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REVIEW

Three-dimensional imaging of the atrial septum and patent foramen ovale anatomy: defining the morphological phenotypes of patent foramen ovale

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Patent foramen ovale (PFO) is known to occur with greater prevalence in those with cryptogenic stroke. These observations support the role of a PFO as a channel for paradoxical embolism and a mechanism for cerebral ischaemic events. Transcatheter closure of PFO may be indicated in this setting. A prerequisite of procedural success is achieving complete closure of the shunt. Studies have shown a varying degree of successful shunt closure. Residual shunts are usually the result of a mismatch between the device shape and PFO anatomy. In this article, we review the features of PFO and their surrounding structures as seen by three-dimensional transoesophageal echocardiography in patients undergoing transcatheter closure and relate these to the variations in morphology on anatomical specimens for a better appreciation of their suitability for closure devices. The salient features of the anatomical variations seen in adults undergoing transcatheter device closure have been summarized and used to produce a practical pre-procedural checklist.

Keywords Patent foramen ovale • Anatomy • Three-dimensional echocardiography • Transoesophageal echocardiography

Introduction

Patent foramen ovale (PFO) is known to occur with greater prevalence in those with cryptogenic stroke.[1–3] This association is more pronounced in the young.[4] These observations support the role of a PFO as a channel for paradoxical embolism, a mechanism for cerebral ischaemic events. Transcatheter closure of PFO is indicated in this setting, where no other cause including cardiovascular risk factors is found, and a PFO is thought to be a likely contributor. This technique is associated with a high success rate, low incidence of procedural and in-hospital complications, and excellent results on long-term follow-up.[5–7]

A prerequisite of procedural success is achieving complete closure of the shunt. Studies have shown a varying degree of successful shunt closure in the intermediate-to-longer term, ranging from 73,[6] 78,[8] 86[5] to 100%.[7] However, the cause of the residual shunt is not clear from the literature. A greater incidence of residual shunting post-procedure has been reported in those with a concomitant atrial septal aneurysm.[9,10] We have reported previously on the morphological features of the PFO,[11] but there are no publications on detailed assessments of the anatomy of the device post-implantation. In our experience, residual shunts are usually the result of a mismatch between the device shape and PFO anatomy. Three-dimensional transoesophageal echocardiography (3D TEE) has revolutionized our ability to understand the anatomy of the atrial septum and PFO morphology in real time. In this article, we review the features of PFO and their surrounding structures as seen by three-dimensional transoesophageal echocardiography in patients undergoing transcatheter closure and relate these to the variations in morphology on anatomical specimens for a better appreciation of their suitability for closure devices.

Anatomy of the atrial septum and patent foramen ovale

The PFO is persistence of the foetal interatrial communication at the site of the embryonic ostium secundum. In foetal life, blood from the inferior caval vein is directed preferentially to the

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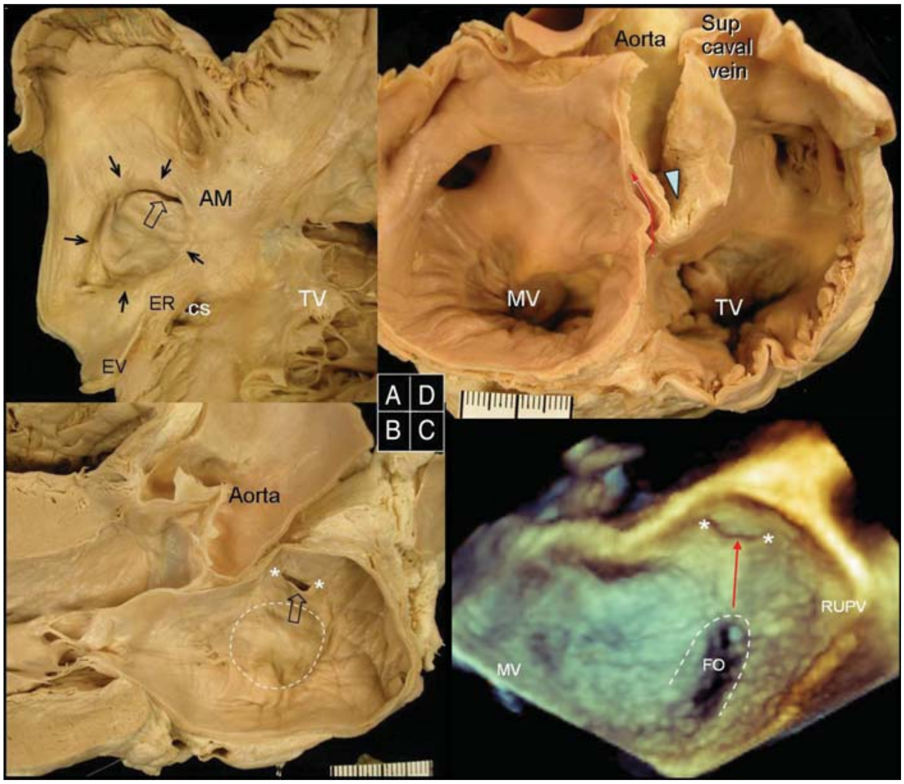

