE). Follow up was performed by the referring physician.

Peri-procedural Transthoracic Echocardiography

All patients underwent TTE prior to the ASD closure procedure. Right ventricular size and function was assessed as per ASE guidelines from para-sternal, apical and subcostal views [10]. The right ventricle (RV) was categorised as being mildly, moderately or severely dilated. If tricuspid regurgitation was present, RV systolic pressure was estimated using the Bernoulli equation in combination with right atrial pressure that was estimated from the inferior vena cava size and respiratory variation. All patients had a complete TTE study on the day following the ASD closure procedure.

Transoesophageal Echocardiography

TOE examination was performed with Philips echocardiography machines (5500 or iE33) utilising a multiplane two-dimensional or three-dimensional probe. TOE studies were either performed in the lead up to the procedure or in the cardiac catheterisation laboratory immediately prior to the procedure. Standard mid-oesophageal views were acquired at 0°, 45°, 90°, and 135° to assess the maximum ASD diameter. All procedures also involved further sizing of the defects with an Amplatzer sizing balloon, which provided a maximal "stretched diameter". The largest diameter obtained at either study was recorded as ASD size.

The anatomical characteristics of ASDs were carefully assessed by a cardiologist experienced in the performance of TOE to document the presence of an aneurysmal septum (defined as total excursion greater than 10 mm) and the presence or absence of a rim of septal tissue at the aortic root, as assessed in the mid-oesophageal short axis (45°) view.

Procedural Success and Follow-up

Transcatheter closure was performed using previously described techniques [11]. Procedural success was defined as successful delivery of the closure device with no peri-procedural complications, satisfactory appearance of the occluder device at the post-procedure TTE (day one) with no pericardial effusion, and patient discharged from hospital day one post-procedure with no additional medical attention required. Procedural complications were defined as bleeding requiring transfusion, advanced heart block requiring cardiac pacing, or abnormalities on the post-procedure TTE including pericardial effusion, new or worsening mitral valve dysfunction due to device interference with the anterior mitral valve leaflet, device migration or embolisation, or aortic root perforation. Clinical follow up visits were used to assess late complications occurring post-discharge.

Table 1. *Baseline characteristics of study patients (n = 42).*

Median age (range), year	40 (12–85)
Male/female, n	10/32
Height, cm	163.7 ± 10.4
Weight, kg	64.3 ± 21.1
Body surface area, m^2	1.73 ± 0.24
Right ventricular size, *n*	
Normal	0
Mildly dilated	14
Moderately dilated	20
Severely dilated	8
Right ventricle systolic function, *n*	
Normal	17
Mildly reduced	15
Moderately reduced	9
Severely reduced	1
Estimated pulmonary systolic pressure, mmHg	37 ± 13

Statistical Analysis

Descriptive statistics described population mean, median, and standard deviation. ASDs were further analysed according to size [moderately large (20–29 mm), very large (30–39 mm) and extremely large (≥40 mm)] defined as the largest diameter obtained at either the pre-procedural TOE or the intra-procedural TOE during balloon sizing of the defect ("stretched diameter"), and the presence or absence of an aortic rim of septal tissue. Group comparisons were made with the student *t*-test. A p value < 0.05 was considered statistically significant.

Results

Patient Characteristics

Baseline characteristics of the 42 patients with large ASD are presented in Table 1. The majority of patients were female (76%) with a mean age of 40 ± 18 years. The population was relatively healthy with only four out of the 42 patients having co-morbidities (hypertension). All patients had normal left ventricular size and ejection fraction. Right ventricular size was at least mildly dilated in all patients with 19% of patients having a severely dilated RV. Right ventricular systolic function was normal in 40% of patients; only one of the 42 patients had severely reduced RV ejection fraction.

ASD Characteristics

ASD characteristics are presented in Table 2. As expected, ASD diameter at the initial TOE was smaller than the "stretched diameter" obtained following intra-procedural

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Table 2. *ASD anatomy.*

Atrial septal defect diameter, mm	
All patients ($n = 42$)	29.0 ± 7.4
20–29 mm ASD group ($n = 23$)	23.0 ± 2.8
30–39 mm ASD group ($n = 13$)	33.1 ± 2.9
≥40 mm group ($n = 6$)	41.3 ± 1.6
Aortic rim present ($n = 20$)	27.2 ± 7.7
Aortic rim absent ($n = 22$)	30.6 ± 6.8
Aortic rim septal tissue, mm	
All patients	2.2 ± 3.1
20–29 mm ASD group	3.0 ± 3.5
30–39 mm ASD group	1.8 ± 2.7
≥40 mm group	0.5 ± 0.8

balloon inflation (23.7 ± 7.6 mm versus 29.0 ± 7.4 mm, $p < 0.001$.) Thirteen patients had very large (30–39 mm diameter) ASD and six patients had extremely large ASDs (diameter ≥40 mm). Twenty-two of the 42 patients (52%) had no aortic rim with the remaining 20 subjects having an average aortic rim of 4.7 ± 2.9 mm. Patients with absent aortic rim had larger defects then patients with aortic rim present (30.6 ± 6.8 mm versus 27.2 ± 7.7 mm, $p < 0.05$). Aortic rim dimension decreased as ASD size increased (Table 2). Atrial septum aneurysm was present in 21% of all patients: 22% of moderate-large ASD's, 23% of very large ASDs and 17% of extremely large ASDs.

