Video Article

Reduction of Iatrogenic Atrial Septal Defects with an Anterior and Inferior Transseptal Puncture Site when Operating the Cryoballoon Ablation Catheter

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Abstract

The cryoballoon catheter ablates atrial fibrillation (AF) triggers in the left atrium (LA) and pulmonary veins (PVs) via transseptal access. The typical transseptal puncture site is the fossa ovalis (FO) – the atrial septum's thinnest section. A potentially beneficial transseptal site, for the cryoballoon, is near the inferior limbus (IL). This study examines an alternative transseptal site near the IL, which may decrease the frequency of acute iatrogenic atrial septal defect (IASD). Also, the study evaluates the acute pulmonary vein isolation (PVI) success rate utilizing the IL location. 200 patients were evaluated by retrospective chart review for acute PVI success rate with an IL transseptal site. An additional 128 IL transseptal patients were compared to 45 FO transseptal patients by performing Doppler intracardiac echocardiography (ICE) post-ablation to assess transseptal flow after removal of the transseptal sheath. After sheath removal and by Doppler ICE imaging, 42 of 128 (33%) IL transseptal patients demonstrated acute transseptal flow, while 45 of 45 (100%) FO transseptal puncture patients had acute transseptal flow. The difference in acute transseptal flow detection between FO and IL sites was statistically significant ($P < 0.0001$). Furthermore, 186 of 200 patients (with an IL transseptal puncture) did not need additional ablation(s) and had achieved an acute PVI by a "cryoballoon only" technique. An IL transseptal puncture site for cryoballoon AF ablations is an effective location to mediate PVI at all four PVs. Additionally, an IL transseptal location can lower the incidence of acute transseptal flow by Doppler ICE when compared to the FO. Potentially, the IL transseptal site may reduce later IASD complications post-cryoballoon procedures.

Video Link

The video component of this article can be found at <https://www.jove.com/video/52811/>

Introduction

Haïssaguerre *et al.* originally described the muscular sleeves surround pulmonary veins (PVs) that are arrhythmogenic and initiate the maintenance of atrial fibrillation (AF) symptoms¹. Since the initial description, pulmonary vein isolation (PVI) has become a cornerstone of the catheter ablation strategy in the treatment of AF². Subsequently, catheter ablation devices have been built to facilitate PVI with a variety of energy sources³, and these purpose-built PVI catheters have been sometimes referred to as "single-shot" ablation catheters. Currently, the cryoballoon is the only FDA approved single-shot catheter, which is approved for the treatment of drug-refractory, recurrent, and symptomatic paroxysmal AF⁴. Uniquely, the cryoballoon system allows for a simplified approach to PVI with a favorable safety profile. In the pivotal STOP AF IDE trial, 69.9% of subjects were free of AF at one year⁴.

Delivery of the cryoballoon catheter to the PVs requires a transseptal catheterization with a 15 French (Fr) outer diameter steerable sheath. A typical transseptal puncture is performed at the fossa ovalis (FO), which is the thinnest part of the septum, and the FO can be an easy point of access into the left atrium (LA) because of the sparsity (or reduction) of septal tissue depth. The cryoballoon system uses guidewire delivery of an inflated balloon catheter, and guidewires can be a traditional J-tip design or a propose-built (multi-polar circular inner-balloon-lumen) mapping catheter for the cryoballoon catheter system. However, different from focal ablation catheters, the cryoballoon catheter uses the anterior balloon surface to push against the atrial tissue surrounding the PV ostium which results in simultaneous delivery of cryothermal energy to the contacting atrial tissue and ultimately the formation of a lesion. Therefore, a cryoballoon catheter approach angle that is more anterior and inferior (near the inferior limbus (IL)) may facilitate a mechanical advantage with regard to push force vectors particularly when ablating the inferior PVs. Also, the IL transseptal position may potentially reduce the occurrence of iatrogenic atrial septal defects (IASD) post-cryoballoon procedure⁵.

In this study, the primary hypothesis was that the location of transseptal puncture could affect the frequency of acute IASD that is detected immediately post-ablation via transseptal Doppler flow while utilizing intracardiac echocardiography (ICE) examination. Additionally, a secondary objective was to assess the acute rate of PVI achieved with the cryoballoon system while using an anterior and inferior transseptal approach

angle (IL location). By examining two alternate transseptal puncture locations (FO versus IL), this study attempted to determine which approach was most beneficial when using the cryoballoon system for the treatment of AF via PVI.