Figure 1 *Long tunnel patent foramen ovale.* (*A*) and (*B*) are right and left atrial views of the septal aspect of the same heart showing a patent foramen ovale (open arrow). The right atrial aspect is characterized by the muscular rim (black arrows), whereas the left atrial aspect is flat with a crescentic opening (between asterisks). The Eustachian valve (EV), Eustachian ridge (ER), and aortic mound (AM) are features of the right atrium. Broken line corresponds to the muscular rim around the fossa on the right atrial side. (*C*) Three-dimensional transoesophageal echocardiography image of left atrium showing an enface view of the atrial septum. Asterisks show opening of patent foramen ovale into left atrium. Red arrow shows course of patent foramen ovale tunnel beginning at the superior aspect of fossa ovalis (FO) from the right atrial aspect and running upwards and opening into the roof of the left atrium. (*D*) This cross-sectional view of the atrial septum shows the tunnel of the patent foramen ovale (red arrow) passing between the infolding (triangle) of the right atrial wall (septum secundum) and the flap valve of the fossa (septum primum). MV, mitral valve; RUPV, right upper pulmonary vein; TV, tricuspid valve.

foramen ovale by the Eustachian valve. The septum primum (primary septum), which forms the floor of the oval fossa is like a flap that is large enough to overlap the rim (or limbus) formed by the septum secundum (secondary septum). The latter is an infolding of the atrial wall on the right atrial side that gives the fossa a raised margin. Thus, the right atrial aspect of the septum is characterized by the rim, which is lacking on the left atrial side (*Figure 1*). The overlap of the flap against the rim allows the foramen ovale to be closed at birth upon increase in left atrial pressure. Soon after, there is adherence of the flap valve to the rim and usually adhesion is complete by the first year of life resulting in total obliteration of the foetal communication. However, a gap, the PFO, persists in the antero-superior margin in 25–35% of hearts examined at routine autopsy.[12] Since the flap valve is larger than the fossa, the length of the overlap can be considerable, resulting in a tunnel-like PFO, especially if the width of the channel is narrow (*Figure 1*). Our small series of heart specimens showed a length of 1–6 mm and widths of 5–13 mm along the curve of the rim.[11] Taking the PFO to be of tunnel-like configuration, the right atrial entrance is bordered by the firm antero-superior rim of the fossa, which is the muscular fold while the posterior border is the pliable and thin flap valve. Its left atrial entrance is marked by the crescentic free edge of the embryonic septum primum. The opening is located close to the antero-superior wall of the left atrium (*Figure 1B*). This proximity should be borne in mind, especially when attempting to negotiate a catheter through a long and narrow tunnel which, in addition, may be meandering. The risk of exiting the heart is particularly relevant because this part of the atrial wall may be exceptionally thin.[13,14]

