

## Review Article

# Anatomo-functional characterization of interatrial septum for catheter-based interventions

Gianluca Rigatelli, Beatrice Magro, Laura Oliva

Section of Congenital Heart Disease Interventions, Cardiovascular Diagnosis and Endoluminal, Interventions Unit, Rovigo General Hospital, Rovigo, Italy

Received July 7, 2011; accepted July 27, 2011; Epub August 10, 2011; published September 30, 2011

**Abstract:** Secundum Atrial septal defect (ASD) and Patent foramen ovale (PFO) is becoming the most popular field of interest for catheter-based interventions. While there is a common agreement about the management of ASD patients, there is no complete agreement on which is the best management of PFO patients. In PFO patients, the real challenge for the clinician, beside secondary prevention of recurrent stroke, is to understand which the higher risk patients to refer for treatment are and which is the proper device to use. In this setting, the anatomo-functional characterization of interatrial septum seems to be of paramount importance for both ASD and PFO, not only for the device selection but also for therapeutic decision-making. In the present review the author overviews the main anatomic and functional characteristics of interatrial septum, obtained with the current available diagnostic tools, such as transcranial Doppler, transthoracic and transesophageal echocardiography and intracardiac echocardiography, and discusses the impact of such characteristics on catheter based closure.

**Keywords:** Secundum Atrial septal defect (ASD), Patent foramen ovale (PFO), catheter-based interventions, anatomo-functional characterization

### Introduction

Interatrial communications usually include a range of different atrial septum pathologies varying from Patent foramen ovale (PFO) to true defects of interatrial septum within the fossa ovalis, the secundum atrial septal defects, and defects of interatrial septum outside the region of fossa ovalis, such as the ostium primum defect and the sinus venosus defect. Only the first two entities are of interest for the interventional cardiologist, being the others of surgical pertinence.

### PFO

The PFO, defined as an incomplete adherence of septum primum and septum secundum at the level of the fossa ovalis, is a common finding in the general population with a prevalence of about 25% [1]. It is mostly a benign condition and its incidental finding in asymptomatic patients doesn't require any specific therapy. On the other hand, PFO is the main cause of right-

to left cardiac shunts followed by pulmonary arteriovenous fistulas, and it is potentially a risk factor for paradoxical embolism. Classical clinical presentations of patent foramen ovale include cryptogenic stroke, decompression syndrome, platypnea-orthodeoxia syndrome and peripheral embolism. Recently, other associations like migraine with aura, became matter of investigation [2]. While many techniques and devices have been developed to make the transcatheter closure an effective and safe therapeutic option for this kind of patients, there is no complete agreement on which is the best management of this patients. The real challenge for the clinician, beside secondary prevention, is to understand which are the higher risk patients to refer for treatment.

### Secundum ASD

Isolated atrial septal defects (ASD) represent 7% of all cardiac anomalies and can present at any age. Adolescents and adults with simple congenital heart disease such as isolated atrial

**Table 1.** Anatomical-functional characteristics of patients with ASD/PFO

Characteristic	Diagnostic tool	Significance
Left-to-Right shunt >2	TEE, MRI	Therapeutic decision-making
Severe Right-to-Left shunt	TDC, TEE	Therapeutic decision-making
Permanent right-to-Left shunt	TDC, TEE	Therapeutic decision-making
ASA	TEE, ICE	Management /device selection
Eustachian valve/Chiari Network	TEE, ICE	Management /Technical challenge
Long tunnel	TEE, ICE	Management /Technical challenge
Left atrial Dysfunction	TTE	Therapeutic decision-making
Associated anomalies	TEE, MRI	Management/technical challenge
Hyperthropy of the rims	TEE, ICE, MRI	Technical challenge

septal defects are more likely to reach adult age without being diagnosed. There are 3 major types of interatrial communications: ostium secundum, ostium primum and sinus venosus defects. Secundum ASD, the only one suitable of transcatheter closure, is by far the most common type, occurring in 1/1500 live births, with 65% to 75% involving females [3-4]. Secundum ASDs can be associated with partial anomalous pulmonary venous return. The magnitude of and direction of flow through an ASD depend on the size of the defect and the relative diastolic filling properties of the left and right ventricles. Conditions that reduce left ventricle compliance and mitral stenosis increase the left-to-right shunt, whereas conditions that reduce right ventricle compliance reduce the left-to-right shunt or cause a right-to-left shunt. A left-to-right shunt is significant when the Qp/Qs ratio is >1.5:1 or when the right chambers are dilated. A significant Qp/Qs ratio is associated with adverse long-term outcomes. Many patients with secundum ASD are free of overt symptoms, although most will become symptomatic at some point in their lives. Exercise intolerance is the most common presentation along with atrial fibrillation or flutter due to the atrial dilation and stretching. This usually occurs around 40 years of age [5]. In older patients, decompensate right heart failure may develop and is often associated with pulmonary hypertension caused by excessive pulmonary flow over a long period of time. Anatomical and functional ASD characteristics suitable for transcatheter closure include defect of < 40 mm and rims at least of 5 mm, absence of anomalous pulmonary venous return, Qp/Qs < 1.5, enlargement of right chambers. Deficiency

of the aortic rim is no longer considered a contraindication to transcatheter closure.

