



Original Article

Impact of transesophageal echocardiography during transseptal puncture on atrial fibrillation ablation

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ABSTRACT

Background: The aim of our study was to demonstrate the added value of routine transesophageal echocardiography (TEE) for correctly positioning the transseptal system in the fossa ovalis (FO), thus potentially preventing complications during fluoroscopy-guided transseptal puncture (TP), and for assessing the optimal puncture site within the FO according to the expected procedure type.

Methods: Ninety-one patients undergoing pulmonary vein isolation (PVI) procedures by cryoballoon technique for drug-resistant paroxysmal or persistent atrial fibrillation (AF) were prospectively included. In 57 patients, the TP procedure was performed under fluoroscopic guidance and septal localization was confirmed by contrast injection through the needle and demonstration of septal tenting in both the anteroposterior and left lateral fluoroscopic projections. In 34 patients, TP was performed under TEE guidance and positioning was targeted to perform the TP procedure in the more anterior and inferior locations of the FO. Two patient groups were compared according to the incidence of complications directly attributable to transseptal catheterization, thromboembolic complications, recurrence rates after the ablation procedure, total procedural time, and fluoroscopy time.

Results: Fluoroscopy time ($p < 0.001$), total cryoablation time ($p = 0.002$), and total procedural time ($p < 0.001$) were shorter in the TEE-guided group. Left inferior pulmonary vein (LIPV) cryoablation time ($p = 0.007$) and right inferior pulmonary vein (RIPV) cryoablation time ($p = 0.004$) were significantly shorter and the number of applications to the LIPV ($p = 0.007$) and RIPV ($p = 0.005$) were significantly fewer in the TEE-guided group. Although there was a trend toward higher complication rates (20.6% vs. 31.6%, $p = 0.37$) and recurrence rates (11.8% vs. 20.1%, $p = 0.26$) in the fluoroscopy-guided group, the differences between the groups were not statistically significant.

Conclusions: TEE-guided TP for AF ablation is associated with shorter fluoroscopy time, shorter total cryoablation time, and shorter total procedural time. Importantly, TEE-guided TP facilitates cryoablation of the inferior pulmonary veins.

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1. Introduction

Over the last decade, the unabated increase in the number of transseptal catheterizations has been related to an increase in atrial fibrillation (AF) ablation procedures. Transseptal puncture (TP) is usually safe in experienced hands [1,2]. However, it can be associated with life-threatening complications [3,4]. Conventionally, the procedure is performed under fluoroscopic guidance and pressure monitoring. To

reduce the incidence of complications, TP can be performed under transesophageal echocardiography (TEE) or intracardiac echocardiography (ICE) guidance [5,6]. The use of echocardiographic guidance for TP allows direct visualization of the transseptal needle tip within the fossa ovalis (FO), and thus, a safe TP in every patient. It is also important to emphasize that the use of echocardiographic guidance enables puncture site selection within the FO according to the expected procedure type (e.g., a more anterior puncture for ablation of an accessory pathway at the mitral annulus or for ablation of ventricular tachycardia vs. a lower and more posterior puncture for ablation of AF). Thus, the puncture site location can make a significant difference in mapping and/or ablation catheter maneuverability. A neglected advantage of echocardiographic guidance during TP is the possibility of initiating anticoagulation safely before TP. This appears to be a very important

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additional benefit, especially in patients with AF. It has to be emphasized that the use of echocardiographic monitoring during the entire AF ablation procedure allows for additional benefits beyond safe TP. Echocardiographic monitoring throughout the ablation procedure may help in understanding the real-time anatomy of relevant cardiac structures such as the pulmonary veins, left atrial appendage, mitral isthmus, cavotricuspid isthmus, etc.

To date, no randomized trial has compared the clinical outcomes and success rates between TEE-guided and traditional fluoroscopic TP. Many studies conclude that cardiac imaging may be better than fluoroscopy for guiding TP [5,6] especially in less experienced hands, but the advantages in routine use of imaging modalities have not yet been demonstrated.

