POLISH HEART JOURNAL

Kardiologia Polska
The Official Peer-reviewed Journal of the Polish Cardiac Society since 1957

Online first
This is a provisional PDF only. Copyedited and fully formatted version will be made available soon

ISSN 0022–9032 e-ISSN 1897–4279

Patent foramen ovale closure for stroke prevention

Authors: Bartosz Czarniak, Krzysztof Kaczmarek, Piotr Jakubowski, Jarosław Drożdż

Article type: Short communication

Received: June 19, 2024

Accepted: September 12, 2024

Early publication date: September 13, 2024

Patent foramen ovale closure for stroke prevention

Short title: PFO closure for stroke prevention.

Bartosz Czarniak[1], Krzysztof Kaczmarek[2], Piotr Jakubowski[2], Jarosław Drożdż[1]

[1]2nd Department Cardiology, Medical University of Lodz, Łódź, Poland
[2]Department of Electrocardiology, Medical University of Lodz, Łódź, Poland

Correspondence to:
Bartosz Czarniak, MD,
2nd Department Cardiology,
Medical University Lodz,
Pomorska 251, 92–213 Łódź, Poland,
phone: +48 505970047,
e-mail: bartoszczarniak@gmail.com

INTRODUCTION

In Poland, around 90 000 people suffer a stroke every year [1]. Despite advances in treatment, the mortality rate from ischemic stroke remains high — about 26.4% after five years, and as high as 39.2% after ten years of observation [2]. In addition, the presence of a patent foramen ovale (PFO) triples the risk of another stroke [3]. Additionally, a direct correlation between the maximum separation of the primary and secondary septal leaflets and the volume of ischemic lesions in the central nervous system was established [4]. The aim of this study was to evaluate the effectiveness of the percutaneous PFO closure for the prevention of stroke recurrence.

METHODS

The study was conducted between December 2017 and April 2019 in the Central University Hospital of the Medical University of Lodz, Poland. The study group included 53 consecutive patients underwent percutaneous closure procedure with a PFO and one of the following: 1) history of ischemic stroke with focal symptoms, 2) history of transient ischemic attack or 3) ischemic lesions in the central nervous system disclosed on imaging modalities such as computed tomography and/or magnetic resonance imaging. The forementioned criteria were defined based on experts consensus of the Polish Cardiac Society [5]. All patients were referred

to the Heart Team discussion including neurologist, who scrutinized individual situation and potential benefits of being qualified for the procedure. If a mechanism other than suspected paradoxical embolization could be found for the stroke or ischemic lesions, patients were excluded. After the PFO closure procedure, postprocedural echocardiographic follow-up was performed twice (after 6 weeks and 3 months). Retrospective analysis of medical records and phone visits was performed. The median follow-up was 22 months (interquartile range 17–27) and the primary outcome was the occurrence of stroke. The obtained results were compared to the estimated risk of stroke based on the Essen Risk Score, which is the recommended tool by the Polish Neurological Society [6]. The characteristics of the population also included an assessment using the Risk of Paradoxical Embolism (RoPE) and the Modified Rankin Scale [6].

Statistical analysis was performed using IBM SPSS and Statistica 13. Continuous data with normal distribution were presented as mean and standard deviation, otherwise (non-normal) as median and range. Categorical data were given as number and percentage. To compare the observed incidence of stroke with the estimated risk of stroke recurrence using the Essen Risk Score, a one-sample Wilcoxon test was used. A *P*-value below 0.05 was deemed as significant for all comparisons. The study was approved by the local ethics committee.

RESULTS AND DISCUSSION

The mean age of the entire cohort was 53 (13) years, and 40% of the cohort were male. Imaging studies revealed cerebral ischemic lesions in 20 patients (38%), and 33 patients (62%) had a history of previous stroke or transient ischemic attack. The median RoPE in the studied population was 6 (4–8) points.

In the group of patients with a clinically symptomatic stroke, the median time to the day of percutaneous PFO closure was 98 (64–192) days. Among comorbidities, the most commonly observed were hypertension (33; 62%) and diabetes (33; 62%), additionally half of the patients were obese (27; 51%). The complete characteristics of the analyzed population are presented in Table 1.

All procedures (100%) resulted in successful implantation of the PFO occluder with the median procedure time of 30 (25–40) minutes. The most common PFO occluder size was 25mm (37 patients; 70%). Neither intraprocedural nor in-hospital complications were detected. The mean length of hospital stay was 3 days.

After the procedure, 51 patients (96%) received dual antiplatelet therapy (acetylsalicylic acid 75 mg/d with clopidogrel 75 mg/d) for 3 months. In 2 patients (4%), dual antiplatelet

therapy was extended to 6 months due to multiple septal defects.