### Imaging techniques

In order to properly managed both these conditions, the anatomo-functional characterization of interatrial septum is of paramount importance not only to define the anatomy helpful to select the occlusion device and the implantation techniques but also, as in the case of PFO, to discriminate patients at high risk to refer for closure from those one to refer to medical treatment.

Different imaging techniques, at preoperative and also intraoperative stages, such as transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), transcranial Doppler ultrasound (TCD), magnetic Resonance Imaging (MRI) and intracardiac echocardiography (ICE) should be used in assessing these conditions (**Table 1**).

### TTE and TEE

TTE and TEE are foundamental for a first screening of patients with suspected PFO as primary cause of their paradoxical embolism (cerebral or extra-cerebral) [6]: when associated with the bubble-test, preferably with the aid of second armonic, TTE allows for a first diagnosis of PFO and atrial septal aneurysm (ASA) and a gross quantification of the shunt also in case of secundum ASD. The TEE is considered the principal imaging tool in defining PFO with or without ASA [7] and of suspected complex ASD,

such as cibrosus ASD or multiple ASD. It allows for confirming the first diagnosis of PFO and ASD and offers a precise quantification of the shunt, it visualizes properly the ASA and it can evaluate the presence of an eventual basal shunt and its direction. It is important for defining presence of eventual embryonal remnants such as an incomplete floor of the fossa ovalis , which is not infrequent in ASD patients also presenting with ASA , and residuals of caval vein valves such as the Eustachian valve and the Chiari network It allows for measuring the diameter of the fossa ovalis and of the defect, the length of the rims, the rims thickness, and eventual enlargement and dysfunction of the right atrium and ventricle in ASD patients and of left atrium and the left ventricle in PFO patients, important elements in deciding the management in particular of PFO patients >50 year-old [8].

### *Transcranial doppler ultrasound*

The TDC is the most sensitive imaging tool in detecting Right-to-Left shunt and remains the most preferred technique in quantifying the presence of basal shunt and Valsalva-induced shunt in PFO patients. Usually the study protocol includes monitoring of both MCAs through the temporal window by the use of 2-MHz probes. The contrast is obtained by mixing 100 cc of saline solution with 2-3 cc of Emagel and loading a 10 cc syringe with this mixture. The solution, agitated between two 10-mL syringes, connected by a 3-way stopcock, is immediately injected with a 20-gauge/32-mm catheter placed in the antecubital vein to obtain a bolus of air microbubbles. This procedure is performed 3 times during normal breathing and the same number of times during a Valsalva maneuver. The bolus of microbubbles is injected in 1 to 2 seconds when this 7-second period ended. The importance of RLSH is evaluated by counting the number of signals in 1 MCA within 7 seconds of the injection, as previously reported [9].

### *MRI*

Magnetic resonance imaging can give us almost the same information as echocardiography as regards right chambers size, fossa ovalis and defect size, shunt ratio, but seems superior in depicting structure and relative rapports of eventual associated pulmonary venous return [10-11].

### *Intracardiac echocardiography*

The use of intra-cardiac echocardiography (ICE) is gaining wide acceptance as one of the most powerful imaging devices in the interventional catheterization laboratory and its usefulness in different clinical settings is well known. Nowadays many electrophysiological, percutaneous congenital heart interventions and some peripheral vascular interventions benefit from the use of ICE.

Two types of ICE catheters are currently used in cardiovascular interventions: one by Siemens, the AcuNav phased-array 10 French, 5.5-10 Mega Hertz catheter with 90° sector image and Doppler capability, and the other by Boston Scientific, the Ultra ICE mechanical, 9 French, 9Mega Hertz catheter, with 360° radial image. Both systems have been fully applied in the daily clinical practice of catheter-based congenital heart disease interventions. ICE has been proved to offer significant advantages not only as effective guidance in even the most challenging procedure, thus avoiding general anaesthesia and reducing fluoroscopy time, but it is also economically competitive as opposed to standard trans-esophageal echocardiography-guided procedures. They also offer advantages over intravascular ultrasound, when large vessels and intra-cardiac structures are to be imaged. Each system has particular characteristics (**Table 2**).

