Zero-fluoroscopy atrial fibrillation ablation in the presence of a patent foramen ovale: a multicentre experience

TITLE PAGE

Title

Zero-fluoroscopy atrial fibrillation ablation in presence of a patent foramen ovale. A multicenter experience.

Short title

Fluoroless AF ablation in PFO patients

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ABSTRACT

Introduction

Atrial fibrillation (AF) ablation has historically been guided by fluoroscopy, with the related enhanced risk deriving from radiation. Fluoroscopy exposure may be confined to guide the transseptal puncture. Small sample size study presented a new methodology to perform a totally fluoroless AF ablation in case of a patent foramen ovale (PFO). We evaluated this methodology in a large sample size of patients and a multicenter experience.

Methods and Results

Two-hundred fifty Paroxysmal AF patients referred for first AF ablation with CARTO3 electroanatomic mapping system were enrolled. In 58/250 a PFO allowed crossing of the interatrial septum, and a completely fluoroless ablation was performed applying the new method (Group A). In the remaining patients a standard transseptal puncture was performed (Group B). Pulmonary vein isolation was achieved in all patients with comparable procedural and clinical outcomes at short and long-term follow-up.

Conclusion

The presence of a PFO may allow a completely fluoroless safe and effective AF ablation. Probing the fossa ovalis looking for the PFO during the procedure is desirable since it is not time consuming and can potentially be done in every patient undergoing AF ablation.

Key words

Atrial fibrillation; Ablation; Fluoroscopy; X-ray; Patent foramen ovale.

INTRODUCTION

X-ray fluoroscopy has conventionally been used to guide electrophysiology procedures, exposing patients and operators to the stochastic and deterministic effects of radiations (1-5).

Since the number of atrial fibrillation (AF) ablations has increased substantially over recent years, making AF procedures the most commonly encountered ablation in clinical practice, fluoroscopy exposure to patients and particularly electrophysiologists is considerable over time. Despite the widespread of 3D mapping systems, which dramatically reduced X-ray exposure, fluoroscopy is still considered a necessary tool for various steps in the ablation procedure, such as performance of the transseptal puncture (6-9).

There is growing evidence that catheter ablation of AF is feasible using various techniques to reduce or eliminate fluoroscopy, such as integration of 3D mapping systems with fluoroscopy images and combination with intracardiac echocardiography (ICE) to guide the transseptal puncture (10,11,12). Despite these promising results, we have to consider that ICE still requires a dedicated operator, an additional venous puncture, potentially increasing the risk of vascular complications, can result in longer ablation procedures and may increase the cost of the procedure.

We already demonstrated that performing an AF ablation with a very limited X-ray exposure is feasible when using a 3D electroanatomic mapping (EAM) system. In our previous experience, our mean X-ray time was 2.28 ± 1.40 minutes indeed and it was mainly confined to manage the transseptal puncture (13).

Based on this consideration fluoroscopy in AF ablation may be strictly confined to guide the transseptal puncture.

Our electrophysiological center started a program dedicated to reduce the X ray exposure early in 2008 using the 3D EAM system that was then carried out through the years (10,11,12). Based on this experience we decided to evaluate prospectively, from June 2014 in a multicenter study, the impact of the patency of the foramen ovale on the procedure and on the X ray exposure. In the

meanwhile in 2016 Kuhne et al (14) published a small sample size single center similar experience. As usual, several centers, may be focused on the same topic at the same time. Once published the experience by Kuhne et al, our ongoing study was not modified because it was reaching the end of the enrollment period. Therefore we thought that a larger multicenter experience would have been useful to add more data about this methodology and its impact on procedural outcome.

METHODS

All paroxysmal AF patients addressed to three university referral centers (1-Città della Salute e della Scienza Hospital, Turin, Italy, 2-Cardinal Massaia Hospital, Asti, Italy, 3-San Eugenio Hospital Rome, Italy) for first AF ablation procedure guided by CARTO3 EAM system (Biosense Webster, Diamond Bar, CA) from June 2014 to January 2016 were prospectively enrolled. Each patient underwent a TEE before ablation in order to assess the atrial dimensions, rule out the presence of thrombi in the left atrium (LA) or in the left atrial appendage (LAA). A contrast-enhanced magnetic resonance imaging (MRI) of the LA was obtained and merged with the cardiac chamber reconstruction performed during the ablation procedure.

The study protocol was approved by the institutional ethics committee and performed according to the principles of the Declaration of Helsinki after written informed consent was obtained from the patient.

