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Original Article

Transcatheter closure of the patent foramen ovale in children: intermediate-term follow-up results

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Abstract The patent foramen ovale is almost a normal anatomical hole between the atria with ~30% incidence in the general population. It has been suggested that the patent foramen ovale is the cause of some neurological events, which is explained by paradoxical embolism. Transcatheter closure of the patent foramen ovale is a common procedure in adult patients with cerebral ischaemic events, but there are limited data investigating the results in children. Between January, 2005 and February, 2014, 17 patients' patent foramen ovales were closed by the transcatheter approach in our department. The indications for closure were transient ischaemic attack in 10 patients, stroke in four patients, and migraine in three patients. The mean age and mean weight at the time of the procedure were 11.1 ± 3.7 years and 42.1 ± 15.4 kg, respectively. We asked our patients whether their previous ailments continued. All patients responded to the study survey. In 15 patients, ailments did not continue after patent foramen ovale closure and they significantly decreased in two of them. We suggest that under the right conditions device closure of the patent foramen ovale is a safe solution for these cryptogenic ischaemic events and migraine.

Keywords: Patent foramen ovale; transient ischaemic attack; stroke; migraine

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The foramen ovale is an interatrial connection that is essential in fetal life; however, after birth, it closes in the majority of people. The foramen ovale does not close in ~25–30% of adults, allowing left-to-right shunt; this is called the patent foramen ovale.[1] Even when it is functionally closed, in some conditions such as straining or coughing the shunt has a potential to become right to left. This may explain some neurological conditions and diseases in patients with patent foramen ovale.[2] Some studies have shown a high incidence of patent foramen ovale in patients with transient ischaemic attack, stroke, and migraine;[3–5] therefore, closing the patent foramen ovale in such patients has become a choice of treatment, especially in adulthood. In children, the approach is mostly conservative, and experience is limited.

We therefore contacted patients who had undergone patent foramen ovale device closure in our hospital and questioned them about the continuity of their ailments that initially led to closure of the patent foramen ovale.

Methods

This retrospective study was carried out at the department of Paediatric Cardiology at Hacettepe University Faculty of Medicine. The medical records of children aged between 0 and 18 years who underwent device closure of the patent foramen ovale between January, 2005 and February, 2014 were systematically reviewed. This study was approved by the ethics committee of the university.

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Relevant demographic and clinical characteristics were retrieved from the medical records and recorded on pre-prepared forms.

We retrospectively collected data on patient demographics, clinical symptoms, findings, and work-up evaluation in the pre-procedural period, procedural details, devices used, complications, and post-procedure outcomes. We obtained details on the post-procedural clinical status of patients who were not followed-up via telephone, whose contact numbers were registered in the library system. Patients who could not be reached for follow-up data were excluded from the study.

Procedure

For the diagnosis of patent foramen ovale, all the patients had been examined by transthoracic echocardiography, and suspected patients had been evaluated with transcranial Doppler and transoesophageal echocardiography. The decision to close the patent foramen ovale had been taken by the council of the paediatric cardiology unit. Families of the patients had been informed about the procedure.

All interventions were performed under general anaesthesia. The implantation procedure was guided by both fluoroscopy and transoesophageal echocardiography. Devices were implanted successfully in all patients by paediatric cardiologists. No residual shunts were seen during the transoesophageal echocardiography performed at the end of the procedure. All patients were discharged on the day after the procedure, following clinical and femoral access-site review and transthoracic echocardiography. After the procedure, all patients were prescribed aspirin for 6 months. No procedural complications or adverse events were observed.

All patients were evaluated by electrocardiography, Holter electrocardiography, and transthoracic echocardiography after 1 month, 6 months, and 1 year after the procedure as a routine. Transcranial Doppler was performed in patients who were suspected of having interatrial residual defects. Patients with normal examinations continued follow-up annually.

