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ORIGINAL PAPER

Incidence and predictors of atrial fibrillation following transcatheter closure of interatrial septal communications using contemporary devices

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Abstract
Background Transcatheter closure of interatrial septal communications (IASC) is being increasingly performed, while less is known about predictors and incidence of new onset atrial fibrillation (AF) after device closure. Hitherto, most studies have only analyzed some parameters potentially influencing the occurrence of AF, variously omitting others and thus limiting interpretation of results.
Methods Descriptive, single author, observational study with 68 consecutive patients [aged 53.6 ± 15.1 years; 32 females (47%)] undergoing IASC closure, being followed up for 16.8 (±9.9; 6–42) months. Two patients with AF previous to device implantation had been excluded. Parameters analyzed included age and gender as well as presence of coronary artery disease, hypertension, atrial size, body mass index, device size, and presence of residual shunt. Device size was normalized to maximal disk diameter as declared by the manufacturer.
Results The incidence of new onset AF was 10.3% in the first 6 months after IASC closure. The only two predictors linked to AF were device size ($P = 0.002$) and, although not reaching significance level, right atrial dilatation ($P = 0.08$).
Conclusion Occluder size was the only significant predictor of post-procedural AF, especially after PFO closure. Although there may be constraints (defect size, presence of an atrial septal aneurysm) that may dictate implantation of a larger device, it is reasonable to implant them "as large as necessary, as small as possible". The influence of atrial dimensions on post-procedural onset of AF must be further investigated.

Keywords Percutaneous closure · Patent foramen ovale · Atrial septal defect · Atrial fibrillation

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Background

Although some reports describing the incidence of atrial fibrillation (AF) after closure of interatrial septal communications (IASC) have been published, most of them have used a few well-established devices [1–3]. Some limitations of these studies have been acknowledged [1], the larger study choosing to omit analyzing atrial and device size as predictors of new onset AF. In addition, other parameters as presence of hypertension, coronary artery disease or body mass index have been inconsistently reported [1–3]. By far, the largest number of new onset AF occurs in the first months after device implantation [1, 2]. Knowledge concerning the incidence of AF after closure of IASC should be diligently sought, as AF remains one of the important causes of cerebrovascular events if not promptly treated. We aimed to define the incidence of AF in the first 6 months after implantation of a variety of contemporary devices in a real-world setting, analyzing more possible predictors of AF than has been the case to date.

Methods

Study population

All patients ($n = 70$,) who underwent transcatheter IASC closure by the author from January 2006 to December 2008

were included, except for two patients with a large atrial septal defect (ASD), one because he had presented with recurrent episodes of AF before closure, another because she had undergone catheter ablation before closure and remained in sinus rhythm. All patients had undergone 24 h ECG monitoring prior to device implantation. For the purpose of this study, frequent atrial ectopics were defined as >1% of all beats during 24 h. Patients experiencing more than 30 consecutive beats (excluding supraventricular and re-entry tachycardia and typical atrial flutter) were defined as having intermittent AF, with the temporal inclusion criteria as described previously [1]. Patient characteristics and devices used are summarized in Table 1.

Left atrial measurement was taken in the short axis parasternal view. Although patients undergoing echocardiography at our institution usually had a 4-chamber long and short axis measurement of right atrial dimensions, some patients were referred by an external cardiologist or hospital and lacked these measurements. The right atrium was thus assessed to be visually enlarged or "normal".

Device selection, description, and implantation

Device size selection was based on transoesophageal echocardiography sizing in the first 30 patients, until undersizing was probably partially causal in subacute device embolization in one patient [4]. In all following patients, device size selection was based on intra-interventional balloon sizing. Device size was reported as diameter of the largest disk as declared by the manufacturer. For example, an Amplatzer® device used for closure of a 36 mm ASD, has a left atrial disk diameter of 52 and a right atrial disc diameter of 46 mm; in this case, 52 mm was chosen as the device size in our study. All devices were implanted and no in-hospital complications occurred. The devices used are shown in Table 2.

Follow up

The follow-up period was 16.8 (±9.9; 6–42) months. Mid-term complications (excluding AF) were one device dislocation that could be retrieved percutaneously [4] and one arteriovenous fistula was treated surgically on an ambulatory basis. Treatment after device implantation consisted of Clopidogrel for 3 months, acetyl salicylic acid, and prophylaxis against infectious endocarditis for 12 months. All patients were seen by the author at least 1 and 6 months after implantation, for transthoracic and transesophageal echocardiography, respectively. All patients and referring physicians were asked to report any change in symptoms or clinical status, with special emphasis on palpitations. Patients suspected of having or those with documented AF were followed up by 12-lead ECG and/or Holter monitoring. The rhythm in asymptomatic patients was documented by a resting ECG and by monitoring during echocardiography at least twice on both follow-up visits by the examining cardiologist. None of the asymptomatic patients had 24 h ECG monitoring.