Procedural Results

Procedural outcomes are presented in Table 3. Amplatzer ASD occluder devices were attempted in 38 patients (90%); the Occlutech Figulla ASD occluder was used in the remaining four patients. An ASD closure device was successfully delivered in 36 of the 42 patients (86%). In the moderately large ASD group (diameter 20–29 mm, $n = 23$), a device was successfully delivered free of complications in all patients. In the very large ASD group (diameter 30–39 mm) procedural success was achieved in 12 of 13 patients (92%). Of the six patients with an ASD diameter ≥40 mm, a device was successfully delivered in only one patient (17%). Immediately following deployment, a residual shunt (by colour Doppler or micro-bubble contrast study) was present in 22% of the patients with ASD 20–29 mm, 33% of patients with ASD 30–39 mm and in one of the two patients with an ASD ≥40 mm. However, these shunts were all trivial and not haemodynamically significant.

The presence or absence of an aortic rim of septal tissue was not related to procedural success. Of 22 patients with an absent aortic rim of septal tissue, an ASD closure device was successfully delivered in 18 patients (82%), with an average device size of 30.9 ± 6.7 mm. In the 20 patients in whom an aortic rim of septal tissue was present, a closure device was successfully delivered in 18 patients (90%), with an average device size that was significantly smaller than the absent aortic rim group (25.5 ± 6.2 mm, $p = 0.012$).

Procedure failure occurred in six patients (14%), five of whom had extremely large defects (mean diameter 41.3 ± 1.6 mm) (Table 4). The remaining patient had a very large defect (34 mm). Deployment of the device in this patient resulted in impingement of the left atrial disc on the anterior mitral valve leaflet. The device was therefore not released. Of the five failures in those with extremely large ASDs, four had deficient postero-inferior septal rims. In two of the four it was judged inappropriate to proceed with device delivery after the inflated balloon repeatedly slipped into the right atrium. Of the remaining two patients with deficient postero-inferior rims, in one the partially deployed device was deemed too unstable to be released; in the other the device was apparently successfully deployed but subsequently was found free in the right atrium on the routine TTE the next day. The patient remained asymptomatic throughout; the device was removed at open heart surgery that day and the ASD closed uneventfully. In remaining patient, the left atrial disc impinged on the anterior mitral valve leaflet and a decision was made not to release the device. Thus of the six failures only one patient left the cardiac catheterisation suite with the device in situ. All six patients with failed deployment subsequently underwent successful surgical closure of the ASD; five on an elective basis.

There were no late complications related to the device documented on clinical follow up ranging from six months to 13 years (median 10 months). All patients had at least one follow up TTE at least three months or greater after the procedure and no patient had a significant residual shunt.

Discussion

The study demonstrates that the vast majority (97%) of large ASDs, defined as maximal ASD diameter in the range 20–39 mm, can be closed with transcatheter techniques with a very low complication rate. However, attempts at transcatheter closure of extremely large defects (≥40 mm) are associated with a low success rate and the potential for complications.

For ASD patients with clinical indications for defect closure, a transcatheter approach, if feasible, is preferable to open heart surgery. Commercially available closure devices are designed to occlude ASDs up to a maximal diameter of 40 mm however the overhang of the left atrial disc (8 mm) and the right atrial disc (6 mm) raises the possibility that some ASDs >40 mm could be successfully closed as was the case in one patient in our series. The challenge presented by ASDs requiring very large devices is the capacity of the left atrium to accommodate the device without interfering with other cardiac structures such as the anterior leaflet of the mitral valve, and device stability after deployment.