2. Materials and methods

2.1. Patients

In this prospective observational study, we enrolled 91 consecutive patients who underwent pulmonary vein isolation (PVI) by cryoballoon technique for documented AF between September 2012 and March 2014. All patients had symptomatic paroxysmal or persistent AF and had failed ≥ 1 antiarrhythmic drug(s) previously. Patients who had AF episodes lasting 7 days were defined as persistent and those whose episodes self-terminated within 7 days were defined as paroxysmal AF [7].

Patients who had moderate-severe valvular disease, thrombus in the left atrium (LA), TEE contraindications, uncontrolled thyroid dysfunction, preprocedural significant coronary artery stenosis, anticoagulation contraindications, previous AF ablation, and LA diameter > 55 mm and patients who were pregnant were excluded from the study. A detailed medical history regarding AF and related cardiovascular and/or systemic conditions was obtained from all patients. The patients' symptomatic severity was recorded according to the European Heart Rhythm Association (EHRA) score. CHA2DS2-VASc scores were calculated for each patient based on relevant guidelines [7]. Informed consent was obtained from each patient before enrollment. The study was conducted in compliance with the principles outlined in the Declaration of Helsinki and approved by the Institutional Ethics Committee.

2.2. Methods

All patients underwent standard transthoracic echocardiography to rule out structural abnormality and TEE to rule out thrombus in the LA. In patients undergoing TEE, sedation was achieved by 2.5 mg midazolam intravenous bolus dose. If necessary, an additional 1 mg or a total maximum 8 mg dose at 5-min intervals was administered intravenously. Antiarrhythmic drugs were discontinued five half-lives before the procedure. Anticoagulation was stopped at least 48–72 h before the procedure. In the patient group in whom the TP procedure was performed under fluoroscopic guidance, a 70 UI/kg heparin intravenous bolus was administered after gaining LA access. In the other patient group in whom the TP procedure was performed under TEE guidance, the same heparin dose was administered at the beginning of the procedure. In all patients, activated clotting time (ACT) > 250 s was maintained during the procedure.

In both groups, all procedures were performed under conscious sedation using midazolam boluses. In all patients, invasive arterial blood pressure, oxygen saturation, and electrocardiogram (ECG) were continuously monitored throughout the procedure.

For the TP procedure in the fluoroscopic guidance group, the TP sheath and dilator were advanced into the superior vena cava (SVC) over a guidewire via the right femoral vein. After removing

the guidewire and aspirating and flushing the dilator, a Brock-enbrough needle (BRK-1, St. Jude Medical, Minnetonka, MN, USA) was inserted in the dilator. Thereafter, the sheath/dilator/needle assembly was slowly withdrawn while monitoring fluoroscopy. Under fluoroscopic guidance (anteroposterior projection), during gradual sheath/dilator/needle withdrawal oriented between the 3:30 and 5:30 handle position, the FO was engaged, indicated by a sudden displacement of the sheath tip and/or septal tenting. Septal localization was also confirmed by contrast injection through the needle and demonstration of septal tenting in both the anteroposterior and left lateral fluoroscopic projections.

In the TEE-guided group, the operator confirmed that the transeptal needle was in a correct position for TP with TEE guidance. After appropriate positioning, TP was performed in the more anterior and inferior locations of the FO. The TEE probe was removed after successful TP.

In both groups, the sheath was then exchanged for a 12-Fr steerable transeptal sheath (FlexCath, Medtronic CryoCath, Minneapolis, USA) over a guidewire (0.032-in., 180-cm Super Stiff, St. Jude Medical, St. Paul, MN, USA). Baseline potentials of all PVs were recorded with a lasso catheter (Biosense Webster, Inc., Diamond Bar, CA, USA). Distal coronary sinus pacing was performed to confirm the presence of the left PV potentials. In all patients, a 28-mm cryoballoon catheter (Arctic Front, Medtronic CryoCath LP) was used for PVI. The cryoballoon was maneuvered to all PV ostia by means of the steerable 12-Fr sheath and a guidewire inserted through the lumen of the balloon catheter. The balloon was inflated in the LA and then directed toward the PV ostia. Assessment of balloon occlusion was performed by injecting 50% diluted contrast through the cryoballoon catheter's central lumen. The duration of each freezing cycle was 240 s. A minimum of two consecutive freezing cycles was performed with excellent or good occlusion for each targeted PV. The procedure systematically began with the left superior PV, followed by the left inferior, right superior, and right inferior PVs, respectively. The right phrenic nerve was constantly paced from the SVC during freezing at the right-sided PVs. Direct palpation of right hemidiaphragmatic excursions was performed during phrenic nerve stimulation. At the end of the procedure, PV conduction was re-evaluated with a lasso catheter. Successful PVI was defined as the elimination (or dissociation) of all PV potentials.

