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Prospective evaluation of iatrogenic atrial septal defect after cryoballoon or radiofrequency catheter ablation of atrial fibrillation—"EVITA" study

Zsofia Nagy[1] · Zsuzsanna Kis[1] · Tamás Géczy[1] · Andras Temesvari[1] · Zoltan Som[1] · Sarolta Borbas[1] · Tamás Breuer[1] · David Molnar[2] · Csaba Foldesi[1] · Attila Kardos[1]

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Abstract

Purpose Iatrogenic atrial septal defect (IASD) after catheter ablation (CA) for atrial fibrillation (AF) due to transseptal puncture (TSP) can occur. The aim of this prospective study was to describe the incidence of IASD and to detect any cerebrovascular accident (CVA) after radiofrequency (RF) and cryoballoon (CB) CA.

Methods Between July 2014 and September 2016, 94 patients (pts) (RF; 48, CB; 46, 30 (31.9%) women, mean age = 60 ± 9.7 years) with paroxysmal AF were enrolled who underwent CA procedure for the first time. During RF ablation a single (n = 30, 62.5%) or double (n = 18, 37.5%) TSP was performed. Transoesophageal echocardiography before the procedure and at the 3-month and 12-month follow-up (FU) was accomplished. During the FU period, we evaluated the occurrence of any postprocedural CVA.

Results At the 3-month FU, IASD was detected in 17/94 (18.1%) pts; in 9/48 (18.8%) pts in the RF while in 8/46 (17.4%) pts in the CB group (p = 0.866), all of them with left-to-right shunt. In the RF group, 6/30 (20%) pts with a single TSP while 3/18 (16.7%) pts in the double TSP group had IASD (p = 0.780). 14/17 (82.4%) IASDs showed high spontaneous closure rate at the 12-month FU. None of the pts died or suffered from CVA.

Conclusion Persistent IASD can occur rather frequently following AF CA. No significant difference was observed between the RF and CB techniques concerning the presence of IASD at 3-month. IASDs showed a high spontaneous closure rate. No cerebral thromboembolic event was observed in the 12-month FU period.

Keywords Iatrogenic atrial septal defect · Transseptal puncture · Atrial fibrillation · Cryoballoon ablation · Radiofrequency ablation

Abbreviations

AAD	Antiarrhythmic drug
AF	Atrial fibrillation
ASD	Atrial septal defect
BMI	Body mass index
CA	Catheter ablation
CB	Cryoballoon
CF	Contact force
CVA	Cerebrovascular accident
DOAC	Direct oral anticoagulant
FU	Follow-up
IASD	Iatrogenic atrial septal defect
LA	Left atrium
LVEF	Left ventricle ejection fraction
PFO	Patent foramen ovale
PV	Pulmonary vein
PVI	Pulmonary vein isolation
RF	Radiofrequency
TEE	Transoesophageal echocardiography
TIA	Transient ischaemic attack
TS	Transseptal
TSP	Transseptal puncture

✉ Zsofia Nagy
zsofianagymd@gmail.com

[1] Department of Cardiology, Gottsegen Gyorgy Hungarian Institute of Cardiology, Haller Street 29, Budapest 1096, Hungary

[2] Department of Internal Medicine, Peterfy Sandor Hospital, Peterfy Sandor Street 8-20, Budapest 1076, Hungary

1 Introduction

Transcatheter puncture of the interatrial septum is an increasingly common procedure to gain access for a variety of cardiac interventions in the left atrium (LA) or ventricle. Atrial septal defect (ASD) caused by transseptal (TS) cardiac interventions is called iatrogenic atrial septal defect (IASD) [1, 2]. IASDs are associated with TS catheter ablation (CA) techniques for atrial fibrillation (AF), most frequently pulmonary vein isolation (PVI), than focal atrial tachycardia or atypical flutter with a left-sided location, or accessory pathway with an anterograde approach and structural heart disease interventions such as MitraClip or transcatheter mitral valve replacement and ventricular tachycardia ablation [3]. AF CA is the most frequent procedure where transseptal puncture (TSP) is needed to access the LA, irrespective of the used technique [4].

The generation of an IASD is unavoidable and thus generally accepted. However, not much is known about IASD-related morbidity and complications.