Cardiac imaging reconstruction and access to the left atrium

CARTO3 EAM system, providing real-time visualization of multiple catheters as in a standard fluoroscopic view, was used to navigate the venous system and perform a right atrium (RA) reconstruction to place all the catheters in the heart. The procedure was performed via both right and left femoral veins. Through a venous femoral approach the coronary sinus catheter (Decanav, Biosense Webster, Diamond Bar, CA) was advanced in the venous system until RA electrical potentials appeared on the catheter's poles. Thanks to CARTO3 ability to create a geometric matrix,

a partial reconstruction of the RA chamber was performed and the catheter was placed inside the coronary sinus. An ablation catheter (Smart-Touch, Biosense Webster, Diamond Bar, CA) was then carefully advanced through an 8F long sheath in the inferior vena cava up to the RA and an EAM of the RA was obtained. Any difficulty in advancing the catheters and navigating the veins was overcome by pulling back the catheter and slightly rotating it; during the entire process the catheters were constantly visualized. After completion of the 3D EAM of the RA, the patency of the foramen ovale was evaluated by pulling back the ablation catheter out of the superior vena cava to the RA, mimicking the transseptal maneuver. After reaching the fossa ovalis position on the interatrial septum, a gentle pressure was applied to tent the septum itself. If the PFO was present, access in the LA was obtained with cautious advancement of the ablation catheter, and an appropriate maneuverability of the catheter itself was demonstrated (Figure 1). The catheter was subsequently covered in an "over-the-catheter" fashion with the long sheath and then removed, leaving the tip of the sheath in the LA. The exact location of the sheath in the LA was assessed by the fact that, when the sheath reaches the ablation catheter, the electrodes on the ablation catheters turn black (Figure 2).

The ablation catheter was then reintroduced through the second femoral vein sheath and a second attempt to cross the PFO was made in the previously described fashion. In case of failure, the mapping catheter (Lasso, Biosense Webster, Diamond Bar, CA) was introduced through the transseptal sheath in the LA without fluoroscopy thanks to the possibility of being visualized by CARTO3, and the sheath itself was withdrawn in the RA (Figure 3). This expedient enhances the possibility of the PFO to be engaged by the ablation catheter because of the smaller size of the Lasso catheter shaft (7F) compared to the 8F of the transseptal sheath.

In case of failure of the previously described approach, a standard transseptal puncture guided by fluoroscopy was performed. The transseptal sheath was advanced over-the-wire into the superior vena cava. The needle was then advanced into the sheath about 2-3 cm short of the tip and the

needle was attached to a pressure transducer. The entire assembly was then withdrawn in left anterior oblique view into the RA, paying attention to the needle rotation. When the expected position along the interatrial septum was reached, the assembly was 1 mm gently advanced to engage the septum itself. The best position was validated in a latero-lateral fluoroscopic view and corrected with a clockwise rotation if necessary. The needle was then gently advanced probing the septum and access in the left atrium was obtained, confirmed by LA pressure waveform and by LA visualization with a small amount of contrast injection. The transseptal sheath was finally advanced into the LA and catheter exchange was performed. The ablation catheter was inserted into the LA through the same septal hole as previously described (12).

Regardless the approach used to enter the LA, as soon as the ablation and the Lasso catheters were on the left side of the heart, the sheath (flushed with a 0.9% heparinezed NaCl solution) was withdrawn again in the RA to reduce the possible risk of embolic events during the procedure.

After LA access was gained, all the patients underwent an EAM reconstruction by navigating the circular mapping and/or the ablation catheter inside the LA and acquiring data points that were subsequently interpolated and displayed by the software. The LA MRI reconstruction was merged with the EAM and the final reconstruction was obtained.

In every patient, total procedural time (skin to RA catheter positioning, left atrium access, LA EAM, ablation time) and total fluoroscopy time were recorded.

For each patient, procedural endpoint was PV isolation, demonstrated as disappearance of PV potentials on the circular mapping catheter and entrance/exit block when pacing from the LA/PV. Radiofrequency (RF) energy was delivered to create a circumferential lesion around the PV antrum using maximum power up to 45 W (range 30-45W), temperature cut-off at 43°C, and irrigation rate from17 ml/min up to 35 ml/min.

All patients performed the ablation procedure on warfarin, with a target INR of 2-2.5 the day of the ablation procedure. One-hundred IU/Kg of heparin were administered during the procedure, one

third of the total dose soon after venous femoral access and two thirds of the dose after gaining access in the LA. After the ablation procedure a transthoracic echocardiography was performed in all patients to assess for the presence of pericardial effusion and evaluate the LA function. Patients were monitored with continuous ECG recording and were discharged the day after the procedure with warfarin therapy for at least 1 month; after 1 month the choice of continuing oral anticoagulation depended on individual CHA_2DS_2-VASc score. Anti-arrhythmic drugs were generally discontinued after 3 months, unless continued for other reasons. Patients were followed-up with a 12-lead ECG, a Holter monitor and a clinical evaluation at 3, 6 and 12 months. Any episode of atrial fibrillation of at least 30 s duration occurring after the blanking period of 3 months was defined as recurrence.