CASE STUDY

From August 2012 to August 2013, this study reviewed 200 consecutive patients who were referred for a cryoballoon AF ablation procedure at a single specialized cardiac-care center. All of the above patients were given a cryoballoon AF ablation, where the transseptal puncture location was near the IL. By retrospective review, these patient charts were examined to determine the rate of acute PVI that was achievable through a singular usage of the cryoballoon ablation catheter without the usage of adjunctive AF ablation catheters. This chart review examination was a single-arm, single-center, data collection. Additionally during the same collection period, 173 patients were examined in a prospective investigation that compared the site of transseptal puncture (FO versus IL) via acute post-procedural ICE imaging of Doppler flow dynamics. This comparison analysis was a double-arm, 3:1 collection (IL to FO transseptal site, respectively), single-center prospective examination. In both evaluations, all patients were symptomatic and drug refractory with a history of AF.

PATIENT SELECTION

In both evaluations, the inclusion criteria for all patients was a documented clinical history of symptomatic AF, a medication refractory treatment of AF by one class I or class III antiarrhythmic drug, and an AF ablation treatment strategy that included a cryoballoon catheter PVI as the primary PV ablation method. Exclusion criteria were patients under 18 years old, patients older than 90 years of age, patients who have had a previous LA ablation, patients who have had a previous transseptal puncture entry, patients who required a double transseptal approach for AF ablation, or patients with permanent AF. All the cryoballoon ablation procedures were conducted at a single experienced cardiac-care center with well over 600 cryoballoon procedures done at this hospital, and all patients were treated with the second generation cryoballoon catheter.

Protocol

Ethical Statement: All methods and procedures performed in these examinations were typical and standard-of-care during this time period of data collection. Informed consent was obtained from all patients, and local institutional review board approval was granted for both studies.

1. Transseptal Access

NOTE: Procedural methods and techniques have now been well described in several publications⁶⁻¹¹, and the cryoballoon ablation strategy used here was similar to published descriptions.

1. Examine patients with a transesophageal echocardiogram on the day of the AF ablation procedure. Use transesophageal echocardiogram imaging to assess the LA for thrombus presence or formation.
2. Re-schedule ablation for any patient with LA thrombus present, and correct the patient anticoagulation strategy.
3. Establish patient sedation with the use of general anesthesia (with an agent such as intravenous propofol) or conscious sedation (with agents such as intravenous fentanyl and versed). In both sedation methods, do not use a paralytic agent so that phrenic nerve monitoring can be used during the ablation procedure.
4. During the AF ablation procedure, use ICE guidance for the transseptal catheterization with a Mullins-type sheath. Use the ICE guidance to position the transseptal needle at the septum, to avoid aortic puncture, and to safeguard against inadvertent LA lateral wall needle-puncture (by examining the needle "tenting" distance during transseptal puncture)¹².
NOTE: In the traditional FO location, the transseptal access point is at the thinnest septal tissue depth near the center of the septum which is evaluated by "tenting" the septum with the transseptal needle under ICE imaging (**Figure 1**).
5. For the IL transseptal location, enter approximately one centimeter below the traditional FO site and at an anterior septal location (**Figure 1; panels A and B**). The IL location is found through evaluation of ICE and fluoroscopy once the FO site is established.
 1. Use ICE plane imaging to define the entry point in the IL location. Sweep the ICE image anterior towards the plane of the mitral valve to define the anterior position of the site.
 2. The inferior location will be dependent on the IL, which is triangular in cross-section. Place the transseptal needle puncture at the center of this triangular area.
6. Facilitate the IL puncture by further bending the transseptal needle approximately ½ inch from this distal tip. Needle bending is customized to the approach angle on LAO view of the inferior vena cava into the right atrium. Use more needle bending when the approach angle is vertical rather than horizontal to the patient's body axis.
 1. Optionally, use a radiofrequency transseptal needle to facilitate the IL position technique; however, only standard transseptal needles were used for this study.
7. Immediately after transseptal puncture, administer heparin bolus using a patient weight-based protocol and then give supplemental doses of heparin throughout the procedure with the goal of maintaining active clotting time between 350 and 400 sec.
8. Establish the transseptal access route with an exchange of the transseptal needle with a guidewire.