The patients remained under continuous hemodynamic and ECG monitoring for 24 h. Immediately after the procedure and 24 h following the procedure, transthoracic echocardiography was performed to ascertain the absence of pericardial effusion. Oral anticoagulation with warfarin was initiated 4–6 h after the procedure and concomitant enoxaparin 1 mg/kg was also administered until the target international normalized ratio of 2.0–3.0 was reached. The patients remained on the antiarrhythmic drug regimen that was prescribed before ablation for a period of 3 months following the procedure. Thereafter, procedural outcomes were assessed off of the antiarrhythmic drug regimen. Regular follow-up visits including medical history, clinical evaluation, 12-lead surface ECG, and 24-h Holter monitoring were conducted 3, 6, 9, and 12 months after ablation and every 6 months thereafter or earlier if symptoms consistent with recurrent AF developed. The need for oral anticoagulation was also evaluated 3 months after ablation, based on the CHA2DS2-VASc score [7].

Acute procedural success was defined as electrical isolation of all PVs. The first 3 months after AF ablation were defined as the blanking period. AF recurrence was defined as the detection of AF (≥ 30 s duration when assessed with 24-h ECG monitoring) after 3 months following AF ablation [8]. The TP success rate was evaluated in terms of number of puncture attempts to gain access to the LA. Procedural time was quantified as the time from catheter positioning in the SVC to time of LA access. Total

procedure and fluoroscopy time, acute procedural success (isolation of all PVs), number of cryoablation applications to each pulmonary vein, and maximum temperature applied were all recorded. Safety was evaluated in terms of complications (TP-related mild pericardial effusion noted on echocardiogram, major systemic arterial embolization, cardiac tamponade, accidental puncture of the aortic root and right atrium, and TP-related cardiac death). The data of patients with and without TEE were compared.

2.3. Statistical analysis

The data were analyzed using SPSS for Windows (version 15.0, SPSS Inc., Chicago, IL, USA). Continuous data are presented as mean \pm SD, and categorical data are summarized as frequencies and percentages. Group percentages were compared with the use of the χ^2 test or Fisher's exact test, as appropriate. Group means for variables with normal and non-normal distributions were compared with the Student's *t*-test for independent groups and the Mann-Whitney *U*, respectively. A *p* value < 0.05 was considered statistically significant.

3. Results

Clinical and echocardiographic data of the study population are given in Table 1. The study population consisted of 91 symptomatic patients with AF. Mean ages of the patients in the TEE-guided group (group 1) and fluoroscopy-guided group (group 2) were 55.5 ± 9.8 years (16 men, 47%) and 55.0 ± 10.4 years (28 men, 49%), respectively. Twenty-five patients (73.5%) in the TEE-guided group and 37 patients (64.9%) in the fluoroscopy-guided group presented with paroxysmal AF. The median durations of AF in the TEE-guided group and fluoroscopy-guided group were 3.5 (2.0–4.25) years and 3.0 (2.0–5.0) years, respectively. The median LA diameter was 40 (interquartile range (IQR): 37–43) mm in the TEE-guided group and 41 (IQR: 38.0–45.5) mm in the fluoroscopy-guided group. The median left ventricular ejection fraction was 60% (IQR: 55–65) in the TEE-guided group and in the fluoroscopy-guided group, similarly. Other demographic characteristics were similar between groups.

