1 Introduction

1.1 The pathophysiology of atrial shunt via a patent foramen ovale

During fetal circulation, the direction of the interatrial flow is from right to left which is achieved via a true atrial septal defect or a patent foramen ovale (PFO). At birth there may be little or no shunt in either direction since both ventricles have the same compliance (1-3). During the neonatal period, the pulmonary vascular resistance falls, the pulmonary arterioles gradually involute, and the relatively thick-walled neonatal right ventricle becomes thinner and offers less resistance to filling than the left ventricle (1, 3, 4). As a consequence of increased left atrial pressure compared to that of the right atrium, the foramen ovale may be closed automatically. In some individuals, the foramen ovale which is a remnant from the fetal circulation remains patent.

PFO is found in approximately one quarter of the general population of adults (5), thus representing the most common persistent abnormality of fetal origin. In these individuals, the PFO permits interatrial right to left shunting whenever the right atrial pressure exceeds the left. Possible situations are:

-. transient instantaneous rather than mean interatrial pressure gradient during the normal cardiac cycle;

- an increase of right atrial pressure caused by a decrease in right ventricular compliance ;

- enhanced pressure gradient between both atria with respiration and the valsalva maneuver;

- a flow phenomenon such that venous blood from the inferior vena cava is directed preferentially toward the foramen ovale (6).

Right-to-left shunt also may occur in the absence of a pressure gradient. Castro et al. (7) suggested that a right to left shunt at rest, in the absence of a significant increase in right atrial mean pressure, is a marker of risk for cerebral ischemia in patients with PFO.

1.2 The relation between PFO and paradoxical embolism

It has been reported that patients with PFO had a significantly higher incidence of cryptogenic stroke (strokes of unknown cause) than those without PFO (8-12). The mechanism involved is presumed to be paradoxical embolism from a venous thrombus that travels via the PFO to the systemic circulation causing a stroke. Since the first report published by Cohnheim in 1877 (13), the association between a PFO and paradoxical embolism is well established (14). The incidence of paradoxical embolism in patients with PFO was 16% (14). Although direct evidence of paradoxical embolism is often lacking, the possibility of paradoxical embolism in patients with cryptogenic stroke and PFO is commonly retained as the cause of the neurological deficit, if all other known causes of cerebral emboli have been excluded. Patients with PFO and paradoxical embolism are also at increased risk for recurrent thrombo-embolic events, with a combined cerebrovascular accident (CVA) and transient ischemic attack (TIA) rate of 3.4% to 3.8% per year (15, 16). Other studies have also identified atrial septal aneurysm (ASA) as more prevalent in people with cryptogenic strokes as compared with asymptomatic control subjects (17). A large PFO and presence of an atrial septal aneurysm have been identified as morphological characteristics of PFO predicting a high risk for paradoxical embolism (18-24).

1.3 Treatment of PFO

The best treatment modality to prevent stroke in patients with PFO has not been defined. There are four major choices: surgical closure, percutaneous device closure, medical therapy with anticoagulation, and medical therapy with antiplatelet agents.

1.3.1 Surgical closure of PFO

Conventionally, many patients with a cryptogenic stroke in the presence of a PFO were treated with an antiplatelet agent or anticoagulants (25,26). However, some patients have contraindications for their use, refuse to take oral agents because of potential restrictions on their lifestyle or experience a recurrence of ischemic events while on medical therapy. For these patients, surgical and transcatheter closure of PFO becomes a potential therapeutic modality.

Surgical closure of PFO has been reported from various centres (27, 28, 31). The main advantage of surgical closure is that it provides a permanent closure of the defect, thereby preventing future paradoxical emboli without the risks associated with long-term anticoagulation. In all reported studies, surgical closure of PFO can be done safely. There was no perioperative morbidity or mortality in surgical closure and it efficiently reduced the risk of stroke recurrence (28). Although perioperative mortality in most cardiac surgical centres approached zero (29, 30), the major disadvantage is that an operation needs general anesthesia, open heart surgery and a hospital stay of several days. It can be associated with complications of cardiac surgery such as tamponade by pericardial effusion, post-pericardiotomy syndrome, cardiac arrhythmia and surgical wound complications (30). Furthermore, cardiopulmonary bypass may affect ventricular function and even cause cerebral complications (32-37).

1.3.2. Transcatheter closure of PFO

Since the first description by King and colleagues of the use of umbrellas to close atrial septal defects (38), the effects of several devices have been studied in ASD and PFO closure (39, 40). Among these are

- the Clamshell double umbrella device which was redesigned and named the CardioSEAL Septal Occluder (Figure 4) by Nitinol Medical Technologies, Inc. Boston, Mass).
- the Amplatzer PFO Occluder (Figure 2) which was approved by the FDA (39, 40) by AGA Medical Corp., Golden Valley, Minn.).
- the Helex Septal Occluder (Figure 3) which was designed by W.L. Gore and Associates, Flagstaff, AZ is a new device with many desirable characteristics.