For overall approach to the atrial septum as viewed from the right atrial aspect, the septum appears extensive at first sight. In reality, the true septum is the floor of the fossa ovale and its immediate muscular rim.[15] Of note to interventionists is the extensive anterior margin, which includes the aortic mound that overlies the aortic root on the epicardial side.[16] The size and location of the fossa ovalis varies from heart to heart.[17] The prominence of its rim also varies. A flat rim blending with the fossa flap occurs in nearly 20% of hearts.[18] The flap valve is usually a thin fibro-muscular sheet, 0.5–1.5 mm thick, rather taut against the fossa margin. Occasionally, there are one or several fenestrations in the flap. These are deficiencies of the septum primum, or oval fossa defects, rather than so-called secundum atrial septal defects. The entire flap can also be redundant and aneurysmal with a tendency to be associated with a large fossa. The infolded rim is filled with epicardial fat to varying thicknesses. In young adults the upper limit of normal fat deposit is defined as 1.5 cm in transverse dimension, not to be mistaken for lipomatous septal hypertrophy.[19]

The orifice of the inferior caval vein is located inferiorly and posteriorly relative to the fossa. It is guarded by the Eustachian valve, which is usually shaped like a crescentic flap of varying heights. The medial insertion of the Eustachian valve toward the cardiac septum is to the Eustachian ridge (sinus septum) that, in turn, continues to the antero-inferior rim of the fossa. Thus, it is conceivable that a prominent flap-like Eustachian valve and ridge can guideflow toward the foramen ovale. In approximately 2% of hearts, the Eustachian valve is large and fenestrated. Rarely, it is an extensive Chiari network. Although not readily visualized on imaging, the network can be entangled during catheter manoeuvres.

Important considerations when assessing PFO anatomy for device closure

Description of anatomy is necessary such that a clear perception of the defect is then possible. This will enable the operator to understand how the defect will or is likely to behave once a percutaneous closure device is deployed through it. There are several types of device available and each has its range of sizes (including Amplatzer® PFO occluder (AGA Medical Corporation), Helix® septal occluder (W.L.Gore and Associates, Inc.), BioSTAR® (NMT Medical, Inc.), Solysafe device® (Swissimplant®) and Premere™ PFO closure system (St Judes)). The aim is to achieve complete closure of the defect so that no right to left shunting remains. The complexity of the PFO anatomy can result in a device position that in fact causes the defect to remain patent and shunting may even be greater than prior to device placement. If at the outset the anatomical description can be precisely understood, it is our belief that such procedure failure could be avoided.

A detailed assessment of the PFO is performed with transoesophageal echocardiography.[20] This assessment is pivotal in deciding the suitability of the defect for device closure. As our clinical experience in imaging PFO and the atrial septum with 3D TEE grows, previous undefined anatomical variations become apparent. Indeed, real-time 3D TEE has brought with it a new era, where, in life, with a blood-filled beating heart the reality of the atrial septum and its neighbouring structures are appreciated. How this impacts on the shape of the defect and issues surrounding its closure, with a percutaneous device, become evident, in a way not appreciated previously. Thus, what is now needed is a detailed understanding of the variation in the types of anatomy. This is best achieved by categorizing these differences. The types of defects possible can be broadly grouped into simple and complex. A simple PFO usually can be closed with most standard devices. Essentially a PFO falls into this group by excluding specific characteristics that, if present, are considered 'complex' and require special consideration of the most suitable type and size of device necessary to achieve long-term closure. *Table 1* summarizes these characteristics.

Table 1 Categories of patent foramen ovale

PFO category	Anatomical characteristics
1. Simple	Standard anatomy, i.e. none of the below
2. Complex	Long tunnel length (≥8 mm)
	Multiple openings into left atrium
	Atrial septal aneurysm
	Hybrid defect
	Thick secondary septum (≥10 mm)
	Eustachian ridge
	Eustachian valve or Chiari network

Defining the morphological phenotypes in the context of suitability for device closure

Simple PFO

This is a standard PFO with tunnel length <8 mm, without an atrial septal aneurysm, without a large Eustachian ridge or valve, without a thickened secondary septum (septum secundum), i.e. <10 mm, and without other defects of the fossa ovalis (see below). Most types of devices will be suitable for this type of PFO. If all other features listed above are not present except the orifice opening(s) are >10 mm then consideration to the size of device, usually a larger device, will be needed.

