Patent Foramen Ovale – Clinical Significance

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Abstract

Probe patent or incomplete seal of the foramen ovale occurs in 25% of adults. Foramen ovale plays a very important role in foetal circulation. PFO acquires significance in various congenital heart diseases leading to right-to-left shunt, and thus to paradoxical embolism. PFO is associated with transient ischaemic attacks, migraine like presentation, and also a host of other problems in particular settings. Practical knowledge about PFO is utilised in cardiac catheterisation labs. also.

Keywords : PFO-patent foramen ovale, ASD-atrial septal defect, PTMC-percutaneous transmitral commissurutomy.

Introduction

Patent foramen ovale (PFO) is known since the time of Galen. It was first described in 1564 by Leonardi Botali and in 1877, Cohnheim described paradoxical embolism due to PFO. Mayo Clinic autopsy studies revealed that size of PFO increases from a mean of 3.4 mm in 1st decade to 5.8 mm in 10th decade of life, as the valve of fossa ovalis stretches with age. PFO by contrast echo is found in only 10-15% cases, but at autopsy its prevalence was 27%, as we can directly visualise FO while contrast echoes rely on secondary physiological phenomenon. To understand PFO, we should have basic knowledge about developmental anatomy and physiological changes in circulation taking place after birth. Foramen ovale is a slit like opening in the atrial septum at the site of foramen secundum of the septum primum. The septum secundum surrounds the foramen secundum in a crescentic shape and leaves a slit-like opening which is covered in a valve-like manner by the free edge of septum primum. In the intrauterine life, foramen ovale has the important role of transmitting highly oxygenated inferior vena caval blood to the left atrium (LA). High right atrial (RA) pressure in foetal life keeps the valve of foramen ovale open. LA pressure rises shortly after birth and the flap is lightly pushed against the septum secundum and closes the foramen ovale functionally. Lend and Wigelius1 could not demonstrate by angiocardiographic methods a functional opening in the foramen ovale at the end of 1st week of life.

Hoffman et al also suggested that an atrial left-to-right shunt resulting from an incompetent foramen ovale may exist in patients without heart disease for more than a year, with eventual closure of the communication. Anatomic patency may occur for several months and 50% of all the infants have probe – PFO at the end of 1st year of life. In 30% of all persons, probably anatomic closure never occurs. We should remember that PFO is a result of the normal developmental process while ASD is the deficiency in the formation of atrial septum. PFO behaves very differently from ASD in many clinical situations.

Basis of clinical significance

PFO is present in 1/5th of the adult population. It can allow only right-to-left shunt because of the flap which covers it from the left side, so communication between RA and LA must go from right to left, unless of course, foramen ovale is stretched by a distended LA or the flap valve is deficient to the extent that it does not cover the foramen secundum completely. Except in conditions with stretch phenomenon and rarely in normal infants, a functional opening in the foramen ovale is likely only in a situation in which resistance to flow in the right side of the heart is higher than in the systemic circuit, and so RA pressure is higher than LA pressure. Clinical picture of PFO is of right-to-left shunt in the cases of obstruction at the level of right ventricle, pulmonary valvular or vascular level. This is usually associated with right ventricular and right atrial hypertension.

There are no risk factors for the development of PFO. If there are no heart defects, usually PFO has no signs and
symptoms. Rarely, intermittent cyanosis is present on crying or straining to pass stools in infants, otherwise PFO is associated with normal health in the majority.

**a. Association with congenital heart diseases:** PFO is present in majority of cases of Ebstein's anomaly. This may be due to right atrial distention caused by regurgitation of blood which prevents complete closure of the valve of FO or ASD secundum sometimes. In pulmonary stenosis also, the communication is by PFO many times. The communication is sometimes due to persistent ostium primum or sinus venosus defect or partial/total anomalous pulmonary venous connection. Pulmonary stenosis with PFO presents as right-to-left shunt and causes redness of the fingertips with central cyanosis. Cyanosis reflects veno-arterial shunting through PFO and is absent in mild stenosis and infrequent in moderate stenosis. It may not be apparent in severe pulmonary stenosis if the atrial septum is intact. In tricuspid atresia, interatrial communication, in 75% of cases, is by PFO and therefore, restrictive. This is reflected as tall 'A' waves in JVP. PFO can be present in many other types of congenital heart disease, e.g., pulmonary atresia with intact ventricular septum. In babies with large PDA (pre-operatively) a sizeable left-to-right shunt may be demonstrated at cardiac catheterisation. After division of ductus and diminution in LA size, atrial shunt can no longer be detected.