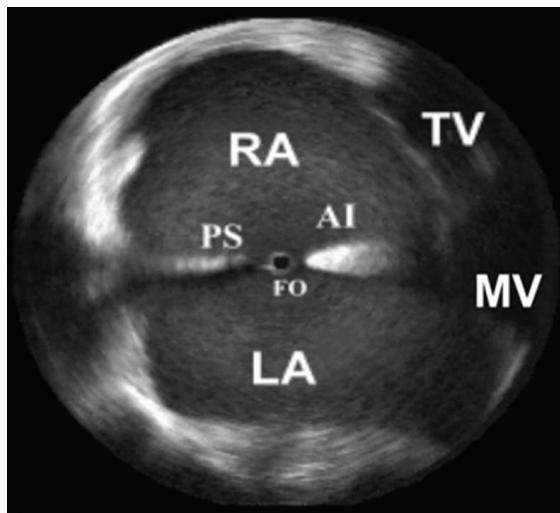
Phased-array equipment is obviously more versatile, thanks to Doppler capability, and has a better image resolution and definition. Pulmonary veins, coronary sinus and valve apparatus and function can be optimally assessed with the electronic probe. The cost is superior to mechanical probe but it can be coupled with multiple and different consoles.

The mechanical probe doesn't have Doppler capability and it has a less good image definition: nevertheless, thanks to the 360° scan has a larger field of view and allows for a more comprehensive depiction of both atrial chambers and atrioventricular valves with their relationships and it also can be used as an IVUS for great vessels. It needs a dedicated console. In the region of interatrial septum, the oval fossa is easily identifiable as a distinct component, characterized by thin membranous tissue, overcome by the thick muscular structure, the septum secundum (**Figure 1**). The absence of such

**Table 2.** Different peculiar characteristic of each intracardiac echocardiography probe

Characteristics	Mechanical	Electronic
Size	9F	10F
Scan	360°	90°
MHz	9	5-10
Introducer	9F precurved (55°, 120°), different curves	10F steerable
Image interpretation	As MRI	As TEE
Doppler	no	yes
Console	Single dedicated (ClearView Ultra or Galaxy)	Multiple (Acuson, Cypress portable)

MRI: magnetic resonance imaging; TEE : transesophageal echocardiography



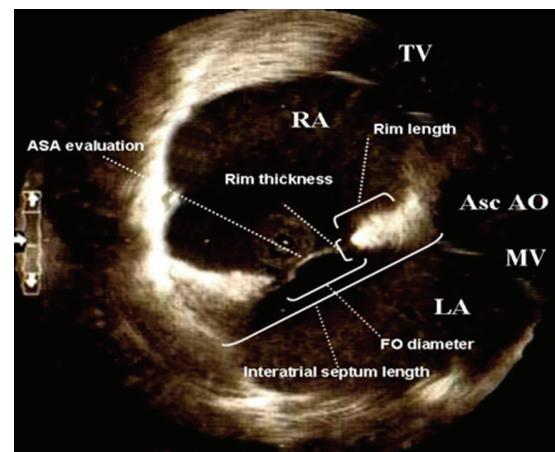
**Figure 1.** 4-chamber view during catheter-based closure of PFO. AI: anteroinferior rim. FO: fossa ovalis. LA: left atrium, PS: posterosuperior rim. MV: mitral valve RA: right atrium, TV: tricuspid valve.

component defines the presence of an ASD.

By ICE, we can obtain some quantitative parameters, such as systolic and diastolic diameters of interatrial septum and oval fossa, the thickness of the rims and their length, the length of the channel in tunneled PFO, the amplitude or severity of the ASA, the presence of the Eustachian valve or Chiari network, sometimes difficult to evaluate even with TEE [12-15] (**Figure 2**).

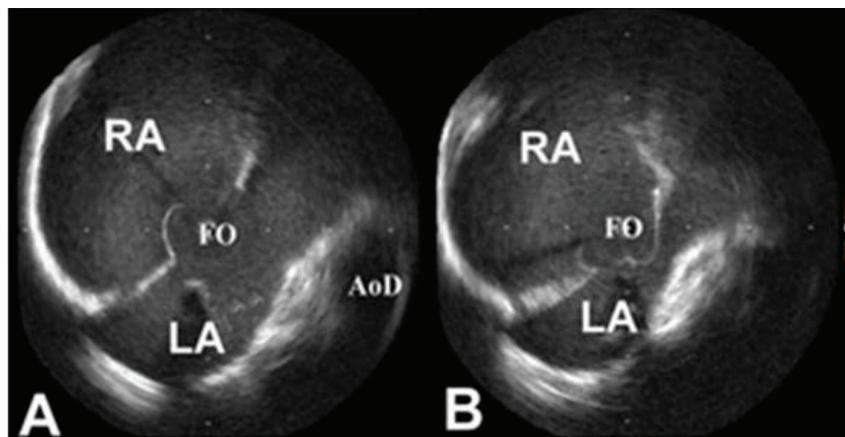
#### Shunt severity

The proper quantification of the Right-to-left shunt remains necessary for any therapeutic indication in PFO patients. The TCD with bubble



