JACC: CARDIOVASCULAR INTERVENTIONS VOL. 9, NO. 24, 2016

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER http://dx.doi.org/10.1016/j.jcin.2016.10.035

STATE-OF-THE-ART REVIEW

Transseptal Techniques for Emerging Structural Heart Interventions

Mohamad Alkhouli, MD, Charanjit S. Rihal, MD, David R. Holmes, Jr, MD

ABSTRACT

The development of new transseptal transcatheter interventions for patients with structural heart disease is fueling increasing interest in transseptal puncture techniques. The authors review contemporary transseptal puncture indications and techniques and provide a step-by-step approach to challenging transseptal access and procedural complications. (J Am Coll Cardiol Intv 2016;9:2465–80) © 2016 by the American College of Cardiology Foundation.

The technique of transseptal puncture (TSP) was developed by Ross, Braunwald, and Morrow (1) in 1959 to allow direct measurement of left atrial (LA) pressure. Over the next several decades, with the growing acceptance of retrograde catheterization of the left ventricle, and the development and expanding use of echocardiography, experience with TSP declined. Substantial renewed application of the TSP technique ensued in the 1980s and 1990s because of the introduction of percutaneous balloon mitral valvuloplasty (PBMV) and catheter ablation of atrial fibrillation (AF) (2,3). In more recent years, the emerging percutaneous transcatheter therapies of valvular and congenital heart disorders have led to the widespread adoption and further modification of the TSP technique. In this paper we aim to: 1) provide an overview of the established and emerging indications for TSP; 2) describe the contemporary techniques of TSP, with an emphasis on the role of multimodality imaging and site-specific puncture; and 3) provide a systematic approach to aid in the management of challenging transseptal access and procedural complications (**Central Illustration**).

INDICATIONS FOR TSP

PERCUTANEOUS TREATMENT OF MITRAL VALVE DISEASE. PBMV. In the 1980s, PBMV became the treatment of choice for rheumatic mitral stenosis with suitable anatomy (3). PBMV using a single-balloon technique (**Figure 1A**) became the most popular PBMV method and virtually replaced surgery in many areas of the world where rheumatic heart disease is prevalent (4).

Transcatheter mitral valve repair. Percutaneous edge-to-edge mitral valve repair (**Figure 1B**) using the MitraClip device (Abbott Vascular, Santa Clara, California) demonstrated superior safety and similar improvement in clinical outcomes compared with conventional surgery in patients with severe degenerative mitral regurgitation (MR) who are at high risk for surgery (5). The MitraClip device has been used in more than 30,000 patients worldwide for both functional and degenerative MR.

Transcatheter mitral valve-in-valve therapy. Initial results with transcatheter transseptal mitral valve-in-valve (**Figure 1C**) implantation are promising (6,7). If this therapy is proved durable, it would provide an excellent alternative to reoperation for patients with failed mitral bioprostheses.

Transcatheter mitral valve implantation. Several dedicated transcatheter mitral valve systems are in the early phase of development. The CardiAQ valve (CardiAQ, Irvine, California) (**Figure 1D**) is

From the Divisions of Cardiovascular Diseases and Internal Medicine, Mayo Clinic College of Medicine, Rochester, Minnesota.
The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received August 22, 2016; revised manuscript received September 25, 2016, accepted October 6, 2016.

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

CB = cryoballoon

FO = fossa ovalis

IAS = intra-atrial septum

ICE = intracardiac echocardiography

IVC = inferior vena cava

LA = left atrial

LAA = left atrial appendage

MR = mitral regurgitation

PBMV = percutaneous balloon mitral valvuloplasty

PFO = patent foramen ovale

PV = pulmonary vein

PVL = paravalvular leak

RF = radiofrequency

SHD = structural heart disease

TEE = transesophageal echocardiography

TSP = transseptal puncture

currently the only transcatheter mitral valve with a transfemoral transseptal delivery system under testing (8).

Mitral paravalvular leak (PVL) repair. PVL occurs in 5% to 17% of patients after valve replacement surgery (9). Repeat surgery has been the traditional treatment for PVL, but it is associated with high operative mortality and variable results (10). Percutaneous repair of mitral PVL using a transseptal route (**Figure 1E**) is an effective alternative to surgery, with feasibility and efficacy demonstrated in multiple studies (11).

PULMONARY VEIN (PV) ISOLATION (PVI). The efficacy of PVI in treating drug-refractory AF has been established, with more than 15 years of clinical studies (**Figure 1F**). This indication has accounted for most of the growth in the use of TSP in the past 2 decades (12).

PERCUTANEOUS LEFT VENTRICULAR ASSIST DEVICES. Percutaneous left ventricular assist devices such as the TandemHeart (CardiacAssist, Pittsburgh, Pennsylvania) (**Figure 1G**) can be used to support patients in cardiogenic shock or as a temporary application during high-risk coronary intervention (13). Another form of percutaneous left ventricular assist device is transseptal extracorporeal membrane oxygenation. This technique is applied in patients with persistent pulmonary edema despite traditional venoarterial extracorporeal membrane oxygenation. In these cases, a "venting" cannula is placed in the left atrium through a TSP and is incorporated into the extracorporeal membrane oxygenation circuit using a Y connection (14).

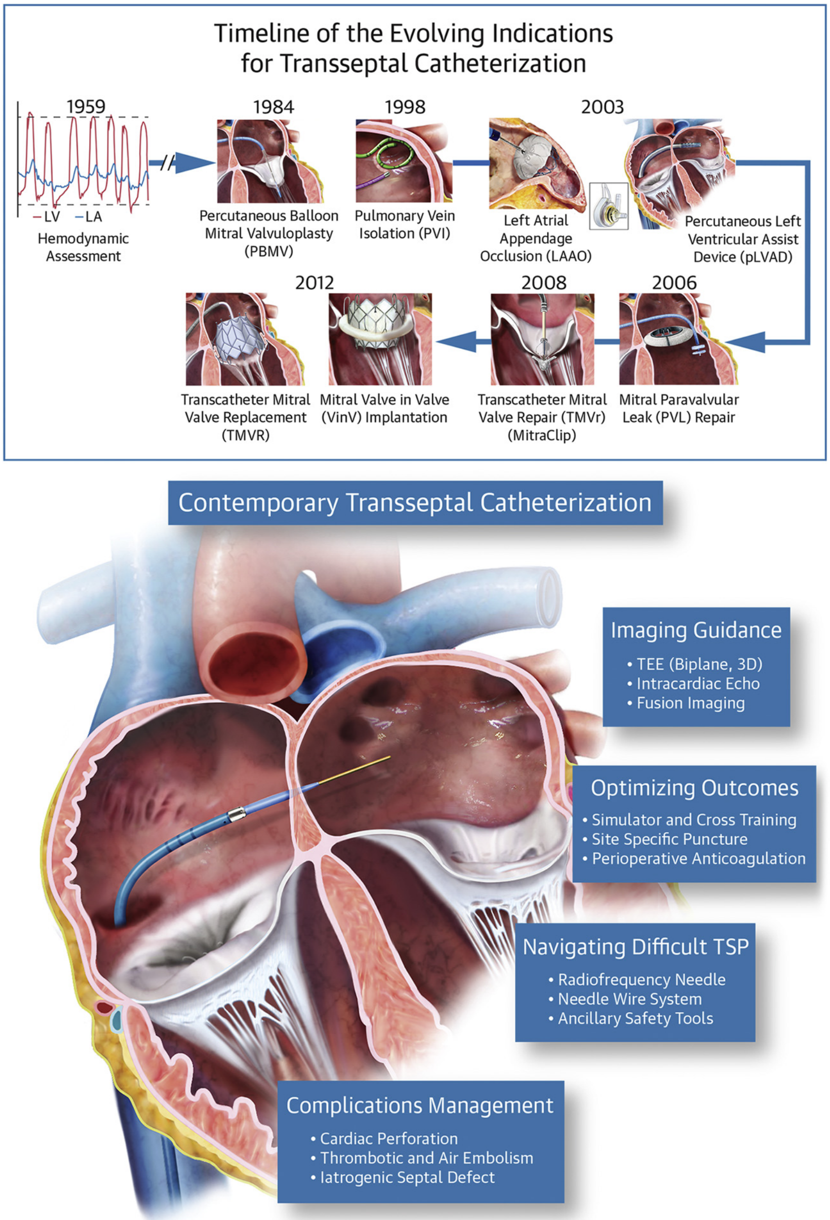
LA APPENDAGE (LAA) CLOSURE. Percutaneous occlusion of the LAA is equivalent to warfarin in preventing stroke in patients with nonvalvular AF and is associated with a lower bleeding risk (15). Percutaneous LAA closure can be achieved with a transseptal approach with the Watchman device (Boston Scientific, Marlborough, Massachusetts) and the Amplatzer Cardiac Plug (St. Jude Medical, St. Paul, Minnesota) (**Figure 1H**), an epicardial approach with the Aegis system (Aegis Medical, Vancouver, British Columbia, Canada), or a hybrid approach with the LARIAT system (SentreHEART, Palo Alto, California). The Watchman device is the only LAA occluder to receive approval for the prevention of systemic thromboembolism in patients with nonvalvular AF in the United States. Several other devices are in CE-mark stages and are available outside of the United States.

ANTEGRADE TREATMENT OF LEFT VENTRICULAR AND AORTIC VALVE DISEASE. The initial transcatheter aortic valve replacement described by Cribier et al. (16) in 2002 was performed through an antegrade transseptal approach, but the procedural complexity led to its replacement with the transfemoral approach. However, in contemporary practice, the transseptal approach is still used on a limited basis for "no-access" patients (17). Similarly, the transseptal route has been used in balloon aortic valvuloplasty in patients with distal aortic occlusion and in patients who are undergoing concurrent mitral valvuloplasty (18,19). Ventricular septal defects are rare complications of aortic valve replacement. Percutaneous closure of these iatrogenic defects through a transfemoral retrograde approach is usually the treatment of choice but can be challenging if a mechanical prosthesis is present. In these cases, an antegrade transseptal approach can be used (20). Likewise, the transseptal approach can provide an excellent access option for percutaneous closure of iatrogenic left ventricular pseudoaneurysms (21).