Raised LA pressure – as seen in mitral stenosis, regurgitation, PDA, and VSD as they can dilate FO and lead to left-to-right shunt while in tricuspid valve stenosis, RV hypoplasia, pulmonary hypertension, chiai network in RA, and others can lead to rise in RA pressure and cause right to left shunt. PFO can act as obligatory shunt in mitral atresia in left-to-right direction, while acts as right-to-left shunt in tricuspid atresia, and anomalous pulmonary venous connections. So, left-to-right shunting through PFO has no signs and symptoms until later in life, while right-to-left shunt can cause cyanosis on crying, valsalva, breath-holding, or any manoeuvre which raises RA pressure. Persistent cyanosis can occur during neonatal period until pulmonary vascular resistance falls, but we should remember that right-to-left shunt causes symmetrical rather than differential cyanosis. There are some typical conditions when PFO can worsen hypoxemia such as valvular PS, Ebstein anomaly, RV myocardial infarction, orthodeoxia platypnoea syndrome, chronic obstructive pulmonary diseases, pulmonary hypertension (primary or secondary). 3 factors which decide the complications arising from PFO are:

1. Size of PFO
2. Pressure gradient between RA/LA
3. Direction of inferior vena cava blood flow.

**b. PFO and neurological problems**: James Lock has postulated that PFO acts as a cul de sac between septum primum and secundum, thus predisposing to haemostasis and clot formation. In some cases of headache – migraine with aura, patient was found to have PFO also, and migraine improved on medical treatment in the form of antiplatelet and anticoagulant drugs or disappeared on the closure of PFO. This was suggested by European Society of Cardiology, Congress Abstract 279 presented on 31st August, 2003 and Stephen Windecker et al at Swiss Cardio Centre and Stephen H Landy: Director Wesley, Headache Clinic, Neurology, University of Tennessee in Memphis also had the same opinion about the relation between PFO and migraine. If true migraine or migraine like symptoms are due to transient ischaemic attacks (TIA) or paradoxical embolism is another query to be solved.

PFO can lead to brain infarction and brain abscess also. Neurological signs and symptoms can be hemiplegia, visual disturbances, and slurred speech. This can be due to paradoxical embolism. An article by Sandy Shah proposes that we should image close family members of a patient with PFO. Cerebrovascular accidents (CVA) can be due to paradoxical embolism and can lead to cryptogenic brain infarction (in absence of any obvious cause). It has increased chances in children with neurosurgical procedures specially in sitting position. It is a medical pitfall to miss PFO as a source of paradoxical embolism in CVA or not to
screen for PFO just prior to setting a neurosurgical procedure. Apart from paradoxical embolism which is due to passing of large venous clots from right to left side, many cases show small arterial thrombus which cannot be explained by right to left shunting alone. It can be due to associated prothrombotic states in PFO. PFO and cryptogenic brain infarction are related to factor V Leiden and prothrombin G 202010A gene mutation. But one study of cryptogenic brain infarction with PFO when compared with controls showed that prothrombotic states were not identified as risk factors except factor VIII along with smoking, high BP, and low HDL. This has been suggested that in tunnel-type PFO, there is sluggish flow leading to arterial thrombus as blood passes through it. PFO raises chances of CVA beyond doubt\textsuperscript{16-20}. One study took 60 adults below 55 years with ischaemic CVA and normal echocardiogram and compared it with 100 controls and found that PFO was found in 40% of cases of stroke and only in 10% in control (P < 0.001). It was present in 21% in 19 patients with identifiable cause of stroke and 40% in 15 patients with no identifiable cause but a risk factor for stroke was present.

High risk PFO are those which are associated with:

(i) atrial septal aneurysm – more than 10 mm tissue sway in either direction from septal plane or more than 15 mm total sway with the base of moving tissue that extends more than 10 mm and is associated with septal perforations.

(ii) spontaneous intracardiac passage of bubble on contrast echocardiogram without any provocative measures.

(iii) tunnel-like PFO

PFO can lead to fat embolism (Nysten, et al) and bilateral central retinal artery occlusion, thus leading to blindness. It can lead to recurrent stroke or TIA – 3.4-3.9%/year\textsuperscript{21}. PFO with atrial septal aneurysm is associated with 1st risk of recurrent stroke within 2 years at 9% and rate of subsequent stroke or TIA within 2 years rises to 22%.

c. PFO and decompression sickness\textsuperscript{22-24}: PFO, not ASD is associated more with decompression sickness. There is an increased risk in Scuba divers, of nitrogen gas embolism across PFO. As only a small percentage of Scuba divers with PFO develop decompression sickness, whether it is feasible to screen all Scuba divers is another controversial issue. PFO can worsen hypoxaemia in Scuba divers at great depths and can lead to deaths especially in improperly trained divers.

d. PFO and obstructive sleep apnoea (OSA)\textsuperscript{25}: It increases chances of hypoxaemia during sleep in OSA at night as there is transient elevation of RA pressure over LA pressure and PFO can augment this shunt and lead to significant fall in oxygen saturation.

e. PFO and post-cardiac surgery: Increased chances of atrial fibrillation and can worsen hypoxaemia, especially in off-pump CABG\textsuperscript{26,27}.

f. LV decompression and PFO: This was seen in case of hypertrophic cardiomyopathy by Ando et al, Department of Cardiac Surgery, University Rome Tor Vergata, Italy, who found that in this case, elevated LV filling pressures was decompressed by PFO in left-to-right direction. Transient sealing of PFO by amplatser device led to abrupt rise in LV filling pressures and risk of pulmonary oedema. So this is very essential to decide occlusion of PFO in relation to other cardiac abnormalities.