**Figure 2.** different measurements obtained by mechanical intracardiac probe: LA: left atrium, RA: right atrium; Asc AO: ascending aorta; MV:mitral valve; TV: tricuspid valve.

test identifies three shunt patterns under Valsalva manoeuvre: Mild (<10 bubbles within three cardiac cycles), moderate (> 10 bubbles within three cardiac cycles) with shower effect (many bubbles but still countable), severe (> 10 bubbles within three cardiac cycles) with curtain effect (many bubbles but not countable). A distinct pattern of shunt occurs when bubbles are identifiable before the Valsalva manoeuvre (basal or permanent shunt) [7]. In PFO patients TEE identifies the shunt under Valsalva manoeuvre in trivial, small, moderate and severe following an old but still valid classification [14]. Usually shower or curtain pattern of shunt correlate with moderate-severe shunt on TEE [16]. Severe and permanent shunt seems to correlate to an increased risk of paradoxical embolism [17-18]. Left-to-Right shunt quantification by TEE or MRI is important for assessing indications to closure



**Figure 3.** (A) Evaluation of atrial septal aneurysm. (B) Measurements obtaining with mechanical probe are important for device selection. Asc ao: ascending aorta; LA: left atrium, MV: mitral valve. RA: right atrium. TV: tricuspidal valve.

of ASD patients.

#### Rims

Accurate rims length measurements remain mandatory in evaluating every case of ASD suitable for transcatheter closure and are becoming important also in selecting the proper device in PFO patients. Usually, deficiency (<5 mm) of the anteroinferior rim is considered a contraindication to transcatether closure because is the only muscular rim of the fossa ovalis, whereas deficiency of the anterosuperior rim or the postero-inferior rims are not considered absolute contraindications but remaining at risk of aortic or atrial wall erosion or perforation in particular with huge ASD (>25 mm). In PFO patients rims are becoming important for device selection, being the deficiency of the anterosuperior rim a risk factor for aortic erosion, an occurrence particularly disturbing when facing with relatively healthy and normal heart and subject, as usually are PFO patients. In such case, when ASA is not associated, soft or asymmetrical device may be preferable compared to stiff metallic simmetrical devices , such as those of the Amplatzer family [19]. TEE, MRI and intraoperatively, ICE should be used in the precise definition of fossa ovalis or defect rims [20].

#### Atrial septal aneurysm (ASA)

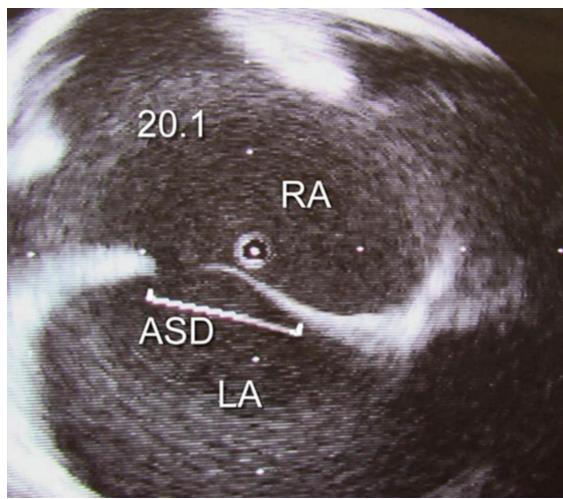
Atrial septal aneurysm (ASA) has prevalence in the general population between 0.22 and 4% [9-12] but it rises to 8-15% in patients with stroke [21-22]. It is a congenital malformation of the atrial septum characterized by bulging of at least 15 mm of the septum overlying the fossa

ovalis region into either atrium [23-24].

Massa and Homma were the first to suggest that concurrence of ASA and PFO identifies a high risk cohort of PFO patients [25-26]. More recently, some studies suggested that PFO and ASA patients have multiple lesions on magnetic resonance imaging more frequently than PFO patients ; Santamarina et al observed that an embolic pattern was more frequent in PFO/ASA patients (44%) compared with PFO patients (26.2%) [27].

The coexistence of PFO and ASA is strongly associated to cerebral ischemic events through a supposed paradoxical embolism mechanism but other new hypothesis are matter of investigation as the one proposed by our study group, consistent with an “atrial fibrillation like” mechanism based on left atrial dysfunction[28].

