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Diagnosis and Evaluation of Patent Foramen Ovale in the Era of Device Therapy: A Mini Review

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Abstract

Patent Foramen Ovale (PFO) causes cryptogenic stroke. Recently, device therapy has become widespread to prevent recurrent cerebral infarction caused by PFO. Therefore, it is important to evaluate the diagnosis of PFO and likelihood of cryptogenic stroke being related to PFO. This review summarizes the current diagnosis and evaluation of PFO.

Keywords: Patent foramen ovale treatment • Cryptogenic stroke • Diagnosis • RoPE score • Microbubble test

Introduction

Patent Foramen Ovale (PFO)

PFO is caused by incomplete fusion of the septum premium and secundum after birth in the cranial portion of the fossa ovalis. Right-left shunt occurs when the right atrial pressure exceeds the left atrial pressure. PFO occurs in about 25% of the general adult population [1,2].

PFO and cryptogenic stroke

Cerebral infarction is a disease that impairs the prognosis of patients. The TOAST classification is commonly used to classify cerebral infarction into five types: large-artery atherosclerosis, cardio embolism, small-vessel occlusion, stroke of other determined etiology, and stroke of undetermined etiology [3]. Of these, unexplained cerebral infarction accounts for as much as 40% and is referred to as cryptogenic stroke [4]. PFO cases cerebral infarction when a thrombus derived from the systemic venous system passes through the shu nt to the systemic arterial system [4].The proportion of cerebral infarction caused by PFO ranges from 21% to 63%, and it is more common in younger patients than other causes of cerebral infarction,its management is important [4].

Cardioembolic stroke

Cardioembolic stroke accounts for 15%-30% of ischemic strokes. Causes of cardioembolic stroke other than PFO are the following differential disease: atrial fibrillation, myocardial infarction, including ventricular aneurysm, intracardiac thrombus, valvular heart disease, cardiac tumor, infective endocarditis, mechanical valve prosthesis, giant Lambl's excrescences, and atrial septal aneurysm [5].

Diagnosis of PFO

Transesophageal Echocardiography (TEE) is considered the golden standard for the detecting PFO [5]. Additionally, the microbubble test with Valsalva maneuver during TEE avoids the increasing false negative rate of up to 20% and is considered an essential technique for PFO diagnosis [5]. The problem with the microbubble test is the complexity of the procedure. Sufficient Valsalva maneuver cannot be performed in the elderly and patients with impaired consciousness. In addition, the mobility of TEE equipment is poor, the procedure invasiveness is high, and repeatability is difficult. Transcranial Doppler Ultrasound (TCD) and Transthoracic Echocardiography (TTE) are alternatives to TEE. However, compared with TEE, the problem is that the sensitivity is 94% and the specificity is 92% for TCD, and the sensitivity is 88% and the specificity is 82% for TTE [6].

PFO Evaluation

In the morphological evaluation of PFO, diameter, tunnel length, septum premium deviation are used [7]. The classification of PFO size was based on the maximum number of microbubbles during the first three cardiac cycles; 0 microbubbles were classified as no shunt, one to five microbubbles as small, six to 25 microbubbles as moderate, and more than 25 microbubbles as large [8]. The presence or absence of Atrial Septal Aneurysm (ASA), Eustachian valve, and Chiari's network will be considered.

Complex PFO

A case of PFO with ASA, or with a long tunnel length of over 8 mm, or with multiple openings into the left atrium, or with septum premium deviation, or with additional multiple small defects on the fossa ovalis, or with the presence of a large Eustachian ridge, or with Chiari network is considered complex PFO [7].

Discussion

Characteristics of PFO cases with cerebrovascular accidents

Comparing PFO cases with and without cerebrovascular accidents, it has been reported that the proportion of complex PFO is high in the PFO cases with cerebrovascular accidents, long diameter (3.4 mm, 2.7 mm), long tunnel>8 mm (55%, 44%), large septum premium deviation (10%, 6%), prominent Eustachian valve (18%, 11%), large shunt (46%, 10%) [7]. TEE with Valsalva maneuver is desirable for PFO diagnosis. In a recent etiology analysis of cardiogenic stroke in a population with a high PFO detection rate in which this method was performed in all cases, PFO-related stroke was 6%, atrial fibrillation-related; 25%, other cardioembolic stroke; 16%, and cryptogenic stroke; 22% [5]. It has been reported that the PFO-related stroke group had a lower severity of stroke on the National Institute of Health Stroke Scale (NIHSS) than the atrial fibrillation group [5].

Likelihood of cryptogenic stroke being related to PFO

RoPE score: The RoPE score is a method for assessing the likelihood of the cryptogenic stroke being related to PFO. Scoring method is based on age, hypertension, diabetes, history of stroke or transient ischemic attack, smoking

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habit, and cortical infarct on imaging [1]. If there are no factors of hypertension, diabetes, stroke or transient ischemic attack, smoking habit, cortical infarct on imaging, 1 point is counted for each. In terms of factor: age, 18-29 years old (y.o); 5 points, 30-39 years old; 4 points, 40-49 years old; 3 points, 50-59 years old; 2 points, 60-69 years old; 1 point, ≥ 70 years old. 0 point, is counted. The scoring system focuses on age [1].