2. Cryoballoon Ablation

1. Use the guidewire to introduce the cryoballoon sheath. Then deploy the cryoballoon catheter and the dedicated inner lumen circular mapping catheter into the LA through the cryoballoon sheath.
2. During each cryoballoon ablation, inflate the cryoballoon and advance it over the inner lumen circular mapping catheter which is wired towards the PV ostium.
3. Inject 5 to 10 ml of radiopaque contrast agent (isovue 300) through the cryoballoon catheter inner lumen.
4. Confirm cryoballoon-to-PV occlusion by using the retention of contrast agent after injection at the distal tip of the balloon.

1. Additionally (or alternatively), confirm cryoballoon-to-PV occlusion by ICE imaging under color-flow Doppler using the lack of flow around the balloon anterior surface as an indicator of occlusion.
5. Start the cryoballoon cryoablation once occlusion is established by pressing the “start” button on the cryoconsole. This action will push cryorefrigerant into the cryoballoon catheter and initiate cryoablation.
6. On right-sided PVs, use a diagnostic catheter in the right atrial/superior vena caval junction and position it to pace the right phrenic nerve.
7. Pace the phrenic nerve at 20 mA amplitude and 2.0 msec pulse width, and monitor phrenic nerve function by manual detection of diaphragmatic contractions. Immediately terminate any ablation if phrenic nerve function is diminished, delayed, or lost.
8. Deliver a minimum of two freezes, each lasting 120 to 180 sec, while using the inner lumen circular mapping catheter to monitor both real-time and post-ablation PVI through entrance and exit block testing.
9. Once entrance and exit block is established at each PV, withdraw the cryoballoon, sheath, and inner lumen circular mapping catheter.
10. Use standard medical care to stop bleeding at vascular entry points and discharge patients via hospital protocols, which may include anticoagulation pharmaceutical therapy and guidance on antiarrhythmic drugs.

Representative Results

The 200 consecutive patients that underwent retrospective chart review were all given a transseptal puncture near the IL position. Examination of the equipment list and ablation records are used to establish the proportion of patients that achieved PVI with a singular usage of the cryoballoon catheter. An additional group of 173 patients were assessed and tested for the differential usage of transseptal entry location. The data is collected in a 3:1 manner, whereby 128 patients are examined with an IL transseptal location and compared to 45 patients who had a FO transseptal site. Acute IASD rates for FO versus IL transseptal locations are assessed by Doppler ICE imaging and later compared by Fisher's exact statistical testing. In this study, statistical significance is set at $P < 0.05$.

In the group of 200 patients undergoing an IL site transseptal puncture, 186 patients (93%) did not require the usage of an additional focal radiofrequency ablation catheter. Representative fluoroscopy images of each of the four PVs during cryoballoon ablation are illustrated in **Figure 2A-D**. Examination of **Figure 2** demonstrates that the cryoballoon catheter and steerable sheath were not required to use full catheter and sheath deflection to achieve PVI at the inferior PVs. Furthermore, analyses of catheter and sheath deflection angles during inferior PV cryoablation via IL transseptal puncture in all 328 patients shows that full cryoballoon catheter and sheath deflection were never necessary to achieve a cryoballoon-to-PV occlusion.

Analysis of the ICE Doppler flow acutely after removal of the ablation sheath revealed that all 45 patients who had a FO puncture site had evidence of atrial septal flow consistent with a small atrial septal defect with left-to-right atrial fluid movement (Q_p — Q_s ratio greater than 1). By contrast, 42 of the 128 patients (32.8%) with the IL puncture site demonstrated acute Doppler ICE flow after removal of the transseptal sheath (**Figure 3**). The difference in acute Doppler flow detection between the IL and FO transseptal puncture site was statistically significant by Fisher's Exact testing ($P < 0.0001$).

Lastly, during the entire examination of 373 patients, no patient experienced a pericardial effusion or tamponade. Also, neither septal dissections nor hematoma formations were observed for either FO or IL transseptal techniques. A combination of ICE and fluoroscopy imaging during all procedures demonstrated qualitatively that the IL position often had ample distance at a lower entry position from collateral tissue puncture. In the IL position, the transseptal needle would point towards the mitral valve rather than the left atrial appendage or left atrial roof. Both of the latter two left atrial lateral structures required more imaging attention when utilizing the FO transseptal approach.

Figure 1 demonstrates that “tenting” of the FO can help to determine an inferior and anterior transseptal location near the IL. This anterior and inferior transseptal location can allow the cryoballoon catheter to be used with minimal catheter and/or sheath deflection. Specifically, with ablations in the lower PVs, the IL transseptal location allows for a “more direct” alignment between the cryoballoon catheter and the tubular section of each PV. As demonstrated in **Figure 2**, this alignment between the PV and cryoballoon catheter allows for the most direct transfer of occlusion force that is necessary to ensure that a complete and circumferential lesion is created surrounding each PV during the cryoballoon ablation procedure. Incomplete cryoballoon lesion sets are created when there are gaps between the cryoballoon and PV contact, which results in reduced transfer of cold between the balloon and tissue.