The cryoablation procedural details are illustrated in Table 2. The median total procedural time was 68 (IQR: 64–74) min in the TEE-guided group and 83 (IQR: 72–97) min in the fluoroscopy-

guided group ($p < 0.001$). The fluoroscopy times in the TEE-guided group and in group 2 were 14 (IQR: 13–15) min and 16 (IQR: 14–22) min, respectively ($p < 0.001$). The median total cryoablation times in the TEE-guided group and in group 2 were 32 (IQR: 32–36) min and 36 (IQR: 33–39) min, respectively ($p = 0.002$). Acute procedural success was 100% in both groups. The maximal temperatures reached at each pulmonary vein were similar between the two groups (Table 2). Comparison of cryoablation times for each pulmonary vein showed shorter cryoablation times at the inferior pulmonary veins (8 [IQR: 8–8] vs. 8 [IQR: 8–11], $p = 0.007$, at left inferior pulmonary veins [LIPVs] and 8 [IQR: 8–8] vs. 8 [IQR: 8–13], $p = 0.004$, at right inferior pulmonary veins [RIPVs], respectively). Upper pulmonary vein cryoablation times were similar. The TEE-guided group was associated with a lower number of cryoenergy applications at the inferior pulmonary veins (2 [IQR: 2–2] vs. 2 [IQR: 2–3], $p = 0.007$, for LIPVs and 2 [IQR: 2–2] vs. 2 [IQR: 2–4], $p = 0.005$, for RIPVs, respectively). Other procedural data as presented in Table 2 were similar among groups.

The TP-related complications are given in Table 3. Pericardial effusion without tamponade was seen in 2 patients (5.9%) in the TEE-guided TP group and 5 (8.8%) in the fluoroscopy-guided group. There was no pericardial tamponade in the TEE-guided group and only one patient experienced tamponade in the fluoroscopy-guided group. One patient in the fluoroscopy-guided group had a transient ischemic attack (TIA) manifesting as right limb weakness that completely resolved before discharge. Diaphragm paralysis was seen in 2 patients (5.9%) vs. 4 (7%) in the TEE-guided group and fluoroscopy-guided group, respectively. Gastroparesis was seen in 3 patients in the fluoroscopy-guided group, whereas none of the patients in the TEE-guided group had gastroparesis. Inguinal hematoma and/or pseudoaneurysm was seen in 3 patients (8.8%) in the TEE-guided TP group and 4 (7.0%) in the fluoroscopy-guided group. None of the study patients required emergent surgery. Total complications seen were 7 (20.6%) and 18 (31.6%) in the two groups. All complication parameters were similar between groups (Table 3).

Table 4 shows the procedural success and recurrence rates. There was no statistical difference in these parameters between groups.

4. Discussion

Previous studies suggest indirectly that the use of echocardiography may increase procedural safety, but to date, there are no data to prove this directly. We showed a similar trend in the present study. However, because of the small size of our study group, it was not possible to show a statistically significant reduction in complication rates by using TEE guidance during the procedure. Conventionally, the procedure is performed under fluoroscopic guidance and pressure monitoring. In experienced hands, various modifications of this method have a reasonable safety profile. However, serious complications such as cardiac tamponade (1.31%) or aortic perforation can still occur and can lead to death (0.15%) [3,4]. To reduce the incidence of such complications, TP can be done under TEE or ICE guidance. TEE necessitates a higher level of sedation and is often not tolerated well. ICE requires additional expertise and remarkably increases procedural cost. In our study, we used TEE as a guide because of the lower procedural cost.

TEE guidance can also be helpful during pulmonary vein cryoablation for AF. Kerut et al. [9] described their first 20 cases of cryoablation for AF using TEE and found TEE to have better overall procedural imaging and monitoring for pericardial effusion or thrombus formation. They found TEE monitoring to be helpful with positioning for interatrial septum (IAS) puncture, catheter tip

Table 1
Patient characteristics.