OTHER INDICATIONS. Hemodynamic assessment of valvular heart disease is commonly achieved with indirect estimation of LA pressure using a Swan-Ganz catheter (1,22). Nevertheless, TSP remains essential in equivocal cases and to assess the transaortic gradient in patients with mechanical aortic prostheses (22). TSP has been used to aid in percutaneous closure of patent foramen ovale (PFO) with long tunnel. However, in contemporary practice, this has been abandoned in the light of excellent devices adapting to all anatomies of PFOs (23). TSP can be a valuable tool for facilitating carotid artery stenting in patients with acutely angulated arch-branch vessels and those with Takayasu arteritis (24) and transcatheter embolization of type I endoleak in the proximal aortic arch (25). In addition, an externalized transseptal guidewire has proved to be an important tool to aid thoracic stent graft passage in tortuous aortas and severely angulated arches (26,27). In rare occasions, transseptal access may provide an alternative route for coronary interventions in patients with no suitable peripheral access (28). Finally, balloon atrial septostomy is another indication for TSP in patients with severe pulmonary hypertension who do not respond to medical therapy or are awaiting lung transplantation (29).

The majority of the aforementioned procedures can also be performed using a transapical approach. However, because of the risks and the steeper learning curve with transapical access, the transseptal route is the preferred approach at most institutions (7,30).

CENTRAL ILLUSTRATION Evolving Indications and Contemporary Techniques of Transseptal Catheterization

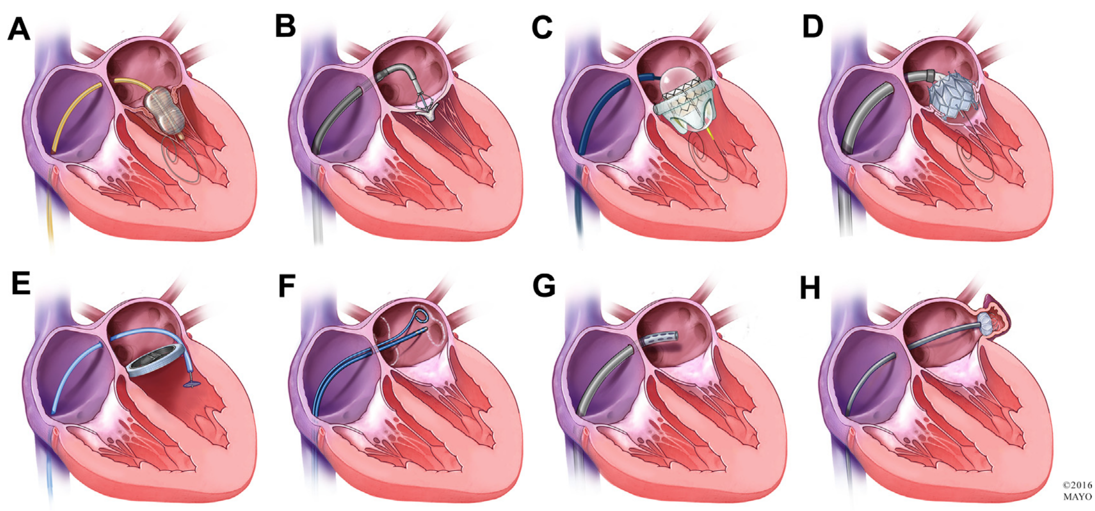


Alkhouli, M. et al. J Am Coll Cardiol Intv. 2016;9(24):2465–80.

SITE-SPECIFIC TSP

Historically, the goal of TSP was to safely traverse the intra-atrial septum (IAS), preferably through the fossa ovalis (FO) (Figure 2). Fluoroscopy-guided TSP is sufficient to achieve this goal in the majority of cases. However, the evolution of a variety of complex interventions that can be performed via the transseptal route has called attention to the importance of site-specific transseptal access. Therefore, transesophageal echocardiography (TEE) and intracardiac echocardiography (ICE) have become essential tools in many structural heart interventions by providing a greater degree of anatomic orientation. Figure 3 illustrates the various suggested locations for TSP for different transseptal procedures.

FIGURE 1 Illustration of the Various Contemporary Transseptal Transcatheter Intracardiac Interventions



(A) Percutaneous mitral balloon valvuloplasty. **(B)** Transcatheter mitral valve repair (MitraClip). **(C)** Mitral valve-in-valve implantation. **(D)** Transcatheter mitral valve replacement. **(E)** Mitral paravalvular leak closure. **(F)** Pulmonary vein isolation. **(G)** Percutaneous left ventricular assist device placement. **(H)** Left atrial appendage closure.

MITRAL VALVE INTERVENTIONS. Proper guiding catheter position is the most important initial step of the MitraClip procedure. Targeted TSP facilitates suitable guide position and allows the clip to reach the middle of the mitral orifice (31). A suboptimal TSP site may result in inadequate treatment of MR (32). For central MR jets, the operator aims for a posterior and slightly superior TSP. Higher TSP heights are needed for more medial jets, while lower transseptal sites are more appropriate when lateral jets are targeted (Figure 3) (32). The position of the TSP for mitral PVL closure requires similar forethoughts. For defects away from the IAS, the location of the puncture is less critical. However, for medial defects, a posterior and slightly superior puncture provides the appropriate working height within the left atrium and allows readily access to the defect. In PBMV and transseptal mitral valve-in-valve implantations, a midposterior puncture is usually adequate and provides a favorable working height in the left atrium and a coaxial plane with the mitral valve.

LAA CLOSURE. The long axis of the LAA is oriented anteriorly, and the plane of the LAA ostium is perpendicular to that axis. Successful coaxial device deployment depends on the ability to position the delivery sheath with sufficient depth into the LAA. This is best accomplished with a posterior-anterior trajectory of the sheath. Therefore, a posterior TSP provides the most favorable sheath orientation (33). There are subtle differences in the recommended TSP height related to the shapes of the transseptal sheathes used for different LAA occlusion technologies. For the Watchman device and the Amplatzer Cardiac Plug, midseptal to slightly inferior TSP is ideal. For the LARIAT device, a more superior location has been suggested (33). A TSP that is too superior or too anterior can make it difficult to align the sheath with the long axis of the LAA and poses a challenge to device delivery, especially with retroverted LAAs (34).

PV INTERVENTIONS. The PVs are posterior structures in the left atrium. Ensuring adequate reach of the radiofrequency (RF) or cryoballoon (CB) catheter is essential to achieve successful ablation, especially when addressing right-sided veins (33). In RF ablation, some experts prefer a relatively anterior crossing of the IAS to allow adequate room for deflectable sheaths and catheters (33). Others suggest that a posterior TSP allows better angling of the ablation catheters toward the PVs (35). In CB ablation, the CB catheter uses the anterior balloon surface to push against the atrial tissue around the PV ostium. Therefore, a more anterior crossing of the IAS provides the most favorable approach for accessing all PVs with the CB, particularly the right inferior PV.

PERCUTANEOUS LEFT VENTRICULAR ASSIST. Mid-FO access for central transseptal catheter positioning allows more room in the left atrium and reduces the likelihood of device malfunction because of cannula-LA wall contact.

Using a PFO for LA access during left-sided structural heart interventions is generally discouraged. However, successful use of a PFO to facilitate LAA occlusion procedures has been reported (36).

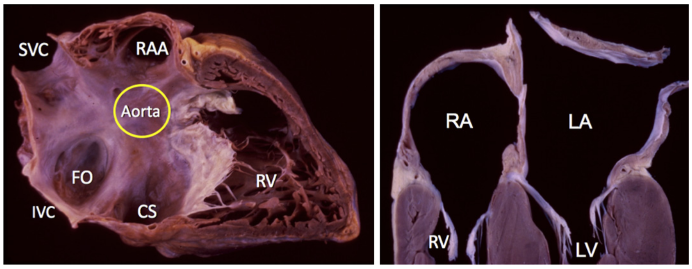
TSP TECHNIQUES

IMAGING GUIDANCE FOR LOCALIZATION OF THE FO. Fluoroscopy has traditionally been the main imaging method for localization of the FO. A pigtail catheter is placed in the aortic root so that its tip marks the location of the aortic valve, while the cardiac silhouette identifies the lateral and posterior borders of the atria. Multiple angiographic projections can be used to puncture the septum safely (Figures 4 and 5). In difficult cases, right atrial angiography with delayed LA angiography can help visualize the septum (overlap area). A septal "staining" technique can also help visualize the FO by injecting 1 to 2 ml of contrast through the needle tip against the IAS (Figure 5). Although TSP performed with fluoroscopic guidance has been the standard since the early days of procedural performance, ultrasound-based imaging (TEE and ICE) has assumed increasing importance because it allows direct imaging of the soft tissue structures that are relevant to TSP and provides reassurance that the specific location of the puncture site is optimal. In addition, the use of TEE and/or ICE may increase the safety and the success rate of TSP in difficult cases, such as in patients with aneurysmal or thickened septum, patients with abnormally rotated hearts, and those with thickened or fibrotic IAS due to patch repair or prior TSP (37,38).

Both TEE and ICE are very useful in achieving site-specific TSP. ICE has the additional advantages of not requiring a second operator or general anesthesia, although TEE with conscious sedation is a common practice outside the United States. In contrast, ICE devices lack multiplanarity, and they may distract the operator, as 2 catheter systems must be handled separately, an additional venous puncture is necessary, and there is a possibility that the 2 catheter systems may get entangled (39).