Complex PFO

PFO with a long tunnel length, usually >8 mm

Tunnel length of a PFO, if more than or equal to 8 mm usually causes a device with a short waist (i.e. most device types) to sit in the defect partially unfolded. This is the case particularly if the tunnel is narrow in addition to being long. Even when the tunnel is wide but with relatively rigid margins, i.e. the primary septum (septum primum) of the fossa ovalis is not aneurysmal, then its length becomes important in the choice of device (*Figure 2*). By 'aneurysmal' we mean thin, excessively mobile and redundant tissue where the overlapping valve tissue can be 'bunched up', so not necessarily causing such an issue.

Multiple openings of PFO on left atrial side

We have observed a number of PFO's, which have multiple openings (of a PFO) into the left atrium. This is created by a strand tissue of the primary septum being 'stuck down' (or tethered) to the secondary septum at the point of its opening into the left atrium causing two separate orifices (*Figure 3*). The morphology is not easily appreciated on 2D TEE imaging. It becomes relevant if one is to ensure both orifices have been covered by a device placed through one of the openings, and the defect(s) completely sealed.

Atrial septal aneurysm

The atrial septal aneurysm essentially is a description of the size and mobility of the tissue of the fossa ovalis, i.e. the primary septum. This mobility has been arbitrarily described in the literature as a sway of the septum in either direction from the midline of >10 mm, by echocardiography.[21] This description can be further refined by describing the margins of the aneurysm. This usually involves describing the proportion of tissue occupied by the fossa ovalis as a percentage of the entire atrial septum. The purpose is to create an understanding of the fragility of the septum when placing a device and hence the risk of device displacement, i.e. the amount of available 'rims' to securely anchor the device. This information helps decide on the size of device to use.

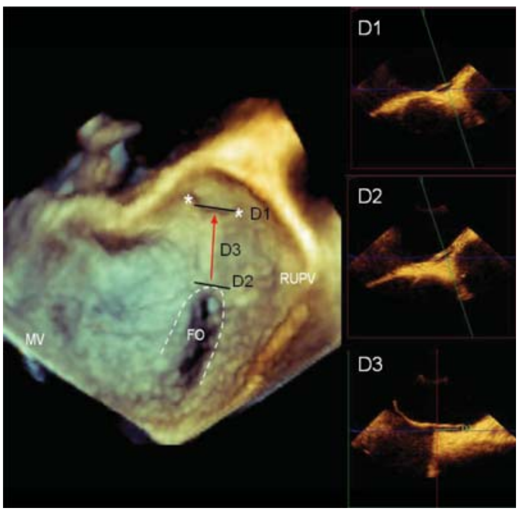

Figure 2 *Dimensions of a patent foramen ovale.* Three-dimensional transoesophageal echocardiography image using 3D QLab software, Philips Healthcare (right panel, D1–3). D1, opening of patent foramen ovale into the left atrium, 10 mm. D2, opening of the patent foramen ovale at the right atrium aspect, situated at the superior aspect of fossa ovalis, 9 mm. D3, length of the tunnel of the PFO, 11 mm.

Hybrid defect

The term 'hybrid defect' is used here to describe the concomitant occurrence of a PFO with additional defects on the fossa ovalis. They may be in the form of multiple small defects or discrete defects either single or multiple (*Figure 4*). They may occur anywhere within the fossa ovalis. Identifying this type of anatomy becomes extremely relevant in the setting of presumed paradoxical embolism. All defects must be included within device(s) coverage. Otherwise a clinically significant shunt may remain.

Excessive thickening of secondary septum (septum secundum)

The thickness of the secondary septum (infolded tissue) varies between individuals. The degree of thickness is due to the amount of extra-cardiac tissue, usually adipose tissue contained within this infolded tissue (*Figure 5*). This has important bearing on how a device may sit through a PFO. The discs of a device may not be able to sit flush against the fossa ovalis if the surrounding secondary septum is excessively bulky. In our experience a thickness of 10 mm or more can cause problems with device position. A small size or softer type of device will usually be considered. The softer type device, such as Biostar® (NMT Medical, Inc.) is able to conform to the change in septum shape from the thin flap valve to the excessively bulky secondary septum.