The two most widely used methods to achieve PVI worldwide are cryoballoon (CB) and radiofrequency (RF) ablation. The aim of our prospective study was to describe the incidence and echocardiographic characteristics of IASD following RF or CB ablation procedures diagnosed by transoesophageal echocardiography (TEE) at 3-month and 12-month follow-up (FU). TSP is an integral part of both CA techniques; however, there are slight differences between the implantation of TSP. CB ablation technique requires a single TSP and a larger diameter TS sheath. RF ablation usually requires two TS sheaths either with a single TSP using "sliding technique" or a double TSP technique. As most centers have a circumferential mapping catheter and an ablation catheter at the same time in the LA, we examined the CA procedures where two long sheaths were introduced into the LA either with the "sliding" technique or the double TSP technique.

Furthermore, we sought to investigate the incidence of cerebrovascular accidents (CVA)—stroke or transient ischaemic attack (TIA)—related to IASD following AF CA.

2 Methods

2.1 Study population

This was an observational, prospective, single-centre cohort study.

The study protocol has been approved by the Ethics Committee of the Investigation Centre and an informed consent was obtained from all pts prior the procedure.

Between July 2014 and September 2016, 94 consecutive, symptomatic, drug refractory pts (30 (31.9%) women, mean age = 60 ± 9.7 years) with paroxysmal AF were enrolled in our study. In all pts, an index procedure of PVI using the CF sensing RF catheter ($n = 48$ (51.1%)) or the second generation CB catheter ($n = 46$ (48.9%)) was performed. The chosen ablation technique depended on the operator's preference. In all pts, only PVI without cavotricuspid isthmus ablation was accomplished. Baseline characteristics are shown in Table 1. Exclusion criteria were considered as previously performed TSP, a previously documented ASD or patent foramen ovale (PFO), congenital heart disease, pregnancy, preprocedural LA thrombus and any contraindications to the TEE and/or the ablation procedure.

2.2 Periprocedural medication

All pts were on therapeutic anticoagulation therapy 4 weeks prior and at least 3 months after the ablation procedure. Anticoagulation with vitamin K antagonists was discontinued before the procedures aiming INR < 2. Direct oral anticoagulants (DOAC) were interrupted the day before the procedure. Antiarrhythmic drug (AAD) administration were not altered prior the ablation procedure.

2.3 Medication therapy after catheter ablation

For the early postprocedural period, therapeutic anticoagulation was used with either enoxaparin or continuing the DOAC. Depending on the CHA_2DS_2-VASc score of the patient, anticoagulation was stopped 3 months following the procedures [5]. Postprocedural AAD therapy was stopped after the 3-month blanking period.

Table 1 Baseline demographic and clinical characteristics.

Baseline demographic and clinical characteristics			
	RF ($n = 48$)	CB ($n = 46$)	p value
Women, n (%)	17 (35.4)	13 (28.2)	n.s.
Age (years)	60.5 ± 9.6	60.4 ± 9.8	n.s.
Hypertension, n (%)	33 (68.8)	31 (67.4)	n.s.
Diabetes mellitus, n (%)	8 (16.7)	3 (6.5)	n.s.
Hyperlipidemia, n (%)	17 (35.4)	22 (47.8)	n.s.
Coronary heart disease, n (%)	15 (31.3)	9 (19.6)	n.s.
Congestive heart failure, n (%)	16 (33.3)	8 (17.4)	n.s.
Body mass index	30.2 ± 5.6	29.2 ± 4.2	n.s.
Duration of AF (months)	45.0 ± 38.9	61.1 ± 59.6	n.s.
CHA_2DS_2-VASc score	2.8 ± 2.0	2.1 ± 1.6	n.s.
Left ventricle ejection fraction (%)	60.9 ± 9.4	63.3 ± 7.7	n.s.
Left atrial diameter (mm)	43.0 ± 7.4	41.5 ± 6.9	n.s.

RF radiofrequency, *CB* cryoballoon, *AF* atrial fibrillation

2.4 Transoesophageal echocardiography

TEE examination was performed the day before the ablation procedure in order to exclude the presence of LA thrombus and to prove an intact interatrial septum. In all pts, at the 3-month FU, TEE was accomplished for the evaluation of persisting IASD. TEE was repeated at the 12-month FU only in those pts who presented with IASD at the 3-month FU. All TEE examinations were performed using the standard commercial echocardiography equipment (IE 33, Philips Medical, Andover, MA, USA). Interatrial septum was analysed with multiple views from the mid to upper oesophagus at angles ranging between 0 and 120°. The colour-Doppler technique and peripheral venous infusion of echocontrast solution—both at rest and during Valsalva manoeuvre—were used to detect persistent IASD [6].