Statistical analysis

Continuous variables are expressed as mean and standard deviations, while categorical variables are reported as absolute values and frequencies. Comparison between PFO and standard transseptal puncture groups was made with T-Student test for continuous variables and Chi-Square test for categorical variables. Kaplan Meier curves were used to measure AF recurrence-free survival over time. Statistically significant P-values were considered with a threshold less than 0.05.

RESULTS

Two hundred fifty patients with paroxysmal AF undergoing PVI as first-time procedure were prospectively enrolled. Baseline clinical characteristics and echocardiographic data are presented in **Table 1**. In 58 out of 250 (23.2%) patients the LA was accessed through the PFO without the use of fluoroscopy. In these patients, no X-ray was used during the entire procedure (to place the catheters in the heart, reconstruct the right and LA anatomy, and perform the ablation procedure). In the remaining 192 patients a standard fluoroscopy guided transseptal puncture was performed. In 41 out of 58 patients, the TEE performed before the ablation procedure, anticipated the presence of a PFO, whereas in the remaining 17 cases the PFO was not unveiled by the TEE. In 1 patient the preprocedural TEE showed the presence of the PFO, but we were unable to cross it with the ablation catheter; therefore a transseptal puncture was performed.

Pulmonary vein isolation was achieved in all patients (regardless the presence of PFO). The procedural parameters and times are reported in **Table 2**. There were no major complications related to the procedure in the acute setting or during in-hospital stay or further follow-up. Minor procedure related complication occurred: 1 (0.4%) artero-venous fistula occluded with manual compression, 2 groin hematoma (0.8%). All patients accomplished the 3, 6 and 12-month follow-up with ECG, Holter ECG recording and clinical examination. To the mean follow up of 12 months freedom from AF was 84.5% (49/58) in the PFO group and 82.3% (158/192) in the general AF cohort (Figure 4). In particular, 68% (39/58) in the PFO group and 65% (125/192) in the general AF cohort were in sinus rhythm without antiarrhythmic drugs.

DISCUSSION

The recent implementation of EAM systems to guide ablation procedures has led to a great impact in the field of reducing fluoroscopy without lowering clinical outcomes or increasing complications (12). AF ablation has always been considered a complex procedure requiring longer fluoroscopy times than other types of ablation. One of the greatest impacts in minimizing or eliminating fluoroscopy might be represented by the prevention of malignancies, since the absolute lifetime risk of fatal cancer increases by 0.05% for every 10 mSV of effective X-ray dose in the adult population (15). Moreover, children, women and obese patients are at even higher risk (16,17). Obesity is strictly related to AF and obese patients receive more than twice the effective dose compared to normal weight patients (18). Many EP laboratories worldwide have started to follow the ALARA concept of minimizing x-ray exposure not only to protect the patient but also for the medical staff (19). In fact harmful biological effects increased directly with radiation dose. Therefore it is essential to reduce the exposure dose to the minimum necessary without forcing to zero-fluoro at any cost. Interventional cardiologists, nurses and laboratory technicians who use fluoroscopy on a daily bases are exposed indeed to the cumulative risk of radiations. This is even more important in high volume centers, where AF ablation is routinely performed. Moreover, among staff that wears protective lead aprons, orthopedic problems such as spine, hip, knee and ankle injuries are extremely common (20). Our previous experience already demonstrated that reducing fluoroscopy was feasible and safe, with only 2 minutes of X-ray necessary to perform the transseptal puncture (13).

The literature reports few studies showing the feasibility of performing a fluoroless AF ablation procedure. However, in these initial experiences, ICE was the crucial element, essential for fluoroscopy elimination. In a study from Reddy et al. (21), 20 consecutive patients with paroxysmal AF underwent zero X-ray ablation with an acute success rate of 97%. They combined the EnSite NavX EAM system with ICE to guide the transseptal puncture. ICE imaging was used also by

Ferguson et al. (22). They were able to perform a zero-fluoroscopy ablation in 19 out of 21 patients, whereas in 2 patients 2-16 minutes of fluoroscopy were needed to facilitate the transseptal puncture. Kuhne et al (14), considering a small sample size, reported a totally fluoroless AF ablation procedure in 87% of PFO patients guided by Carto3 mapping system. This study demonstrated a new method to cross the interatrial septum and position all catheters in the LA in patients with PFO completely without fluoroscopy and without additional tools like ICE to assist the AF ablation procedure. Our study strongly enhances these results. To the best of our knowledge this is the largest experience ever published on this topic. In our experience, we were able to handle without problems both the ablation and the circular mapping catheter inside the LA with a good maneuverability, despite entering the chamber through the PFO; in no case bringing the sheath in the LA to confer more stability to the ablation catheter was necessary, thus reducing the risk of embolization.