Various transesophageal echocardiographic imaging maneuvers can display IAS anatomy in detail. Superior and inferior localization is seen best in the bicaval view (90°), and anterior and posterior localization is seen best in the short-axis (30°) and 4-chamber (0°) views. An x-plane view that displays both the bicaval and the short-axis view is extremely helpful in puncturing the IAS at the desired location (Figure 6).

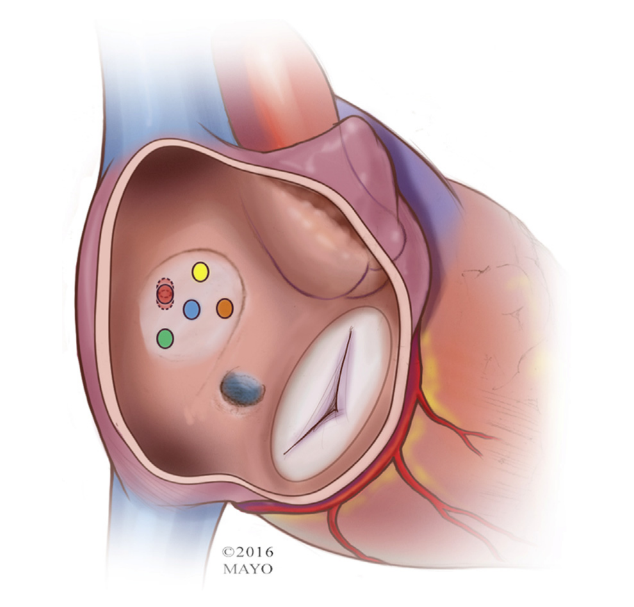
FIGURE 2 Anatomy of the Atrial Septum



CS = coronary sinus; FO = fossa ovalis; IVC = inferior vena cava; LA = left atrium; LV = left ventricle; RA = right atrium; RAA = right atrial appendage; RV = right ventricle; SVC = superior vena cava.

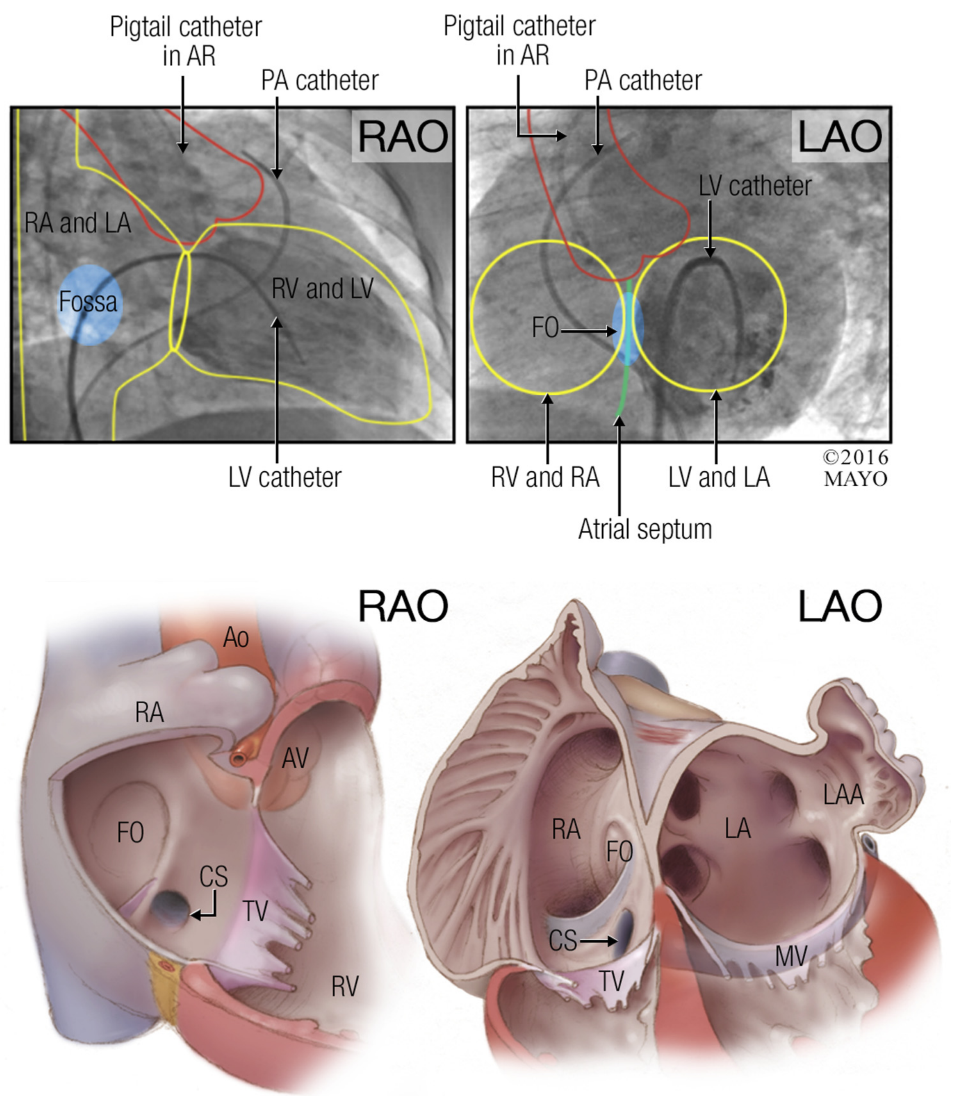
In ICE-guided procedures, a phased-array intracardiac echocardiographic catheter (AcuNav, Siemens, Malvern, Pennsylvania; or ViewFlex, St. Jude Medical) is advanced to the right atrium and manipulated to identify the "home" view (Figure 7). The initial survey of the IAS is then performed; from the home view, a posterior tilt of the transducer and a

FIGURE 3 Site-Specific Transseptal Puncture for Various Intracardiac Interventions



Red: MitraClip, paravalvular leak closure (a higher crossing site is recommended for medial leaks, and a lower crossing site is recommended for lateral leaks; **dashed red circles**). **Yellow:** transseptal patent foramen ovale closure. **Blue:** percutaneous left ventricular assist device placement, hemodynamic studies. **Green:** left atrial appendage closure. **Orange:** pulmonary vein interventions.

FIGURE 4 **Fluoroscopic Projections for Transseptal Puncture Guidance**



Ao = aorta; AR = aortic root; AV = aortic valve; CS = coronary sinus; LAA = left atrial appendage; LAO = left anterior oblique; PA = pulmonary artery; RAO = right anterior oblique; TV = tricuspid valve; other abbreviations as in Figure 2.

clockwise rotation of the catheter bring the IAS and FO into view (septal view) (Figure 7). With the sheath and dilator apparatus engaged against the FO in the septal view, the height of the TSP can be readily assessed. The anterior-posterior location of the TSP can then be determined with an anterior (counterclockwise rotation) and posterior (clockwise rotation) of the transducer, allowing needle adjustment before puncturing the FO (33). This survey also allows screening for PFO and characterization of the IAS properties (thick septum, septal aneurysm, prior patch repair, and so on). After successful TSP, ICE allows direct visualization of the needle tip and its relationship to the surrounding cardiac structures (39).

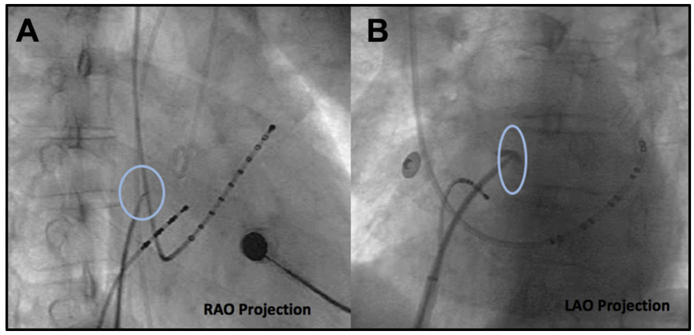
Fusion of different imaging modalities has gained increasing popularity in structural heart disease (SHD) interventions over the past decade. Currently, the combination of TEE and fluoroscopy (e.g., EchoNavigator, Philips, Amsterdam, the Netherlands) is the only modality that allows real-time image fusion of high quality during SHD interventions. The utility of the EchoNavigator system to facilitate a targeted TSP has been demonstrated in several studies (37,40). Newer imaging techniques are emerging as useful guiding tools for TSP, but their additional value to the current imaging modalities remains to be fully evaluated. These modalities include 3-dimensional echocardiography, computed tomography-derived 3-dimensional augmented fluoroscopy (CARTO3, Biosense Webster, Diamond Bar, California), real-time magnetic resonance imaging, and rotational angiography (41–43).

TSP TOOLBOX. The basic TSP kit consists of a transseptal sheath, an introducer, and the transseptal needle. Novel ancillary tools have been added to the TSP toolbox and served to increase the safety and success of the TSP procedure (**Figure 8**).

Transseptal sheaths. Transseptal sheaths are generally categorized in 2 broad groups: fixed-curve sheaths and steerable sheaths. Traditionally, fixed-curve sheaths of various shapes and sizes have been used in the majority of transseptal procedures. However, the wide adoption of PVI techniques for AF ablation led to the development of steerable sheaths to improve LA access, maneuverability, and tissue contact (44,45). Steerable sheaths may be associated with superior clinical outcomes in PVI procedures, but are 4 to 5 times more expensive than traditional fixed-curve sheaths (45,46). A brief description of the available transseptal sheaths and their characteristics is shown in Online Table 1.