Presence of Eustachian ridge

Increasingly, it is being recognized that the presence of a large bulky Eustachian ridge (ER) may pose issues with device placement (*Figure 6*). This ridge limits the space available over the fossa ovalis on the right atrial side and may cause a PFO device to sit away

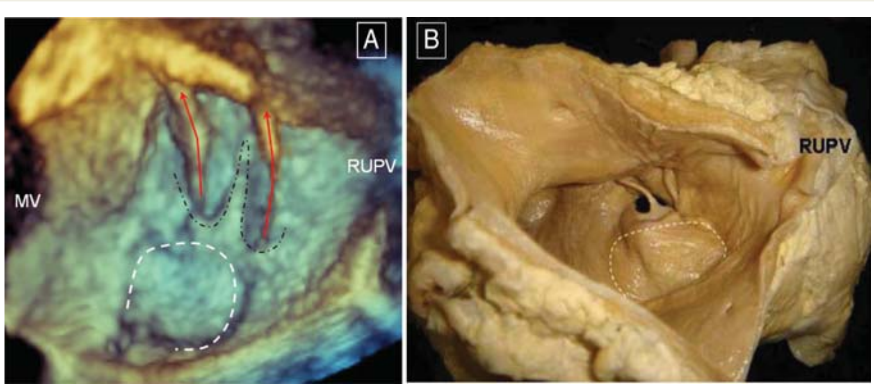

Figure 3 *Double orifice patent foramen ovale.* (*A*) Three-dimensional transoesophageal echocardiography view of atrial septum from left atrium. There are two openings of the patent foramen ovale into the left atrium, outlined by dotted black line. The primary septum (septum primum) is attached to the secondary septum (septum secundum) in the middle of the patent foramen ovale opening on the left atrial side creating two orifices. The red lines depict the passage of two separate guidewires, each passing through the two orifices. Fossa ovalis position on the right atrial side is shown by the white dotted line. (*B*) A heart specimen with the corresponding morphology of the patent foramen ovale displayed in the same orientation. MV, mitral valve and RUPV, right upper pulmonary valve.