Figure 3 illustrates another acute advantage of using the IL location during a cryoballoon ablation procedure. When the FO location is used, immediate withdrawal of the cryoballoon and sheath will often leave an acute left-to-right blood-shunt at the transseptal puncture location, which can be observed with color-flow Doppler imaging. Alternatively the IL location for a transseptal puncture is typically in a thicker part of the septum. Consequently, when the cryoballoon and sheath are removed from the LA, there is less left-to-right shunting of blood, and in some cases there is no detectable blood shunting when viewed by color-flow Doppler imaging.

Transseptal Puncture Location by ICE Imaging

Figure 1: ICE images of FO and IL transseptal puncture. (A) The traditional placement of transseptal entry at the fossa ovalis will demonstrate “tenting” of the septum tissue due to the sparsity of tissue when viewed by fluoroscopy. (B) An inferior and anterior transseptal approach at the inferior limbus will provided a mechanical advantage when using the cryoballoon catheter. Yellow arrows indicate the transseptal puncture locations. [Please click here to view a larger version of this figure.](#)

Fluoroscopy Images of Cryoballoon Ablation

Figure 2: Cryoablation at the PVs. Cryoballoon placement at four pulmonary vein (PV) locations with antral balloon positioning at each vein as view by fluoroscopy. All PV are viewed in LAO positioning with an inferior and anterior transseptal entry position (IL location). **(A)** The left superior PV is an almost straight-on approach from the transseptal entry, and it is typically the first PV that is ablated because of the ease of guidewire approach. **(B)** The left inferior PV will use sheath deflection to achieve proper PV-to-balloon occlusion. **(C and D)** Phrenic nerve pacing will be used to monitor nerve function during right-sided ablations. Both PVs will use sheath deflection, and the right inferior PV (RIPV) will typically use the highest degree of deflection. However, note that with an inferior and anterior approach, the RIPV ablation does not require the maximal deflection capability that is provided in the cryoballoon system. Yellow brackets are the cryoballoon and blue brackets are the steerable sheath. [Please click here to view a larger version of this figure.](#)

ICE Image After Procedure at Transseptal Location

Figure 3: ICE imaging with color-flow Doppler. Doppler images from intracardiac echocardiography. Notice the amount of Doppler flow that is present after catheter removal at the septum when comparing the fossa ovalis transseptal position (A) compared to the inferior limbus position (B). Yellow arrows indicate the transseptal puncture location. [Please click here to view a larger version of this figure.](#)

Angle of Approach by FO or IL Location

Figure 4: Angles of cryoballoon approach into PVs. A virtual reconstruction of FO versus IL transseptal locations. The FO puncture site achieved complete occlusion at the following deflection angles: 131°, 32°, 206°, and 329°. By comparison, the IL transseptal site achieved occlusion with the following deflection angles: 121°, 45°, 182°, and 349°. Note that less catheter deflection is needed in the inferior PVs for the IL location. Green lines are representative of the cryoballoon catheter direction from a FO site, and red lines denote the cryoballoon direction from an IL site. [Please click here to view a larger version of this figure.](#)

Discussion

This study observed that using the anterior and inferior transseptal site approach resulted in 93% of the patients not requiring an additional focal ablation with an adjunctive focal ablation catheter to achieve acute procedural PVI. By comparison, the STOP AF trial reported a rate of 83% acute procedural PVI when only the cryoballoon catheter was used⁴. A rate of 97.6% acute procedural PVI was obtained when adjunctive focal ablation catheters were used during STOP AF⁴, and a typical transseptal needle puncture during the STOP AF study was located in the FO position. However, more recently, higher rates of acute PVI have been reported when using the second-generation cryoballoon catheter, which does not require perfect cryoballoon-to-PV axial alignment to achieve PVI⁶⁻¹¹.

