Original Article

Assessment of Long- and Short-Term Complications of Percutaneous Patent Foramen Ovale Closure in Patients With Cerebrovascular Events or Peripheral Embolism Over a 12-Year Period Starting in 1998

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ABSTRACT

Background: Observational studies have favored percutaneous patent foramen ovale (PFO) closure over medical treatment for the reduction of recurrent stroke, whereas randomized trials have failed to demonstrate the significant superiority of percutaneous PFO closure. A few long-term studies are available on post-PFO closure outcome. This study reports long- and short-term clinical outcomes after percutaneous PFO closure.

Methods: Between January 1998 and January 2015, we enrolled 51 (32 men [62.7%] and 19 [37.3%] women) consecutive eligible patients with cerebrovascular events or peripheral embolism, presumably related to PFOs, who underwent percutaneous PFO closure in our center. All the patients' documents and clinical data were assessed. Of the entire study population, telephone contacts were applied in 47 cases. The mean follow-up time was 46.51 ± 43.43 months. The main criterion for closure was patients with at least 1 cryptogenic stroke or peripheral embolism associated with PFOs.

Results: Percutaneous PFO closure was successfully performed in 51 patients. No cardiovascular or cerebrovascular deaths occurred. The mean follow-up time was 46.51 ± 43.43 months. Long-term device-related complications were cerebrovascular accidents in 3 (5.88%) patients (2, 3, and 4 y after the procedure) and open heart surgery in 1 (1.96%). The short-term complications were atrial fibrillation in 1 (1.96%) patient, air embolism in 2 (3.92%), hematoma in 2 (3.92%), and tamponade in 1 (1.96%).

Conclusions: Percutaneous PFO closure was associated with a very low risk of recurrent stroke. We observed no cardiovascular or cerebrovascular mortality; however, there were a few short- and long-term device-related complications. Thus, percutaneous PFO closure is a safe treatment even in the long term. ***(Iranian Heart Journal 2017; 17(4): 6-16)***

Keywords: Patent foramen ovale ● Cryptogenic stroke● Long-term follow-up● PFO closure● Short-term follow-up● Atrial septal aneurysm● Transient ischemic attack● Transesophageal echocardiography

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A patent foramen ovale (PFO) is a common heart defect presenting in about 25% of the general population. [1] A few studies have shown the relationship between PFOs and cryptogenic stroke in young adults. Likewise, an association between an increased risk for recurrent thromboembolic events, PFOs, and cryptogenic stroke has been previously described. [2-5] PFOs and atrial septal aneurysms are associated with an increased risk of recurrent thromboembolic stroke, and a large PFO is a predictor for cerebrovascular ischemic events. [6-9] Long-term oral anticoagulation or antiplatelet medication, surgical PFO closure, and percutaneous PFO closure with a catheter-based procedure using a septal occluder device are considered the potential therapeutic strategies for the secondary prevention of paradoxical embolic stroke. Percutaneous PFO closure is a safe, feasible, and practical procedure. [10-13] Numerous different devices are used at present. Five observational trials have indicated that, in comparison to medical treatment, the device closure of PFOs reduces the relative risk of recurrent cerebrovascular events by nearly 80%. [14-18] Nevertheless, 3 randomized trials [19-21] have shown no significant benefits of device closure over medical therapy during a 2-year follow-up. The primary outcomes of the most recent trials such as the RESPECT and the PC Trial were not significantly affected by which treatment was given. Low annual rates of recurrent stroke (1%–2%) have been reported by previous research, [22-23] citing the long-term clinical outcomes of device closure and showing a need for much larger follow-up studies—either by enrolling more patients or by maintaining a longer follow-up period. Confusing results can be avoided by keeping the number of patients lost to follow-up to a minimum, especially when the event rate is low. In observational studies, the AMPLATZER PFO Occluder has been shown to have advantageous safety features as a closure device. [24]

The aim of the present study was to provide short- and long-term clinical follow-ups of patients with a previous percutaneous PFO closure as a secondary prevention after cryptogenic stroke or peripheral embolism and to monitor mortality, complications, recurrent stroke, and other clinical significant conditions.