2.5 Transseptal and ablation technique in cryoballoon ablation

CB ablation procedure was performed using the second-generation 28-mm CB (Arctic Front Advance™, Medtronic, Minneapolis, MN, USA) in all pts. LA access was achieved with a single TSP approach. TSP was carried out with the Brockenbrough needle (BRK-1™, St. Jude Medical, St. Paul, MN, USA) inserted in the SL0 dilator sheath system (SL0™, St. Jude Medical, St. Paul, MN, USA). Then a 0.032″ standard guidewire (Emerald Cordis®, Johnson and Johnson, Diamond Bar, CA, USA) was introduced in the SL0 sheath that was changed over the wire for a 15-Fr outer diameter steerable sheath (FlexCath Advance™, Medtronic, Minneapolis, MN, USA). In the next step, the circular mapping catheter (Achieve Mapping Catheter™, Medtronic, Minneapolis, MN, USA) together with the CB was positioned in each pulmonary vein (PV) ostium. Contrast injection into the PVs was applied to reach the best-fit occlusion. Firstly, a 240-s initial cryoablation was applied for each vein and was continued until total isolation of the PVs, at a minimal temperature no colder than minus 55 °C. The diaphragm excursion was monitored routinely during cryoablation of the right superior PV to minimize the risk of phrenic nerve damage.

2.6 Transseptal and ablation technique in radiofrequency ablation

During RF ablation procedures, contact force (CF)–sensing ablation catheters (Navistar Thermocool SmartTouch®, Biosense Webster Inc., Diamond Bar, CA, USA) and the CARTO® system (BiosenseWebster Inc., Diamond Bar, CA, USA) were utilized. We used two different TSP techniques: a single and a double TSP method. In 30/48 (62.5%) pts, a single TSP technique with the Brockenbrough needle and SL0 sheath was performed. The multipolar, steerable, circular mapping catheter (Lasso®Nav, Biosense Webster Inc., Diamond Bar, CA, USA) was inserted in the SL0 sheath, positioned in the LSPV, and the sheath was withdrawn to the right atrium. Then from a separate femoral venous puncture, the steerable 8.5-Fr-long sheath (Agilis ™ NxT, St. Jude Medical, St. Paul, MN, USA) was positioned in the superior caval vein, gently withdrawn and stabilized against the intraatrial septum. After penetration of the sheath's guidewire to the LA under fluoroscopic and/or intracardiac echocardiography guidance, the Agilis was passed over the TS defect beside the shaft of the Lasso catheter. In 18/48 (37.5%) pts, where the Agilis steerable long sheath was not successfully passed through the atrial septum with only guidewire use, a double TSP approach was performed. In these cases, after inserting the Lasso catheter in the SL0 dilator sheath system, a second TSP with 90-mm Brockenbrough needle was used to get the second access to the LA with the Agilis long sheath. The second access was needed to introduce the CF sensing ablation catheter in the Agilis steerable long sheath into the LA. The ablation catheter was set in a power-controlled mode with a maximum power of 25 W at the posterior wall of the LA and 35 W at the other regions of the LA, using a maximum temperature of 48 °C, while PV potentials were visible.

During all ablation procedures, conscious sedation was performed (iv. midazolam up to 5 mg and fentanyl up to 200 μg). Before initial TS access, full anticoagulation with intravenous heparin bolus was given and repeated as required to reach the targeted activated clotting time above 300 s. Figure 1 demonstrates the position of the TS sheaths and the ablation catheters during RF and CB ablation procedures. In all cases, TSP was evaluated under fluoro-guidance. If necessary, ICE guidance was used to help to visualize the site of the puncture.