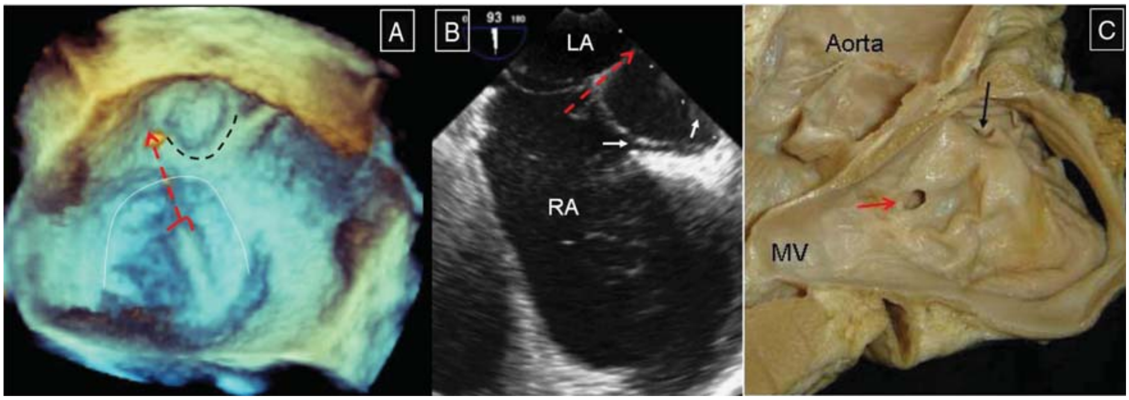

Figure 4 *Hybrid defect.* (*A*) Three-dimensional transoesophageal echocardiography enface view of atrial septum viewed from left atrium and (*B*) two-dimensional transoesophageal echocardiography image. The fossa ovalis (demarcated by white line) has redundant aneurymal tissue, a guidewire (red dotted arrow) has entered the left atrium through a small fenestration, of which there are several, in the fossa ovalis. A PFO is also present, its opening into the left atrium is demarcated in (*A*) by the dotted black line and in (*B*) by white arrows. (*C*) This left atrial aspect of an aneurysmal fossa valve shows the PFO opening (black arrow) and another defect (red arrow). LA, left atrium; MV, mitral valve; RA, right atrium.

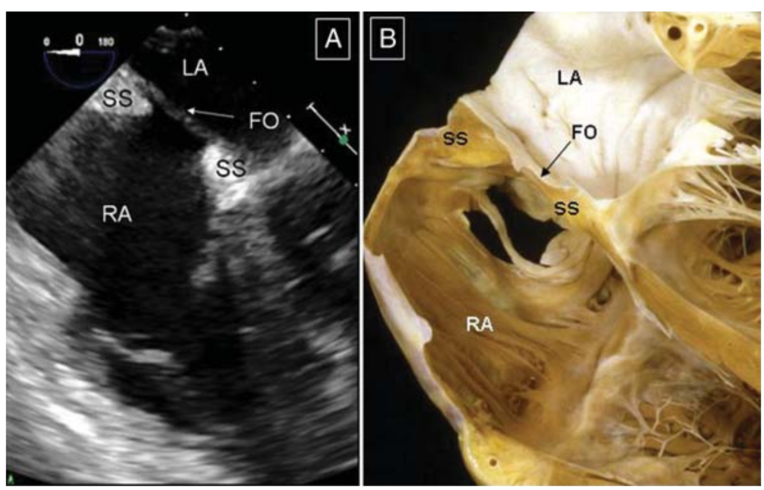

Figure 5 *Thick secondary septum*. (*A*) Two-dimensional transoesophageal echocardiography image shows a thickened secondary septum (SS), measuring 11 mm. (*B*) A heart section in similar orientation shows fatty tissues filling the infolding of the SS. FO, fossa ovalis; LA, left atrium; RA, right atrium.

from the fossa ovalis. The disc may rest on the Eustachian ridge and result in the PFO tunnel being held open and a residual shunt remaining. In addition, attachment of primary septum on the left atrial side may be under tension (presumed to be a result of the ER pulling on the atrial septum) such that it is held away from secondary septum with a persistently open PFO. A very careful assessment on 2D TEE imaging is needed if 3D TEE is not available. In our experience 3D is needed to accurately assess how such a structure will impact on device choice and size.

Presence of Eustachian valve (or Chiari network)

Excessive redundant tissue may attach to the Eustachian ridge and guard the inferior vena cava (IVC) orifice. This Eustachian valve has the potential to interfere with device placement. Passing the guidewire may be difficult. The Eustachian valve can become caught in the device during deployment and this may interfere with the device position or pose an embolic risk if drawn across the septum into the left atrium. A Chiari network, although rare, is usually more extensive and will present similar concerns.

Pre-procedural checklist

Practical approach to describing atrial septum characteristics for suitability to device closure is suggested below, see also *Figure 2*. Essentially we propose a pre-procedural checklist.