How to diagnose PFO

Clinically, there are no characteristics findings. Other conditions which can mimic PFO are: ASD, PS, total/partial anomalous pulmonary venous connection, left superior venacava joining LA or RA. There are no specific ECG features of PFO.

Imaging methods\textsuperscript{28,29}

TEE (Trans-oesophageal Echo) is better than trans-thoracic echo in diagnosing PFO. We can see the gap in mid inter – atrial septum or evidence of septal aneurysm with septal perforation. Contrast/bubble
Echocardiography is very helpful in the diagnosis and appearance of micro bubbles (agitated saline) in LA within 3 cardiac cycles of appearance in RA which confirms PFO. This can be made simpler by Valsalva manoeuvre during contrast echo. Dye oximetry methods are also helpful but TEE is a gold standard for diagnosis.

**Cardiac catheterisation and PFO**

We should note that simple passage of cardiac catheter from RA to LA does not indicate ASD as it may also pass through a functionally closed FO. True deficiency of atrial septum (ostium secundum type, including fossa ovalis) should not be confused with ASD. As septal puncture during PTMC in cases of mitral stenosis (MS) may lead to cardiac perforation and puncture of an inappropriate atrial septal site, so, safety of using PFO for crossing atrial septum instead of atrial septal puncture during PTMC in cases of MS was seen by Buruah *et al* at Apollo Hospital, Vishakapatnam, India. Choosing PFO in cases of MS with huge LA and RA may be associated with problems as in such LA enlargement, PFO migrates downward making its relationship with mitral orifice more horizontal or even low. Practically, they found many problems during PTMC in such cases.

Cardiac catheterisation can quantitate shunt across PFO.

**Drug therapy**

There is no consensus to treat asymptomatic PFO, but high risk PFO should be treated with antiplatelet and anticoagulant drugs. In the presence of history of stroke or TIA, patient should be put on aspirin and warfarin to maintain INR at 2-3 and opinion of neurologist should be sought. There is a controversy regarding the duration of these drugs, but at present it is believed that these should be given for six months at least.

**Role of oxygen therapy**

It is helpful to some extent in cases of cyanosis and hypoxaemia.

**Exercise in symptomatic PFO**

Large right-to-left shunt shows increase in cyanosis on performing exercise, so patient should be advised against strenuous exertion in large PFO with significant shunt.

**Device closure of PFO**

In cryptogenic brain stroke and failed drug therapy we consider device closure. The devices are:

i. Cardioseal double umbrella device (smallest is 17 mm). It is US-FDA approved device. It requires hospitalisation for only 24-48 hours.

ii. Amplatzer septal occluder device.

Complication of devices are: embolism, bleeding, infection, frame fracture, device entrapment in chlari network regurgitation, apnoea, perforation of atrial wall, etc. Contraindication to device procedure are: active infection, blood clots in veins or very narrow vein so it becomes very difficult to put the device. These implants are not affected by MRI or metal detectors as they are not metallic in nature.

**Surgical closure** is recommended when PFO is more than 25 mm in size or cases of device failure. Procedures are: Double continuous suture of PFO or closure by Dacron and Pericardial Patch. Closure procedures, specially devices, are followed by antiplatelet and anticoagulants for at least six months.

**Risk of infective endocarditis in PFO**

There is no risk of infective endocarditis (IE) with PFO, so there is no role of antibiotic prophylaxis for IE in PFO.

**Prognosis**

It depends on underlying cardiac defects, but it is good in isolated PFO. In neonates, there is complete resolution of shunt as pulmonary vascular resistance falls. Associated congenital heart diseases, like Ebstein anomaly, show increase in size of PFO with the growth of the child and right-to-left shunt increases with exercise.

**Unsettled issues**

1. Treatment of asymptomatic patients with PFO
2. Optimal duration of medical therapy after stroke/TIA or device or surgical closure of PFO.
3. Optimal time to close PFO.
Conclusions

Knowledge about PFO is very important as it can be a cause of cryptogenic brain infarction and play a crucial role in various congenital and other valvular heart diseases. PFO has practical significance in cardiac cath labs also. More studies should be undertaken about unresolved issues, as PFO is present in 25-30% of normal adult population.

References

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