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Should we consider patent foramen ovale and secundum atrial septal defect as different steps of a single anatomo-clinical continuum?

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1 Introduction

Isolated atrial septal defects (ASD) represent 7% of all cardiac anomalies and can present at any age.[1] Adolescents and adults with simple congenital heart disease such as isolated atrial septal defects are more likely to reach adult age without being diagnosed. Secundum ASD (sASD) is by far the most common type, occurring in 1/1500 live births, with 65% to 75% involving females.[2] On the other hand, patent foramen ovale (PFO) represents an endemic variant in the normal population with a prevalence of 25%–27%.[3] These two entities appear so different that is difficult to find a conjunction ring: nevertheless we use the same philosophy for the treatment. Indeed, device–based closure has been proved to be effective in both settings.[4,5]

2 Anatomy, pathophysiology, and haemodynamic

From an anatomic and pathophysiologic point of view, these two entities are absolutely different. The ostium sASD is a true defect of the atrial septum which involves the fossa ovalis region and causes usually a left-to-right shunt. 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 ratio of pulmonary to systemic blood flow (Qp/Qs) is > 1.5: 1 or when the right chambers are dilated.[6]

The PFO is defined as the incompetence of the fossa ovale valve determining a right-to-left shunt. The cause of right-to-left atrial shunting despite normal intracardiac pressures and normal or near-normal pulmonary function through a PFO has still not been completely clarified. Despite modern diagnostic methods, the underlying anatomophysiologic and pathogenic mechanisms of right-to-left atrial shunting without abnormal intracardiac pressures remain a matter of debate and controversy. An explanation may derive form few considerations. Firstly, despite the mean right atrial pressure is normally lower than the mean left atrial pressure, a physiologic transient spontaneous reversal of the left-to-right atrial pressure differential is present during early diastole and during isovolumetric contraction of the right ventricle of each cardiac cycle; this reversal gradient may drastically increase under substantial hemodynamic changes caused by physiologic manoeuvre that increase the right atrial pressure such as posture, inspiration, cough or Valsalva maneuver, or under same pathologic conditions resulting in high pulmonary vascular resistances, such as acute pulmonary embolism, hypoxemia due to obstructive sleep apnea, severe chronic obstructive pulmonary disease, right ventricular infarction and positive end-expiratory pressure during neurosurgical procedures in the sitting position, causing right-to-left shunting when they are coupled with a secondary PFO. Secondly, another anatomophysiologic theory to explain the right-to-left shunting with both normal atrial and pulmonary vascular pressures involves the "flow phenomenon", i.e., a preferential blood flow streaming from the inferior vena cava towards the atrial septum as a part of the remnant prenatal circulatory pattern, but there is still only limited understanding of its potential significance in relation to right atrial anatomy and physiology.[7]

Thirdly, in the same way, a physiologic change in the relationship of right and left sided chambers compliance, that is probably exacerbated with age, with the right sided chambers becoming stiffer than the left sided counterpart, has been advocated. Finally, an anatomic disarray of the inferior vena cava relative to the atrial septum due to mediastinal shift or heart counter-clockwise rotation and/or distortion, following an ascending aorta enlargement, right pneumectomy or pericardial effusion may result in a atypi-

cally horizontal reorientation of the plane of the atrial septum, which overlies the inlet of the inferior vena cava into the right atrium, facilitating part of the flow to stream directly into the left atrium via a PFO.[8]

Even from a haemodynamic point of view, ASD obviously differs from PFO. ASD are usually associated with pulmonary hypertension of different degree, an increased Qp/Qs ratio and enlarged right chambers, whereas the usual findings in PFO patients is a normal or slightly elevated pulmonary pressure, normal Qp/Qs ratio, and normal right chambers. Sometimes in presence of a PFO associated with large atrial septal aneurysm (ASA), a mild impairment of the left atrial function can be observed.[9]

Usually fenestrated sASD with or without ASA also tends to present less right chambers enlargement and only slightly increase in mean pulmonary pressure compared to sASD.[10]

3 Searching for a conjunction ring

Despite the differences in anatomy, pathophysiology and haemodynamic, we can find some contact points when we look to the clinical presentation. Excepted for supraventricular arrhythmias and dyspnoea, usually present in sASD,[6] and in fenestrated ASD, paradoxical embolism may occur in both entities and also may be the first appearance of fenestrated ASD with or without ASA.[11]