2.7 Follow-up

All pts were recalled for outpatient clinical visits including physical examination, 12-lead ECG and 1-week transtelephonic ECG monitoring at 3, 6 and 12 months after the PVI procedure. AF recurrence was defined as atrial tachycardia/AF/atrial flutter lasting > 30 s [7]. We assumed all symptoms as AF recurrence which was similar to the previous symptomatic AF episodes. During all FU visits, we focused on the neurological status and all recorded medical files were checked up to reveal any CVAs following the CA procedures. TEE was accomplished in all pts at the 3-month FU while repeated TEE at the 12-month FU was accomplished only in those who had IASD at the 3-month FU. The incidence, diameter and shunt flow of IASD following CB (single TSP) or RF (single/double TSP) CA were investigated at the 3- and 12-month FU. The most important clinical (gender, age, hypertension, body mass index (BMI)) and echocardiographic parameters (left ventricle ejection fraction

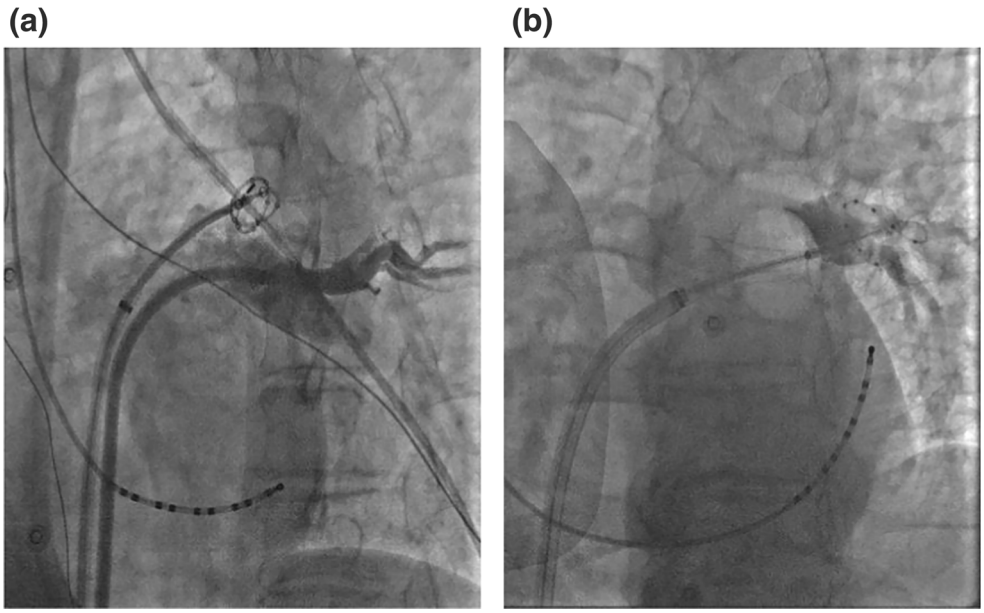

Fig. 1 Fluoroscopic LAO 30° projections are demonstrating the position of the transseptal sheaths (SLO and Agilis) during radiofrequency (A) and cryoballoon (FlexCath) (B) ablation procedure

(LVEF) and LA diameter) were compared in pts with IASD and without IASD at the 3- and 12-month FU, which will be referred as pts in IASD or NoIASD group.

2.8 Statistical analysis

Continuous variables are presented as mean ± standard deviation and were compared between groups with the two-sided *t*-test. Among pts with successful ablation procedure, the probability of freedom from AF was calculated with Kaplan and Meier survival analysis and differences between the groups were determined by the log rank statistic test. Binary endpoints were multivariately modelled with logistic regression, time-to-event endpoint were modelled with Cox proportional hazard model. Continuous covariates were first expanded with restricted cubic splines and checked whether there is any deviation from linearity. Effects with $p < 0.05$ were considered significant. All analyses were performed in R statistical program package, version 3.6.0 (R Core Team (2019). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.).

3 Results

3.1 Baseline demographic and clinical characteristics

Present study included 94 consecutive pts ([30 (31.9%) women, mean age = 60 ± 9.7 years) with paroxysmal symptomatic AF refractory to at least one AAD. In all pts, an index procedure of PVI using the CF sensing RF catheter ($n = 48$ (51.1%)) or the second generation CB catheter ($n = 46$ (48.9%)) was performed between July 2014 and September 2016. The investigated clinical and echocardiographic parameters did not differ significantly between the RF and CB groups (Table 1).