Continuous data are presented as a mean ±SD and range, and compared using a paired Student's *t* test. All data were analyzed using the StatView 5.0® program, SAS systems™, Cary, NC, USA).

Table 2 Device types used

	Amplatzer®	Occlutec®	Solysafe®	Premere®	Cardia®
Total number	28	20	9	8	3
AF	1 (3.6%)	5 (20%)	1 (11%)	0	0

AF number of patients having experienced atrial fibrillation after device implantation

Results

Incidence of AF and treatment

Seven patients (10.3%) experienced one or more episodes of AF with palpitations as presenting symptom in all seven and additionally dyspnea and precordial pain in three. All episodes occurred in the first 6 months after device implantation (1–24 days; 14.6 ± 9.6). None of the episodes was intermittent at presentation. The patient experiencing AF peri-interventionally was immediately cardioverted and treated with Betablockers. One patient was on oral anticoagulation because of recurrent deep venous thrombosis and was cardioverted and given Betablocker. Two patients with a CHADS 2 score ≤1 were given

Table 1 Patient characteristics

All patients (women)	Age in years	Hypertension	Coronary artery disease	LA size	RA dilated	Residual shunt
68 (32; 47%)	53.6 ± 15.1; 24–83	12 (17.6%)	6 (8.8%)	3.52 ± 0.52; 2.1–4.9	11 (16.1%)	3 (4.4%)

LA left atrium size in mm (upper limit of normal 40 mm)

RA right atrium (semi quantitative assessment: dilated versus not dilated. Pre-intervention dimensions available only in 12 patients)

Betablockers and low molecular heparin. All of them converted spontaneously within a few days. Three patients with a CHADS 2 score >1 were put on oral anticoagulation, Amiodarone, and cardioverted. In one patient, cardioversion had to be applied twice after a recurrence and the seventh patient also experienced a recurrence and is receiving oral anticoagulation with established AF, she had declined a second cardioversion and Amiodarone medication. No patient experienced any complication due to AF (no embolic events, cardiac decompensation or syncope). Except for the latter patient, all antiarrhythmic medication and oral anticoagulation were stopped after 2 months, after a 24 h-ECG.

Predictors of AF

The following parameters showed to bear no relation to the new onset of AF after closure of an IASC: residual shunt, hypertension, body mass index, coronary artery disease, gender, age, and left atrial size. Significance for right atrial size as a predictor for AF was narrowly missed ($P = 0.08$). The only significant predictor of AF was found to be device size (Table 3). Four out of seven patients experiencing post closure AF had right atrial enlargement. Of the 68 patients studied, 62 (91.2%) had a patent foramen ovale (PFO) and 6 (8.8%) an ASD. Of the latter, one patient (17%) experienced AF after defect closure, the other six patients developing AF had a PFO (9.6%; $P =$ ns). Frequent atrial ectopics had been found in two patients that developed AF after IASC, and in four patients that remained free of AF ($P =$ ns).

Discussion

The incidence of AF after closure of an IASC seems to be higher in our series than in others published so far [1–3].

Table 3 Predictors of atrial fibrillation

Variable	No AF	AF	*P*
Age in years	53 ± 15.4; 24–83	58 ± 13; 32–71	NS; 0.8
Gender (F)	28 (45.9%)	4 F (57%)	NS
BMI	25.3 ± 4.4; 18.8–37.8	24 ± 2; 21.5–27.5	NS; 0.17
LA size	3.5 ± 0.56; 2.1–4.9	3.6 ± 0.38; 3–4.1	NS; 0.24
RA dilatation	7/61 (11.5%)	4/7 (57%)	NS; 0.08
Device size[a]	26.4 ± 5.6; 15–52	31.6 ± 2.7; 30–36	0.002
Hypertension	11/61	0/7	NA
CAD	4/61	2/7	NS; 0.17
Residual shunt	3/61	0/7	NA

AF new onset atrial fibrillation after device implantation, *BMI* body mass index, *CAD* coronary artery disease, *NA* Not analyzed, *NS* not significant

[a] Diameter of largest disc of device used as declared by manufacturer

This may be a bias due to the numbers studied, or to different definition, selection, or follow-up criteria. Basically, most studies suspect some factors to be implicated in the occurrence of AF in this setting. Left atrial and device size [3] are cited by some, residual shunting [1] by others, yet the data are not always congruent.