Only 1 patient (2%) suffered from a thromboembolic event. The patient was a 36-year-old man who had ischemic stroke after 32 months after the PFO closure due to protein C and protein S deficiency. A follow-up echocardiographic examination revealed no leak and interatrial shunt. There were no deaths or long-term complications related to the device.

Baseline risk (before PFO closure) was assessed using the Essen Stroke Risk Score and the median was 3.3% (2.9%–4.7%) in the first year after PFO closure. No strokes were recorded during the year. The analysis showed that the observed risk of stroke recurrence was lower than the estimated risk (0% vs. 3.3%; P <0.001). Over the entire observation period, one patient (2%) suffered a stroke, which was significantly lower than the median estimated risk of stroke 7.3% (5%–8.8%) recurrence based on the Essen Stroke Risk Score (7.3% vs. 2.0%; P <0.001).

In conclusion, a statistically significant reduction in the incidence of recurrent strokes compared to the estimated risk using the Essen Risk Score was observed. The results presented are consistent with data from the currently available literature.

The study group has a high score on the RoPE scale, with the median 6 (4–8) points, which is approximately consistent with patient populations in published studies. For example, the population mean score in the CLOSE study was 7.4 (1.3) points [7].

In the results from the Gore REDUCE study with extended 5-year follow-up published in 2021, a total of 20 clinically apparent recurrent strokes were observed — 8 (1.8%) in the percutaneously treated group and 12 (5.4%) in the conservatively treated group [8]. Unfortunately, long-term follow-up did not include clinically silent ischemic events assessed by magnetic resonance imaging. In the CLOSE study, the 5-year cumulative stroke risk was 0% in the invasively treated group, while it was 4.9% in the pharmacologically treated group [9]. In the DEFENSE-PFO study, the occurrence of stroke was recorded only in the pharmacologically treated group (antiplatelet therapy), affecting a total of 6 patients (10%) [10].

Recently published results of randomized clinical trials have confirmed the benefit of PFO closure compared to pharmacological treatment in stroke prevention. The GoreREDUCE Trial, CLOSE Trial and RESPECT Trial [11] have shown that the risk of stroke is lower after percutaneous PFO closure compared to pharmacological treatment. However, these results are controversial because they are not blinded randomized prospective studies, especially with regard to the comparison to anticoagulant therapy. For patients requiring anticoagulant therapy, the benefit of percutaneous closure of a PFO has not yet been proven [12]. On the other hand, there are no clinical data confirming the effectiveness of anticoagulant therapy in patients with PFO after ischemic stroke [13].

The Polish Neurological Society recommends the use of the RoPE score as a tool in its published guidelines [6]. Recent reports also confirm that the lower the RoPE score, the greater the benefit to the patient of percutaneous closure of a PFO [14].

According to the available algorithm presented in the European consensus, the greatest benefit of PFO closure is expected to be achieved in patients aged 18 to 60 years with a high probability of paradoxical embolism and recurrent stroke. However, it should be emphasized that qualification for interventional treatment must be individualized and based on a thorough evaluation of clinical data [15].

Limitations

This is a single-center retrospective study with relatively small number of patients without a control group. The obtained results were compared to the estimated risk of stroke recurrence.

Article information

Conflict of interest: BC, KK, PJ — consultants for and received grants from Abbott. JD declared no conflict of interest.

Funding: None.

REFERENCES

1. Health Needs Map in the scope of hospital Treatment for Poland (30.08.2018). http://www.mz.gov.pl/wp-content/uploads/2016/04/17_polska-1.pdf (accessed: June 18, 2024).
2. Mohan KM, Wolfe CDA, Rudd AG, et al. Risk and cumulative risk of stroke recurrence: a systematic review and meta-analysis. Stroke. 2011; 42(5): 1489–1494, doi: 10.1161/STROKEAHA.110.602615, indexed in Pubmed: 21454819.
3. Pristipino C, Sievert H, D'Ascenzo F, et al. European position paper on the management of patients with PFO. Eur Heart J. 2019; 40(38): 3182–3195, doi: 10.1093/eurheartj/ehy649, indexed in Pubmed: 30358849.
4. Benvenuti F, Meucci F, Vuolo L, et al. Relation between the size of patent foramen

ovale and the volume of acute cerebral ischemic lesion in young patients with cryptogenic ischemic stroke. Neurol Sci. 2022; 43(1): 453–458, doi: 10.1007/s10072-021-05330-y, indexed in Pubmed: 34050831.