	TEE-guided group, N=34	Fluoroscopy-guided group, N=57	<i>p</i> Value
Age, years (mean \pm SD)	55.5 \pm 9.8 (37–72)	55.0 \pm 10.4 (33–71)	0.82
Sex (male/female)	16/18	28/29	0.85
Hypertension, <i>n</i> (%)	15 (44.1)	25 (43.9)	0.98
Diabetes mellitus, <i>n</i> (%)	4 (11.8)	8 (14.0)	1
Coronary artery disease, <i>n</i> (%)	4 (11.8)	5 (8.8)	0.72
Cerebrovascular accident, <i>n</i> (%)	1 (2.9)	1 (1.8)	1
Lone atrial fibrillation, <i>n</i> (%)	9 (26.5)	27 (47.4)	0.08
Paroxysmal atrial fibrillation, <i>n</i> (%)	25 (73.5)	37 (64.9)	0.39
CHA2DS2-VASc score (median)	1.5 (IQR: 0–2.0)	1.0 (IQR: 0–2.5)	0.68
Left ventricular ejection fraction, % (median)	60 (IQR: 55–65)	60 (IQR: 55–65)	0.22
Atrial fibrillation duration, years (median)	3.5 (2.0–4.25)	3.0 (2.0–5.0)	0.92
Left atrium size, mm (PLAX)	40 (IQR: 37–43)	41 (IQR: 38.0–45.5)	0.19

Table 2
Procedure characteristics.

	TEE-guided group, N=34	Fluoroscopy-guided group, N=57	p Value
Septal thickness, mm	1.88 ± 0.33 (1.0–2.5)	1.86 ± 0.34 (1.0–2.5)	0.68
Median transseptal puncture time, s	433 (IQR: 372–474)	421 (IQR: 322–579)	0.67
Number of transseptal punctures, n	1 (IQR: 1–1)	1 (IQR: 1–2)	< 0.001
Median total cryoablation time, min	32 (IQR: 32–36)	36 (IQR: 33–39)	0.002
Median total fluoroscopy time, min	14 (IQR: 13–15)	16 (IQR: 14–22)	< 0.001
Median total procedure time, min	68 (IQR: 64–74)	83 (IQR: 72–97)	< 0.001
LSPV maximum temperature (°C)	50 (IQR: 48–52)	49 (IQR: 48–51)	0.35
LIPV maximum temperature (°C)	48 (IQR: 45–50)	47 (IQR: 44–49)	0.13
RSPV maximum temperature (°C)	51 (IQR: 50–56)	51 (IQR: 49–53)	0.11
RIPV maximum temperature (°C)	46 (IQR: 44–49)	45 (IQR: 41–48)	0.11
LSPV cryoablation time, min	8 (IQR: 8–8)	8 (IQR: 8–8)	0.69
LIPV cryoablation time, min	8 (IQR: 8–8)	8 (IQR: 8–11)	0.007
RSPV cryoablation time, min	8 (IQR: 8–8)	8 (IQR: 8–8)	0.77
RIPV cryoablation time, min	8 (IQR: 8–8)	8 (IQR: 8–13)	0.004
LSPV number of applications	2 (IQR: 2–2)	2 (IQR: 2–2)	0.75
LIPV number of applications	2 (IQR: 2–2)	2 (IQR: 2–3)	0.007
RSPV number of applications	2 (IQR: 2–2)	2 (IQR: 2–2)	0.72
RIPV number of applications	2 (IQR: 2–2)	2 (IQR: 2–4)	0.005

IQR: interquartile range; LCPV: left common pulmonary vein; LIPV: left inferior pulmonary vein; LSPV: left superior pulmonary vein; RCPV: right common pulmonary vein; RIPV: right inferior pulmonary vein; RSPV: right superior pulmonary vein.

Table 3
Complications.

	TEE-guided group, N=34	Fluoroscopy-guided group, N=57	p Value
Pericardial effusion without tamponade, n (%)	2 (5.9)	5 (8.8)	0.71
Pericardial effusion with tamponade, n (%)	0 (0.0)	1 (1.8)	1
Thromboembolic events, n (%)	0 (0.0)	1 (1.8)	1
Diaphragm paralysis, n (%)	2 (5.9)	4 (7.0)	1
Gastroparesis, n (%)	0 (0.0)	3 (5.3)	0.29
Inguinal hematoma and/or pseudoaneurysm, n (%)	3 (8.8)	4 (7.0)	0.75
Emergent surgery, n (%)	0 (0.0)	0 (0.0)	–
Total number of complications, n (%)	7 (20.6)	18 (31.6)	0.37