Transseptal needles. Historically, the stainless steel Brockenbrough needle (Medtronic, Minneapolis, Minnesota) has been the standard needle used to mechanically puncture the FO. The BRK series of transseptal needles (St. Jude Medical) are similar to

FIGURE 5 Septum Crossing in Fluoroscopy-Guided Transseptal Puncture

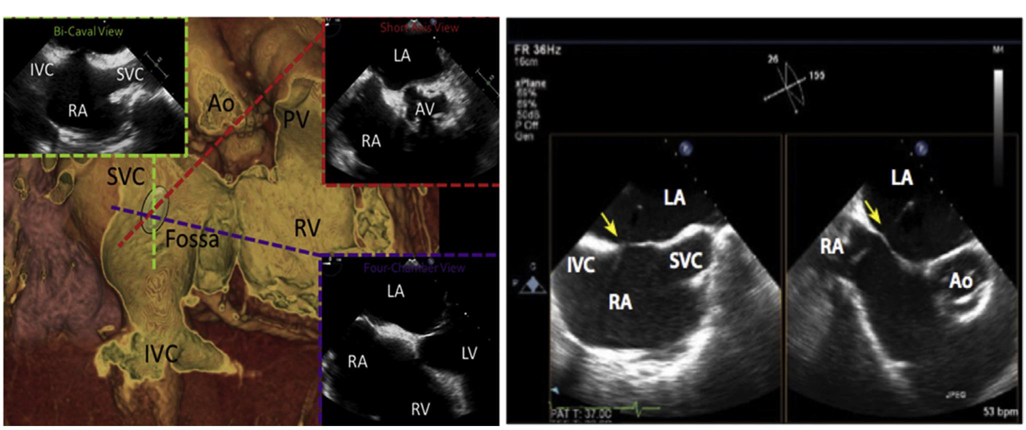


Engaging the fossa ovalis in the right anterior oblique (RAO) **(A)** and left anterior oblique (LAO) **(B)** projections. The **blue circle/oval shapes** indicate the fossa ovalis. Note the staining of the fossa ovalis in the LAO view. A pigtail is present in the RAO projection to mark the anterior location of the aorta.

the Brockenbrough needle but are available in multiple lengths and curves. The NRG RF transseptal needle (Baylis, Montreal, Quebec, Canada) uses RF energy and allows the operator to cross the IAS in a controlled manner without using excessive force (**Figure 9B**). The use of RF needles has been shown to improve the safety and efficacy of TSP for AF ablation compared with conventional transseptal needles (47). The commercially available transseptal needle systems are listed in Online Table 2.

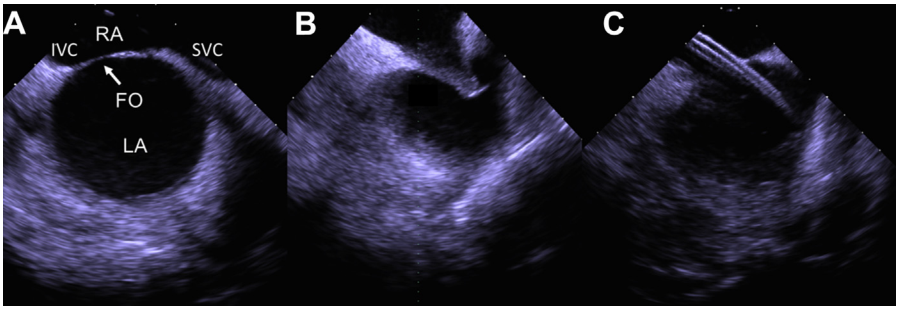
Ancillary devices. *Needle-wire system.* The SafeSept wire (Pressure Products, San Pedro, California) is a 120-cm nitinol guidewire with 0.014-inch diameter that has a sharp and floppy "J tip" that assumes a

FIGURE 6 Biplane Transesophageal Echocardiography for Transseptal Puncture



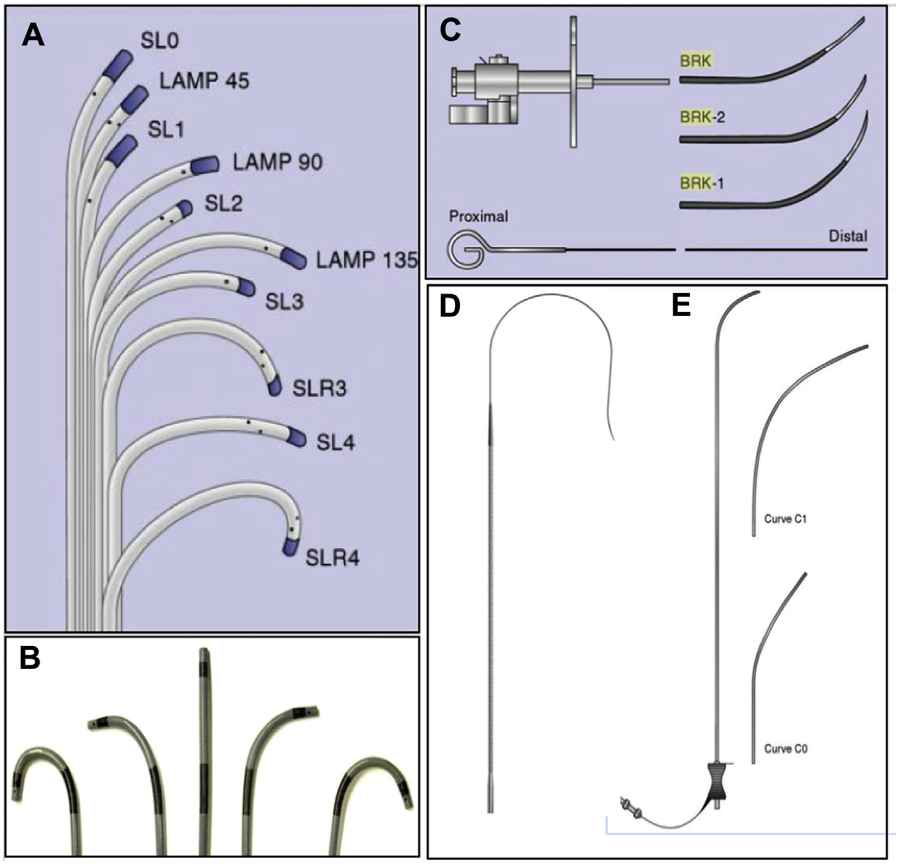
AV = aortic valve; PV = pulmonary vein; SVC = superior vena cava; other abbreviations as in **Figure 2**. Reprinted with permission from Singh et al. (32).

FIGURE 7 **Intracardiac Echocardiography for Transseptal Puncture**



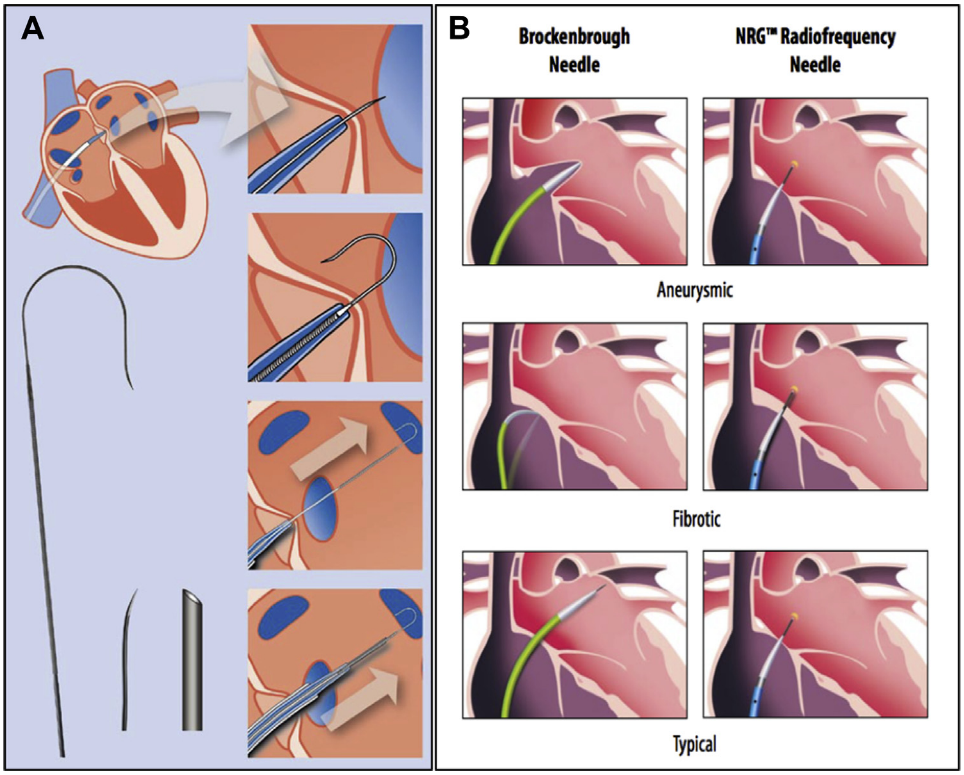
(A) The fossa ovalis (FO) as seen in the "septal" view. **(B)** Tenting of the FO with the transseptal needle. **(C)** The transseptal sheath across the FO in the left atrium (LA). Abbreviations as in Figures 2 and 6.

FIGURE 8 **Commonly Used Transseptal Sheaths and Needles**



(A) Fixed-curve sheath. **(B)** Steerable sheath (Agillis). **(C)** BRK (Brockenbrough) transseptal needle. **(D)** SafeSept wire. **(E)** NRG radiofrequency needle.

FIGURE 9 Navigation Tools for Difficult Atrial Septum



(A) SafeSept wire system. **(B)** NRG radiofrequency needle.

straight orientation while inside the transseptal needle, allowing crossing the septum, but immediately prolapses, assuming a J shape, upon entry into the left atrium (**Figure 9A**) (48). The SafeSept is also available in a 0.035-inch needle-free platform.

Pre-curved LA guidewires. The TorayGuide 0.025-inch guidewire (Toray, Tokyo, Japan) can be used to provide stable access in the left atrium. Other guidewires, such as the Confida 0.035-inch wire (Medtronic) and the Safari 0.035-inch wire (Boston Scientific), can be used off-label to maintain stable access in the left atrium during catheter and sheath exchanges.

