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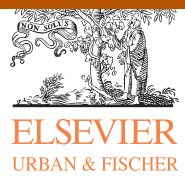

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Italian patent foramen ovale survey (I.P.O.S.): Early results

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Patent foramen ovale;
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Summary
Background: Percutaneous patent foramen ovale (PFO) closure is gaining wide acceptance. Aims of the study were to analyse clinical practice regarding PFO closure in Italy, to study indications, devices, results, and the follow-up of large series of patients treated by percutaneous PFO closure.
Methods and patients: Italian patent foramen ovale survey (IPOS) is a prospective, observational, multi-centric survey that uses a web-based database. The survey lasted 12 months, (November 2007—October 2008). 50 centres participated. Ongoing follow-up will continue up to 36 months. 1035 patients (m.a. 46 years, 60% females) were included in the registry. Most subjects were treated due to a previous history of TIA/ischemic stroke (~80% of patients). PFO diagnosis and right-to-left shunt (RLS) were assessed by contrast-enhanced transesophageal (cTEE) and/or transthoracic echocardiography and/or transcranial doppler. An aneurysm of the

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interatrial septum was associated in 41% of patients. Intraprocedural monitoring was assessed by using cTEE and fluoroscopy in 70% and intracardiac echocardiography in 30% of subjects. Procedures were performed under general anesthesia and local anesthesia/conscious sedation in 54% and 46% of patients respectively. The most used device for PFO closure was Amplatzer (~70% of cases).

Results: The procedure was successful in all patients. Early complications occurred in 24/1035 patients (2.3%): 12/24 (50%) of them had cardiac arrhythmias, 1 subject had a TIA. Data regarding both clinical and cardio-neurosonological follow-up were assessed in 444/1035 (43%) subjects. The rate of neurological events and cardiac and extra-cardiac complications were around 3% and 9% up to the 24-month follow-up respectively. A large permanent residual RLS and no RLS were observed in less than 1% and in ~82% of patients at the 1-year follow-up, respectively.

Conclusions: Our data confirm that percutaneous PFO closure is a safe procedure. Early complications and those during follow-up are mostly related to arrhythmias. Longer follow-up is under way.

Introduction

During the last years, percutaneous patent foramen ovale (PFO) closure has gained wide acceptance with a huge number of patients successfully undergoing this procedure. Few large databanks exist with mid-long term follow-up after PFO closure [1—8]. Moreover, the rate of peri- and post-procedural clinical complications was differently characterized in many studies all over the world.

The aim of our study was, therefore, to analyse clinical practice regarding PFO closure in Italy, to study indications, devices used, results of percutaneous PFO closure and to evaluate a 36-month follow-up of a large series of patients treated by percutaneous closure.

Waiting for the final results, this paper describes early results concerning crucial aspects related to PFO closure up to the 24-month follow-up.

Methods and patients

Study design

IPOS is a prospective, observational, multi-centric survey that uses a web-based database. An independent neurological evaluation of all cases included in the registry was assessed. Doubtful or inconsistent reports regarding a neurological recurrence were ruled out.

Study period

The survey lasted 12 months and the patients were enrolled between November 2007 and October 2008. Ongoing follow-up will continue up to 36 months.

Flow-chart

Patients' screening consisted with demographic characteristics, current medical treatment, neurological evaluation, indication for PFO closure and RLS evaluation.

Imaging with cardiomorphological data, different devices and possible complications were indicated during the procedures.

In the post-procedural phase early complications, length of hospitalization and treatment at discharge were described.

Follow-ups were within the 6th, 12th, 24th and 36th month. Data regarding cardiac imaging, residual RLS, neurological recurrences and/or cardiac extra-cardiac complications were specified.

Indications

Most subjects who underwent PFO closure had a previous history of TIA/cryptogenic ischemic stroke (~80% of patients). The remaining indications were consistent with migraine with aura, other events of paradoxical embolism as myocardial or retinal ischemia, residual PFO after a previous procedure, platypnea—ortheodoxia syndrome, neurosurgical procedures in sitting/semisitting position, diving, thrombophilic status and asymptomatic patients with neuroradiological ischemic lesions.

Baseline data and PFO diagnosis

Fifty Italian cardiology departments accepted to participate. Forty of them enrolled at least one patient in the registry. 1035 patients (mean age 46 years [range 5—75], 619/1035 [60%] females) were included in the registry.

PFO diagnosis and right-to-left shunt (RLS) were assessed by contrast-enhanced transesophageal (cTEE) and/or transthoracic echocardiography (cTTE) and/or transcranial Doppler (cTCD).

RLS was assessed in a visual semi-quantitative method by cTEE and cTTE: RLS was diagnosed if at least 1 microbubble (MB) appeared early in the left atrium either spontaneously or after provocative manoeuvres, thus indicating no shunt if no MB were revealed up to a severe shunt if >20 MB occurred.

cTCD methods regarding RLS diagnosis were previously described [9]. cTCD was performed according to the standardized procedure agreed on in the Consensus Conference of Venice [10]. Briefly, the total MB count consisted of all MB detected during a time interval of 20 s or less after the appearance of the first MB. The proposed classification is as follows: small (0—10 MB), moderate (>10 MB, without shower or curtain pattern), and large (shower or curtain pattern)

RLS. All our patients who exhibited RLS of 5 or more MB were considered to have a positive test result [11].