avoidance of the left atrial appendage (LAA), and guidance of the balloon catheter into each PV, with proper positioning within each PV orifice and documentation of PV occlusion for the cryoballoon procedure. Use of TEE monitoring resulted in a perceived reduction in radiopaque contrast agent use and fluoroscopy time. In our study, we aimed to demonstrate the added value of routine TEE use for correctly positioning the transseptal system in the FO, thus potentially preventing complications during fluoroscopy-guided TP, and for assessing the optimal puncture site within the FO according to the expected procedure type. Although there was a trend toward higher complication rates in the fluoroscopy-guided group, the differences between the groups were not statistically significant. This is probably because of lower complication rates in both groups and the small study size. Kautzner et al. [10] reported that a retrospective analysis of 1692 TP procedures guided by ICE between 2006 and 2009 revealed no complications associated with the puncture and they added that this provides indirect evidence that the use of online imaging may increase procedural safety, especially in anatomical variants of the intraatrial septum, which make the procedure challenging. They also emphasized that the use of echocardiographic guidance enables puncture site selection within the FO according to the expected procedure type (e.g., a more anterior puncture for ablation of an accessory pathway at the mitral annulus or for ablation of ventricular tachycardia and a lower and more posterior puncture for ablation of AF). They stated that even 1-cm difference in the puncture site location can

Table 4
Recurrence and follow-up.

	TEE-guided group, N=34	Fluoroscopy-guided group, N=57	p Value
Acute success, n (%)	34 (100)	57 (100)	–
Recurrence (after 3 months), n (%)	4 (11.8)	12 (21.1)	0.26
Recurrence time, days, and median	239 (IQR: 222–274)	243 (IQR: 213–286)	0.40
Follow up, days, and median	239 (IQR: 222–274)	243 (IQR: 214–286)	0.89

IQR: interquartile range.

make a significant difference in mapping and ablation catheter maneuverability, and this seems to be even more important when using “one-size-fits-all” devices such as a cryoballoon. In general, a posterior crossing is optimal when targeting posterior LA structures (e.g., the pulmonary veins during AF ablation). For patients undergoing AF ablation with either magnetic navigation or balloon technologies, it may be more favorable to puncture the fossa in a more anterior and inferior location. An anterior and inferior fossa approach for balloon pulmonary vein ablation greatly facilitates access to the right inferior pulmonary vein. Su et al. [11] also recommended a low anterior TP that was near or on the limbus of the septum to allow more space for the balloon to be rotated posteriorly to the right inferior PV as well as mechanical advantages while accessing the other PVs. They noted that without sufficient distance between the puncture site and the right inferior PV, optimal balloon positioning and occlusion might be difficult. The authors also emphasized that a low puncture location improved balloon contact with the inferior aspects of the PVs. They highly recommended using ICE to improve the safety of transseptal catheterization, and they reported that ICE would also provide early detection of complications (e.g., catheter-related and pericardial thrombus) in ablation cases. The authors concluded that the location of transseptal access was best at the lower third of the septum, and anterior reach at the plane of ICE, where the mitral valve was in view and bending of the distal 15-cm portion of the typical transseptal needle could improve transseptal needle engagement with the anterior portion of the septum. In our study,

the shorter total procedural time and total fluoroscopy time can be related to the easy access to the pulmonary veins by using TEE guidance. Importantly, TP facilitates cryoablation of the inferior pulmonary veins. LIPV and RIPV cryoablation time was significantly shorter and the numbers of LIPV and RIPV applications were significantly fewer in the TEE-guided group.

An important advantage of echocardiographic guidance during TP is the possibility of initiating anticoagulation safely before TP. This appears to be a very important benefit, especially in patients with AF, in whom the risk of thrombus formation is high, despite anticoagulation to ACT >250 s. In one study, the incidence of thrombosis was significantly lower when heparin was given before the first or second TP compared with heparin administration after the TP (3.1% vs. 9%, $p < 0.001$). A thrombus was observed on a mapping or ablation catheter in 16 of 29 patients, and in the remaining 13, it was detected in the left atrium or appendage. Additionally, a thrombus aspiration was safely performed through the sheath in 21 of 29 cases [12]. In our study, we also aimed to evaluate the advantages of echocardiographic guidance during TP by initiating anticoagulation safely before TP, but only one patient in the fluoroscopy-guided group experienced a thromboembolic event, which was not statistically different from the TEE-guided group.

