PREVALENCE OF PATENT FORAMEN OVALE IN YOUNG PATIENTS WITH CRYPTOGENIC ISCHEMIC STROKE

Masoumeh Sadeghi[(1)], Masoud Poormoghaddas[(2)], Hamidreza Roohafza[(3)]

Farideh Mazaheri[(4)], Mortaza Abdar Esfahani[(5)], Aliakbar Tavassoli[(1)]

Abstract

BACKGROUND: Patent foramen ovale (PFO) is the most commonly persistent abnormality of fetal origin. PFO has long been recognized as a potential risk factor for ischemic stroke. This study has shown the prevalence of PFO among young patients with cryptogenic stroke.

METHODS: In our case-control study we had 32 patients, 18 to 55 years old with cryptogenic stroke and 64 participants among normal population with matched age and sex in control group. We studied them for stroke risk factors like hypertension, diabetes mellitus, ischemic heart disease, dyslipidemia and then election of PFO by contrast trans-thoracic echocardiography.
Data entered in $SPSS_{11}$ and analyzed by Chi-Square and logistic regression. P value less than 0.05 was considered statistically significant.

RESULTS: We found that 37.5 % of patients in case group and 7.7 % of patients in controls had PFO and this difference was statistically significant (P = 0.001). They had no significant difference in other atherosclerosis risk factors. In control group we saw small shunt but in stroke group large shunt was more prevalence (P < 0.05).

CONCLUSION: Our findings supported this idea that PFO is a predisposing factor for stroke and it had a higher prevalence among patients with cryptogenic stroke. Besides, large shunt was more concomitant with ischemic attack. Then we suggest any patient with undefined cause of stroke must be evaluated for PFO.

Keywords: Patent foramen ovale, Stroke, Young.

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Introduction

Patent foramen ovale (PFO) is the most commonly persistent abnormality of fetal origin, occurring in 10% to 15% of the normal adult population.[1] PFO has been recognized as a potential risk factor for ischemic stroke through paradoxical cerebral embolism.[2] Ischemic stroke in young adults has been considered a relatively rare event, with fewer than 5% of all cerebral ischemic infarctions occurring below the age of 45 years, although cerebral ischemic infarction more than 10% has been reported.[3,4]

The cause of ischemic stroke in young patients is often not found despite systemic investigations. Such strokes are classified as cryptogenic in patients with cryptogenic stroke. PFO can be detected in up to 50%, whereas its prevalence in general population is low.[5,6] So with case-control studies which demonstrating a higher prevalence of PFO among elderly patients with strokes with unknown origin, led to acceptance of PFO as stroke risk factor.[7] However because direct evidences for paradoxical embolization are rare in the individual clinical situation, the potential role of the PFO in stroke is still a matter of debt.5 Earlier studies have suggested that a PFO is an incidental finding in patients with stroke and dose not represent a risk factor for it.[8,9]

On the other hand, later studies and a meta-analysis support PFO as risk factor for stroke and more recent investigations also found a strong association between the morphological characteristics of the PFO and size of it and the risk of embolic cerebrovascular events.[10,11] But establishing a causal relationship between PFO and stoke remains the clinical point in the diagnosis of paradoxical cerebral embolism.

In our study we evaluated the prevalence of PFO

1) Associate Professor of Cardiology, Isfahan Cardiovascular Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.
2) Professor of Cardiology, Isfahan Cardiovascular Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.
3) Psychologist, Isfahan Cardiovascular Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.
4) Neurologist, Isfahan Cardiovascular Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.
5) Associate Professor, Department of Cardiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.
Corresponding author: Masoumeh Sadeghi, E-mail: sadeghimasoumeh@gmail.com

in young patient with cryptogenic stroke and co morbid conditions in these patients.

Materials and Methods

We selected 32 patients aged 18 to 55 years old and who had an ischemic stroke (defined as a neurological deficit that lasted more than 24 hours) within the preceding three months for which no definite cause had been identified after a standardized workup.

Patients were excluded if the work-up had been incomplete, if there was a contraindication for aspirin therapy, hemorrhagic stroke subjects or if certain circumstances made follow-up impractical.

At first we recorded their demographic data. Then risk factors for stoke, post vascular events, neurological deficit and the severity of stroke were systematically recorded. In addition to cerebral computed tomography (CT scan) all patients had a standardized workup to rule out definite causes of stoke. The workup comprised routine blood tests and a coagulation study (including tests for protein S, protein C, antithrombin III and antiphospholipid antibodies), 12-lead electrocardiography ,echocardiography and cervical ultrasonography (carotid and vertebral). The following disorders were considered to be definite causes of stroke and led to exclusion: large artery atherosclerosis(defined by stenosis of at least 50 percent or occlusion of the corresponding vessel); lacunar stroke (defined by small deep infarct less than 15mm in diameter in a patient with hypertension); cardio-embolic causes, such as arterial fibrillation; recent (within 4 months before the stroke) myocardial infarction, dilated cardiomyopathy; rheumatic mitral stenosis, mitral or aortic vegetations or prostheses, left arterial or left ventricular thrombus or tumor, akinetic left ventricular segment, spontaneous echo contrast of the left atrium, complex atheroma of the aortic arch, and coagulopathies, hematologic or systemic disorders (e.g. antiphospholipid antibody syndrome) or migrainous infarction.