The PFO-attributable fraction to cerebral infarction is estimated to be 88% at a maximum of 10 points, 8 points: 84%, 7 points: 72%, 6 points: 62%, 5 points: 34%, 4 points: 38%, 0-3 points: 0% on RoPE scoring system [1]. It has been shown that young patients with no other factors have possibility to be induced stroke by PFO. The Rope scoring system also estimates the recurrence rate over two years for each score. The recurrence rate in each score group was 9-10 points: 2%, 7-8 points: 6%, 6 points: 8%, 5 points: 7%, 4 points: 12%, 0-3 points: 20% [1].

Nakayama score: There is a report of a scoring system that estimates attributable fraction in cryptogenic stroke by scoring each independent factor of PFO; long-tunnel PFO ≥ 10 mm, hypermobile interatrial septum, Eustachian valve or Chiari's network, large RL shunt during Valsalva maneuver, low-angle PFO ≤ 10° [9]. In that scoring system, the PFO attributable fraction to cryptogenic stroke was 5% or 17% with a score of 0 or 1 [9]. However, with a score of 2,3 or 4 points, it was 80%, 87%, or 89% [9]. It has been reported that the PFO attributable fraction to cryptogenic stroke is significantly increased with a score of 2 or more [9]. 91% sensitivity and 80% specificity have been reported for 2 points for an association to Cryptogenic stroke [9].

MorPFO score: Recently, in the MorPFO scoring system, PFO independent factors, PFO channel length reduction ≥ 21%: 7 points, short septum secundum (<8.6 mm): 5 points, thin septum premium (<1.6 mm): 3 points, large right-to-left shunt: 3 points, low PFO channel length/height ratio during Valsalva (≤ 2.1): 2 points, the presence of atrial septal aneurysm: 1 point, are scored to evaluate the risk of cerebral infarction [10]. In this scoring system, the PFO attributable fraction to cryptogenic stroke is evaluated as 0-7 points: low-risk PFO (0%-25%), 8-11 points: moderate-risk (25%-50%), 12-21 points: high-risk [10]. This scoring system emphasizes PFO channel length reduction and short septum secundum [10]. Many scoring systems have been published. It is important to evaluate PFO in a multifaceted and objective manner by using these scoring systems, for PFO treatment strategies.

Device therapy for PFO

RESPECT, CLOSE, DEFENSE-PRO, and REDUCE results show the superiority of PFO closure compared with optimal medical therapy [11]. It is also more cost effective than drug therapy [12]. The recurrence rate of cerebrovascular events in the PFO group was 3.8% per year, the recurrence rate after PFO closure was 1.86%, and in the standard treatment was 5.4% [13]. Thrombus in the PFO occluder, aortic plaque, pulmonary arteriovenous fistula, atrial fibrillation, is considered causes of recurrence [7]. Recent reports have reported the usefulness of PFO closure with a recurrence rate of stroke of 1.1% in the PFO closure group and 13.3% in medical therapy [14]. Additionally, in patients at high risk of thrombotic stroke, the usefulness of PFO closure has been suggested even in the group of patients aged 60 years and older [14]. Even when PFO is closed, the benefit of postoperative combination of anticoagulant therapy has been mentioned when the risk of thrombosis is high [14]. When considering the indications for PFO closure, it is necessary to consider not only the evaluation by the scoring system but also the individual pathological conditions [14].

Since the high RoPE score cases tend to be younger population, it is essential to prevent the recurrence of stroke. Alternatively, in the low-scoring group: the elderly with cardiovascular risk factors, PFO is less associated with stroke, so the indications for PFO treatment should be considered. However in the lower PFO-related stroke cases, the recurrence and severity of stroke are also high, therefore, it is also important to diagnose the stroke etiology and prevent recurrence [1,5]. PFO treatment is considered for younger patients with low cardiovascular risk factors because of their higher likelihood of cryptogenic stroke [1]. However, there are PFO cases with atrial fibrillation and PFO cases in which paroxysmal atrial fibrillation has not been detected [5]. It has been denied that PFO closure itself induces new atrial fibrillation. The incidence of new atrial fibrillation has also been shown to be comparable to that of the age-matched normal population in the group of patients after PFO closure [15].

Conclusion

Device therapy for PFO has possibility to make it difficult to perform catheter ablation therapy for atrial fibrillation. Therefore, for the likelihood of the cryptogenic stroke being related to PFO is low in elderly patients with high cardiovascular risk factors, prior evaluation is important to diagnose whether device therapy should be performed. Since device treatment has high advantages in PFO treatment, appropriate device therapy should be considered in young patients with cryptogenic stroke who caused by PFO. However, in older cases, careful evaluation of another stroke causes is important.

Conflict of Interest

All authors declare no conflict of interest.

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