Although in our study the TEE probe was removed after successful TP, there are many other possible advantages of continuous TEE usage during the cryoablation of AF. Siklody et al. [13] studied 124 PVs in 30 patients. Under continuous TEE assessment, a cryoballoon was placed in the antrum of each PV aiming for complete PV occlusion as documented by color Doppler. They reported that, compared to their previously published data [14], times with the cryoballoon were shorter (including both ablation time and mapping time after ablation), similar to previously published cryoballoon data [15]. Fluoroscopy times were not longer and tended to be shorter at the end of the study, as they had advanced in their learning curve. They also noted that TEE allowed them to observe some undescribed phenomena, as well as to resolve them during the procedure. Whenever PV occlusion cannot be achieved, particularly by complex anatomies such as extremely oval PV or supplementary right-sided PVs, echocardiography precisely localized the site of leakage and permitted the development of alternative strategies. In the last cases of their series, oval PVs were successfully ablated by freezing the balloon at the cranial part of the PV antrum, and then pulling it gently back after approximately 45 s under attentive TEE supervision, aiming to close the gap by slightly pulling the frozen PV balloon toward the caudal aspect of the antrum. This maneuver could only be echocardiographically documented, as contrast fluid could not be injected through the balloon once the temperature fell below 0 °C. Whenever this last “pull-back” strategy was not feasible, the PV antrum was ablated in 2 stages, sequentially aiming at the cranial and the caudal aspects of the PV antrum. Supplementary right-sided PVs were specifically targeted by selecting them with the guidewire: this approach permitted the creation of more complete overlapping lesions around the septal PVs, as it includes LA tissue located between the superior and the inferior septal PV. Additionally, they reported that TEE also avoided inflating the balloon across the interatrial septum while attempting to isolate a right inferior PV. In the study of Siklody et al., all patients underwent a computed tomography scan, 3D anatomical models of the LA were reconstructed, and if all PVs presented a diameter < 18 mm, the PV isolation was performed using a 23-mm diameter cryoballoon. If any PV was > 18 mm, they chose a 28-mm balloon (Arctic Front, Cryocath, Montreal, Quebec, Canada, 11-Fr shaft size) in order to create wider lesions including part of the LA surrounding the PV. The main observed complication was a transient phrenic nerve paralysis. The ratio between the vein size and the balloon size

seems to play a crucial role in the appearance of this complication [15,16]. TEE has been reported as strongly correlated to magnetic resonance (MR) angiography in assessing PV anatomy [17], and Peyrol et al. [18] suggested that TEE was an easily available and effective tool to select the cryoballoon size for PVI according to evaluated PV diameters and anatomy. Instead of using MR angiography for evaluating the PV diameter and selecting the cryoballoon size, we think that it is reasonable to use TEE. This way, continuous TEE usage can enable us to evaluate the size of right-sided PVs before choosing the balloon size and a large balloon can be preferred. Although cryoballoon positioning at the PV antrum may be influenced not only by the TP site but also by the anatomical findings of both the left atrium and the PV antrum in each case, TEE-guided TP can shorten fluoroscopy, total cryoablation, and total procedural times. Importantly, it can also facilitate cryoablation of inferior pulmonary veins.

4.1. Study limitations

This study was conducted in a single center with a small sample size. In addition, because the patients could not tolerate continuous TEE guidance, we had to remove the TEE probe after successful TP. For this reason, unfortunately, we do not have any additional data showing that the puncture location facilitates inferior PV isolation when using the cryoballoon.

5. Conclusions

Despite its small size, our study showed that TEE-guided TP for AF ablation was associated with shorter fluoroscopy time, total cryoablation time, and total procedural time. Importantly, TEE-guided TP can facilitate cryoablation of the inferior pulmonary veins.