Transcatheter closure has recently become an alternative to the surgical operation in the treatment of PFO. Compared with the surgical procedure, advantages of this technique are a lower complication rate, avoidance of the need for sternotomy and cardiopulmonary bypass, and the short period of hospital stay (43). The devices have been in various stages of development and testing for more than a quarter of a century. With the advent of newer devices and increasing experience, transcatheter closure of PFO can be performed with increasing success and a decreasing complication rate. However, whether device closure affects cardiac function has not been clarified. The main complications of this method are residual shunt, device frame fracture, device embolization, distortion or compression of the atrioventricular valves, chronic stresses between the heart and device that can lead to myocardial friction lesions, laceration of the atrial wall, and cardiac perforation (44, 45-50).

1.4. Non-invasive assessment of the ventricular function after PFO closure

1.4.1. Echocardiography

Conventional echocardiography is routinely used in the evaluation of cardiac function and colour Doppler echocardiography is used for assessment of blood flow velocities in the cardiac chambers and great vessels (51). Many parameters such as peak

velocity, acceleration time and deceleration time of the early diastolic wave can be determined from the transmitral flow velocity (52, 53), but these parameters are influenced strongly by volume status and aortic or left atrial pressures (54-56).

1.4.2 Tissue Doppler Imaging

TDI is a modified Doppler technique that allows measurements of low velocities from the myocardial wall. This technology can be easily incorporated into conventional ultrasonographic equipment and offers unique information regarding myocardial shortening and lengthening velocities along the long and short axes of the left and right ventricle.

Isaaz et al.(64) first reported the use of pulsed wave TDI in the apical four-chamber view for assessment of diastolic myocardial velocities, and concluded that pulsed Doppler recording of low velocity wall motion may provide a unique method for studying non-invasively the systolic and diastolic performance of the left and right ventricle in the longitudinal direction and for quantifying systolic and diastolic haemodynamic events during isovolumic periods that are not easily measurable by other non-invasive techniques. Since then, this method has been used to evaluate the ventricular wall motion velocity quantitatively in patients with various kinds of heart disease (58-60).

Tissue Doppler imaging may be recorded in pulsed wave, colour-encoded M-mode or two-dimensional mode. The spectral pulsed wave TDI method provides the highest temporal resolution and can be appropriately used for analysis of temporal relation between myocardial systolic and diastolic velocity waves. With this modality, a sample volume is placed within the myocardium, and the low Doppler shift of frequencies recorded from the heart wall moving through the sample volume during the cardiac cycle is recorded. The pulsed wave TDI can record both the systolic (Sm wave) and diastolic (Em, Am wave) myocardial velocities. The S wave reflects systolic and the E wave diastolic function. The velocity profiles of the mitral annulus

can be used to evaluate left ventricular function (65), and the tricuspid annular velocity measured from the right ventricular (RV) free wall can be used to assess the RV function. The major advantage of pulsed wave velocity measurements is that the ultrasound beam is parallel to the ventricular contraction, without the influence of trabeculae and myocardial dropouts.

A recent review by Garcia et al.(65) provides a description of the application of pulsed TDI in the assessment of ventricular diastolic function. It had been shown that TDI is more sensitive than traditional methods (63), such as transmitral pulsed Doppler.
Regional Doppler tissue velocities in one area, however, are affected by motion in adjacent tissue and global cardiac motion. Therefore it might not differentiate between active contraction and passive motion.

1.4.3 Strain Rate Imaging

Strain rate imaging is a recently developed technique derived from TDI that adds further details to detect cardiac function by overcoming some of the limitations of the TDI measurements. It allows the determination of velocity gradients between two tissue Doppler points oriented in the same plane. It describes myocardiac deformation, theoretically less susceptible to translation or tethering. It is potentially superior to TDI in regional myocardial function assessment (70,71).

Some studies demonstrated that SRI may be more accurate and sensitive than tissue velocity alone for evaluating regional longitudinal myocardial function (67,68,69).

Strain rate imaging is a novel parameter of regional myocardial function. It calculates velocity gradients between two distinct points along the ultrasound beam and is less susceptible than tissue velocity to translation and tethering artefacts. SRI wave form was also characterised by three peaks: systolic (SRs), early (SRe) and late diastolic (SRa) peaks.

“ Shortening” (S wave), which occurs when the two points are moving toward each other, can be used to describe the contraction properties; “lengthening” (E wave and A wave), when the two points are moving away from each other, can be used to describe the relaxation properties of a specific region of the myocardium. Peak systolic strain rate may accurately reflect local systolic function and peak diastolic strain rate may reflect local diastolic function because they measure myocardial deformation, not displacement (70-73).