3.2 Procedural data

The duration of the procedure was significantly shorter in the CB group (CB 66.0 ± 18.3 min vs. RF 99.0 ± 25.5 min, $p < 0.001$), while fluoroscopy time was significantly shorter in the RF group (CB 11.6 ± 4.4 min vs. RF 8.6 ± 5.7 min, $p = 0.004$). CB ablation resulted in a higher radiation exposure caused by verifying PV occlusion after contrast injection (CB 988.1 ± 770.4 vs. RF 620 ± 554.6 cGycm^2, $p = 0.016$). No major periprocedural complications are presented in the RF group. In 2 pts within the CB group, temporary phrenic nerve palsy occurred, which resolved still during the procedure. No TSP-related complication occurred during the total of 94 ablation procedures. Procedural characteristics are summarized in Table 2.

Table 2 Procedural data

Procedural data			
	RF ($n = 48$)	CB ($n = 46$)	*p* value
Procedural time (min)*	99.0 ± 25.5	66.0 ± 18.3	< 0.001
Fluoroscopy time (min)	8.6 ± 5.7	11.6 ± 4.4	0.004
Fluoroscopy exposure (cGycm^2)	620.1 ± 554.6	988.1 ± 770.4	0.016
Pericardial tamponade	0	0	–
Phrenic nerve palsy, *n* (%)	0	2 (4.3)	–

*Lasts from the first venous puncture until the end of the procedure

RF radiofrequency, *CB* cryoballoon

3.3 Transoesophageal echocardiography at the 3- and 12-month FU

Table 3 shows the incidence of IASD at 3 and 12 months in the CB and in the RF group using a single or double TSP technique. At the 3-month FU, IASD was observed in 17/94 (18.1%) pts. Nine out of forty-eight (9/48) (18.8%) pts had a persistent IASD in the RF group. In the RF group, IASD was revealed in 6/30 (20%) pts following the single TSP while in 3/18 (16.7%) pts after double TSP ($p = 0.780$). In the CB group, the IASD incidence was 17.4% (8/46 pts). Concerning the IASD incidence at 3 month, no significant difference was found between the RF and CB ablation groups ($p = 0.866$). The mean IASD diameters were 2.2 ± 1.1 mm in the RF and 2.5 ± 1.4 mm in the CB groups ((range 1–7 mm) ($p = 0.624$)). All IASDs demonstrated spontaneous left to right flow not only with colour Doppler but also with microbubble contrast study.

At the 12-month echocardiographic FU, IASDs investigated at the 3-month FU showed a spontaneous closure rate of 82.4% (14/17 pts), in 8/9 (88.9%) pts in the RF while in 6/8 (75%) pts in the CB group. Two out of forty-six (4.3%) pts had persistent IASD in the CB group and 1/48 (2.1%) pts in the RF single TSP group ($p = 0.529$) (Fig. 2).

3.4 Clinical characteristics of patients with and without IASD at the 3- and 12-month FU

In the study population, pts with IASD at 3 months had a significantly higher BMI than pts without IASD ($(32.4 \pm 6.1$ vs. $28.9 \pm 4.2)$ ($p = 0.01$)). IASD pts in the RF group had a significantly higher BMI as compared with the NoIASD group at the 3-month FU ($(34.6 \pm 6.7$ vs. $28.8 \pm 4.5)$ ($p = 0.01$)). IASD and NoIASD groups showed no difference comparing the main echocardiographic parameters. The clinical and echocardiographic characteristics of the IASD and NoIASD pts at the 3- and 12-month FU are shown in Table 4 and Table 5.

3.5 AF-free survival and cerebrovascular event rate

At the 12-month FU, 34/48 (70.8%) pts in the RF group and 31/46 (67.4%) pts in the CB group were free from AF recurrence ($p = 0.72$). 6/48 (12.5%) pts after RF and 3/46 (6.5%) pts after CB ablation required a redo ablation following 10.4 ± 4.6 months on average after the index procedure ($p = 0.33$).

Anticoagulation was stopped at the 3-month FU visit in 58/94 (61.7%) of the pts depending on the CHA_2DS_2-VASc score. No pts with IASD in either ablation group presented with CV event after an index PVI procedure.

3.6 Predictors of IASD at the 3-month FU

In the multivariate model for IASD at the 3-month FU, ablation method, sex and LA size were insignificant ($p = 0.8956$, $p = 0.4380$ and $p = 0.8538$, respectively), but age was significant ($p = 0.0489$, 7.1% higher odds of having IASD at 3 months for each year increase in age, 95% confidence interval 1.00–1.15).