The three patients (4.4%) in our series showing a minimal [2] and moderate [1] residual shunt 6 months after closure, defined as described previously [5], did not develop AF. Atrial dysrhythmias after IASC closure may be due to an inflammatory response of the atrial myocardium [1]. New macro-reentry circuits may be favored [1]; more so when the left atrial disk is in the vicinity of right pulmonary veins ostia. Alternatively, mechanical irritation by the device, analogous to catheter-induced atrial dysrhythmias sometimes seen during right heart catheterization, may occur. The larger the size and the contact surface of the device with the atrial walls, the larger the potential for mechanical irritability. One of the reasons why in our series, left atrial dilatation did not correlate with AF development may be that in all nine patients with left atrial enlargement, device sizes happened not to exceed 25 mm (2 device diameters of 15 mm, one of 20 mm and 6 of 25 mm). Of the 11 patients with enlarged right atrial dimensions, 4 experienced postprocedural AF, 3 of them with device sizes of 30 mm diameter, and one of 35 mm (the only patient with ASD and AF). Two patients with ASD and very large devices (48 and 52 mm) remained in sinus rhythm; the right atrial dimensions regressed to normal at 6 months' follow-up. The three patients with RA enlargement and AF had received 30 mm devices. Four of the five remaining patients with RA enlargement remaining in sinus rhythm had a 25 mm, the last one a 30 mm device.

A partial explanation for the apparent contradiction why only one out of six patients with a large ASD developed AF after closure of the defect may be that, in contrast to PFO, atrial volume overload is seen with significant shunting in ASD, leading to atrial enlargement. Often there is a rapid decrease of atrial dimensions after ASD closure [6, 7], probably by leading to decrease in wall tension and reduction of the arrhythmic substrate. This is also exemplified by one of the patients in our series, who had been excluded because of persistent AF before ASD closure. Immediately after device implantation, left atrial size was 5.1 cm and right atrial size 5.8 × 6 cm. On the first transthoracic examination 1 month post implantation, the left atrium measured 4.8 cm and the right one 5 × 5.4 cm. The patient was cardioverted and remained in sinus rhythm. A second reason may also be related to the (literal) contact area between the device and the atrial wall. In a large ASD, the defect itself is no substrate for "contact-dysrhythmia", the active interface "device-atrial tissue" is limited by the surface of the rim covered by the device

edges. For example, for an ASD measuring 32 mm, we use a 32 mm Amplatzer® device with a left atrial disc diameter of 46 mm. The surface area of the device would maximally be 16.6 cm^2 ($\pi r^2 = 3.14 \times [2.3]^2$), of which 8.04 cm^2 ($3.14 \times [1.8]^2$) would cover the defect, leaving 8 cm^2 device rim in contact with atrial myocardium. This is not much more than the 7.1 cm^2 ($3.14 \times [1.5]^2$) of a 30 mm Amplatzer® device used to cover a slit-like PFO with an atrial septal aneurysm. A study reporting on symptomatic AF after ASD (not PFO) closure quotes an incidence of 15% [8], which is more in line with our results.

One of the devices seemed to be numerically associated with higher rates of AF (Table 2); statistically this was not significant. At this stage, it would be purely speculative to link any physical characteristic (stiffness of metal, device bulkiness, etc) with occurrence of AF in this small series.

Limitations

Obviously, caution has to be exerted when talking about statistical significance and while dealing with small patient numbers. Also, the small numbers render a multivariate analysis inapplicable.

Dimensions of the RA have only be qualified, not numerically quantified, because most echocardiography studies of patients referred for PFO closure described the RA either as enlarged or normal. Then again, the long axis dimensions of the LA were not systematically registered, even in our patients. Although theoretically some spontaneously converted episodes of AF may have been missed, despite routine 24 h ECG in all patients pre-procedurally, our feeling is rather that post IASC episodes have been underreported in the literature to date. It is more than probable that not all transient episodes of AF can be attributed to an anatomical or mechanical cause. There may be other less tangible factors as exemplified by one of our younger patients who reported with AF after a week of overwork followed by indulgence of excessive alcohol over the weekend [9].

Conclusion

More data on the incidence of postprocedural AF after IASC are needed as its incidence seems to be underreported. This may be due to the fact that the majority of these episodes are transient and asymptomatic, yet they remain potentially dangerous. Occluder size was the only significant predictor of post-procedural AF, especially after PFO closure. Although there are some obvious constraints (defect size, presence of an atrial septal aneurysm, etc.) that sometimes may dictate implantation of a larger device, it may be reasonable to implant occluders "as large as necessary, as small as possible". Larger studies examining the correlation between atrial and device size on one hand and AF on the other, are necessary.

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