Conflict of interest

All authors declare no conflict of interest related to this study.

References

- [1] Fagundes RL, Mantica M, De Luca L, et al. Safety of single transseptal puncture for ablation of atrial fibrillation: retrospective study from a large cohort of patients. *J Cardiovasc Electrophysiol* 2007;18:1277–81.
- [2] Hanaoka T, Suyama K, Taguchi A, et al. Shifting of puncture site in the fossa ovalis during radiofrequency catheter ablation: intracardiac echocardiography-guided transseptal left heart catheterization. *Jpn Heart J* 2003;44:673–80.
- [3] Cappato R, Calkins H, Chen SA, et al. Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circ Arrhythm Electrophysiol* 2010;3:32–8.
- [4] De Ponti R, Cappato R, Curnis A, et al. Trans-septal catheterization in the electrophysiology laboratory: data from a multicenter survey spanning 12 years. *J Am Coll Cardiol* 2006;47:1037–42.
- [5] Hahn K, Gal R, Sarnoski J, et al. Transesophageal echocardiographically guided atrial transseptal catheterization in patients with normal-sized atria: incidence of complications. *Clin Cardiol* 1995;18:217–20.
- [6] Epstein LM, Smith T, TenHoff H. Nonfluoroscopic transseptal catheterization: safety and efficacy of intracardiac echocardiographic guidance. *J Cardiovasc Electrophysiol* 1998;9:625–30.
- [7] European Heart Rhythm Association, European Association for Cardio-Thoracic Surgery, Camm AJ, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Europace* 2010;12:1360–420.
- [8] Calkins H, Kuck KH, Cappato R, et al. h/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *Europace* 2012;2012(14):528–606.
- [9] Kerut EK, Hanawalt C, McKinnie J. Transesophageal echocardiography during pulmonary vein cryoballoon ablation for atrial fibrillation. *Echocardiography* 2015;32:281–90.

- [10] Kautzner J, Peichl P. You get what you inspect, not what you expect: can we make the transeptal puncture safer? *Europace* 2010;12:1353–5.
- [11] Su W, Kowal R, Kowalski M, et al. Best practice guide for cryoballoon ablation in atrial fibrillation: the compilation experience of more than 3000 procedures. *Heart Rhythm* 2015;12:1658–66.
- [12] Bruce CJ, Friedman PA, Narayan O, et al. Early heparinization decreases the incidence of left atrial thrombi detected by intracardiac echocardiography during radiofrequency ablation for atrial fibrillation. *J Interv Card Electrophysiol* 2008;22:211–9.
- [13] Siklódy CH, Minners J, Allgeier M, et al. Cryoballoon pulmonary vein isolation guided by transesophageal echocardiography: novel aspects on an emerging ablation technique. *J Cardiovasc Electrophysiol* 2009;20:1197–202.
- [14] Arentz T, Weber R, Bürkle G, et al. Small or large isolation areas around the pulmonary veins for the treatment of atrial fibrillation? Results from a prospective randomized study *Circulation* 2007;115:3057–63.
- [15] Neumann T, Vogt J, Schumacher B, et al. Circumferential pulmonary vein isolation with the cryoballoon technique results from a prospective 3-center study. *J Am Coll Cardiol* 2008;52:273–8.
- [16] Chun KR, Schmidt B, Metzner A, et al. The 'single big cryoballoon' technique for acute pulmonary vein isolation in patients with paroxysmal atrial fibrillation: a prospective observational single centre study. *Eur Heart J* 2009;30:699–709.
- [17] Toffanin G, Scarabeo V, Verlato R, et al. Transoesophageal echocardiographic evaluation of pulmonary vein anatomy in patients undergoing ostial radiofrequency catheter ablation for atrial fibrillation: a comparison with magnetic resonance angiography. *J Cardiovasc Med* 2006;7:748–52.
- [18] Peyrol M, Sbragia P, Quatre A, et al. Pulmonary vein isolation using a single size cryoballoon chosen according to transesophageal echocardiography information. *Int J Cardiol* 2013;168:108–11.