METHODS

Patient Selection

The present study, conducted between January 1998 and January 2015, recruited 51 consecutive patients (32 [62.7%] men and 19 [37.3%] women), who were referred to our tertiary care center for percutaneous PFO closure. In all the patients, cryptogenic stroke or transient ischemic attack (TIA) or peripheral embolism associated with PFOs were diagnosed by their neurologists and cardiologists at primary local hospitals via transesophageal echocardiography (TEE), computerized tomography scan, or magnetic resonance imaging of the brain. The patients were referred from their 1st hospitals due to the complexity of their cryptogenic stroke and PFOs, and further evaluation of the patients' clinical data and medical records was made by our interventional cardiologists, who took the final decision on PFO closure after consulting TEE imaging experts and stroke experts. For both index stroke/TIA and at follow-up, a diagnosis of TIA was made by the treating neurologist if acute neurological deficits with a probable vascular ischemic cause were completely resolved within 24 hours. Ischemic stroke was defined as a sudden new focal neurological deficit lasting > 24 hours. [25] Stroke etiology was defined according to the modified TOAST (Trial of Org 10172 in Acute Stroke Treatment) criteria. [26]

The documents and clinical records of 51 patients were assessed. Forty-seven cases were followed up by telephone calls. In 4

cases, telephone contact was not possible, so they were only followed up through their records. The main criterion for closure was patients with at least 1 cryptogenic stroke or embolic event with PFOs as no clear cause for stroke or embolic event was found such as atrial fibrillation, myocardial infarction during the preceding 4 weeks, and large apical infarction. The present study was approved by the Review Board of Iran University of Medical Sciences, Tehran, Iran. Informed consent was obtained from the whole study population. Twenty-eight cases had already discontinued their medication at the time of telephone intervention follow-up, and 3 of those patients developed cerebrovascular complications and were, therefore, administered aspirin (ASA). Our results demonstrated that after PFO closure, while we had discontinued the medication, the rate of recurrent events was very low.

Patent Foramen Ovale Closure

The patients, who were selected for PFO closure, underwent TEE. The PFO size and the underlying diseases were all assessed via echocardiography. PFO closure was performed under fluoroscopy guidance without using TEE. The femoral vein access was achieved in 27 patients. The AMPLATZER, Figulla, Cardi-O-Fix, and other devices were applied in the patients for PFO closure. Out of the 51 patients, 39 cases underwent transthoracic echocardiography (TTE) and TEE for a 2nd time and were evaluated regarding residual shunting and location of the device during the 1st 48 hours. The complications of death, bleeding requiring blood transfusion, tamponade, air embolism, arrhythmias, device embolization, device thrombosis, arteriovenous fistula formation, shunts before and after the procedure, pseudoaneurysms, endocarditis, cerebrovascular accidents (CVAs), and embolic events were all assessed.

Patients' Follow-Up

TEE was also performed 48 hours following PFO closure with color Doppler and contrast injections during the Valsalva maneuver in 39 patients. Residual shunting was defined as "small" when 1–20 bubbles were seen in the left atrium or when the shunt was seen only with color Doppler, despite multiple contrast injections during the Valsalva maneuver. Once in excess of 20 bubbles were seen in the left atrium, the shunt was considered substantial. [28] The patients underwent treatment with ASA and Plavix for the duration of 6 months after PFO closure.

A structured medical history—including items on recurrent stroke/TIA, risk factors for stroke, and potential complications to percutaneous treatment—was obtained from all the patients. The patients who agreed to attend follow-up at our center were examined via ECG and TTE. The patients' neurological status was assessed using the modified Rankin Scale. [29-31] Those who could not attend our tertiary care center were followed up with a structured telephone interview.