3.7 Relationship of IASD and AF burden

In multivariate model for AF with IASD as a—time-varying—covariate, the effect of IASD was not significant on the hazard of the onset of AF ($p = 0.3210$), after controlling for age, sex, LA size and ablation method.

4 Discussion

To the best of our knowledge, this is the first prospective study which aimed to investigate the presence of IASD and cerebrovascular event rate after CB or RF ablation using a single or double TSP technique confirmed by TEE at the 3- and 12-month FU. Furthermore, this is the first study reporting on the comparison of IASD occurrence following single or double TSP in RF ablation procedures. The main findings of our study are the following: IASDs were not associated with increased risk of cerebrovascular event rate (stroke/TIA). IASD occurrence was

Table 3 Iatrogenic atrial septal defect incidence

Incidence of IASD at the 3 and 12-month follow-up		
	3 month, *n* (%)	12 month, *n* (%)
Study population ($n = 94$)	17 (18.1)	3 (3.2)
RF ($n = 48$)	9 (18.8)	1 (2.1)
RF, single TSP (slide technique) ($n = 30$)	6 (20.0)	1 (3.3)
RF, double TSP ($n = 18$)	3 (16.7)	0 (0.0)
CB ($n = 46$)	8 (17.4)	2 (4.3)

IASD iatrogenic atrial septal defect, *RF* radiofrequency, *CB* cryoballoon, *TSP* transseptal puncture

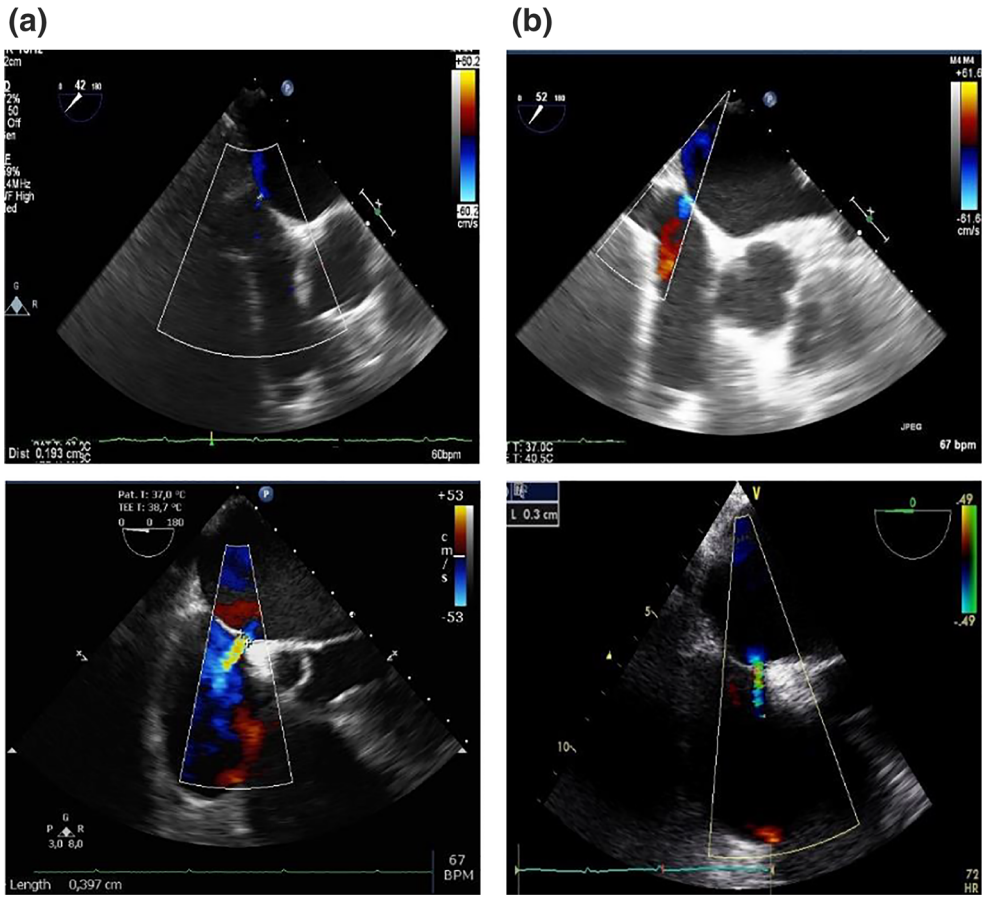

Fig. 2 Persistent iatrogenic atrial septal defects with left-to-right shunt in a patient at 3-month (A) and 12-month (B) follow-up following radiofrequency (above) and cryoballoon (below) ablation procedure as shown by transoesophageal echocardiography