The observation (that the use of an IL site transseptal puncture resulted in a smaller angle between the cryoballoon and the PV) may explain the high degree of success since the puncture site is more likely to be at the same level as the inferior PVs. This smaller angle of cryoballoon catheter and sheath deflection results in a more direct path for the positioning of cryoballoon-to-PV ostium which facilitates the ease of occlusion. In contrast, a larger angle between the cryoballoon and the PV typically makes occlusion of the PV more difficult to achieve and therefore results in reduced PVI. Consequently, prior studies (with the first generation cryoballoon catheter) have described the use of a “hockey stick” approach configuration of the cryoballoon when the transseptal site is above the level of the inferior PVs^{13,14}. This procedural movement (hockey stick) is not necessary with the second-generation cryoballoon when an IL transseptal site is employed.

In a virtual intracardiac reconstruction (**Figure 4**), the cryoballoon catheter takes a sharp turn to reach the right-sided PVs from the FO transseptal location. With the traditional FO puncture site, the cryoballoon-to-PV angles needed to achieve complete occlusion are 131°, 32°, 206°, and 329° for the right superior PV (RSPV), left superior PV (LSPV), right inferior PV (RIPV), and left inferior PV (LIPV), respectively. By comparison, the lower IL transseptal site allows the cryoballoon-to-PV occlusion angles to achieve complete occlusion at 121°, 45°, 182°, and 349°, respectively. When comparing the angles needed to achieve cryoballoon occlusion, the mechanical advantage of the anterior and inferior transseptal site becomes apparent.

Additionally, by direct comparison, this study demonstrated that the IL position was statistically better than the FO transseptal site at preventing acute IASD as monitored by Doppler flow on ICE. Acute left-to-right shunts were detected in 100% of the patients given a FO transseptal puncture while it was reduced to a 33% rate when examining patients with an IL puncture site. A seemingly apparent explanation is that the thicker and more muscular septum, in an anterior and inferior approach, allows for compaction and minimization of the tissue disruption. By comparison the thin-walled FO does not have enough tissue to establish closure by tissue contact once the 15 Fr septal portal has been established. However, further follow-up examination will be necessary to determine the longer-term persistence of transseptal access-induced IASDs. By systematically examining transseptal access locations, this study was able to demonstrate an advantage of using an anterior and inferior approach near the IL.

This current study only examined the acute instance of IASD via Doppler flow ICE imaging. Longer-term and persistent left-to-right atrial shunts are more relevant to the overall health of patients. It is possible (and likely) that most (if not all) patients show no detrimental cardiac symptomology in longer-term follow-up care. Also, while the IL transseptal puncture did have certain advantageous in this study, it is important to clarify that many other cryoballoon using physicians have successful ablation procedures utilizing the FO transseptal position, and that the ultimate point of transseptal entrance should be selected at the physician’s medical discretion. This study represents the clinical results from a single center retrospective examination, and thus the reproducibility and utility of the technique may rely heavily on physician-user experience.

When choosing to use the IL position, ICE imaging is a required recommendation. The more anterior and inferior location of the IL transseptal puncture may predispose the patient to a higher risk of atrial perforation and/or aortic puncture. ICE imaging is critical to maintain safety during the transseptal puncture and importantly, it can be used to determine a location that is well posterior to the aortic root. In the anterior direction, ICE imaging will ensure that the transseptal puncture is not too anterior and not near the Kock triangle anatomically, which will avoid any potential AV node injury. While using ICE during all 373 procedures reported in this study, there were no complications related to transseptal puncture, and there were no instances of atrial septal dissection and left atrial hematoma formation which have been previously noted during the usage of radiofrequency focal-tip ablation catheters¹⁵.

By locating the transseptal access site to approximately one centimeter below the typical level of the FO, there were several benefits that were introduced during the operation of a cryoballoon catheter for AF ablation. The improved angle between the transseptal puncture site and each of the four PVs resulted in a better alignment and a mechanical advantage between the cryoballoon and PV ostium. As an immediate result, the rate of “balloon-only” PVI was robust. Additionally, the lower puncture site (at the thicker septum) decreased the incidence of acute IASDs, which may have further implications in longer-term patient care.

Lastly, the study physicians in this examination qualitatively observed that it was easier to push a 15 Fr sheath through the IL position compared to the FO location. The mechanical advantage (of pushing through a more central and rigid cardiac structure) facilitated large sheath pushing during entry and more controlled motion during passage. By comparison, the FO position was prone to “hanging” because of a thinner (and compliant) septum during the “step-up” entry of the 15 Fr sheath.

Disclosures

Conflicts of interest: Michael Rich – none; Andrew Tseng – none; Hae Lim- an employee of Medtronic plc; Paul Wang – none; Wilbur Su – research and honorarium; Medtronic, AtriCure, St. Jude Medical.

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