We collected all relevant medical records and documentation of the imaging procedures between 1998 and 2015 by a professional interventionist. Forty-seven (92%) cases were followed up by telephone. The entire study population received ASA and Plavix treatment. Atrial fibrillation rhythm before and after the procedure, PFO diameter, tunnel length > 10 mm or < 10 mm, presence of coronary artery disease, other diagnostic problems such as left ventricular clot or concomitant disease, existence of thrombosis on the PFO on echocardiography, and finally occurrence of stroke as well as its type and status on imaging were also determined.

Statistical Analysis

The continuous data are summarized as means ± SDs (or median ranges), as appropriate. Univariate comparisons were made using paired or unpaired *t*-tests for the continuous data and the Fisher exact test or

the χ^2 test for the categorical data. The level of significance was considered at a *P* value < 0.05. The distributions are presented as means and SEMs. The logistic regression test was applied to remove the confounding effects of the variables. The statistical analyses were performed using SPSS, version 18.0 (software IBM Corporation, Armonk, NY, USA).

RESULTS

In the present study, carried out between January 1998 and January 2015, 51 consecutive patients—comprising 32 men (62.7%) and 19 (37.3%) women—who were referred to our tertiary care center for PFO closure were enrolled. The mean age at PFO closure was 39.61 ± 0.38 years (age range = 16–66 y). The mean follow-up duration was 46.51 ± 43.43 months (1–230 mon).

Among the 51 patients, the minor complications were comprised of atrial fibrillation (n = 1, BioSTAR), hematoma (n = 2, AMPLATZER Occluder and Figulla), and air embolism (n = 2, Figulla). Among these patients, there was a 29-year-old man with a previous history of pulmonary stenosis. He underwent percutaneous transluminal pulmonary commissurotomy (PTPC) but suffered intraprocedural tamponade due to right atrium-inferior vena cava (RA-IVC) rupture and finally underwent surgery. The major complications were device removal 1 year after closure in 1 patient (AMPLATZER Occluder) with a PFO size of 3 mm and mild-to-moderate residual shunting after PFO closure on follow-up echocardiography, CVA in a 47-year-old man (Figulla device) with a PFO diameter of 4.5 mm and a PFO length of 12 mm and unknown shunting 2 years after closure, and CVA in a 35-year-old patient with a PFO diameter of 8 mm without residual shunting 4 years after PFO closure (25-mm DEVIE device). There was also a 32-year-old patient, who experienced CVA 3 years after PFO closure and had a history of 2 cerebrovascular events. This patient had pulmonary stenosis, for which he underwent PTPC but developed intraprocedural tamponade. The diameter of the PFO was 4 mm in 1 case with the Figulla device and after closure, there was no residual shunt. All the mentioned complications were not accompanied by underlying diseases apart from 1 patient, who had pulmonary stenosis, experienced tamponade because of RA-IVC junction rupture, and suffered 2 CVAs within a 3-year period afterward. The device most frequently used in the patients was the Figulla in 28 (54.9%) cases and the AMPLATZER Occluder in 12 (23.5%). The average PFO diameter was 3.49 ± 1.38 mm (min of 1 mm and max of 8 mm), and the mean length of the PFO was 11.61 ± 6.02 mm (min of 5 mm and max of 24 mm). Out of the 51 patients, 20 (39.2%) cases had hemiparesis associated with dysarthria, 18 (33.3%) had hemiparesis, and 2 (3.9%) had visual loss. ASA was used totally in 8 (11.8%) cases. According to the study population's medical records, among the 51 cases, TIA was seen in 10 (19.6%), CVA in 37 (72.5%), TIA in conjunction with CVA in 3 (5.9%), and peripheral embolism in 12% of the cases. Furthermore, among the 51 patients, PFOs with atrial septal aneurysms were seen in 8 (11.8%) cases. Diabetes mellitus was seen in 11.96% of the patients, hypertension in 6 (11%), smoking in 6 (11.76%), and hyperlipidemia in 6 (11.8%). The most frequently used drugs were respectively ASA in 15 (29.4%) cases, Plavix and ASA in combination in 14 (27.5%), warfarin in 9 (17.6%), ASA and warfarin in 8 (15.7%), and Plavix in 1 (2%). Out of the 51 patients, 41 cases had PFO closure while they experienced their 1st embolic events and in 10 cases, PFO closure was performed when they had recurrent cerebrovascular events (Table 1).