PUNCTURE OF THE FO. The transseptal sheath is advanced over a 0.032-inch or 0.035-inch wire (Online Table 1) into the superior vena cava in the anterior-posterior projection, and the transseptal needle is then advanced to the distal end of the sheath without exiting the sheath. The sheath and needle assembly is retracted to the right atrium with clockwise rotation. Two characteristic "jumps" of the dilator tip are usually described: one as the tip passes under the aortic knob and one as the tip passes under the muscular septum in to the fossa. Under fluoroscopic or ultrasound guidance, the needle's tip is advanced into the left atrium. The LA position of the tip can be verified by aspirating oxygenated blood, measuring LA pressure, injecting contrast into the left atrium, or advancing a coronary or a SafeSept wire into a PV. The sheath and dilator apparatus is then advanced over the needle into the left atrium. If 2 accesses to the left atrium are needed, 2 wires can be advanced inside the sheath into the left upper PV, the sheath is removed, and the 2 sheaths are advanced side to side over the 2 wires into the left atrium. However, it has been suggested that this technique may result in a higher chance of a persistent residual septal defect than the double-puncture technique (49). The following steps (catheter insertion via the sheath, sheath exchange, IAS dilation, and so on) vary depending on the specific procedure being performed.

NAVIGATING CHALLENGING TRANSSEPTAL ACCESS

The TSP procedure can be achieved with a high level of success and excellent safety (12). However, several

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 9, NO. 24, 2016
DECEMBER 26, 2016:2465–80

difficulties may arise at various stages of the procedure. Knowledge of the unique challenges of the TSP and the development of a systematic troubleshooting approach are key to improving procedural success and reducing the risk for serious complications (50).

DIFFICULTY WITH ACCESS TO THE RIGHT ATRIUM. The right femoral vein provides the easiest access for TSP. However, there are several scenarios in which obtaining a TSP through right femoral vein access is challenging or not possible.

First, extreme venous tortuosity can make the advancement of a transseptal needle through the sheath quite challenging. In these cases, the transseptal sheath can be exchanged with a long (45-cm) sheath that is ≥2 F larger in diameter. The transseptal sheath will then be reinserted inside the larger sheath, which will provide support and facilitate navigation of the venous tortuosity. It should be noted that in these cases, advancing the sheath and needle system as a unit is critical. Attempting to advance the needle in a kinked sheath can result in perforation of the sheath. The tortuosity can also impede engagement of the FO with the transseptal needle. A secondary bend in the transseptal needle 2 to 3 cm proximal to the primary bend provides adequate reach and allows a targeted TSP (32).

Second, the presence of an indwelling inferior vena cava (IVC) filter does not preclude successful execution of the procedure, even when large sheaths and cannulas must be advanced through the filter (51–53). However, remote IVC filters are associated with high filter thrombosis rates, and therefore partially or totally occluded IVCs should be excluded.

Third, if iliofemoral veins and/or the IVC are patent but have severe stenosis, percutaneous revascularization may be considered to allow access for the transseptal procedure (51).

Fourth, if iliofemoral veins and/or the IVC are occluded, alternative access should be considered. Left femoral and right internal jugular venous access has been successfully used to perform catheter ablation of AF and balloon mitral valvuloplasty (54–56). These approaches, nevertheless, may be inadequate for SHD procedures that mandate site-specific TSP, such as transcatheter mitral valve repair. In these cases, transapical access is the alternative access of choice. On rare occasions, direct right atrial access can be used as a last resort (57).

DIFFICULTY WITH ENGAGEMENT OF THE FO. Severe kyphoscoliosis, abnormally rotated heart due to ventricular hypertrophy or prior surgery, enlarged left or right atrium, dilated ascending aorta, and excessive cardiac motion with respiration can pose significant technical and safety challenges during TSP (58). These challenges can be successfully overcome using a large-curved transseptal needle, manually adding a secondary bend to the transseptal needle, and using adjunctive real-time imaging guidance (32).

DIFFICULTY WITH NEEDLE ADVANCEMENT. Several IAS characteristics can lead to difficulties in gaining access to the left atrium.

Thickened septum. Many patients with AF or SHD had prior TSP or a hypertrophied or fibrotic IAS. Repeat TSPs are more difficult, less often successful, and potentially associated with more complications compared with the first TSP because of increased thickness of the FO, local scarring, or distorted IAS anatomy (59,60). Techniques to overcome these difficulties include the use of a large-curved transseptal needle (e.g., BRK-1), advancement of transseptal needle stylet or sharp-tipped wires (e.g., SafeSept) through the needle to facilitate needle crossing, and using an RF transseptal needle (**Figure 9B**) (60,61). If RF needles are not available, brief application of RF energy using an electrocautery system connected to the proximal end of the transseptal needle may assist with passage of the needle across the FO (62). Adjunctive imaging with ICE has also been shown to facilitate crossing a scarred or highly resistant IAS (63).

Aneurysmal septum. In these cases, there is a reduced distance between the apex of the tented FO and the opposite LA wall during TSP. It is therefore crucial not to apply excessive force on the needle, to avoid damaging the LA wall from unanticipated and uncontrolled forward movement after the device passes through the FO. Again, a brief application of electrocautery or RF energy can be useful in this circumstance (**Figure 9B**).

Prior septal occluder. In case of a prior septal occluder device, transseptal access can be obtained in portions of the native IAS in the majority of cases. Direct transoccluder puncture is rarely necessary but has been reported (64,65). In patients with surgically repaired IAS, puncture can be performed through neighboring native IAS tissue or through the patch itself in case of a pericardial or Dacron patch, but not in case of a Gore-Tex patch (W. L. Gore, Flagstaff, Arizona) because of its resistant texture (66).

DIFFICULTY WITH SHEATH AND GUIDE ADVANCEMENT. Even if the transseptal needle is able to cross the IAS, significant difficulty may be encountered with advancing the sheath across the FO. This is particularly a problem with braided or steerable sheaths because of the “step” in size between the dilator and the sheath.

Forceful advancement of the transseptal apparatus can reduce fine control and potentially lead to atrial perforation. Several maneuvers can be used in this circumstance: redirecting the sheath and dilator apparatus with careful clockwise or counterclockwise torsion often allows the apparatus to penetrate the resistant IAS. This is best done over a SafeSept or a coronary wire to avoid perforating the left atrium. Alternatively, lower profile sheath-dilator combinations (e.g., SR0, Mullins) may be used to further dilate the FO. Finally, balloon septostomy may be needed to adequately dilate the FO (67). Balloon septostomy is often required in transseptal interventions that use large-bore sheaths (e.g., mitral valve-in-valve) (7,49).

MANAGING COMPLICATIONS

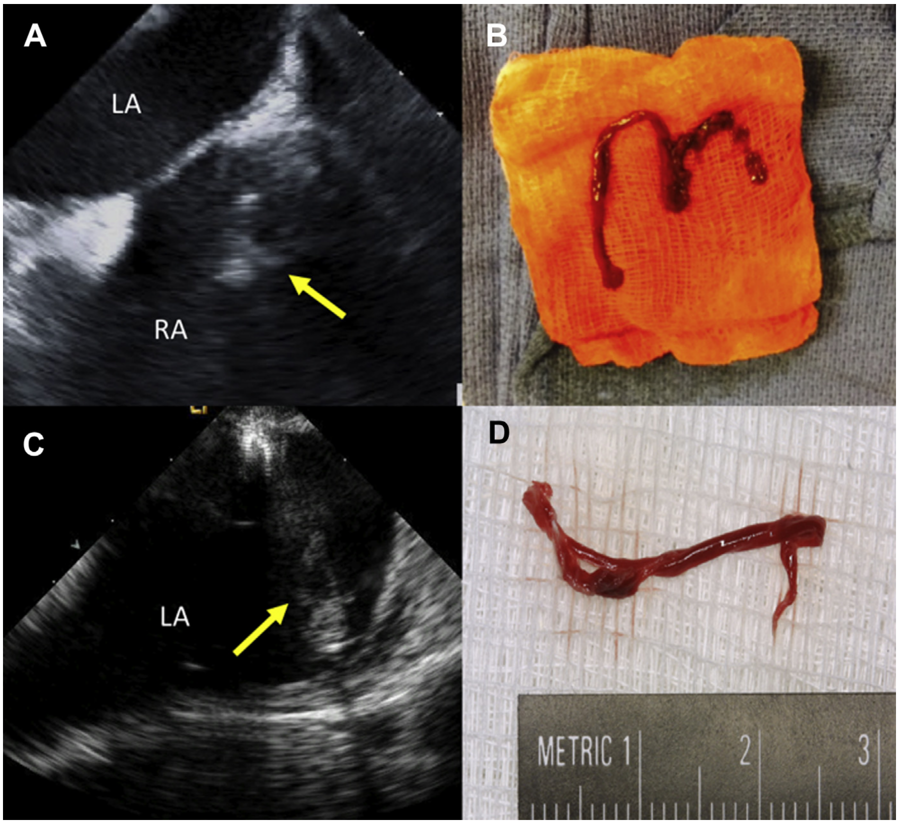
TSP is a reasonably safe procedure with a major complication rate of 1% to 2% (12,68). However, complications related to TSP could be life threatening, and operators should be familiar with their management. Avoiding complications starts with careful patient selection, knowledge of the contraindications to TSP, and periprocedural management of anticoagulation. The only absolute contraindication to TSP is thrombus at the IAS. Relative contraindications are thrombus within the right atrial or LA cavity, therapeutic anticoagulation, or marked cardiac or thoracic deformity. Hypertrophied or aneurysmal IAS and prior surgical patch repair are not contraindications to TSP.