Besides feasible, our approach seemed safe as well; no major complications were observed in the acute setting or during follow-up. Indeed, the presence of the long sheath into the LA is identifiable thanks to the EAM system: the exact location is revealed by the progressive color change of the ablation catheter electrodes once the sheath covers it (Figure 2). Moreover, catheter shape and visualization with CARTO3 EAM is reliable as already demonstrated in our previous paper (13).

We have also to consider that, theoretically, every time a transseptal puncture is performed, the patient has an additional risk of complication. Compared to the group of patients undergoing AF ablation with a standard transseptal puncture and thus with the use fluoroscopy, the PFO group showed the same effectiveness of PV isolation. Ablation success was 100% in the acute setting in both groups and AF recurrence was also similar in the long-term.

In line with previously published papers, fluoroless ablation does not take more time to be performed than standard PV isolation guided by fluoroscopy (7,11,23). In our report, procedural times were unaffected by crossing the interatrial septum through the PFO versus performing the

transseptal puncture, demonstrating that probing the fossa ovalis and searching or a PFO is a feasible and not time consuming operation that can potentially be done in every patient.

The only discriminating factor to obtain a complete fluoroless AF ablation was the presence and/or the capability to cross the PFO. The patency had been found during gentle tenting of the fossa ovalis only performed with the ablation catheter at the time of catheter positioning. In our experience, this maneuver has been accomplished without affecting the safety of the procedure, and an attempt might be considered as part of a standard ablation procedure before proceeding to transseptal puncture. However, we have to stress that this maneuver has to be carried out carefully, using a contact force enable catheter with a gentle probing of the fossa in order to avoid dissection of the inter-atrial septum.

In fact Lehrmann et al (24) reported a 1.5% complication rate during the insertion of the ablation catheter into the LA through the same septal hole of the previous transseptal puncture or crossing the PFO. However, in this experience, in all patients the first access to the LA was obtained with a transseptal puncture, even when a PFO was present, consequently we may speculate that this maneuver may favor inter-atrial septum dissection considering also that the ablation catheters used were not contact force enable.

LIMITATION

A limitation of the study may be the fact that some possible complications could have been missed due to the deliberate avoidance of X ray usage.

CONCLUSION

The presence of a PFO may allow completely fluoroless safe and effective AF ablation.

This approach does not seem to affect negatively the procedural times, acute and long-term outcome. Probing the fossa ovalis looking for the PFO during the procedure is desirable since it is not time consuming and can potentially be done in every patient undergoing AF ablation.

TABLE 1

Baseline characteristics

	Group A (58 pts)	Group B (192 pts)	P value
Mean age (years)	59.7 ± 11.2	59.0 ± 10.5	0.66
Male Sex	12 F, 46 M	41 F, 151 M	0.92
BMI	25.1 ± 3.8	24.5 ± 4.1	0.32
Hypertension	25/58 (43%)	92/192 (48%)	0.62
Diabetes	3/58 (5%)	18/192 (9%)	0.47
Hyperlipidemia	9/58 (16%)	35/192 (15%)	0.79
Previous Stroke/TIA	3/58 (5%)	4/192 (2%)	0.40
Cha2ds2-Vasc	2.2 ± 0.6	2.3 ± 0.5	0.20
Antiarrhythmic drugs:			
-Class Ic AAD	38/58 (66%)	112/192 (58%)	0.41
-Class III AAD	3/58 (5%)	11/192 (6%)	0.91
Oral Anticoagulation:			
-VKA	20/58 (35%)	71/192 (37%)	0.85
-DOAC	26/58 (45%)	93/192 (47%)	0.74
Echocardiography:			
-LA diameter AP (mm)	46 ± 5.7	45.3 ± 6.1	0.43
-LA Volume (ml)	85.1 ± 29.3	89.9 ± 28.0	0.25
-Mean EF (%)	59.7 ± 7.3	61.3 ± 6.5	0.11

F = females; M = males; BMI = body mass index; TIA = transient ischemic attack; AAD = antiarrhythmic drug; VKA = vitamin K antagonist, DOAC = direct oral anticoagulant; LA = left atrium; AP = antero-posterior, EF = ejection fraction