Table 1. Demographic and clinical data

Variables	Mean ± SD N=51
Age	36.61±0.38 (16-66 y)
Sex male female	32 (62.7%) 19 (37.3%)
DM	11.96%
HTN	6 (11%)
Smoking	6 (11%)
Hyperlipidemia	6 (11.8%)
ASA	15 (29.4%)
Warfarin	9 (17.6%)
Warfarin + ASA	8 (15.7%)
Plavix ± ASA	14 (27.5%)
Plavix	1 (1.96%)
No anticoagulant	4 (7.84%)
Hemiparesis	18 (33.3%)
Dysarthria	8 (15.68%)
Hemiparesis + dysarthria	20 (39.2%)
Visual loss	2 (3.9%)
Peripheral embolism	1 (1.96%)
Unknown cerebrovascular symptoms	2 (3.9%)

ASA, Aspirin; HTN, Hypertension; DM, Diabetes mellitus

Short-Term Complications

According to our results, the short-term complications were atrial fibrillation in 1 (1.96%) patient, air embolism in 2 (3.92%), hematoma in 2 (3.92%), and tamponade in 1 (1.96%). Atrial fibrillation was seen in a 29-year-old patient with a 23-mm BioSTAR device without any cardiac risk factors. Hematoma was seen in 2 cases with the Figulla device; 1 of these patients received warfarin and the other one received ASA and Plavix together. Air embolism was seen in 2 cases with the Figulla device. Tamponade was observed in a 29-year-old man with the Figulla device. He had pulmonary stenosis, for which he underwent PTPC and due to stroke was candidated for PFO closure. During the procedure, however, tamponade occurred owing to the rupture of the RA-IVC junction and finally he underwent open heart surgery (Table 2).

Table 2. Long- and short-term complications

Complication	N(%) N=51
CVA	3 (5.88%)
Open heart surgery	1 (1.96%)
AF	1 (1.96%)
Tamponade	1 (1.96%)
Air embolism	2 (3.92%)
Hematoma	2 (3.92%)

CVA, Cardiovascular accident; AF, Atrial fibrillation

Long-Term Complications

The long-term complications were comprised of CVAs, seen in 3 (5.88%) patients with recurrent CVAs (2, 3, and 4 y afterward), and residual shunting in 1 patient, who underwent open heart surgery and device removal. No death due to cardiovascular or cerebrovascular events was seen. Out of the 3 cases with CVAs, the Figulla device was used in 2 (66.6%) and the DEVIE device was applied in 1 (33.3%). In the 2 cases, follow-up echocardiography was performed and no residual shunt was observed. Follow-up echocardiography was not performed in the other case. One patient had a history of pulmonary stenosis and underwent PTPC. Open heart surgery was performed in 1 male patient due to residual cardiac shunting and he was found to have a PFO diameter of 3 mm but no history of underlying heart disease was found. (The implanted device was the AMPLATZER Occluder, and mild-to-moderate residual shunting after PFO closure was observed on follow-up echocardiography.) Totally, the long-term complications were observed in 4 patients: 1 patient underwent surgery for a 2nd time for

PFO closure and 3 patients had CVAs (Table 2).

Incidence of the Underlying Diseases

Out of the 51 patients with PFOs, interatrial septal aneurysms were seen in 6 (11.76%) patients, lipomatous hypertrophy of the interatrial septum (thickness = 4.9 mm) in 2 (3.94%), previous coronary artery bypass graft surgery in 1 (1.96%), and history of pulmonary stenosis and PTPC in 1 (1.96%) (Table 3).