Statistical analyses

All statistical analyses were performed using the Statistical Package for the Social Sciences programme for Windows, version 16.0. Descriptive statistical methods were used to analyse the results. Normality of distribution of numerical variables was evaluated by the Kolmogorov–Smirnov or the Shapiro–Wilk test. Values for numerical variables are given as mean ± standard deviation or as medians (minimum–maximum), depending on the normality of distribution.

Results

Patients

A total of 17 patients (7 males; 10 females) with a mean age of 11.1 ± 3.7 years (with a range from 4 to 16 years) underwent closure of the patent foramen ovale with different devices. Among them, 10 patients had recurrent transient ischaemic attacks, four patients had stroke history, and three patients had significant migraine attacks. On transthoracic echocardiography, there were no coexisting pathological findings except for minimal mitral insufficiency in two patients and minimal aortic insufficiency in one patient. The diagnosis of right-to-left shunt was confirmed with both transcranial Doppler and transthoracic echocardiography in all patients. Patient general characteristics and procedural data are illustrated in Table 1. The details of all 17 patients are summarised in Table 2.

We examined 8 patients for predisposition to thrombophilia. Electroencephalographies of these patients were found to be normal, except the third patient who had a subacute infarct in the left parietal lobe, observed during cranial magnetic resonance. Patient number 12 had a diagnosis of Crohn's disease, and patient number 16 had a diagnosis of Hashimoto's disease.

Follow-up

The median follow-up time was 5 years (2–10 years). No pathological findings were observed on electrocardiography, transthoracic echocardiography, and Holter electrocardiography during the follow-up period. No residual shunts were detected in the transcranial Doppler in 10 patients. We contacted all 17 patients and asked them about continuity of their ailments after the procedure: 15 patients were symptom free, and two patients with migraine had

Table 1. General characteristics of the patients and procedural data.

Patient population	17
Gender	
Female	10 (58.8%)
Age (years)	11.1 ± 3.7
Weight (kg)	42.1 ± 15.4
Indication for intervention	
Transient ischaemic attack	10 (58.8%)
Stroke	4 (23.5%)
Migraine	3 (17.6%)
Transcranial Doppler	
Low-grade shunt	2 (11.7%)
Medium- or large-grade shunt	15 (88.3%)
Procedural complication	0 (0%)
Mean procedural duration (min)	69 ± 21.9
Mean flouroscopy duration (min)	7.3 ± 3.7

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Table 2. Detailed features of the patients in the study group.

Patient	Age/sex (year)	Weight (kg)	Indication for procedure	Neuroimaging findings	Trombophilia	TCD (shunt grade)	Device	Follow-up (year)	Complication	Symptoms after procedure
1	14/M	46	Recurrent TIA	Cr MR → Normal	NP	Medium–large	Amp PFO 25 mm	2	No	No
2	10/M	44	Recurrent TIA	Cr MR → Normal	MTHFR 677/1298 heterozygous PAI 4 G/5 G heterozygous	Low	Amp PFO 18 mm	2	No	No
3	4/M	22	Stroke	Subacute infarct in the left parietal lobe	MTHFR 677/1298 heterozygous, F V Leiden heterozygous	Medium–large	Gore 20 mm	3	No	No
4	13/F	65	Stroke	Subcortical ischaemic gliozis in both frontoparietal regions	Normal	Medium	Gore 25 mm	3	No	No
5	14/M	41	Recurrent TIA	Cr MR → Normal	NP	Medium	Amp PFO 18 mm	10	No	No
6	13/F	40	Stroke	Lacuner infarct in the right lentiform nucleus	Normal	Medium–large	Cribriform ASO 25 mm	8.5	No	No
7	13/F	54	Recurrent TIA	Cr MR → Normal	NP	Medium–large	Biostar 23 mm	5	No	No
8	14/F	49	Recurrent TIA	Cr MR → Normal	Normal	Medium–large	ASO 4 mm	3.5	No	No
9	5/F	22	Recurrent TIA	Cr MR → Normal	NP	Medium	Biostar 23 mm	3.5	No	No
10	12/F	57	Migraine	Cr MR → Normal	NP	Large	Gore 25 mm	2.5	No	Rarely headaches
11	15/M	55	Migraine	Cr MR → Normal	NP	Large	Amp PFO 25 mm	5.5	No	No
12	8/F	19	Stroke	Chronic infarct	Normal	Medium	Occlutech PFO 18 mm	6	No	No
13	14/M	54	Migraine	Cr MR → Normal	NP	Medium	Amp PFO 25 mm	6	No	Rarely headaches
14	5/M	20	Recurrent TIA	Cr MR → Normal	MTHFR 1298 homozygous	Large	Amp PFO 18 mm	6.5	No	No
15	10/F	31	Recurrent TIA	Cr MR → Normal	Normal	Low	Amp PFO 18 mm	6	No	No
16	10/F	33	Recurrent TIA	Cr MR → Normal	MTHFR 677 heterozygous	Large	Amp PFO 18 mm	6.5	No	No
17	16/F	65	Recurrent TIA	Cr MR → Normal	Normal	Large	Amp PFO 25 mm	5	No	No