Most cases of paradoxical embolism were associated with PFO, less commonly, sASD, pulmonary arterio-venous fistula, and other intracardiac septal defects may be responsible for paradoxical embolism.[12] Microemboli might navigate from a thrombosis at the level of deep vein circulation, or as recently postulated,[9] they might be generated even on the surface of a huge ASA or in the left atrium itself as a result of a left atrial dysfunction induced by the PFO and ASA itself. On the contrary, the pathophysiology of paradoxical embolism associated with sASD seems clearer, being probably based on a transient increase in right heart pressure inducing a right-to-left shunting which allows a venous thromboembolus to enter the arterial circulation.[11] Alternatively, a pre-existing bidirectional shunting precipitated in its right-to-left component by Valsalva maneuver, coughing, or straining might explain the occurrence of a paradoxical embolism in sASD patients especially in elderly patients, more prone to rapid change of right chambers pressure because of the increasing stiffness of the chambers.

Recently in an analysis of our institutional database, we found 24 (6.2%) out of 386 patients who underwent transcatheter repair for paradoxical embolism had a sASD. The defects were cribrosus in 41.6% (10/24). All single sASD (58.3%) had a peculiar so-called flat elliptical shape with a major axis of 7.6 ± 2.4 mm and minimal axis of 2.5 ± 1.6 mm when assessed with intracadiac echocardiography. Patients with sASD-related paradoxical embolism had a higher frequency of deep venous thrombosis and more severe clinical presentation compared to the usual spectrum of paradoxical embolism patients. When evaluated with transcranial Doppler, all patients had massive curtain shunt on Valsalva maneuver. In comparison to non-emboligenous sASD, such patients had lower mean pulmonary pressure, a lower mean Qp/Qs, and had bidirectional shunt at rest.[12]

As a matter of fact, flat elliptical shape ASD and cribrosus ASD with or without ASA appear to represent the conjunction ring between ASD and PFO, being a hybrid haemodynamic and clinical profile compared to each of the others.

4 The single anatomo-clinical continuum theory

From what we have discussed above, sound likely to theorize that, at least from an anatomo-clinical point of view, ASD and PFO might be considered at the edge of a single continuum which pass throughout flat elliptical ASD and cribrosus ASD (Figure 1). In this continuum, paradoxical

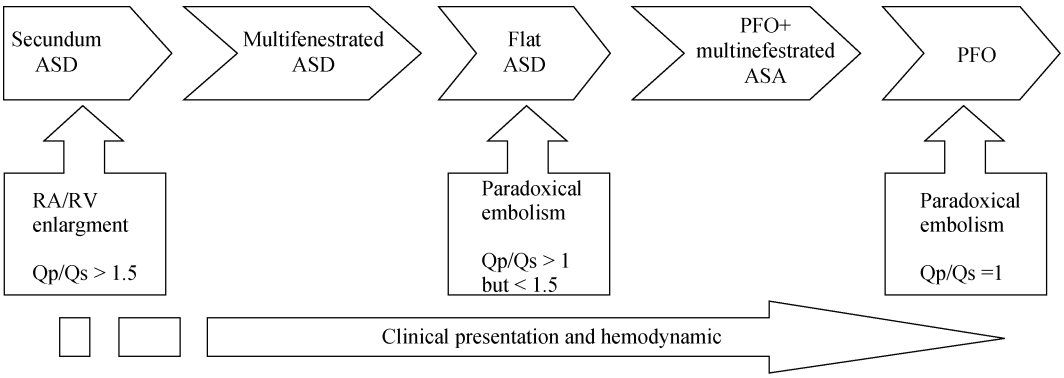

Figure 1. Graphic representation of the pathophysiological spectrum of interatrial shunt with haemodynamic and clinical main features. ASA: atrial septal aneurysm; ASD: atrial septal defect; PFO: patent foramen ovale; Qp/Qs: the ratio of pulmonary to systemic blood flow; RA: right atrial; RV: right ventricles.

embolism seems to be the common clinical presentation whereas device–based closure represents the common treatment strategy.

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