Table 3. Frequency of the long-term complications associated with the device, PFO diameter, and residual shunts

Variables	Device Type	PFO Diameter	Follow-Up Echo	Shunt	
CVA	Figulla	4 mm	yes	no	2 (66.6%)
	DEVIE	8 mm	yes	no	1 (33.3%)
Open heart surgery	AMPLATZER	3 mm	yes	yes	1 (33.3%)

PFO, Patent foramen ovale; CVA, Cerebrovascular accident

Table 4. Frequency of the underlying concomitant diseases

Type	N(%) N=51
ASA	6 (11.75%)
Lipomatous hypertrophy of the septum	2 (3.94%)
Severe PS and PTPC	1 (1.96%)
CABG history	1 (1.96%)
No underlying disease	41 (80.39%)

ASA, Atrial septal aneurysm; PS, Pulmonary stenosis; PTPC, Percutaneous transluminal pulmonary commissurotomy; CABG, Coronary artery bypass graft surgery

Relationship between atrial fibrillation and the device type

We found 1 instance of atrial fibrillation in a 23-year-old man with a BioSTAR device without any risk factors.

Relationship between the device type and the long-term complications (cerebrovascular accidents and surgery)

A small-to-moderate residual shunt or fenestration after PFO closure was found in 1 patient, who had PFO closure with the AMPLATZER Occluder device (25 mm) and underwent open heart surgery due to continuous shunting 1 year after PFO closure. The size of the PFO before closure was 3 mm, and the patient had no history of underlying heart diseases. Out of the 3 patients with CVAs, 2 cases had the Figulla device and 1 had the DEVIE device. The Figulla was utilized in a 45-year-old male smoker with a PFO diameter of 4.5 mm; he had no residual shunting on follow-up echocardiography. The Figulla device was also used in a 29-year-old man without any cardiac risk factors and with a PFO diameter of 4 mm; he had no residual shunting on follow-up echocardiography. The DEVIE device was used only in a 31-year-old man without any history of cardiac risk factors and with a PFO diameter of 8 mm; there was no residual shunting on follow-up echocardiography (Table 3).

Frequency of cardiovascular accidents due to remaining shunts

Out of the 51 patients, 39 cases had follow-up echocardiography. Eight (20.51%) of these patients had residual shunts on follow-up echocardiography.

Frequency of the remaining shunts according to the device type

There were 51 patients with considerable residual shunts; 5 (9.80%) of these patients had the Figulla device and 3 (5.88%) had the AMPLATZER Occluder device.

DISCUSSION

The rate of recurrent neurological events in the present study is high in comparison with a recently published meta-analysis of 48 studies, which showed a recurrence rate of 0.8% per year for PFO closure and 5% per year for pharmacologically treated PFO patients. [32] The recurrence rate of complications for PFO closure in our study was 1.5% annually. It should be noted, however, that our sample size is too small. PFO closure in a long-term follow-up study of 12.4 years was associated with a very low recurrent event rate of 0.3% per year and a success rate of 99%. According to our study, the recurrence rate was about 1.5% in 1 year, which is approximately twice that reported by another 2 meta-analyses. The differences may be more due to various inclusion criteria. In our study, the recurrence rate of stroke was low and the coincidence of PFOs and atrial septal aneurysms was infrequent. Therefore, if we had included high-risk patients, the differences would have been reduced.

So far, there have been 3 randomized clinical trials on device PFO closure. The 1st study, CLOSURE I, [19] presented no significant benefits of PFO closure on the primary end point to prevent recurrent stroke but had a trend toward a slight reduction in recurring TIAs: 3.3% for PFO closure vs 4.6% for medical therapy alone. The RESPECT trial [20] and the PC Trial [21] have both been published recently and, as with the CLOSURE I study, their primary outcome was not significantly affected by which treatment was given. However, the results of these studies should be interpreted more carefully because the event rate was lower than expected.