Amp = Amplatzer; ASO = Amplatzer septal occluder; Cr MR = cranial magnetic resonance; F = female; F V = factor 5; M = male; MTHFR = methylenetetrahydrofolate reductase; NP = not performed; PAI = plasminogen activator inhibitor; PFO = patent foramen ovale; TCD = transcranial Doppler; TIA = transient ischaemic attacks

significant improvement in their headaches; they were not using preventive treatment anymore.

Discussion

There are several reports that establish a relationship between patent foramen ovale and some neurological events. It has been clearly shown that patent foramen ovale incidence is higher in patients with stroke, transient ischaemic attack, or migraine than in the normal population. Most of these reports involve adult age groups. McCandless et al[6] and Choi et al[7] showed high prevalence of patent foramen ovale in children with migraine, especially migraine with aura. As cerebrovascular events are lower in children than in adults, there are no enough data investigating patent foramen ovale in children with cryptogenic stroke or transient ischaemic attack. Benedik et al[8–10] showed high incidence of patent foramen ovale in children with transient ischaemic attack and high incidence of right-to-left shunt in children with arterial ischaemic stroke. Agnetti et al[9] reported patent foramen ovale as the cause for stroke in two children. Most of these studies made an expectation that closing the patent foramen ovale may be the cure for these neurological events.

In 1999, Cujec et al[11] declared that surgical closure of the patent foramen ovale prevented recurrences of cerebral ischaemic events in their 14 patients. Orgera et al[12] found that surgical patent foramen ovale closure in these patients is comparable with warfarin therapy in their meta-analysis. Butera et al[13] found no recurrence of thromboembolic events during their 1-year follow-up of patients with patent foramen ovale and cryptogenic stroke after transcatheter closure. Many studies with the same results have been published since then. Schwerzmann et al[14] showed similar benefit in migraine with aura.

There are only a few studies questioning the patent foramen ovale–neurological events relationship, however. Davis et al[15] mentioned that these pairwise associations do not strongly suggest a casual role for patent foramen ovale in their meta-analysis. Garg et al[16] found no relationship between migraine and patent foramen ovale.

In light of these arguments, in our department, transcatheter closure of the patent foramen ovale is a very rarely performed procedure. In these last 10 years, there were only 17 children with this condition among ~9000 catheter angiography patients. Patients were chosen very carefully, and decisions were taken by both neurologists and cardiologists. All diagnoses of patent foramen ovale were made not only by transthoracic echocardiography but also by transcranial Doppler and transoesophageal echocardiography. After the procedure, patients were followed-up by transthoracic echocardiography. As there were no further complaints, we did not require any other examination for follow-up, except in ten patients who underwent control transcranial Doppler.