There is no universally accepted definition for large ASDs. Studies have variously described the lower cut-off levels for large ASDs in the diameter range 20–30 mm and an upper cut-off level of between 36 and 40 mm [5,6,12,13]. As such, direct comparison with other studies is difficult particularly as some studies report outcomes only in terms of devices that were actually deployed and released at the time of catheterisation and do not mention cases where no attempt was made to deploy a device after balloon sizing or cases where a device was deployed but not released either because of device instability or device

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Table 3. *Procedural success in all patients and according to ASD size.*

	All patients ($n = 42$)	ASD 20–29 mm ($n = 23$)	ASD 30–39 mm ($n = 13$)	ASD $\geq$ 40 mm ($n = 6$)
ASD diameter, mm	29.0 ± 7.4	23.0 ± 2.8	33.1 ± 2.9	41.3 ± 1.6
Aortic rim, *n*, present/absent	20/22	13/10	5/8	2/4
Device size, mm	28.4 ± 6.9	23.9 ± 3.2	34.7 ± 2.9	40 ± 0
Device type	33	22	9	2
Amplatzer, *n* Occlutech, *n*	4	1	3	0
Procedure success, *n* (%)	36 (86)[a]	23 (100)	12 (92)	1 (17)
Procedural complications *n*, (%)	1 (2.4)	0	0	1 (17)
Late complications	0	0	0	0

ASD, atrial septal defect.
[a] 37 devices were used, however 36 were classed as procedural successes as one device dislodged following implantation.

Table 4. *Characteristics of patients with failed ASD closure attempt (n = 6).*

Pt	Age	ASD TOE diameter (mm)	Balloon diameter (mm)	Aneurysmal septum	Aortic rim (mm)	Reason for failure
1	33	33	42	No	1.1	Deficient posterior rim
2	30	33	44	No	2.0	Deficient posterior rim
3	34	38	40	Yes	0	Deficient posterior rim
4	22	31	40	No	0	AMVL impingement by LA disc
5	33	33	34	No	0	AMVL impingement by LA disc
6	50	40	42	No	0	Device embolisation detected on day 1 post-procedure TTE

AMVL, anterior mitral valve leaflet; Ø, not able to be accurately measured.

interference with other cardiac structures [6]. Two studies that have particular similarities with ours are the studies of Varma et al. [5] and Rodriguez et al. [12]. Using a definition of large as >25 mm diameter on balloon sizing Varma et al. [5] described 34 patients with mean ASD diameter of 30 ± 3 mm. In 31 cases (91%) deployment was successful. In two of the three remaining patients, device instability precluded release and in the third patient device embolism occurred. Using a definition of >30 mm balloon diameter Rodriguez et al. [12] described 34 patients with mean ASD diameter of 33 ± 3.4 mm (range 30–40 mm). Successful device deployment occurred in 23 patients (74%).

In our study we used a broad definition of large ASDs by choosing a lower cut-off level of 20 mm and allowing a higher cut-off level of >40 mm on balloon sizing as opposed to echocardiographic sizing on pre-procedural TOE. This allowed us to divide our patients into three groups – those with moderately large ASDs (diameters 20–29 mm), those with very large ASDs (diameters 30–39 mm) and those with extremely large ASDs ($\geq$40 mm). We chose 20 mm as the lower cut-off level as ASDs of this size require an occluding device with discs large enough to potentially interfere with other cardiac structures, such as the anterior mitral valve leaflet, especially in the more antero-inferiorly located ASDs. After balloon sizing we did not choose an upper cut-off level as we wished to analyse our results on a strictly intention to treat principle. That is all patients in our series had presented to the cardiac catheterisation laboratory with the specific intention of transcatheter closure of the ASD if at all possible.

In our series the success rate for closure of moderately large ASDs (20–29 mm) was 100%, and 92% for those with very large ASDs (30–39 mm) – figures that compare favourably to those reported by Varma et al. [5] and Rodriguez et al. [12]. In contrast, the success rate in those with extremely large ASDs ($\geq$40 mm) was poor (17%) indicating that such defects are generally not suitable for transcatheter closure. Five of the six failures and the only complication in our series occurred in those with extremely large ASDs ($\geq$40 mm). Four of those five had deficient postero-inferior rims – an anatomical finding well known to be associated both with difficulty in obtaining a stable position of the device and a high risk of device embolism [14–17]. Based on our experience we now no longer attempt closure of ASDs $\geq$40 mm in diameter. This recommendation is in compliance with the current "instructions for use" guidelines for both the Amplatzer and the Occlutech devices.

Large ASDs are often associated with deficient aortic rims. A deficient aortic rim has been proposed by some to be a relative contraindication to transcatheter closure [18]. Others have demonstrated that in experienced hands such deficiency does not materially affect success or complication rates, however the absence of an aortic rim does make the procedure more challenging [4,11,18,19]. In our series the presence or absence of an aortic rim did not influence the results. As such we do not regard an absent aortic rim as a contra-indication to percutaneous closure.

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Limitations of our study were that it was conducted retrospectively, the numbers were relatively small and not all patients had long term follow up TTE beyond three months following the procedure. Nevertheless clinical follow up has been complete and we think it unlikely that we have missed any very late device related complications such as device embolism or cardiac perforation.

In conclusion, our study has demonstrated that percutaneous closure of large ASDs in the range of 20–39 mm diameter can be safely performed with high success rates. In contrast the success rate for ASDs $\geq$40 mm in diameter is low and such patients are more appropriately considered as surgical candidates.

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