The present study provides reliable short- and long-term follow-up and adds to our understanding of the long-term consequences of PFO closure in patients with a history of cerebrovascular events associated with PFOs. The mean follow-up post PFO closure was 46.51 ± 43.43 months. This is both short-term and long-term clinical follow-ups of PFO cases with a follow-up rate of 47 (92%) according to telephone contacts with the patients. The mean follow-up time in a study by Fischer et al [22] was found to be 15.4 years, but the follow-up rate was only 89% post PFO closure. In addition, the mean follow-up after index event in a study by Wahl et al [23] was 10 years, with a mean follow-up rate of 98%. When the event rate is low, it is of vital importance to have a high follow-up rate in order to eliminate the risk of bias. In the present study, the follow-up rate according to the patients' documents and records was 100% and in terms of telephone contacts was 92%. The 10.47% incidence of atrial fibrillation was the only potential procedure-related minor complication in the present study. However, the observed atrial fibrillation was transient; no chronic atrial fibrillation could be observed and it was spontaneously recovered. The incidence of atrial fibrillation varies in other studies from 0.6% [33] to 7.6% [34] during the 1st year post PFO closure. Khairy et al [35] in 2003 reported a rate of 7.9% for major complications and 1.5% for minor complications. In 2009, Wahl et al [33] reported a complication rate of 0.8%. In our study, the long-term event rate was 4 (7.84%) and the short-term event rate was 6 (11.76%). We also showed that the rate of major complications was approximately in concordance with that reported by the Khairy trial; however, the rate of minor complications was higher than that reported in the trial, which may be due to the occurrence of air embolism and hematoma during the procedure. The reduction in the complication rate over time is most likely a result of better patient selection, better devices, and greater experience among interventional cardiologists. [36]

It is supposed that clinical results will be more optimal with devices providing a higher complete closure rate. [37] Our initial experience with 51 patients treated with different devices and a follow-up period of

about 46.51 ± 43.43 years showed air embolism in 2 cases (Figulla device) and CVAs in 3 (5.9%) cases (Figulla device in 2 cases and DEVIE device in 1). This contrasts favorably with the literature on the natural course of patients with PFOs and cryptogenic stroke. [38] In light of the results of our study, it can be concluded that the most frequently used device in the patients undergoing surgery and PFO closure was the AMPLATZER Occluder.

PFO closure with the AMPLATZER Occluder device has been reported to be associated with a low risk of device thrombus formation compared to the other PFO occluding devices. [39] We found no thrombus formation at the AMPLATZER Occluder device location or the other devices. In an investigation, an 88% success rate for PFO closure with the AMPLATZER Occluder device at 6 months' follow-up and 93% after a mean follow-up of 18 months was demonstrated, compared to 86.1% at 6 months and 86.7 at 24 months in the CLOSURE I study, which used the STARFlex device in another study. [20] In our investigation, *vis-à-vis* residual shunts, a successes rate of 79.48% was observed during 48 hours of follow-up after PFO closure. We did not evaluate the success rates at 6 months and 24 months. On the other hand, out of the 39 patients who underwent follow-up echocardiography, 8 cases had residual shunts (Figulla device in 5 patients and the AMPLATZER Occluder device in 3). In regard to the use of these 2 kinds of device in those patients, the differences were not significant. The AMPLATZER Occluder device was modified for PFO indication and was initially implanted on September 10, 1997 by the author in the presence of Kurt Amplatzer, the inventor. Similar to all AMPLATZER Occluder devices, it consists of a nitinol mesh double disk containing polyester fabric inside the 2 disks. Three sizes of AMPLATZER PFO closure devices are available and named after the diameter of the right-sided disk. The most commonly used is the 25-mm AMPLATZER PFO Occluder, which features a right-sided disk (25 mm in diameter) and a left-sided disk (18 mm in diameter). The 18-mm AMPLATZER PFO Occluder device comprises two 18-mm disks and is meant for small PFOs with a stable septum primum. The 35-mm AMPLATZER PFO Occluder device is designed for large PFOs with an extremely redundant and flimsy septum primum atrial septum aneurysm and features a 35-mm disk on the right side and a 28-mm disk on the left side. It requires a 9-Fr sheath in contrast to the 2 smaller devices fitting through an 8-Fr sheath. The most widely used devices so far for PFO closure are the CardioSEAL device (the only device available in the USA between 2000 and 2002) and the AMPLATZER PFO Occluder in the rest of the world and available in the USA since 2002. [39] In our study, the AMPLATZER Occluder device was implanted in 12 (23.5%) cases and the Cardi-O-Fix device in 4 (7.84%) patients, but the device implanted the most was the Figulla, which was seen in 28 (54.90%) cases. According to our study, it can be concluded that larger sizes of a PFO and also of label devices such as the DEVIE may lead to more complications. A PFO was defined as TEE evidence of infused microbubbles in the left atrium within 3 cardiac cycles after their appearance in the RA, at rest or during the Valsalva release. The shunt size was graded on a standard scale, [8, 9] with grade 0 indicating no microbubbles; grade 1, 1 to 9 microbubbles; grade 2, 10 to 20 microbubbles; and grade 3, > 20 microbubbles. The complete closure of the PFO was defined as a shunt grade of 0 and effective closure as a shunt grade of 0 or 1. [39]