CARDIAC PERFORATION AND TAMPONADE. Cardiac tamponade during transseptal intracardiac procedures is usually the result of a perforation (69). Cardiac perforation may be caused by factors related to the TSP such as inadvertent advancement of the needle or the dilator or sheath into the free atrial wall or could be related to the specific intracardiac procedures (excessive ablation energy, manipulation of the delivery sheath inside the appendage, and so on). Patients with large atria are at a particularly high risk for perforation when a posterior TSP is performed. The incidence of perforation and tamponade varies according to the specific type of procedure: <1% in diagnostic hemodynamic studies, 1% to 2% in PBMV, and 2% to 3% in PVI and LAA closure (12,69). The presentation depends on the size of the device responsible for the perforation, the structure that is perforated, the hemodynamic state at the time of perforation, the properties of the pericardium, and the coagulation status. Cardiac tamponade is the most common cause of death during PVI procedures (70). Early recognition and prompt treatment with pericardiocentesis is lifesaving and should be a core competency for all laboratories performing TSP. When the perforation is a result of inadvertent passage of the needle into the pericardial space or the aorta, withdrawing the needle and reversing anticoagulation is usually sufficient. However, if a sheath or a catheter is advanced through the perforation, it is imperative not to prematurely withdraw the perforating catheter to maintain access to the hole for potential closure (71). Several reports demonstrated the feasibility of various Amplatzer occluders in sealing iatrogenic cardiac and aortic perforations (72,73).

THROMBOEMBOLISM. A number of studies reported higher than expected incidences of intraoperative thrombus detected on the transseptal sheath and in the left atrium during PVI procedures (8% to 11%) (**Figure 10**) (74). There are also several reports concerning thrombus formation in the left atrium during PBMV and transcatheter mitral valve repair (75,76). Although clinical stroke remains rare, cerebral lesions are detected on magnetic resonance imaging in 7% to 13% of patients undergoing PVI (77,78). In a small study of patients undergoing MitraClip treatment with cerebral protection, embolic debris potentially conducive to cerebrovascular events was found in all patients (79). Periprocedural anticoagulation management varies depending on the specific procedure. However, developing guideline-supported institutional algorithms for pre-procedural management of oral anticoagulant agents is paramount to minimize bleeding and thromboembolic complications. It is a common practice to hold anticoagulant agents 2 to 5 days before procedures involving TSP. We reserve bridging anticoagulation for “high-risk” patients (e.g., patients with mechanical valves and those with acute venous thrombosis). We routinely administer 2,000 to 5,000 U of unfractionated heparin before TSP and a total of 200 U/kg to achieve an activated clotting time >300 seconds after obtaining access to the left atrium. Maintaining an activated clotting time >300 seconds during PVI has been suggested to prevent LA thrombus formation (74). Cerebral protection with bilateral carotid filters can be used in patients undergoing TSP who are at higher risk for stroke (e.g., those with LAA thrombus or dense spontaneous echocardiographic contrast) (79). Nevertheless, the role of routine cerebral protection during transseptal procedures has not been established. If detected on TEE or ICE, intracardiac thrombus can be effectively removed with vigorous aspiration (80).

AIR EMBOLISM. Air embolism is often a clinically silent event because of its transient nature and the procedural sedation. However, coronary ischemia, stroke, hypotension, and cardiac arrest have been

FIGURE 10 **Thromboembolism During Transseptal Cardiac Interventions**

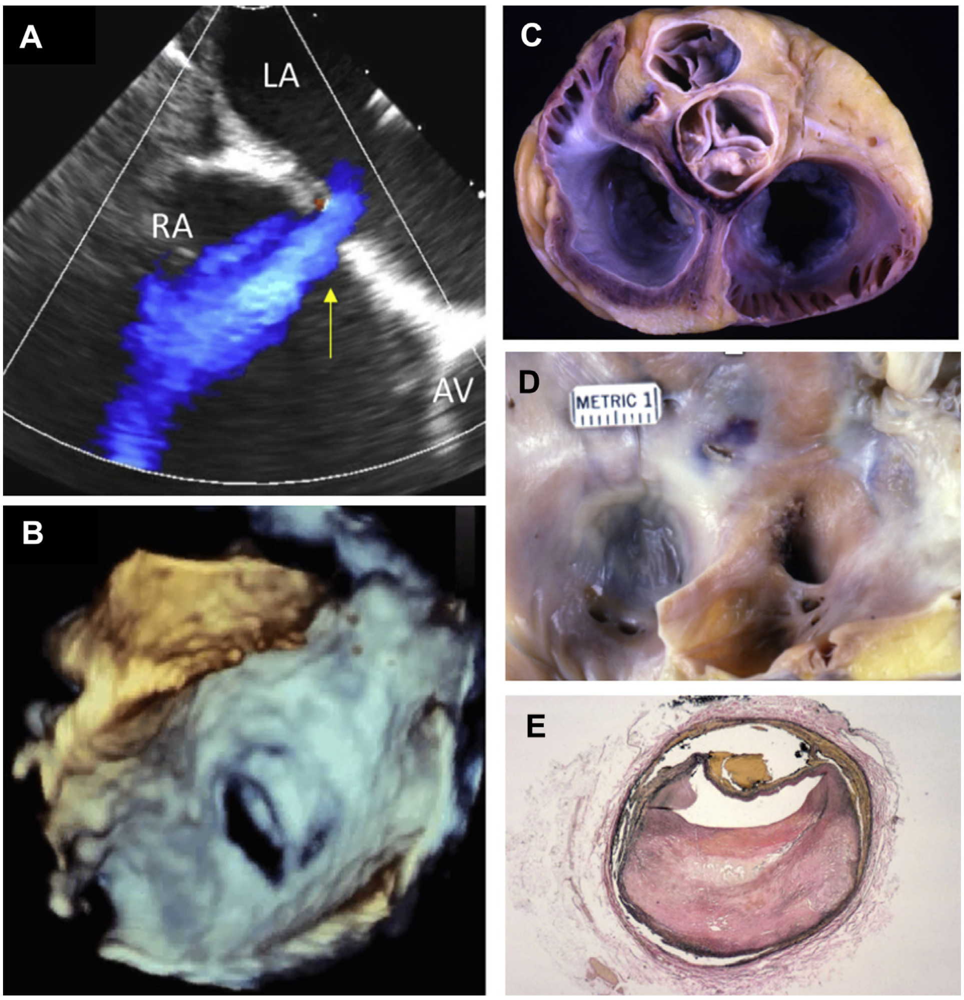


(A, B) Thrombus on the transseptal sheath in the right atrium detected on transesophageal echocardiography **(arrow)**. **(C, D)** Large thrombus formed on the transseptal sheath in the left atrium detected on intracardiac echocardiography.

reported (15,81). Air emboli may enter the left atrium because of accidental injection of air or inadequate de-airing of the system (81). Prevention of air embolism can be achieved largely with meticulous de-airing of the system. Saline infusion to increase LA pressure during the procedure may decrease the likelihood or air embolism (82). However, high-pressure infusion through the side arm of the guiding catheter should be avoided, as it can lead to air embolism when opening the stopcock. Although most cases of air embolism are self-limiting, prompt interventions including volume loading, oxygenation, lidocaine, manual thrombectomy, vasopressors, and hyperbaric oxygen can be effective in treating patients with large air emboli and those with dramatic symptoms (83). It should be noted that transient ST-segment elevation during transseptal procedures is not always explained by coronary air embolism. A vasospastic neurally mediated mechanism (also known as Bezold-Jarisch-like reflex) may be implicated; the mechanical effects of the TSP on the IAS can activate vagal network leading to coronary spasm and ST-segment elevation (84). This hypothesis has been supported by the resolution of electrocardiac abnormalities and hypotension with the administration of atropine or dopamine (85).

IATROGENIC ATRIAL SEPTAL DEFECT. Hypoxemia resulting from large right-to-left shunt can occur after withdrawal of the transseptal sheath but is rare (49). Persistent iatrogenic atrial septal defect after structural and electrophysiological procedures that use the transseptal route are, however, not uncommon, especially when large-bore transseptal sheaths are used. The current research is inconclusive with regard to the clinical significance of persistent iatrogenic atrial septal defect but suggests possible detrimental effects (hypoxemia, heart failure, and systemic embolization) in some patients (49,86).

FIGURE 11 **Complications of Transseptal Puncture**



(A, B) Persistent atrial septal defect **(C to E)** Coronary artery dissection.

Systematic surveillance with serial echocardiography following large-bore access into the left atrium might be necessary, and elective closure of the iatrogenic septal defect should be considered in selected patients (86). Less common complications of TSP include vena cava perforation, coronary artery dissection, detachment of the tip of the transseptal sheath, and acute pericarditis (**Figure 11**) (12,87).

TRAINING IN TSP

The TSP procedure has become an integral part of many electrophysiological and SHD interventions. Although major complications are uncommon, adequate training for TSP is essential to limit potential increases in complication rates because of increasing demand for this procedure (88). Current training for TSP relies on performance on patients with supervision by an experienced operator. Approximately 30 TSPs are needed for a trainee to pass the steepest area of the learning curve (89). Virtual reality simulators (Procedicus VIST, Mentice AB, Gothenburg, Sweden; and Simbionix, Cleveland, Ohio) are novel models that aim to complement the apprenticeship of trainees. The use of such simulators can result in shorter training times and superior post-training performance (88). Partnering among different specialties involved in transseptal procedures (electrophysiology, SHD, congenital heart disease) affords trainees with an excellent opportunity to acquire the necessary TSP skills within the short span of their training programs. At our institution, cardiology fellows are offered a dedicated time in the electrophysiology laboratory to gain experience in TSP during their interventional cardiology and SHD fellowships.

CONCLUSIONS

The field of left-sided SHD interventions continues to grow, leading to a substantial renewed interest in transseptal heart catheterization. Imaging guidance to achieve site-specific puncture and continuous improvement in the available equipment have enhanced the safety and the success of this procedure. Although incremental experience remains pivotal to successful and safe TSP, simulator training and interdisciplinary collaboration can effectively supplement traditional training models.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. David R. Holmes, Jr., Mayo Clinic College of Medicine, Division of Cardiovascular Diseases, 200 First Street SW, Rochester, Minnesota 55905. E-mail: holmes.david@mayo.edu.

