Transcatheter closure of patent foramen ovale in patients with cryptogenic stroke

Gianfranco Butera, Margherita Roberta Bini, Massimo Chessa, Francesco Bedogni*, Michele Onofri*, Mario Carminati

*Pediatric Cardiology, Istituto Policlinico S. Donato, S. Donato Milanese (MI), *Department of Cardiology, Istituto Clinico S. Ambrogio, Milan, Italy*

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Background. **About 50% of patients with cryptogenic stroke have a patent foramen ovale (PFO). The recurrence rate of paradoxical embolism is higher if a PFO is detected.**

Methods. **Thirty-five patients with PFO and ≥ 1 thromboembolic event due to paradoxical embolism were included in the study (23 males, 12 females, mean age 47.8 ± 14 years, mean weight 75 ± 15 kg). Twenty-three patients had a transient ischemic attack whereas 12 experienced an ischemic stroke. Twenty-nine patients had one thromboembolic event, 4 patients had two thromboembolic events, and 2 patients had three thromboembolic events. The implantation procedure was performed, as previously reported, under general anesthesia, fluoroscopic guidance and during transesophageal echocardiography.**

Results. **The implantation procedure was successful in all patients. There were no complications related to the procedure. Four different devices were implanted (Amplatzer 3 patients; Cardioseal 12 patients; Starflex 12 patients, PFO Star 8 patients). The procedure time and fluoroscopic time were 50 ± 21.8 and 12.2 ± 8.3 min respectively. At transesophageal echocardiography performed after the procedure, 11 patients had a trivial shunt. None of the patients had a residual shunt at 1 month of follow-up. The mean follow-up was 12.3 ± 8 months (median 11.0 months, range 3-37 months). In no patient did recurrence of a thromboembolic event occur during follow-up.**

Conclusions. **Percutaneous PFO closure is a feasible and safe technique for the prevention of recurrent paradoxical embolism.**

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Address:

Dr. Mario Carminati

Cardiologia Pediatrica
Istituto Policlinico
S. Donato
Via Morandi, 30
20097 S. Donato
Milanese (MI)
E-mail: carminati.mario
@lycos.com

Among the population, one third of subjects have a patent foramen ovale (PFO). The incidence of PFO is higher, about 50-60%, in patients with cryptogenic cerebral infarcts[1-4]. Finally, the recurrence rate of cryptogenic stroke is higher if a PFO is detected[5-7].

These facts suggest a strong role of a PFO in cryptogenic stroke. A large PFO[8,9] and the presence of an atrial septal aneurysm[1,10,11] have been identified as risk factors for paradoxical embolism. These relationships are less strongly defined in patients older than 55 years[4,12].

Various therapeutic strategies have been developed to prevent recurrence of cryptogenic stroke in patients with PFO. Medical treatment (using either aspirin or oral anticoagulants)[6,7] and surgical PFO closure[13-17] have been used in such patients. Percutaneous PFO closure was initially performed by Bridges et al.[18].

We report our experience regarding percutaneous PFO closure in a group of 35 consecutive patients with cryptogenic stroke.

Methods

Patients. Since January 1998, 35 patients have undergone percutaneous PFO closure. In all cases, patient history included a thromboembolic event attributed to paradoxical embolism. The following criteria were used to define a thromboembolic event due to paradoxical embolism: a) presence of a PFO with or without an atrial septal aneurysm with spontaneous or induced right-to-left shunt during contrast transesophageal echocardiography; b) clinically and neuroradiologically confirmed ischemic stroke or symptoms of transient ischemic attack (TIA) with or without neuroradiologically identified intracranial ischemic or clinically and radiologically identified peripheral thromboembolism; c) no known causes for the thromboembolic event other than PFO. Twenty-nine patients had one thromboembolic event, 4 patients had two thromboembolic events, and 2 patients had three thromboembolic

events. The time interval between the last ischemic event and PFO closure was 8 ± 5 months. In patients with multiple thromboembolic events, the mean time (± SD) between such events was 26 ± 22 months.

In all cases, written informed consent was obtained prior to the procedure.

Patient characteristics are summarized in table I.

Table I. Patient characteristics.

No. patients	35
Mean age (years)	47.8 ± 14
Mean weight (kg)	75 ± 15
Sex (M/F)	23/12
Thromboembolic events	35
TIA	23
Stroke	12
Atrial septal anatomy	
PFO only	29
PFO and ASA	6

ASA = atrial septal aneurysm; PFO = patent foramen ovale; TIA = transient ischemic attack.