It can have different degree of amplitude or severity (1 to 5), and it can be fixed or mobile toward the Right (R) or left (L) atrium following the Olivares classification [27]. Large ASA (3 to 5), seems to be correlate to an increased risk or recurrent paradoxical embolism [29]. From a technical point of view, TEE and ICE are mandatory in properly identifying severity of ASA. The presence of moderate to large ASA associate with a PFO usually induces the operator to select a stiff metallic device to stabilize the interatrial septum increasing the risk of misalignment and residual shunt after closure (**Figure 3**). Not infrequently incomplete floppy or frankly aneurysmal floor of the fossa ovalis can be associated with a secundum ASD, complicating transcatheter closure by interfering with the



**Figure 4.** Intracardiac echocardiography demonstrating the association of a 20.1 mm secundum ASD with an incomplete aneurysmal floor of the fossa ovalis. (LA: left atrium; RA: right atrium).

long sheath or facilitating a device misalignment (**Figure 4**).

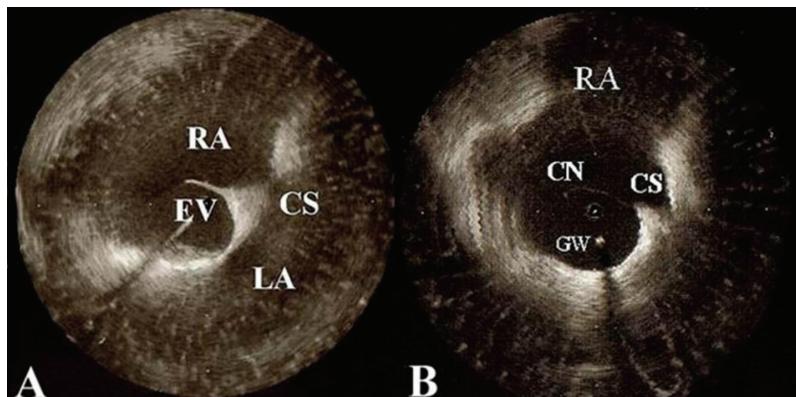
#### Eustachian valve and Chiari network

From an embryological point of view the EV is derivative of the right sinus venosus valve, it has a semicircular shape and is facing the anterior-inferior aspect of the inferior vena cava. The CN represents a very huge multi-perforated Eustachian valve with a network-like appearance and it has been found in 1.3% to 4% of autopsies. The EV and CN guarding the anterior-inferior aspect of the inferior vena cava, have a crucial role in deflecting the blood flow through the foramen ovale during the foetal life predis-

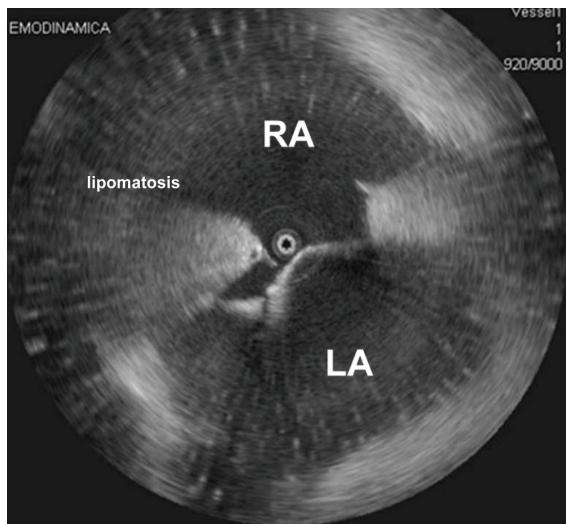
posing to paradoxical embolism [27-28]. Large PFO and prominent EV or right atrial filamentous strands were found more frequently in patients with septal aneurysm compared with those without (37.7% vs. 10.9%,  $p < 0.001$  and 59.4% vs. 43.1%,  $p = 0.02$ ) [31]. As previously reported by TEE studies an EV is present in 48% of patients with cryptogenic stroke [31] and a large CN is associated with PFO in 83% of cases [32]. TEE and ICE seem to be the most sensitive imaging tools for detecting these embryonic remnants: ICE has been found to be extremely accurate in detecting both entities which have been suggested to be predictors of large shunt and recurrent paradoxical embolism also in recent studies [33]. From a technical point of view, the presence of such structures should be taken in account during transcatheter closure, representing potential technical difficulties (**Figure 5**).