For each patient, the clinical, laboratory and imaging data were reviewed by a neurologist and patients with diagnosis of cryptogenic stroke were referred to cardiovascular out patient clinic.

A cardiologist did trans-thoracic echocardiography with contrast. Patients that assessed for a PFO as a right-to-left shunt were diagnosed if at least three microbubbles appeared in the left atrium, either spontaneously or after provocative maneuvers, within three cardiac cycles after the complete opacification of right atrium. The shunting was defined as small if 3 to 9 microbubbles appeared, moderate if 10 to 30 microbubbles and large if more than 30 microbubbles were detected.

Controls were selected among normal population with same age and sex. Controls were 64 people.

Statistical analysis

Data entered in $SPSS_{11}$ and were analyzed with use of the chi-square test and logistic regression.

Results

A total of 96 patients enrolled in the study. 32 patients were in case group (young patient (18-55 years oldwith cryptogenic stroke), and 64 patients were in control group. Mean and standard deviation of age was 43.8±5 years in case group and in controls was 45.87±6 years. 35 patients were female, 12 patients in case and 23 in control, and 61 patients were male, 20 patients in case and 41 patients in control groups.

In control groups only 5 patients(7.7 %) had PFO but in case group 12 patients (37.5 %) had PFO and this deference was statistically significant (P=0.001). We found no statistically important difference between cases and controls in risk factors like hypertension, diabetes mellitus, hyperlipidemia, smoking status and previous ischemic heart disease.

In logistic regression analysis none of these risk factors could anticipate the stroke in youth.

Then we compared these risk factors between patients with PFO (in case and control groups) and without PFO. We found no statistically significant difference between patients with PFO and without PFO in these risk factors (P>0.05).

According to PFO size, from 12 patients in case group 10 patients (83.3%) had large shunt and 2 (16.7%) had moderate shunt. In control group 4 (80%) had small shunt and 1 (20%) had moderate shunt and no control subject had large shunt. Then small and large shunt were seen statistically significant in control and stroke group respectively (P<0.05).

Discussion

Our study showed that PFOs (especially with large shunt) were more prevalent in young patient with stroke rather than healthy subject.

Our results are compatible with Lechat et al. study that found among young adult with stroke 40% had PFO.[12]

Steiner et al. revealed that stroke patient with larger PFOs show more brain imaging feature of embolic infarcts than those with small PFOs. Thus larger PFO may be more likely to cause paradoxical embolization and may help to explain the stroke mechanism among patients with no other definite cause.[7] Current study didn't evaluate severity of stroke through brain imaging but this survey showed that stroke patient had larger shunt than healthy ones.

Both case and control groups were adjusted for atherosclerotic risk factors; in this way there were no significant difference between them. Considering no

significant major risk factors differences among case and control groups, it can be suggested that PFO will be more possible cause for stroke in IRAN.

The prevalence of PFO in healthy group (7.7%) was lower than the estimated PFO prevalence (10-15%). This differences may be due to selection of control according to case, also exclusion of all participant less than 18 years.

More than 30 millions Americans have PFOs, but only 1 in 1000 will have an embolic stroke of "unknown" origin. If the PFO was the only cause, the recurrence rate would be tiny, yet recurrence rates have been estimated to be 3.4% to 11% per patient-year.[13]

The annual recurrence rate after PFO closure in 80 patients was reasonably low at 2.5% for transient ischemic attack and 3.4% for all embolic events.[1]

Although in our study we found a higher prevalence of PFO among stroke patients but this finding never shows a causal relationship between them.

Must we evaluate every patient with stroke for PFO or must treat them?

The PFO stands accused. The evidence is strong and getting stronger. Acquittal or conviction will only occur after a randomized trial in patients who have a PFO and a first event, comparing closure (either by catheter or surgery) with anticoagulation. Given the accumulating data, one hopes that our general hospitals interested in adult stroke prevention, will organize such trials. Until such a trial is completed, neurologists and cardiologists have real patients with real strokes to manage. A review of the available data, including those presented by Windecker et al. would support the following recommendation: those embolic stroke patients who are younger, who have largish PFOs and no other stroke source, may be considered candidates for anatomic closure of their PFO.[14]

We concluded that as we have shown high prevalence of PFO in stroke patients, we must organize another study to follow this patient for recurrence and if needed closure of PFOs.

Study Limitation

Considering the ethnical committee prohibited invasive procedure including trans-esophageal echocardiography in healthy people, and the necessity of similar measurement for both groups we evaluated them with transthoracic echocardiography.

With firm eligibility criteria, finding proper cases lasted three years.

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