5. Araszkiewicz A, Bartuś S, Demkow M, et al. Interventional closure of patent foramen ovale in prevention of thromboembolic events. Consensus document of the Association of Cardiovascular Interventions and the Section of Grown-up Congenital Heart Disease of the Polish Cardiac Society. Kardiol Pol. 2019; 77(11): 1094–1105, doi: 10.33963/KP.15058, indexed in Pubmed: 31723115.
6. Diener HC, Chutinet A, Easton JD, et al. Dabigatran or aspirin after embolic stroke of undetermined source in patients with patent foramen ovale: Results from RE-SPECT ESUS. Stroke. 2021; 52(3): 1065–1068, doi: 10.1161/STROKEAHA.120.031237, indexed in Pubmed: 33504190.
7. Søndergaard L, Kasner SE, Rhodes JF, et al. Patent foramen ovale closure or antiplatelet therapy for cryptogenic stroke. N Engl J Med. 2017; 377(11): 1033–1042, doi: 10.1056/NEJMoa1707404, indexed in Pubmed: 28902580.
8. Kasner SE, Rhodes JF, Andersen G, et al. Five-year outcomes of PFO closure or antiplatelet therapy for cryptogenic stroke. N Engl J Med. 2021; 384(10): 970–971, doi: 10.1056/NEJMc2033779, indexed in Pubmed: 33704944.
9. Saver JL, Carroll JD, Thaler DE, et al. Long-term outcomes of patent foramen ovale closure or medical therapy after stroke. N Engl J Med. 2017; 377(11): 1022–1032, doi: 10.1056/NEJMoa1610057, indexed in Pubmed: 28902590.
10. Lee PH, Song JK, Kim JS, et al. Cryptogenic stroke and high-risk patent foramen ovale. J Am Coll Cardiol. 2018; 71(20): 2335–2342, doi: 10.1016/j.jacc.2018.02.046, indexed in Pubmed: 29544871.
11. Bhatt DL, Kandzari DE, O'Neill WW, et al. A controlled trial of renal denervation for resistant hypertension. N Engl J Med. 2014; 370(15): 1393–1401, doi: 10.1056/NEJMoa1402670, indexed in Pubmed: 24678939.
12. Angelini F, Fortuni F, Tsivgoulis G, et al. Comparison of antithrombotic strategies in patients with cryptogenic stroke and patent foramen ovale: An updated meta-analysis. Cardiovasc Drugs Ther. 2021; 35(5): 987–993, doi: 10.1007/s10557-020-07068-9, indexed in Pubmed: 32918655.
13. Błażejewska-Hyżorek B. Guidelines for the management of stroke. Pol Neurol Rev . 2019; 15.
14. Kent DM, Saver JL, Ruthazer R, et al. Risk of Paradoxical Embolism (RoPE)-estimated

attributable fraction correlates with the benefit of patent foramen ovale closure: An analysis of 3 trials. Stroke. 2020; 51(10): 3119–3123, doi: 10.1161/STROKEAHA.120.029350, indexed in Pubmed: 32921262.

15. Nachoski D, Schroeder J, Almalla M, et al. Dual-center experiences with interventional closure of patent foramen ovale: A medium-term follow-up study comparing two patient groups aged under and over 60 years. Clin Cardiol. 2021; 44(3): 386–391, doi: 10.1002/clc.23548, indexed in Pubmed: 33595868.

Table 1. Characteristics of the patients population

Parameter	Value n = 53
Sex	
Women	32 (60%)
Men	21 (40%)
Age, years	53 (13)
Risk of Paradoxical Embolism Score (RoPE)	6 (4–8)
Modified Rankin Scale (mRS)	
Rankin 0–2 points	52 (98%)
Rankin 3–5 points	1 (2%)
Ischemic lesions CT/MR	20 (38%)
History of ischemic stroke/TIA	33 (62%)
Time from Stroke Onset to Procedure, days	98 (64–192)
Obesity (BMI >30)	27 (51%)
Atrial fibrillation	10 (19%)
— Paroxysmal atrial fibrillation	6 (11%)
— Persistent atrial fibrillation	4 (8%)
— Permanent atrial fibrillation	0 (0%)
Venous thromboembolic disease	8 (15%)
Oral contraception	6 (11%)
Active smoking	9 (17%)
Chronic heart failure (EF <55%)	4 (8%)
Hypertension	33 (62%)
Diabetes	33 (62%)
Chronic coronary syndrome	10 (19%)
Hypercholesterolemia	15 (28%)
Essen Risk Score, %	3.3 (2.9–4.7)
Procedure time, min	30 (25–40)
Length of hospital stay, days	3 (1)
Follow-up	22 (17–27)

Values are presented as mean (standard deviation), median (interquartile range) or number (%)

Abbreviations: BMI, body mass index; CT, computed tomography; EF, ejestion fraction; MR, magnetic resonance; TIA, transient ischemic attack