Implantation procedure. Venous access was gained via the right femoral vein. A pig-tail 6F catheter was used to perform right atrial angiography in the left anterior oblique view. Contrast transesophageal echocardiography was performed with the pig-tail catheter inserted into the right atrium (Figs. 1 and 2). Sometimes, a Valsalva maneuver was started at the time of injection of the contrast medium. Under fluoroscopic guidance a 6F multipurpose catheter was passed through the PFO. Using a standard 0.035-inch exchange wire, the multipurpose catheter was substituted with a sizing balloon (Fig. 3) which, in turn, was exchanged with an 8F to 12F transseptal sheath. The PFO occluder was delivered through the transseptal sheath and placed within the PFO under fluoroscopic and transesophageal echocardiographic guidance (Fig. 4).

Before release of the PFO device, the occluder position was checked by right atrial contrast angiography which permitted delineation of the atrial septum. Contrast transesophageal echocardiography was performed with and without a Valsalva maneuver in order to check for any residual shunt (Fig. 5).

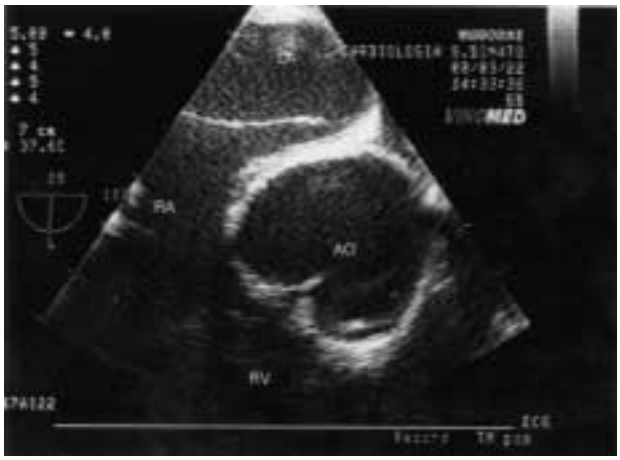

Figure 1. *Patent foramen ovale (transesophageal echocardiography). AO = aorta; LA = left atrium; RA = right atrium; RV = right ventricle.*

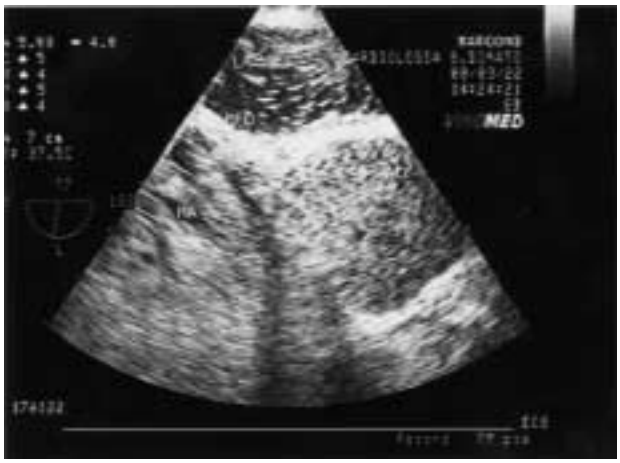

Figure 2. *Contrast echocardiography before patent foramen ovale (PFO) closure. Abbreviations as in figure 1.*