#### Interatrial septum thickness and lipomatosis

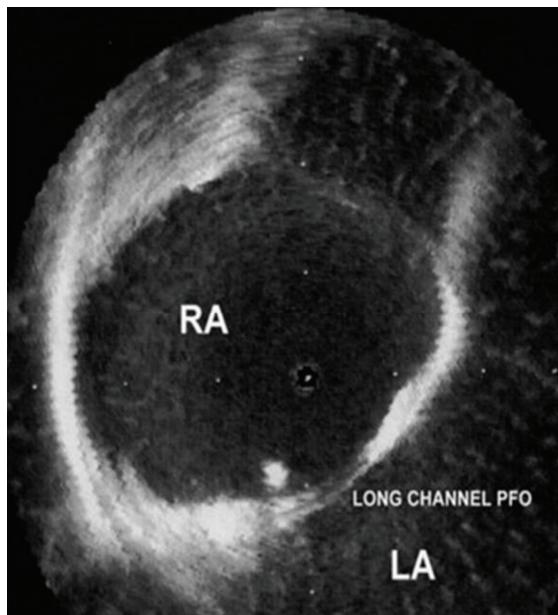
Interatrial septum thickness in the general population is about 6 mm and usually it increases to about 7 mm in aged population [34]. Interatrial septum hypertrophy (IASH) and lipomatosis have been defined when thickness is  $>8$  mm and  $>15$  mm, respectively. IASH is common in elderly people and is related with hypertension and smoke but not with vascular disease [35-38] (**Figure 6**). Lipomatosis of Interatrial septum is a benign tumoral process characterized by fat accumulation in the interatrial septum [39]. Both conditions may have a deep impact on transcatheter closure because in case of both PFO and ASD, a stiff device such as those of the Amplatzer family should be contraindicated, due to the inability of such device



**Figure 5.** (A) A huge Eustachian valve as it has been observed on Intracardiac echocardiography during a PFO closure procedure. (B) A Chiari's network as it has been observed on Intracardiac echocardiography during a PFO closure procedure: note the thickness  $< 1$  mm and the filamentous appearance (CS: coronary sinus; CN: Chiari's network; EV: huge Eustachian valve, GW: guide wire in the attempt to cross the fossa ovalis; RA: right atrium).



**Figure 6.** Lipomatosis of Fossa ovalis rims and Interatrial septum on ICE study in a 60-year old patient with recurrent stroke and coronary artery disease. LA: left atrium, RA: right atrium.



**Figure 7.** Long channel PFO. LA: left atrium; RA: right atrium.

to stretch the waist zone more of 7-8 mm [40].

#### Tunnelized PFO

Not infrequently, PFO appears as a tunnel -like opening between the right and left atrium and this feature can be associated with a variety of

other anatomical variants, such as hyper trophy of the rims, different degree of ASA, etc. Recently this kind of anatomy has been correlated with an increased risk of paradoxical embolism [41], for its potential role in causing thrombosis in situ within the channel, in particular if long > 10-12 mm. From a technical point of view, TEE and in particular ICE can be useful in determining the length of the tunnel and in selecting the proper device, which should be an asymmetrical opening device which could adapt to this anatomy better than stiffer metallic symmetrically opening double disk device (Figure 7).

#### Conclusions

Transcatheter closure of ASD/PFO is usually a safe and effective procedure when a meticulous study of the anatomy and functional characteristics of the interatrial septum is accomplished. It allows for properly managing of patients, in particular of PFO patients, and for avoiding procedural failures and complications, whom the interventionalist can face with when dealing with such procedures.

**Address correspondence to:** Gianluca Rigatelli, MD, PhD, EBIR, FACP, FACC, FESC, FSCAI, Via Mozart 9, 37048 Legnago, Verona-Italy, Tel: +3903471912016, Fax: +39044220164, E-mail: jackyheart@libero.it

#### References

- [1] Marelli AJ, Mackie AS, Msc RI, Rahme E, Pilote L. Congenital Heart Disease in the General Population. Changing Prevalence and Age Distribution. *Circulation*. 2007 Jan 8; [Epub ahead of print]
- [2] Rigatelli G, Rigatelli G. Congenital heart diseases in aged patients: clinical features, diagnosis, and therapeutic indications based on the analysis of a twenty five-year Medline search. *Cardiol Rev*. 2005; 13: 293-6.
- [3] Bernier FP, Spaetgens R. The geneticist's role in adult congenital heart disease. *Cardiol Clin* 2006;24:557-69
- [4] Webb G, Gatzoulis MA. Atrial septal defects in the adult: recent progress and overview. *Circulation* 2006; 114: 1645-53.
- [5] Rigatelli G. Patent foramen ovale: the evident paradox between the apparently simple treatment and the really complex pathophysiology. *J CardiovascMed (Hagerstown)* 2007; 8: 300-4.
- [6] Rigatelli G, Cardaioli P, Dell'Avvocata F, Giordan M, Braggion G, Aggio S, et al. The association of different right atrium anatomical-functional characteristics correlates with