TABLE 2

Procedural characteristics

	PFO group (58 pts)	**Transseptal group (192 pts)**	**P-value**
Total procedural time (min)	88.5 ± 26.7	99.1 ± 30.0	0.15
Skin-to-catheter positioning time (min)	23.2 ± 11.9	26.8 ± 16.1	0.34
LA mapping time (min)	16.5 ± 9.5	19.5 ± 9.8	0.20
PVI radiofrequency delivering time (min)	46.3 ± 12.2	47.7 ± 17.2	0.73
Fluoroscopy time (min)	0	3.9 ± 1.6	0.0001
Contact Sensor Force guided Procedure (%)	35 (60.3%)	112 (58.3%)	0.49
Mean Periprocedural ACT (sec)	298±32	305±38	0.11

PVI = pulmonary vein isolation; LA = left atrium; PFO = patent foramen ovale; ACT = activated clotting time.

FIGURES

Figure 1

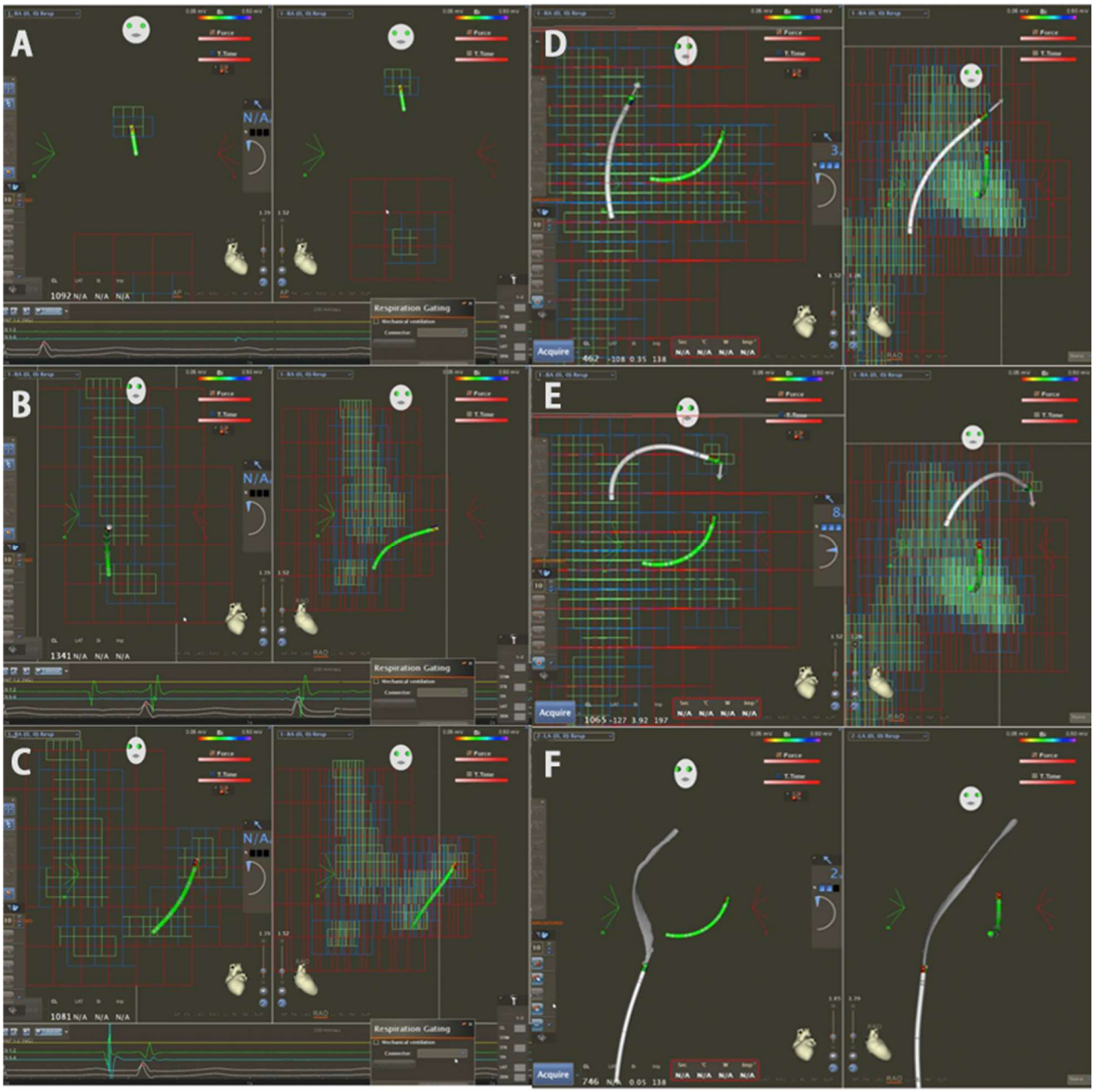

Figure 2

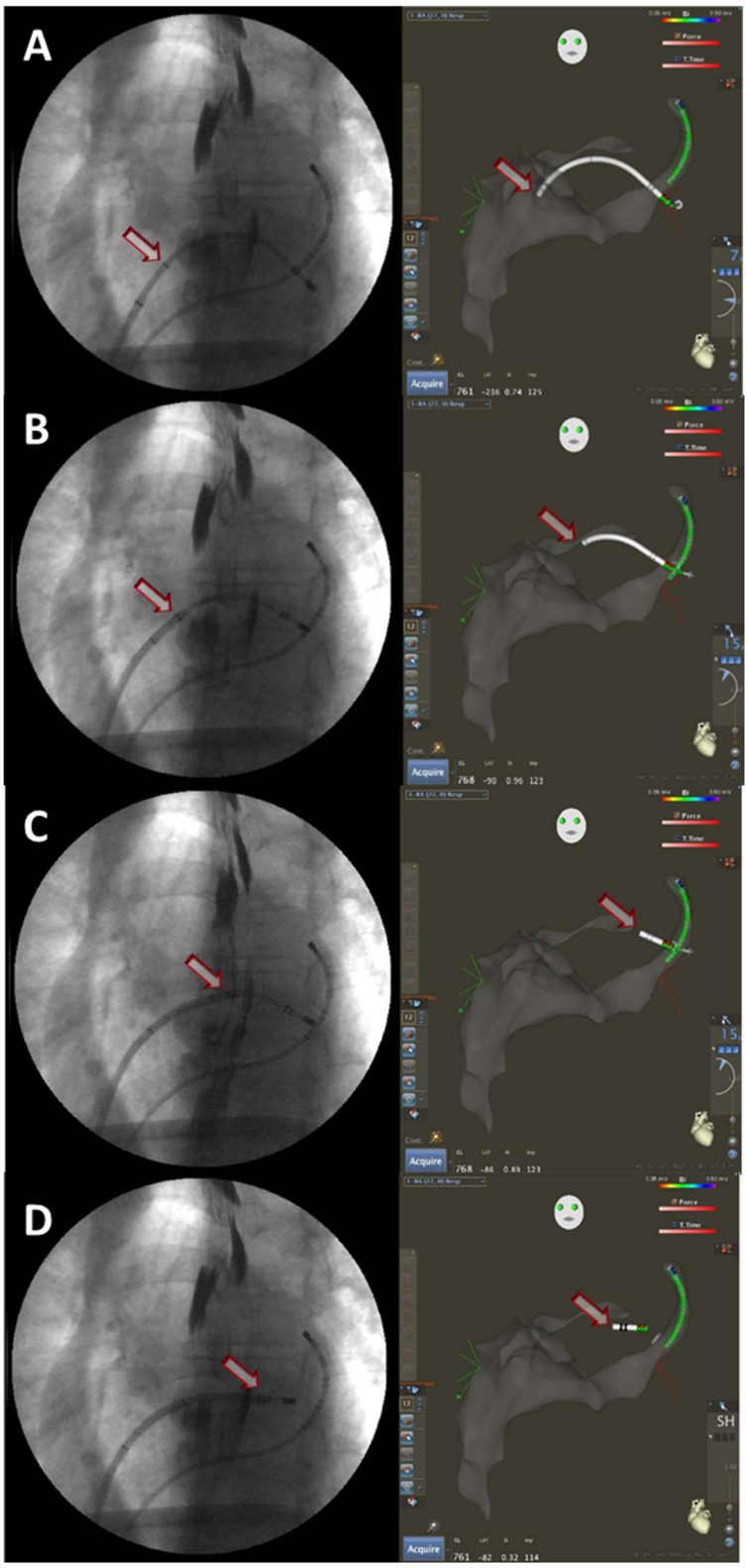

Figure 3

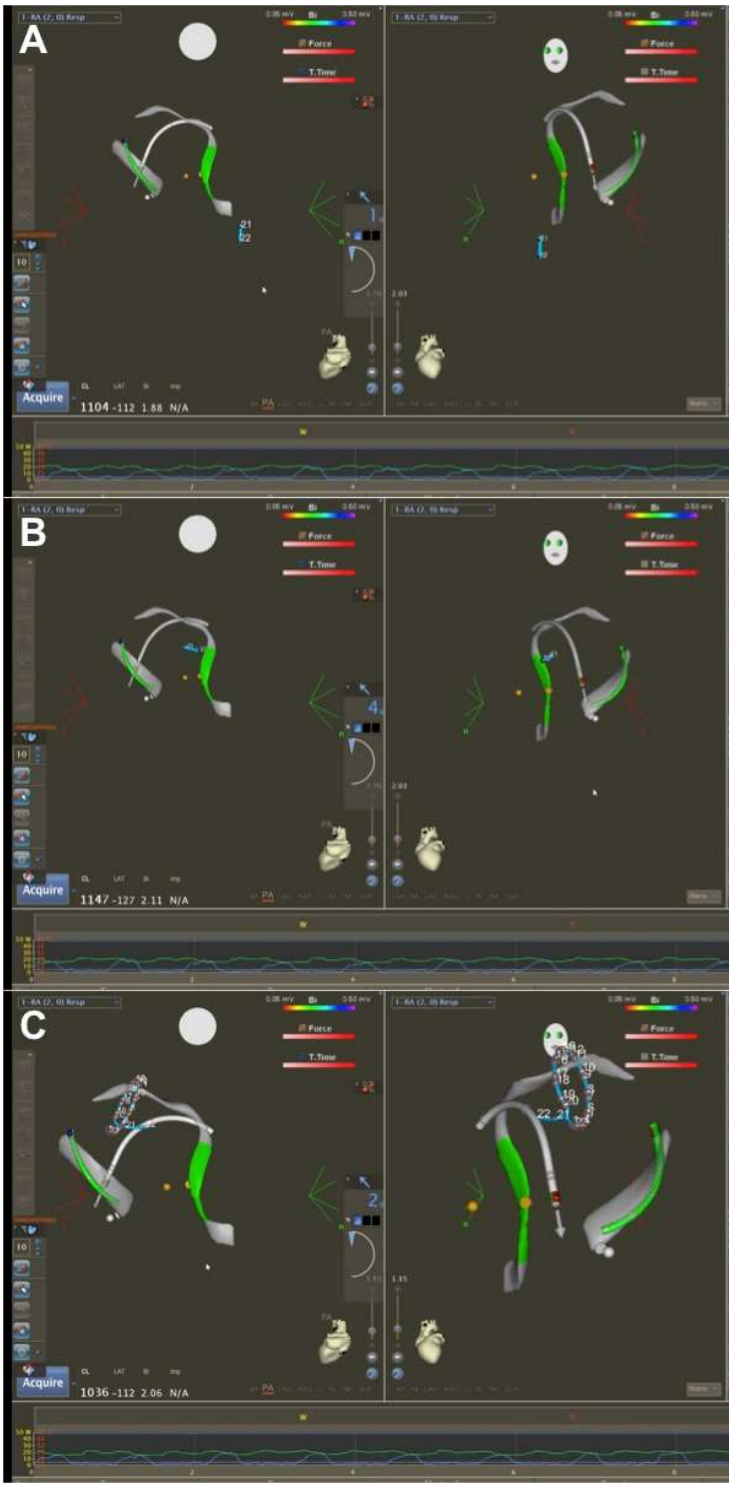
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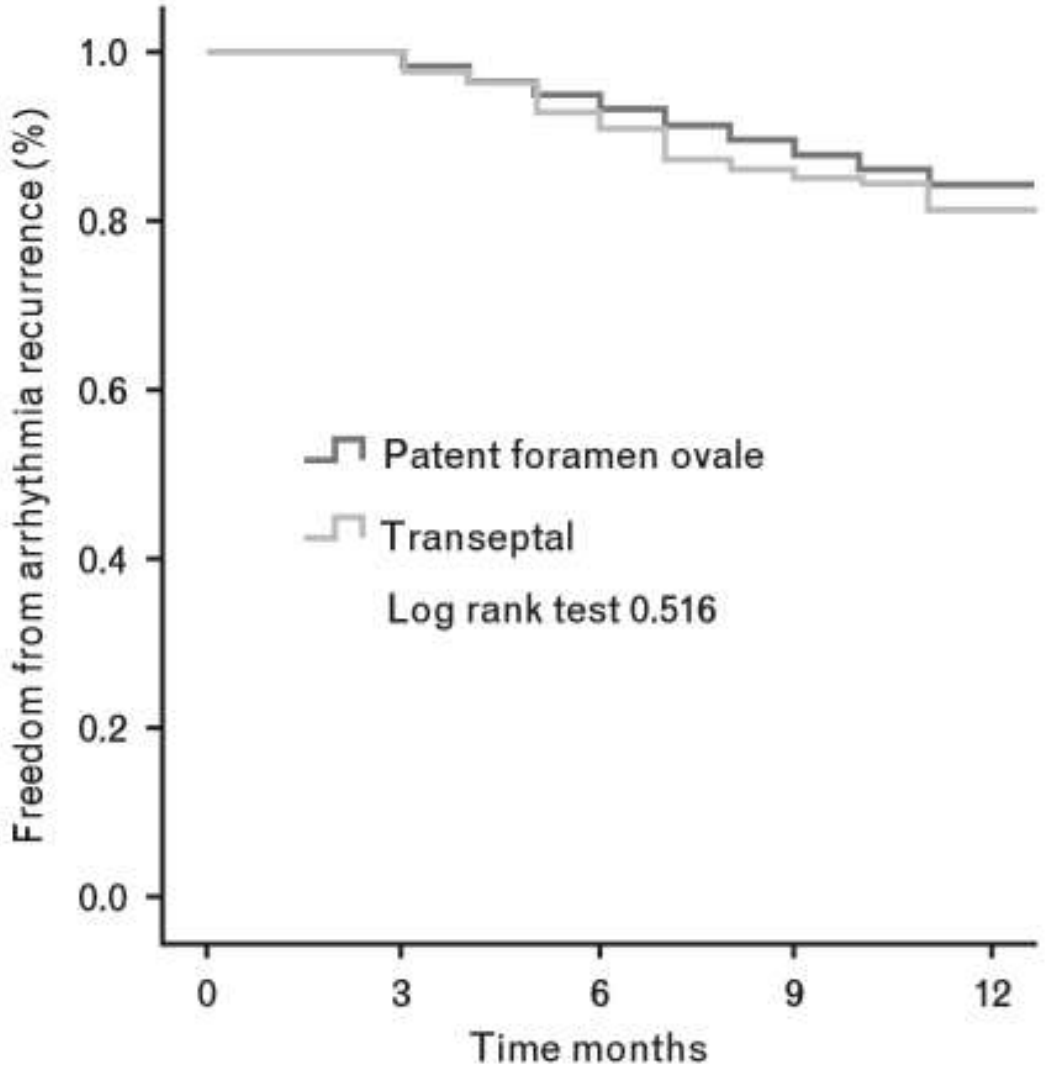
Figure 4