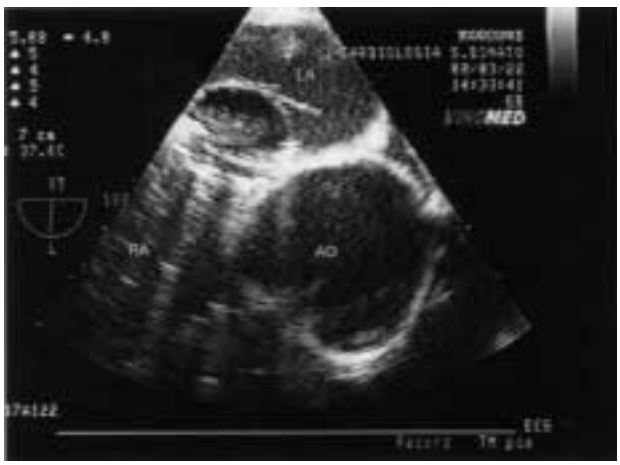

Figure 3. *Sizing of the patent foramen ovale. Abbreviations as in figure 1.*

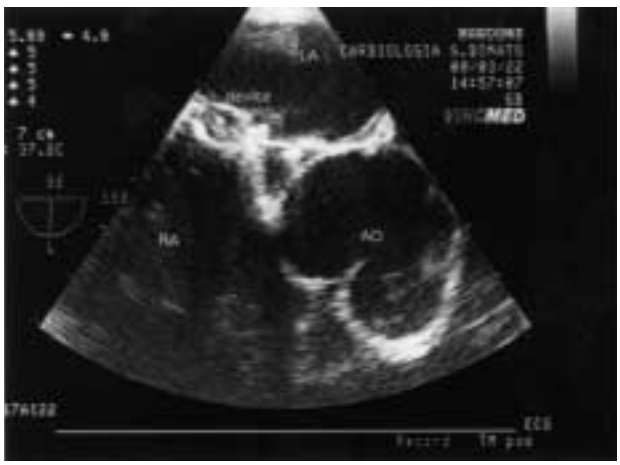

Figure 4. *Patent foramen ovale closure. Abbreviations as in figure 1.*

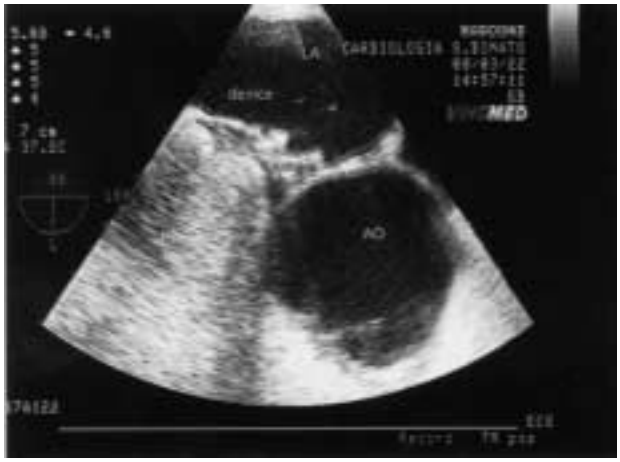

Figure 5. *Contrast echocardiography after patent foramen ovale closure. Abbreviations as in figure 1.*

Follow-up. Patients were studied by means of transthoracic echocardiography at discharge and at 1, 6 and 12 months after the procedure. They were treated with aspirin, 5-10 mg/kg once daily for 6 months.

The mean follow-up was 12.3 ± 8.0 months (median 11.0 months, range 3-37 months).

Results

The implantation procedure was successful in all patients. There were no complications related to the procedure. A total of four different devices were implanted (Table II).

The procedure and fluoroscopic times were 50 ± 21.8 and 12.2 ± 8.3 min respectively and were independent of the type of device.

Postoperative transesophageal echocardiography revealed the presence of a trivial residual shunt in 11 patients. In these patients the following devices were implanted: a PFO Amplatzer occluder in 2 cases, a Cardioseal device in 1, a Starflex device in 1, and a PFO Star device in 7 cases. None of 31 patients with a follow-up of 6 months and of 12 patients with a follow-up of 12 months had a residual shunt.

Discussion

PFO is a strong risk factor for paradoxical embolism[1-7]. This is particularly true for large PFOs or for a PFO associated with an atrial septal aneurysm[1,8-11]. These correlations are weaker in patients older than 55 years[4,12].

In patients with no treatment[5] the recurrent-event rate was 16% per year.

Different treatments have been used in order to prevent thromboembolic events in patients with cryptogenic stroke or TIA and PFO.

Medical treatment was studied by Mas and Zuber[6] and by Bogousslavsky et al.[7]. Mas and Zuber[6] retrospectively evaluated 132 patients younger than 60 years treated, during a follow-up period of 23 months, using either aspirin (250-500 mg/die) or oral anticoagulants (target INR 2 to 3). The average annual rate of recurrence was 1.2% for stroke and 3.4% for the combined endpoint of TIA and stroke. In the Lausanne Stroke Registry[7], 92 patients were treated with aspirin (250-500 mg/die) and 37 with oral anticoagulants (target INR 2 to 3). The average annual recurrence rate during follow-up lasting 3 years was 1.9% for stroke and 3.8% for the combined endpoint of TIA and stroke.