Data on patent foramen ovale closure in childhood are limited. Bartz et al[17] reported device closure of the patent foramen ovale as a safe alternative therapeutic option for children and young adults. Their median patient age was 29 years, and the median follow-up time was 5.3 months. Menon et al[18] found complete resolution or reduction of symptoms in 143 of their 153 patients (93%) after patent foramen ovale closure. In this largest study in the literature, the median age was 16 years, and the median follow-up time was 12 months; however, a strong placebo effect was found. In our study, 15 patients were symptom-free, and two patients showed significant decrease in headaches after device closure of the patent foramen ovale. All of them were in the paediatric age group, and the follow-up time was long enough to rule out a placebo effect. Even the patient number was less to form a precise opinion, we suggest that under the right circumstances device closure of the patent foramen ovale is a safe solution for cryptogenic ischaemic events and migraine.

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Conflicts of Interest

None.

References

1. Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. Mayo Clin Proc 1984; 59: 17–20.
2. Kenny D, Turner M, Martin R. When to close a patent foramen ovale. Arch Dis Child 2008; 93: 255–259.
3. Lechat P, Mas JL, Lascault G, et al. Prevalence of patent foramen ovale in patients with stroke. N Engl J Med 1988; 318: 1148–1152.
4. Webster MW, Chancellor AM, Smith HJ, et al. Patent foramen ovale in young stroke patients. Lancet 1988; 2: 11–12.
5. Del Sette M, Angeli S, Leandri M, et al. Migraine with aura and right-to-left shunt on transcranial Doppler: a case-control study. Cerebrovasc Dis 1998; 8: 327–330.
6. McCandless RT, Arrington CB, Nielsen DC, Bale JF Jr, Minich LL. Patent foramen ovale in children with migraine headaches. J Pediatr 2011; 159: 243–247.

7. Choi DY, Shin DH, Cho KH, Lee SP, Park S. Migraine with aura: a predictor of patent foramen ovale in children and adolescents. Cephalalgia 2013; 33: 463–468.
8. Perkovič-Benedik M, Zaletel M, Pečarič-Meglič N, Podnar T. A right-to-left shunt and prothrombotic disorders in pediatric patients presenting with transient ischemic attack. Eur J Pediatr 2013; 172: 239–245.
9. Agnetti A, Carano N, Sani E, et al. Cryptogenic stroke in children: possible role of patent foramen ovale. Neuropediatrics 2006; 37: 53–56.
10. Benedik MP, Zaletel M, Meglic NP, Podnar T. A right-to-left shunt in children with arterial ischaemic stroke. Arch Dis Child 2011; 96: 461–467.
11. Cujec B, Mainra R, Johnson DH. Prevention of recurrent cerebral ischemic events in patients with patent foramen ovale and cryptogenic strokes or transient ischemic attacks. Can J Cardiol 1999; 15: 57–64.
12. Orgera MA, O'Malley PG, Taylor AJ. Secondary prevention of cerebral ischemia in patent foramen ovale: systematic review and meta-analysis. South Med J 2001; 94: 699–703.
13. Butera G, Bini MR, Chessa M, Bedogni F, Onofri M, Carminati M. Transcatheter closure of patent foramen ovale in patients with cryptogenic stroke. Ital Heart J 2001; 2: 115–118.
14. Schwerzmann M, Wiher S, Nedeltchev K, et al. Percutaneous closure of patent foramen ovale reduces the frequency of migraine attacks. Neurology 2004; 62: 1399–1401.
15. Davis D, Gregson J, Willeit P, Stephan B, Al-Shahi Salman R, Brayne C. Patent foramen ovale, ischemic stroke and migraine: systematic review and stratified meta-analysis of association studies. Neuroepidemiology 2013; 40: 56–67.
16. Garg P, Servoss SJ, Wu JC, et al. Lack of association between migraine headache and patent foramen ovale: results of a case-control study. Circulation 2010; 121: 1406–1412.
17. Bartz PJ, Cetta F, Cabalka AK, et al. Paradoxical emboli in children and young adults: role of atrial septal defect and patent foramen ovaledevice closure. Mayo Clin Proc 2006; 81: 615–618.
18. Menon SC, Grove A, McFadden M, Korgenski KE, Cowley CG. Clinical practice, resource utilization, and outcomes of device closure of patent foramen ovale in pediatrics. Pediatr Neurol 2014; 50: 213–217.