Number at risk

	Baseline	3 months	6 months	12 months
PFO group	58	58 (1)	57 (4)	53 (4)
Transeptal group	192	192 (5)	187 (16)	171 (16)

FIGURE LEGEND

Figure 1

Panel A. The coronary sinus catheter located at the RA-superior vena cava junction, as confirmed by the appearance of RA electrical potentials on the catheter's poles; **Panel B.** The coronary sinus catheter at coronary sinus os (left anterior oblique and right anterior oblique views); **Panel C.** The catheter is placed inside the coronary sinus. **Panel D.** The ablation catheter is pulled back out of the superior vena cava to the RA and reaches the fossa ovalis position on the interatrial septum; **Panel E.** A gentle pressure is applied to tent the septum and access in the LA is obtained through the PFO with cautious advancement of the ablation catheter; **Panel F.** The ablation catheter is withdrawn into the RA and an EAM of the crossing pathway is obtained meanwhile.

Figure 2

All panels show the fluoroscopy image, in the left, and the corresponding Carto3 EAM reconstruction

Panel A. The ablation catheter is located in the LA, crossing the interatrial septum through the PFO (Arrows pointing at the ablation catheter exiting the sheath); **Panel B.** and **C.** The ablation catheter is progressively covered by the long sheath in an "over-the-catheter" fashion. On Carto3 the long sheath is not visualized, but the exact location can be established by the disappearance of the catheter shaft (Arrows pointing at the ablation catheter exiting the sheath); **Panel D.** Once the tip of the ablation catheter is covered the electrodes on it turn black (Arrows pointing at the ablation catheter exiting the sheath).

Figure 3

Panel A. The ablation catheter is located in the LA, crossing the septum through the PFO, while the circular mapping catheter is advanced through the transseptal sheath; **Panel B.** The circular

mapping catheter is located inside the transseptal sheath, at the interatrial septum level; **Panel C.** The circular mapping catheter is deployed in the LA and the sheath is withdrawn in the RA.

Figure 4

Cumulative atrial fibrillation free survival. Kaplan Meier Curve showing that freedom from AF recurrence did not differ between Patent Foramen Ovale and Transeptal Group (Log rank test 0.516)

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