- the risk of paradoxical stroke: an intracardiac echocardiographic study. *J Interv Cardiol* 2008; 21: 357-62.
- [7] Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al; American Society of Echocardiography's Nomenclature and Standards Committee; Task Force on Chamber Quantification; American College of Cardiology Echocardiography Committee; American Heart Association; European Association of Echocardiography, European Society of Cardiology. Recommendations for chamber quantification. *Eur J Echocardiogr* 2006; 7: 79-108.
- [8] Messe SR, Silverman IE, Kizer JR, Homma S, Zahn C, Gronseth G, et al.; Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: recurrent stroke with patent foramen ovale and atrial septal aneurysm: report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2004; 62: 1042-50.
- [9] Serena J, segura T, Perez-Ayuso MJ, Bassagranjas J, Molins A, Davalos A. The need to quantify right-to-left shunt in acute ischemic stroke: a case-control study. *Stroke* 1998; 29: 1322-8
- [10] Marcu CB, Beek AM, van Rossum AC. Clinical applications of cardiovascular magnetic resonance imaging. *CMAJ*. 2006; 175: 911-7.
- [11] Weber OM, Higgins CB. MR evaluation of cardiovascular physiology in congenital heart disease: flow and function. *J Cardiovasc Magn Reson* 2006; 8: 607-17.
- [12] Rigatelli G. Patent foramen ovale in elderly people. *J Am Geriatr Soc* 2008; 56: 953-4.
- [13] Rigatelli G, Cardaioli P, Giordan M, Dell'Avvocata F, Braggion G, Piergentili C, et al. Transcatheter intracardiac echocardiography-assisted closure of interatrial shunts: complications and midterm follow-up. *Echocardiography* 2009; 26: 196-202.
- [14] Bartel T, Konorza T, Neudorf U, Ebralize T, Eggebrecht H, Guttersohn A, et al. Intracardiac echocardiography: an ideal guiding tool for device closure of interatrial communications. *Eur J Echocardiogr* 2005; 6: 92-6.
- [15] Rigatelli G, Cardaioli P, Braggion G, Aggio S, Giordan M, Magro B, et al. Transesophageal echocardiography and intracardiac echocardiography differently predict potential technical challenges or failures of interatrial shunts catheter-based closure. *J Interv Cardiol* 2007; 20: 77-81
- [16] Rigatelli G, Hijazi ZM. Intracardiac echocardiography in cardiovascular catheter-based interventions: different devices for different purposes. *J Invasive Cardiol* 2006; 18: 225-33.
- [17] Anzola GP, Morandi E, Casilli F, Onorato E. Different degrees of right-to left shunting predict migraine and stroke: data from 420 patients. *Neurology* 2006; 66: 765-7.
- [18] Anzola GP, Morandi E, Casilli F, Onorato E. Does transcatheter closure of patent foramen ovale really "shut the door"? A prospective study with transcranial doppler. *Stroke* 2004; 35: 2140-4.
- [19] Rigatelli G, Dell'Avvocata F, Ronco F, Giordan M, Cardaioli P. Patent oval foramen transcatheter closure: results of a strategy based on tailoring the device to the specific patient's anatomy. *Cardiol Young* 2010; 20: 144-9.
- [20] Rigatelli G, Cardaioli P, Giordan M, Dell'Avvocata F, Braggion G, Piergentili C, Roncon L, Faggian G. Transcatheter intracardiac echocardiography-assisted closure of interatrial shunts: complications and midterm follow-up. *Echocardiography* 2009; 26: 196-202.
- [21] Giardini A, Donti A, Formigari R, Salomone L, Palareti G, Guidetti D, et al. Spontaneous large right-to left shunt and migraine headaches with aura are risk factors for recurrent stroke in patients with a patent foramen ovale. *Int J Cardiol* 2007; 120: 357-62.
- [22] Agmon Y, Khandheria BK, Meissner I, et al. Frequency of atrial septal aneurysm in patients with cerebral ischemic events. *Circulation* 1999; 99: 1942-4.
- [23] Pearson AC, Nagelhout D, Castello R, Gomez CR, Labovitz AJ. Atrial septal aneurysm and stroke: a transesophageal echocardiographic study. *J Am Coll Cardiol* 1991; 18: 1223-9.
- [24] Zabalgoitia M, Norris LP, Garcia M. Atrial septal aneurysm as a potential source of neurological ischemic events. *Am J Card Imaging* 1994 Jan; 8(1): 39-44.
- [25] Hanley PC, Tajik AJ, Hynes JK et al: Diagnosis and classification of atrial septal aneurysm by two-dimensional echocardiography: report of 80 consecutive cases. *J Am Coll Cardiol* 1985; 6:1370-82.
- [26] Homma S, Sacco RL, Di Tullio MR, Sciacca RR, Mohr JP; PFO in Cryptogenic Stroke Study (PICSS) Investigators. Effect of medical treatment in stroke patients with patent foramen ovale: patent foramen ovale in Cryptogenic Stroke Study. *Circulation* 2002; 105: 2625-31.
- [27] Mas JL, Arquizan C, Lamy C, Zuber M, Cabanes L, Derumeaux G, et al.; Patent Foramen Ovale and Atrial Septal Aneurysm Study Group. Recurrent cerebrovascular events associated with patent foramen ovale, atrial septal aneurysm, or both. *N Engl J Med* 2001; 345: 1740-6.
- [28] Santamarina E, Gonzalez-Alujas MT, Munoz V, Rovira A, Rubiera M, Ribo M, et al. Stroke patients with cardiac atrial septal abnormalities: differential infarct patterns on DWI. *J Neuroimaging* 2006; 16: 334-40.17.