REFERENCES

1. Ross J Jr., Braunwald E, Morrow AG. Transseptal left atrial puncture; new technique for the measurement of left atrial pressure in man. Am J Cardiol 1959;3:653–5.

2. Jais P, Haissaguerre M, Shah DC, et al. A focal source of atrial fibrillation treated by discrete radiofrequency ablation. Circulation 1997;95:572–6.

3. Inoue K, Owaki T, Nakamura T, Kitamura F, Miyamoto N. Clinical application of transvenous mitral commissurotomy by a new balloon catheter. J Thorac Cardiovasc Surg 1984;87:394–402.

4. Remenyi B, ElGuindy A, Smith SC Jr., Yacoub M, Holmes DR Jr. Valvular aspects of rheumatic heart disease. Lancet 2016;387:1335–46.

5. Feldman T, Foster E, Glower DD, et al. Percutaneous repair or surgery for mitral regurgitation. N Engl J Med 2011;364:1395–406.

6. Ye J, Cheung A, Yamashita M, et al. Transcatheter aortic and mitral valve-in-valve implantation for failed surgical bioprosthetic valves: an 8-year single-center experience. J Am Coll Cardiol Intv 2015;8:1735–44.

7. Eleid MF, Cabalka AK, Williams MR, et al. Percutaneous transvenous transseptal transcatheter valve implantation in failed bioprosthetic mitral valves, ring annuloplasty, and severe mitral annular calcification. J Am Coll Cardiol Intv 2016;9:1161–74.

8. Ussia GP, Quadri A, Cammalleri V, et al. Percutaneous transfemoral-transseptal implantation of a second-generation CardiAQ mitral valve bioprosthesis: first procedure description and 30-day follow-up. EuroIntervention 2015;11:1126–31.

9. Hwang HY, Choi JW, Kim HK, Kim KH, Kim KB, Ahn H. Paravalvular leak after mitral valve replacement: 20-year follow-up. Ann Thorac Surg 2015;100:1347–52.

10. Taramasso M, Maisano F, Denti P, et al. Surgical treatment of paravalvular leak: long-term results in a single-center experience (up to 14 years). J Thorac Cardiovasc Surg 2015;149:1270–5.

11. Sorajja P, Cabalka AK, Hagler DJ, Rihal CS. Long-term follow-up of percutaneous repair of paravalvular prosthetic regurgitation. J Am Coll Cardiol 2011;58:2218–24.

12. De Ponti R, Cappato R, Curnis A, et al. Transseptal catheterization in the electrophysiology laboratory: data from a multicenter survey spanning 12 years. J Am Coll Cardiol 2006;47:1037–42.

13. Myat A, Patel N, Tehrani S, Banning AP, Redwood SR, Bhatt DL. Percutaneous circulatory assist devices for high-risk coronary intervention. J Am Coll Cardiol Intv 2015;8:229–44.

14. Alkhouli M, Narins CR, Lehoux J, Knight PA, Waits B, Ling FS. Percutaneous decompression of the left ventricle in cardiogenic shock patients on venoarterial extracorporeal membrane oxygenation. J Card Surg 2016;31:177–82.

15. Holmes DR Jr., Kar S, Price MJ, et al. Prospective randomized evaluation of the Watchman left atrial appendage closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. J Am Coll Cardiol 2014;64:1–12.

16. Cribier A, Eltchaninoff H, Bash A, et al. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. Circulation 2002;106:3006–8.

17. Cohen MG, Singh V, Martinez CA, et al. Transseptal antegrade transcatheter aortic valve replacement for patients with no other access approach—a contemporary experience. Catheter Cardiovasc Interv 2013;82:987–93.

18. Eisenhauer AC, Hadjipetrou P, Piemonte TC. Balloon aortic valvuloplasty revisited: the role of the Inoue balloon and transseptal antegrade approach. Catheter Cardiovasc Interv 2000;50:484–91.

19. Abdou SM, Chen YL, Wu CJ, Lau KW, Hung JS. Concurrent antegrade transseptal Inoue-balloon mitral and aortic valvuloplasty. Catheter Cardiovasc Interv 2013;82:E712–7.

20. Matsumoto T, Yeow WL, Kar S. Percutaneous closure of iatrogenic ventricular septal defect following surgical aortic valve replacement using two different approaches. J Invasive Cardiol 2013;25:E42–4.

21. Matsumoto T, Okuyama K, Cheng W, Makkar RR, Kar S. Transseptal closure of left ventricular pseudoaneurysm post-transapical transcatheter aortic valve replacement. J Am Coll Cardiol Intv 2014;7:e177–8.

22. Ross J Jr. Transseptal left heart catheterization a 50-year odyssey. J Am Coll Cardiol 2008;51:2107–15.

23. Thompson AJ, Hagler DJ, Taggart NW. Transseptal puncture to facilitate device closure of "long-tunnel" patent foramen ovale. Catheter Cardiovasc Interv 2015;85:1053–7.

24. Yoon YS, Shim WH. Transseptal approach for stent implantation in right internal carotid artery stenosis. J Invasive Cardiol 2000;12:70–4.

25. Joseph G, Chacko ST, Stephen E, Joseph E. Transseptal ascending aortic access facilitates transcatheter embolization of proximal type I endoleak associated with bird-beak configuration of an endograft in the proximal aortic arch. J Endovasc Ther 2014;21:805–11.

26. Joseph G, Stephen E, Chacko S, Sen I, Joseph E. Transseptal ascending aortic access and snare-assisted pull down of the delivery system to facilitate stent-graft passage in the aortic arch during TEVAR. J Endovasc Ther 2013;20:223–30.

27. Kolbel T, Rostock T, Larena-Avellaneda A, Treede H, Franzen O, Debus ES. An externalized transseptal guidewire technique to facilitate guidewire stabilization and stent-graft passage in the aortic arch. J Endovasc Ther 2010;17:744–9.

28. Wang R, Souza Filho NS, Lima Filho A, Moreira MV. Transseptal coronary angioplasty in patients with severe peripheral vascular disease. Arq Bras Cardiol 2013;101:e11–4.

29. Galie N, Corris PA, Frost A, et al. Updated treatment algorithm of pulmonary arterial hypertension. J Am Coll Cardiol 2013;62:D60–72.

30. Alkhouli MA, Raybuck BD, Badhwar V. Navigating the S-curve of transapical therapy. J Thorac Cardiovasc Surg 2016;152:781–2.

31. Cavalcante JL, Rodriguez LL, Kapadia S, Tuzcu EM, Stewart WJ. Role of echocardiography in percutaneous mitral valve interventions. J Am Coll Cardiol Img 2012;5:733–46.

32. Singh GD ST, Rogers JH. Targeted transseptal access for MitraClip percutaneous mitral valve repair. Intervent Cardiol Clinic 2016;5:55–69.

33. Merchant FA DD. Site-specific transseptal cardiac catheterization guided by intracardiac echocardiography for emerging electrophysiology applications. J Innov Card Rhythm Manage 2013;4:1415–27.

34. Bazaz R, Schwartzman D. Site-selective atrial septal puncture. J Cardiovasc Electrophysiol 2003;14:196–9.

35. Ruisi CP, Brysiewicz N, Asnes JD, et al. Use of intracardiac echocardiography during atrial fibrillation ablation. Pacing Clin Electrophysiol 2013;36:781–8.

36. Koermendy D, Nietlispach F, Shakir S, et al. Amplatzer left atrial appendage occlusion through a patent foramen ovale. Catheter Cardiovasc Interv 2014;84:1190–6.

37. Gafoor S, Schulz P, Heuer L, et al. Use of EchoNavigator, a novel echocardiography-fluoroscopy overlay system, for transseptal puncture and left atrial appendage occlusion. J Interv Cardiol 2015;28:215–7.

38. Bayrak F, Chierchia GB, Namdar M, et al. Added value of transoesophageal echocardiography during transseptal puncture performed by inexperienced operators. Europace 2012;14:661–5.

39. Kim SS, Hijazi ZM, Lang RM, Knight BP. The use of intracardiac echocardiography and other intracardiac imaging tools to guide noncoronary cardiac interventions. J Am Coll Cardiol 2009;53:2117–28.

40. Sundermann SH, Biaggi P, Grunenfelder J, et al. Safety and feasibility of novel technology fusing echocardiography and fluoroscopy images during MitraClip interventions. EuroIntervention 2014;9:1210–6.

41. Bourier F, Reents T, Ammar-Busch S, et al. Transseptal puncture guided by CT-derived 3D-augmented fluoroscopy: transseptal puncture guided by 3D-fluoroscopy. J Cardiovasc Electrophysiol 2016;27:369–72.

42. Nazarian S, Kolandaivelu A, Zviman MM, et al. Feasibility of real-time magnetic resonance imaging for catheter guidance in electrophysiology studies. Circulation 2008;118:223–9.

43. Koektuerk B, Yorgun H, Koektuerk O, et al. Rotational angiography based three-dimensional left atrial reconstruction: a new approach for transseptal puncture. Cardiovasc Ther 2016;34:49–56.

44. Rajappan K, Baker V, Richmond L, et al. A randomized trial to compare atrial fibrillation ablation using a steerable vs. a non-steerable sheath. Europace 2009;11:571–5.

45. Piorkowski C, Eitel C, Rolf S, et al. Steerable versus nonsteerable sheath technology in atrial fibrillation ablation: a prospective, randomized study. Circ Arrhythm Electrophysiol 2011;4:157–65.

46. Winkle RA, Mead RH, Engel G, Kong MH, Patrawala RA. Physician-controlled costs: the choice of equipment used for atrial fibrillation ablation. J Interv Card Electrophysiol 2013;36:157–65.