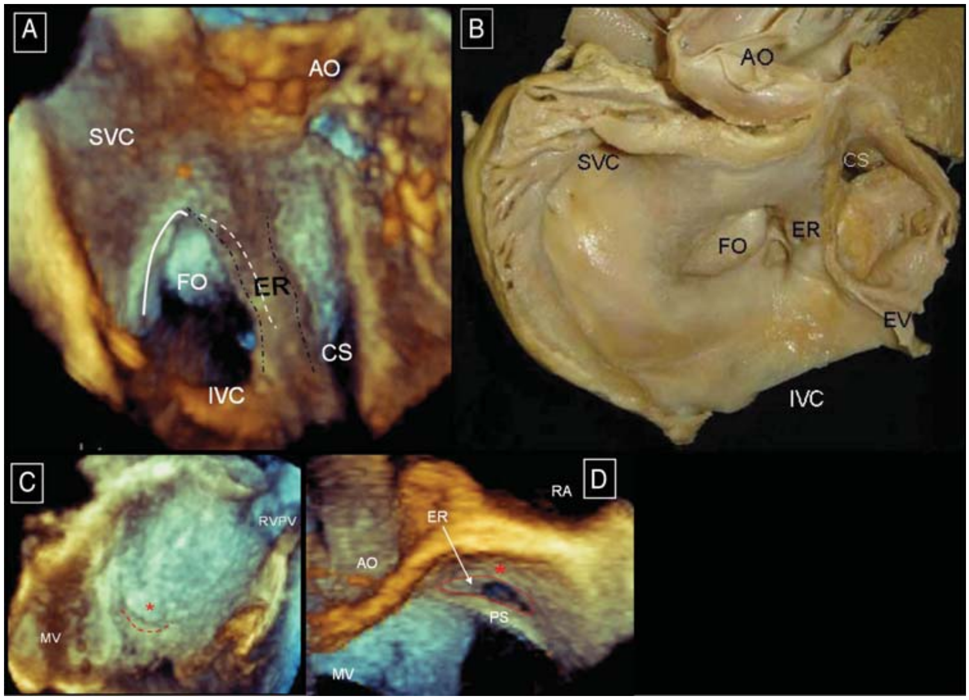

Figure 6 *Eustachian ridge*. (*A*) Three-dimensional transoesophageal echocardiography image, enface view of atrial septum seen from the right atrium. A large Eustachian ridge (ER, black dotted line) is seen to extend from the orifice of the IVC and attach to the superior aspect of the fossa ovalis (FO). FO is demarcated by white line. The dotted white line shows the remainder of the FO which is hidden behind the ER. (*B*) A heart specimen tilted in comparable orientation shows the continuation of the ER into the rim of the FO. In this heart there are depressions between the FO and the ER. (*C*) Three-dimensional transoesophageal echocardiography image, left atrial view of septum. Red dotted line demarcates the PFO opening. Red asterisk shows concave recess formed by tension on septum by ER. (*D*) Three-dimensional transoesophageal echocardiography image, dotted red line shows PFO opening viewed from above, directly looking into the PFO from left atrium. CS, coronary sinus orifice; AO, aorta; SVC, superior vena cava; RA, right atrium; MV, mitral valve; RUPV, right upper pulmonary vein; PS, primary septum.

Measurements of the entrance (right atrium) and exit (left atrium) of PFO and its tunnel length can be performed very accurately using real-time 3D TEE image data sets. Software is available on line (QLab 3DQ, Philips Healthcare), which allows rapid analysis of the 3D data sets. If the atrial septum is aneurysmal then any measurements made of the PFO tunnel length and openings (left and right side) may not be adequate alone. Some operators may prefer to balloon size the defect at the time of closure.

- (i) Size of left atrial opening (performed with 3D TEE, see *Figure 2*).
- (ii) Size of right atrial opening (performed with 3D TEE, see *Figure 2*).
- (iii) Total length of the PFO tunnel, from right to left atrial opening (see *Figure 2*).
- (iv) Presence of other defects, usually within the fossa ovalis.
- (v) Multiple openings of the PFO into the left atrium.
- (vi) Atrial septum aneurysm, mobility, and margins.
- (vii) Thickness of secondary septum (septum secundum).
- (viii) Eustachian ridge, extent, and location.
- (ix) Eustachian valve (or Chiari network) presence, extent, and location.

Conclusion

We have presented a new approach to characterizing PFO morphology, combining 3D imaging with anatomical findings. To achieve procedure success with complete PFO closure, an understanding of the PFO defect shape is necessary in order to relate how a particular device will behave once deployed. The salient features of the anatomical variations seen in adults undergoing transcatheter device closure have been summarized and used to produce a practical pre-procedural checklist.

Conflict of interest: none declared.

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