## Interatrial septum characterization

- [30] Rigatelli G, Aggio S, Cardaioli P, Braggion G, Giordan M, Dell'Avvocata F, Chinaglia M, Rigatelli G, Roncon L, Chen JP. Left atrial dysfunction in patients with patent foramen ovale and atrial septal aneurysm: an alternative concurrent mechanism for arterial embolism? *JACC Cardiovasc Interv* 2009 Jul; 2: 655-62.
- [31] Olivares-Reyes A, Chan S, Lazar EJ, Bandlamudi K, Narla V, Ong K. Atrial septal aneurysm: a new classification in two hundred five adults. *J Am Soc Echocardiogr* 1997; 10: 644-56.
- [32] Rigatelli G, Cardaioli P, Giordan M, Dell'Avvocata F, Braggion G, Piergentili C, et al. The CARPE criteria: implications for transcatheater closure of patent foramen ovale. *J Interv Cardiol* 2009; 22: 398-403.
- [33] Schuchlenz HW, Saurer G, Weihs W, Rehak P. Persisting eustachian valve in adults: relation to patent foramen ovale and cerebrovascular events. *J Am Soc Echocardiogr* 2004; 17: 231-3.
- [34] Schneider B, Hofmann T, Justen MH, Meinertz T. Chiari's network: normal anatomic variant or risk factor for arterial embolic events? *J Am Coll Cardiol* 1995; 26: 203-10.
- [35] Rigatelli G, Dell'Avvocata F, Braggion G, Giordan M, Chinaglia M, Cardatoli P. Persistent venous valves correlate with increased shunt and multiple preceding cryptogenic embolic events in patients with patent foramen ovale: an intracardiac echocardiographic study. *Catheter Cardiovasc Interv* 2008; 72: 973-6.
- [36] Schneider B, Hofmann T, Justen MH, Meinertz T. Chiari's network: normal anatomic variant or risk factor for arterial embolic events? *J Am Coll Cardiol* 1995; 26: 203-10
- [37] Swinger ME, Gindea AJ, Freedberg RS, Kronzon I. The anatomy of the interatrial septum: transesophageal echocardiographic study. *Am Heart J* 1990; 119: 1401-5.
- [38] Galzerano D, Tuccillo B, Lama D, Paolisso G, Mirra G, Giasi M. Morpho-functional assessment of interatrial septum: a transesophageal echocardiographic study. *Int J Cardiol* 1995; 51(1): 73-7
- [39] Agmon Y, Meissner I, Tajik AJ, Seward JB, Peterson TM, Christianson TJ, O'Fallon WM, Wiers DO, Khandheria BK. Clinical, laboratory, and transesophageal echocardiographic correlates of interatrial septal thickness: a population-based transesophageal echocardiographic study. *J Am Soc Echocardiogr* 2005; 18: 175-82
- [40] Christoph MH, Thomas K, Stefan PL, Torsten TB, Volkmar N. Lipomatous hypertrophy of the interatrial septum: A prospective study of incidence, imaging findings, and clinical symptoms. *Chest* 2003; 124: 2068-2073
- [41] Marshall AC, Lock JE. Structural and compliant anatomy of the patent foramen ovale in patients undergoing transcatheater closure. *Am Heart* 2000; 140: 303-7
- [42] Goel SS, Tuzcu EM, Shishehbor MH, de Oliveira El, Borek PP, Krasuski RA, Rodriguez LL, Kapadia SR. Morphology of the patent foramen ovale in asymptomatic versus symptomatic (stroke or transient ischemic attack) patients. *Am J Cardiol* 2009; 103: 124-9.