A previous analysis to determine the potential heterogeneity of the treatment effects according to baseline covariates suggested that closure might provide a greater benefit in patients with a substantial grade 3 right-to-left shunt and in those with an atrial septal aneurysm. [39] The implantation of the AMPLATZER PFO Occluder was associated with a high rate of procedural success

(96.1%), with minimal or no residual shunting in 93.5% of the treated patients in a previous study. [24] In our study, the success rate on the basis of a residual shunt grade 0 was 79.48%, which chimes in with the result of the other similar studies. In our study, only 4 (7.84%) long-term complications were reported: 1 (1.96%) patient undergoing open heart surgery and PFO closure and 3 (5.88%) cases with recurrent CVAs.

In our study, the DEVIE device was used only in a 31-year-old man without any history of cardiac risk factors and with a PFO size of 8 mm; he had no residual shunting on follow-up echocardiography. After DEVIE implantation, the patient had transient atrial fibrillation, which was resolved spontaneously. Atrial fibrillation occurrence in this patient may have been due to a larger PFO size or the performance of the device, which are less prevalent. Consequently, larger studies with greater sample sizes are required. According to an investigation, no shunts were detected by TTE in the long-term follow-up. [36] In the present study, 39 patients were followed up via echocardiography during a 48-hour period following PFO closure. Of the 39 patients, 8 cases had residual shunts. Among the patients with CVAs, 2 cases had no residual shunts and 1 case had no follow-up echocardiography. Nevertheless, 1 patient with open heart surgery had residual shunts on follow-up echocardiography.

CONCLUSIONS

In this long-term follow-up study, percutaneous PFO closure was associated with a low risk of recurrent stroke. No mortality related to cerebrovascular or cardiovascular diseases was found. There were only a few short- or long-term device-related complications. Accordingly, percutaneous PFO closure is a safe and efficient treatment option. Nonetheless, our sample size is too small and long-term randomized trials are needed to determine the efficacy of different therapeutic measures and the importance of patient selection.

Study Limitations

In our study, only 10 cases had recurrent cerebrovascular events before PFO closure and 41 patients underwent PFO closure after the 1st embolic event. Our study evaluated only 10 (20%) of the recurrent cases. One of the salient limitations of the current study might be related to incomplete or no follow-up of some cases. Further studies with greater sample sizes and comprehensive follow-up times are recommended. The evaluation of cryptogenic stroke was performed only by neurologists and cardiologists, who referred the patients with cryptogenic stroke and PFOs together: This might have biased the case selection. In this study, not all the patients underwent follow-up echocardiography: comprehensive echocardiography is required to diagnose residual shunts at follow-up. Finally, it was hard to diagnose cryptogenic TIA or CVA in the patients.

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