47. Hsu JC, Badhwar N, Gerstenfeld EP, et al. Randomized trial of conventional transseptal needle versus radiofrequency energy needle puncture for left atrial access (the TRAVERSE-LA study). J Am Heart Assoc 2013;2:e000428.

48. Wieczorek M, Hoeltgen R, Akin E, Salili AR. Use of a novel needle wire in patients undergoing transseptal puncture associated with severe septal tenting. J Interv Card Electrophysiol 2010;27:9–13.

49. Alkhouli M, Sarraf M, Zack CJ, Holmes DR, Rihal CS. Iatrogenic atrial septal defect following transseptal cardiac interventions. Int J Cardiol 2016;209:142–8.

50. Sy RW, Klein GJ, Leong-Sit P, et al. Troubleshooting difficult transseptal catheterization. J Cardiovasc Electrophysiol 2011;22:723–7.

51. Alkhouli M, Morad M, Narins CR, Raza F, Bashir R. Inferior vena cava thrombosis. J Am Coll Cardiol Intv 2016;9:629–43.

52. Chiam PT, Ruiz CE, Cohen HA. Placement of a large transseptal cannula through an inferior vena cava filter for TandemHeart percutaneous left ventricular assist. J Invasive Cardiol 2008;20:E197–9.

53. Martinez G, Lindefjeld D, Martinez A. Transfemoral approach through inferior vena cava filters for complex cardiac interventions: expanding the limits. J Invasive Cardiol 2013;25:E57–9.

54. Vyas C, Shah S, Patel T. Percutaneous transvenous mitral commissurotomy via left femoral vein approach—exploring an unusual approach for left atrial entry. J Invasive Cardiol 2011;23:E145–6.

55. Baszko A, Kalmucki P, Dankowski R, Lanocha M, Siminiak T, Szyszka A. Transseptal puncture from the jugular vein and balloon cryoablation for atrial fibrillation in a patient with azygos continuation of an interrupted inferior vena cava. Europace 2015;17:1153–6.

56. Sullebarger JT, Coto H, Lopez E, Sayad D, Fontanet HL. Transjugular percutaneous Inoue balloon mitral commissurotomy in a patient with inferior vena cava obstruction after liver transplantation. Catheter Cardiovasc Interv 2003;59:261–5.

57. Frerker C, Meincke F, Seibert HP, et al. MitraClip® via direct right atrial access in case of a missing inferior vena cava. EuroIntervention 2013;9:643–7.

58. Ramasamy D, Zambahari R, Fu M, Yeh KH, Hung JS. Percutaneous transvenous mitral commissurotomy in patients with severe kyphoscoliosis. Cathet Cardiovasc Diagn 1993;30:40–4.

59. Hu YF, Tai CT, Lin YJ, et al. The change in the fluoroscopy-guided transseptal puncture site and difficult punctures in catheter ablation of recurrent atrial fibrillation. Europace 2008;10:276–9.

60. Marcus GM, Ren X, Tseng ZH, et al. Repeat transseptal catheterization after ablation for atrial fibrillation. J Cardiovasc Electrophysiol 2007;18:55–9.

61. Shirani J, Zafari AM, Roberts WC. Morphologic features of fossa ovalis membrane aneurysm in the adult and its clinical significance. J Am Coll Cardiol 1995;26:466–71.

62. Capulzini L, Paparella G, Sorgente A, et al. Feasibility, safety, and outcome of a challenging transseptal puncture facilitated by radiofrequency energy delivery: a prospective single-centre study. Europace 2010;12:662–7.

63. Arkles J, Zado E, Supple G, et al. Feasibility of transseptal access in patients with previously scarred or repaired interatrial septum. J Cardiovasc Electrophysiol 2015 Jun 15 [E-pub ahead of print].

64. Li X, Wissner E, Kamioka M, et al. Safety and feasibility of transseptal puncture for atrial fibrillation ablation in patients with atrial septal defect closure devices. Heart Rhythm 2014;11:330–5.

65. Santangeli P, Di Biase L, Burkhardt JD, et al. Transseptal access and atrial fibrillation ablation guided by intracardiac echocardiography in patients with atrial septal closure devices. Heart Rhythm 2011;8:1669–75.

66. Lakkireddy D, Rangisetty U, Prasad S, et al. Intracardiac echo-guided radiofrequency catheter ablation of atrial fibrillation in patients with atrial septal defect or patent foramen ovale repair: a feasibility, safety, and efficacy study. J Cardiovasc Electrophysiol 2008;19:1137–42.

67. Zadeh AA, Cannom DS, Macrum BL, Ho IC. The use of balloon atrial septostomy to facilitate difficult transseptal access in patients undergoing catheter ablation for atrial fibrillation. J Cardiovasc Electrophysiol 2011;22:822–4.

68. Roelke M, Smith AJ, Palacios IF. The technique and safety of transseptal left heart catheterization: the Massachusetts General Hospital experience with 1,279 procedures. Cathet Cardiovasc Diagn 1994;32:332–9.

69. Holmes DR Jr., Nishimura R, Fountain R, Turi ZG. Iatrogenic pericardial effusion and tamponade in the percutaneous intracardiac intervention era. J Am Coll Cardiol Intv 2009;2:705–17.

70. Cappato R, Calkins H, Chen SA, et al. Prevalence and causes of fatal outcome in catheter ablation of atrial fibrillation. J Am Coll Cardiol 2009;53:1798–803.

71. Wasmer K, Zellerhoff S, Kobe J, et al. Incidence and management of inadvertent puncture and sheath placement in the aorta during attempted transseptal puncture. Europace 2016 Mar 21 [E-pub ahead of print].

72. Mijangos-Vazquez R, Garcia-Montes JA, Zabal-Cerdeira C. Aortic iatrogenic perforation during transseptal puncture and successful occlusion with Amplatzer ductal occluder in a case of mitral paravalvular leak closure. Catheter Cardiovasc Interv 2016;88:312–5.

73. Hartono B, Razakjr OA, Munawar M. Amplatzer septal occluder sealed the complicating aortic root perforation during transseptal procedure. J Am Coll Cardiol Intv 2012;5:450–1.

74. Ren JF, Marchlinski FE, Callans DJ, et al. Increased intensity of anticoagulation may reduce risk of thrombus during atrial fibrillation ablation procedures in patients with spontaneous echo contrast. J Cardiovasc Electrophysiol 2005;16:474–7.

75. Hamm K, Barth S, Diegeler A, Kerber S. Stroke and thrombus formation appending to the MitraClip: what is the appropriate anticoagulation regimen? J Heart Valve Dis 2013;22:713–5.

76. Aizawa Y, Nakai T, Kurosawa T, et al. Giant thrombus formation immediately after mitral valvuloplasty. Int Heart J 2015;56:668–70.

77. Martinek M, Sigmund E, Lemes C, et al. Asymptomatic cerebral lesions during pulmonary vein isolation under uninterrupted oral anticoagulation. Europace 2013;15:325–31.

78. Ichiki H, Oketani N, Ishida S, et al. Incidence of asymptomatic cerebral microthromboembolism after atrial fibrillation ablation guided by complex fractionated atrial electrogram. J Cardiovasc Electrophysiol 2012;23:567–73.

79. Frerker C, Schluter M, Sanchez OD, et al. Cerebral protection during MitraClip implantation: initial experience at 2 centers. J Am Coll Cardiol Intv 2016;9:171–9.

80. Maleki K, Mohammadi R, Hart D, Cotiga D, Farhat N, Steinberg JS. Intracardiac ultrasound detection of thrombus on transseptal sheath: incidence, treatment, and prevention. J Cardiovasc Electrophysiol 2005;16:561–5.

81. Franzen OW, Klemm H, Hamann F, et al. Mechanisms underlying air aspiration in patients undergoing left atrial catheterization. Catheter Cardiovasc Interv 2008;71:553–8.

82. Mobius-Winkler S, Majunke N, Sandri M, et al. Percutaneous left atrial appendage closure: technical aspects and prevention of periprocedural complications with the watchman device. World J Cardiol 2015;7:65–75.

83. Mofrad P, Choucair W, Hulme P, Moore H. Case report: cerebral air embolization in the electrophysiology laboratory during transseptal catheterization: curative treatment of acute left hemiparesis with prompt hyperbaric oxygen therapy. J Interv Card Electrophysiol 2006;16:105–9.

84. Letsas KP, Pappas LK, Gavrielatos G, Efremidis M, Sideris A, Kardaras F. ST-segment elevation induced during the transseptal procedure for radiofrequency catheter ablation of atrial fibrillation. Int J Cardiol 2007;114:e12–4.

85. Tang RB, Dong JZ, Long DY, et al. Incidence and clinical characteristics of transient ST-T elevation during transseptal catheterization for atrial fibrillation ablation. Europace 2015;17:579–83.

86. Alkhouli M, Sarraf M, Holmes DR. Iatrogenic atrial septal defect. Circ Cardiovasc Interv 2016;9:e003545.

87. Schricker AA, Feld GK, Tsimikas S. Retrieval of a detached transseptal sheath tip from a right pulmonary artery branch following catheter ablation. Catheter Cardiovasc Interv 2015;86:1131–5.

88. De Ponti R, Marazzi R, Ghiringhelli S, Salerno-Uriarte JA, Calkins H, Cheng A. Superiority of simulator-based training compared with conventional training methodologies in the performance of transseptal catheterization. J Am Coll Cardiol 2011;58:359–63.

89. Yao Y, Ding L, Chen W, et al. The training and learning process of transseptal puncture using a modified technique. Europace 2013;15:1784–90.

KEY WORDS fossa ovalis, left atrial appendage, mitral valve repair, transseptal puncture, pulmonary vein isolation, site-specific puncture

APPENDIX For supplemental tables, please see the online version of this article.