Surgical closure of PFO has been reported[14-16]. Homma et al.[14] studied 28 patients (mean age 41 years) submitted to surgical PFO closure at open thoracotomy; the recurrence rate was 20% at 13 months. Guffi et al.[15] submitted 11 patients (mean age 39.4 years) to surgical PFO closure. None experienced recurrence of thromboembolic events during a median follow-up of 12.2 months.

Similar results were obtained by Ruchat et al.[16] who surgically treated 59 patients with a mean age of 42 years. Dearani et al.[17] retrospectively studied 91 patients (mean age 42 years) who underwent surgical PFO closure. The median follow-up was 2 years. No TIAs were observed at 1 and 4 years of follow-up in 92 and 83% of patients respectively. Percutaneous PFO closure was initially reported by Bridges et al.[18], who treated 36 patients (mean age 39 years) with the clamshell device. Eight patients had a residual shunt after the procedure. During a mean follow-up of 8 months, 4 patients experienced a TIA.

In a multi-institutional study[19] using the ASDOS device, only 1 of 46 patients (mean age 44 years) had a recurrent TIA 7 months after the procedure.

Table II. Device characteristics.

PFO Amplatzer septal occluder	3
Cardioseal	12
Starflex	12
PFO Star	8
Device diameter	
Amplatzer	
9 mm	1
19 mm	1
25 mm	1
Starflex	
23 mm	9
28 mm	2
33 mm	1
Cardioseal	
17 mm	7
23 mm	2
28 mm	1
33 mm	2
PFO Star	
3 × 26 mm	2
3 × 30 mm	3
3 × 35 mm	1
5 × 30 mm	1
5 × 35 mm	1

Windecker et al.[20] studied 80 patients (mean age 52 years) with PFO and at least one paradoxical event. Five different devices were used. During 5 years of follow-up (mean 1.6 years) the actuarial annual risk of a recurrent thromboembolic event was 2.5% for TIA, 0% for stroke, 0.9% for peripheral emboli, and 3.4% for the combined endpoint. A post-procedural shunt was a predictor of recurrent paradoxical embolism (relative risk 4.2, 95% confidence interval 1.1-17.8).

Hung et al.[21] submitted 63 patients (mean age 46 years) to transcatheter PFO closure. During a mean follow-up of 2.6 ± 2.4 years the risk of recurrent stroke or of a transient neurological event was 3.2% per year.

In our study, we submitted 35 patients (mean age 47.8 years) to percutaneous closure of a PFO. Four different devices were used. The procedure was successful in all patients and none experienced complications related to the procedure. This is probably due to the use of safer and retrievable devices.

In fact, major complications were reported with the use of buttoned devices[20] which are associated with a significant risk of a residual shunt[20]. In our report, no patient had a residual shunt.

During a mean follow-up of 12.3 months, none of our patients experienced a recurrent thromboembolic event. This is probably related to the fact that none had a significant post-procedural residual shunt at discharge. In fact, a post-procedural shunt is a strong predictor of recurrent thromboembolic events with a relative risk of 4.2[20].

Limitations of the study. This study has certain limitations. First, the follow-up of our study is short. In fact, the mean follow-up was 12.3 months and only 12 patients had a follow-up of 12 months. The risk of recurrent thromboembolic events is reported to be higher in the first 2 years after percutaneous PFO closure[20]. Secondly, our patients are a selected cohort of subjects referred to our center specifically for percutaneous PFO closure. Thirdly, the number of patients is probably too small to observe any recurrent event. Finally, this study was without a control group and treatment was not randomly assigned.

In conclusion, percutaneous PFO closure is a promising technique for the prevention of recurrent paradoxical embolism in patients with PFO. In experienced hands, it is a feasible and safe technique. In our opinion, it should be considered the procedure of choice.