moderately frequent 3 months after AF ablation in the RF (18.8%) and CB (17.4%) group, but the ablation technique did not significantly affect the incidence of postprocedural IASD. After RF ablation, the presence of IASD did not depend on the TSP approach (single or double). IASDs showed a high spontaneous closure rate of 82.4% at 12-month FU in both ablation groups. Obese pts had a higher risk of persisting IASD.

4.1 Comparison of the incidence of IASD after RF and CB ablation

PVI is the most common procedure where TSP is performed. The different AF ablation techniques require various TSP approaches. During CB ablation, a single TSP approach was achieved in all pts [8]. RF ablation was performed using a single TSP method or a double TSP access [9]. In the

Table 4 Risk factors of iatrogenic atrial septal defect at the 3-month follow-up

Characteristics of patients with and without iatrogenic atrial septal defect at 3-month follow-up

	Study population ($n = 94$)			RF ($n = 48$)			CB ($n = 46$)		
	NoIASD	IASD	p value	NoIASD	IASD	p value	NoIASD	IASD	p value
Number of pts., n (%)	77 (81.9)	17 (18.1)	–	39 (81.3)	9 (18.7)	–	38 (82.6)	8 (17.4)	–
Women, n (%)	25 (32.5)	5 (29.4)	n.s.	14 (35.9)	3 (33.3)	n.s.	11 (28.9)	2 (25)	n.s.
Age (years)	59.5 ± 9.4	64.7 ± 10.0	n.s.	59.4 ± 9.5	65.5 ± 9.4	n.s.	59.7 ± 9.5	63.7 ± 11.1	n.s.
Hypertension, n (%)	53 (70.1)	11 (70.6)	n.s.	28 (71.8)	5 (55.6)	n.s.	25 (65.8)	6 (75)	n.s.
Body mass index	28.9 ± 4.2	32.4 ± 6.1	$p = 0.01$	28.8 ± 4.5	34.6 ± 6.7	$p = 0.01$	29.0 ± 3.9	30.1 ± 4.7	n.s.
Left ventricle ejection fraction (%)	51.8 ± 5.2	59.4 ± 8.7	n.s.	62.7 ± 8.6	54.7 ± 9.9	$p = 0.04$	63.1 ± 8.3	64.0 ± 4.2	n.s.
Left atrial diameter (mm)	41.3 ± 6.2	42.9 ± 5.3	n.s.	42.0 ± 6.4	44.7 ± 7.6	n.s.	41.4 ± 6.7	42.2 ± 5.4	n.s.

IASD iatrogenic atrial septal defect, *RF* radiofrequency, *CB* cryoballoon

Table 5 Risk factors of iatrogenic atrial septal defect at the 12-month follow-up

12-month follow-up of those patients who presented with IASD at 3-month follow-up			
Study population ($n = 17$)			
	NoIASD ($n = 14$)	IASD ($n = 3$)	p value
Ablation technique			
RF, n (%)	8 (57.1)	1 (33.3)	–
CB, n (%)	6 (42.9)	2 (66.7)	–
Women, n (%)	5 (35.7)	0	–
Age (years)	63.2 ± 10.1	71.4 ± 6.6	n.s.
Hypertension, n (%)	9 (64.3)	2 (66.7)	n.s.
Body mass index	32.5 ± 6.4	31.6 ± 5.0	n.s.
Left ventricle ejection fraction (%)	58.8 ± 9.2	63.0 ± 4.2	n.s.
Left atrial diameter (mm)	43.7 ± 7.7	40.5 ± 5.4	n.s.
Stroke/paradoxical embolism	0	0	–