References

1. Cabanes L, Mas JL, Cohen A, et al. Atrial septal aneurysm and patent foramen ovale as risk factors for cryptogenic stroke in patients less than 55 years of age. Stroke 1993; 24: 1865-72.
2. Lechat P, Mas JL, Lascault G, et al. Prevalence of patent foramen ovale in patients with stroke. N Engl J Med 1988; 318: 1148-52.
3. Webster MW, Chancellor AM, Smith HJ, et al. Patent foramen ovale in young stroke patients. Lancet 1988; 2: 11-2.
4. Hausmann D, Mugge A, Becht I, Daniel WG. Diagnosis of patent foramen ovale by transesophageal echocardiography and association with cerebral and peripheral embolic events. Am J Cardiol 1992; 70: 668-72.
5. Comess KA, DeRook FA, Beach KW, Lytle NJ, Golby AJ, Albers GW. Transesophageal echocardiography and carotid ultrasound in patients with cerebral ischemia: prevalence of findings and recurrent stroke risk. J Am Coll Cardiol 1994; 23: 1598-603.
6. Mas JL, Zuber M. Recurrent cerebrovascular events in patients with patent foramen ovale, atrial septal aneurysm, or both and cryptogenic stroke or transient ischemic attack. French Study Group on Patent Foramen Ovale and Atrial Septal Aneurysm. Am Heart J 1995; 130: 1083-8.
7. Bogousslavsky J, Garazi S, Jeanrenaud X, Aebischer N, Van Melle G. Stroke recurrence in patients with patent foramen ovale: the Lausanne Study. Lausanne Stroke with Paradoxical Embolism Study Group. Neurology 1996; 46: 1301-5.
8. Homma S, Di Tullio MR, Sacco RL, Mihalatos D, Li Mandri G, Mohr JP. Characteristics of patent foramen ovale associated with cryptogenic stroke: a biplane transesophageal echocardiographic study. Stroke 1994; 25: 582-6.
9. Hausmann D, Mugge A, Daniel WG. Identification of patent foramen ovale permitting paradoxic embolism. J Am Coll Cardiol 1995; 26: 1030-8.
10. Mugge A, Daniel WG, Angermann C, et al. Atrial septal aneurysm in adult patients: a multicenter study using transthoracic and transesophageal echocardiography. Circulation 1995; 91: 2785-92.
11. Agmon Y, Khandheria BK, Meissner I, et al. Frequency of atrial septal aneurysm in patients with cerebral ischemic events. Circulation 1999; 99: 1942-4.
12. De Belder MA, Tourikis L, Leech G, Camm AJ. Risk of patent foramen ovale for thromboembolic events in all age groups. Am J Cardiol 1992; 69: 1316-20.
13. Devuyst ST, Bogousslavsky J, Ruchat P, et al. Prognosis after stroke followed by surgical closure of patent foramen ovale: a prospective follow-up study with brain MRI and simultaneous transesophageal and transcranial Doppler ultrasound. Neurology 1996; 47: 1162-6.
14. Homma S, Di Tullio MR, Sacco RL, Sciacca RR, Smith C, Mohr JP. Surgical closure of patent foramen ovale in cryptogenic stroke patients. Stroke 1997; 28: 2376-81.
15. Guffi M, Bogousslavsky J, Jeanrenaud X, Devuyst G, Sadeghi H. Surgical prophylaxis of recurrent stroke in patients with patent foramen ovale: a pilot study. J Thorac Cardiovasc Surg 1996; 112: 260-3.
16. Ruchat P, Bogousslavsky J, Hurni M, Fischer AP, Jeanrenaud X, von Segesser LK. Systematic surgical closure of patent foramen ovale in selected patients with cerebrovascular events due to paradoxical embolism: early results of a preliminary study. Eur J Cardiothorac Surg 1997; 11: 824-7.
17. Dearani JA, Ugurlu BS, Danielson GK, et al. Surgical patent foramen ovale closure for prevention of paradoxical embolism-related cerebrovascular ischemic events. Circulation 1999; 100 (Suppl II): II171-II175.
18. Bridges ND, Hellenbrand W, Latson L, Filiano J, Newburger JW, Lock JE. Transcatheter closure of patent foramen ovale after presumed paradoxical embolism. Circulation 1992; 86: 1902-8.
19. Sievert H, Babic UU, Haysdorf G, et al. Transcatheter closure of atrial septal defect and patent foramen ovale with ASDOS device (a multi-institutional European trial). Am J Cardiol 1998; 82: 1405-13.
20. Windecker S, Wahl A, Chatterjee T, et al. Percutaneous closure of patent foramen ovale in patients with paradoxical embolism. Long-term risk of recurrent thromboembolic events. Circulation 2000; 101: 893-8.
21. Hung J, Landzberg M, Jenkins K, et al. Closure of patent foramen ovale for paradoxical emboli: intermediate term risk of recurrent neurological events following transcatheter device placement. J Am Coll Cardiol 2000; 35: 1311-6.