IASD iatrogenic atrial septal defect, *RF* radiofrequency, *CB* cryoballoon

literature, only one study compared the presence of persisting IASDs using two ablation techniques: Mugnai et al. reported the incidence of IASD at 1-year FU after CB or RF ablation using a double TSP technique. They found a significantly higher IASD incidence in the CB group (22.2%) than in the RF group (8.5%) [10]. Concerning the RF ablation, there is one retrospective study which examined the incidence of IASD (5.6%) by TEE with a median FU of 12 months but not with 3- and 12-month FU (Anselmino et al.) [11]. Besides, CB-related IASD was examined in four studies using TEE following the CA procedure. Chan et al. discovered persistent IASD in 4/12 cases (31%) 9 months following CB ablation procedure [12]. Sieira et al. reported that IASD was present in 20% of pts 1 year after CB ablation [13]. In the study of Davies et al., IASD was revealed in 7/27 pts (25.9%) with a median FU time of 553 days [14]. Linhart et al. recently published their long-term results, the prevalence of IASD after CB ablation was 37% after 2.9 years [15]. After CA with the second-generation CB, in the study of Watanabe et al., IASDs were found in 8.4% of pts with a median FU of 15.5 months, but IASD was examined only with transthoracic echocardiography [16]. The wide range of variety concerning the IASD incidence seen in the referred studies might derive from their various inclusion criteria. They used heterogeneous patient population, not excluding preprocedural PFO or IASD, evaluating the postprocedural IASD with transthoracic echocardiography. The lower rate of IASD in our study might be explained by our inclusion criteria such as only pts with paroxysmal AF and only pts with excluded preprocedural PFO or IASD were finally enrolled.

4.2 Risk factors of persisting IASD

In our study, pts who presented with IASD at 3 months had a higher BMI than pts without IASD. Pts with IASD 3 months after the RF ablation had lower LVEF as compared with those without IASD in the same ablation group. Age was a significant predictor of IASD at the 3-month FU; older pts had higher odds of having IASD at 3 months. Other investigated parameters showed no further difference between the groups.

4.3 The clinical relevance of IASD

Postinterventional IASD is relatively common following LA procedures, but its clinical significance is not clear yet [4, 17]. The interventional closure of IASDs following AF ablation procedures is extremely rare because of the high spontaneous closure rate of the IASDs [18]. Only limited data is available about the risk of cerebrovascular events in pts with IASD [3, 19]. In our patient cohort, none of the pts suffered from stroke or TIA during the 12-month FU period, subsequently the presence of IASD was not associated with an increased risk of cerebrovascular event rate. The spontaneous closure rate of the IASD was high (82.4%) between the 3- and 12-month FU. Consequently, the risk of stroke or TIA associated with IASD was the highest in the first 3 months after AF ablation. In our protocol, every patient who underwent AF ablation generally received oral anticoagulant for 3-month postprocedural therapy which may reduce the risk of paradoxical embolism in this period. No relationship was observed between the presence of IASD and the onset of atrial fibrillation during the FU period.

4.4 Strengths and limitations

The strengths of this prospective study are the following. First of all, this study has a homogenous patient cohort, enrolled only pts with paroxysmal AF. Secondly, PFO or IASD was excluded in all pts with preprocedural TEE. Thirdly, not only CB with single TSP RF technique but also RF CA performed with two different TSP methods (single or two-separate TS access) was compared. Furthermore, IASD was confirmed not

only short after PVI—3-month FU—but also 1 year after CA investigated by TEE. Nevertheless, the study has a systematic FU focusing on neurological events.

Limitations of the present study include the observational nature, due to which comparisons between RF and CB groups might be subject to confounding, the small sample size (limited power) and the short FU duration. Silent cerebral embolism caused by the procedure itself, or due to paradoxical embolism through IASD, was not investigated using neurocognitive function tests or cerebral brain imaging.

5 Conclusion

IASD irrespective of the ablation method is a moderately frequent phenomenon after CA procedure at the 3-month FU. Using single or double TSP technique during RF ablation did not significantly influence the presence of IASD in the FU period. IASDs showed a high spontaneous closure rate in the first year following AF ablation. No cerebrovascular event was recorded in this patient cohort, subsequently the RF and CB ablation procedures in paroxysmal AF pts were safe in the investigated population. However, the clinical relevance of IASD after AF ablation still requires further investigations.

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Compliance with ethical standards

Conflict of interest All authors declare no conflict of interest.

Ethics approval and consent to participate This study was approved the Ethics Committee of the Investigation Centre. Informed consent was obtained from all individual participants included in the study.

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