Aneurysm of the interatrial septum (ASA) was diagnosed in the presence of atrial septal excursion greater than 10 mm beyond the plane of the interatrial septum in the presence of a base width greater than 15 mm. ASA was associated in 423/1035 (41%) patients.

Cardiac monitoring

Intraprocedural monitoring was assessed by using TEE and fluoroscopy in 70% and intracardiac echocardiography in 30% of subjects. Procedures were performed under general anesthesia and local anesthesia/conscious sedation in 58% and 42% of patients, respectively. The most used device for PFO closure was Amplatzer (~70% of cases).

Results

The procedure was successful in all patients.

Early complications

They occurred in 24/1035 (2.3%) patients in the periprocedural phase. 12/24 (50%) subjects experienced cardiac arrhythmia: 5 patients had transient atrial fibrillation (AF), one patient a transient bradycardia, one patient a I° atrioventricular block, 4 had AF and 1 had a wide QRS tachycardia, before starting the procedure, and needed electrical cardioversion. 2/24 (8.3%) patients had a femoral arteriovenous fistula, thus needing vascular surgery. 4/24 (16.6%) subjects had respiratory problems after general anesthesia. One patient experienced a device embolization, retrieved percutaneously. One patient had a transient visual loss and 4 patients had a vagal reaction, allergy to antibiotics, right coronary spasm and mild pericardial effusion.

Follow-up

Both clinical and cardio-neurosonological follow-ups were assessed in 444/1035 (43%), 243/1035 (23.5%) and in 31/1035 (3%) subjects, at the 6- 12- 24-month follow-up, respectively. Up to the 12-month follow-up, fourteen neurological recurrences were observed in 12/444 (2.7%) patients: 8 TIA and 2 hemorrhagic and 4 ischemic strokes. 10/14 (71.5%) neurological recurrences occurred within the 6-month follow-up. 41 cardiac and extra-cardiac complications occurred in 40/444 (9%) subjects, up to the 12th month. 34/41 (83%) complications were related to arrhythmias, 16 of them had AF, one atrial flutter, 10 supraventricular paroxysmal tachycardia and the remaining 7 patients non specific arrhythmic patterns. 7/41 (17%) complications were related to myocardial ischemia, atrial erosion, device malposition, gluteal hematoma, apical thrombus, pericardial effusion and dyspnoea. Most cardiac complications (34/41, 83%) occurred within the 6-month follow-up. Neither neurological recurrences nor cardiac-extra-cardiac complications were observed at the 24-month follow-up.

Data concerning residual RLS were available in 401/444 (90.3%) and in 198/243 (81.5%) subjects, at the 6- and 12-month follow-up, respectively. A large permanent residual RLS was observed in 1/401 (0.25%) and 1/198 (0.5%) patient at the 6- and 12-month follow-up, respectively.

cTTE was the most utilized diagnostic technique during the follow-up (47.1%, 42.4% and 74.2% at the 6- 12- 24-month follow-up, respectively); successively, in a lesser extent, were the data obtained by cTTE plus cTCD (23.2%, 24.3% and 16.1% at the 6- 12- 24-month follow-up, respectively).

Discussion

The aim of our study was to analyse the clinical practice regarding PFO closure in Italy by a prospective, observational and multi-centric survey using a web-based database.

The number of the entire population that underwent PFO closure was, to our knowledge, one of the highest among similar studies. Although there was a considerable drop in number of patients at the follow-up, the absolute amount is still worthy of note, mostly at the 6- and 12-month. This could be explained by the fact that the study was conducted by cardiologists whose aims were, first, to evaluate the success of the procedure and possible early complications and, second, to assess neurological recurrence and residual RLS.

Nowadays, the only neurological indication for PFO closure is a cryptogenic stroke or TIA. In our study ~20% of the subjects underwent the procedure with other clinical indications. The ''enlargement'' of indications might be due to a greater effort in primary prevention. The question at issue was, therefore, whether all indications were assessed by neurologists or by other specialists. A closer collaboration between neurologists and cardiologists or other specialists who work together in the patient's management is desirable.

Our study showed an absolute technical procedural success, comparable to previous reports [4,8—11]. The occurrence of early complications are mostly related to cardiac arrhythmias as described in previous reports [12—15].

We observed that a 2.7% of patients had neurological recurrences with major complications (i.e. ischemic and hemorrhagic stroke), and up to the 1.3% at the 12-month follow-up. It is noteworthy that about 70% of these patients had neurological recurrences within the 6-month follow-up. This would indicate that the medical therapy should be carefully monitored, mostly during the critical process of endothelization. Previous reports described similar incidence of recurrent thromboembolic events ranging from 0 to 4% per year [16—21].

Cardiac and extra-cardiac complications were around 9% up to 12-month follow-up, with 83% of them within the 6th month. Major, even transient, complications (i.e. AF, atrial flutter, myocardial ischemia, apical thrombus) were observed in 19/40 (47.5%) patients. Our data, in line with previous studies [13,22, Furlan A. CLOSURE I trial. Presented at the AHA 2010 meeting], draw attention to these critical adverse events, mostly related to cardiac arrhythmias, thus indicating the need to improve the peri- and postprocedural safety and prevention both with technical advances and medical therapy.

Finally, given the low rate of large permanent residual RLS at the 6- and 12-month follow-up (<1%), considered

crucial for increased risk of paradoxical embolism, we would substantially rule out that the re-occurrence of neurological events in our patients be correlated with the patent foramen ovale, as sole cause. Remarkably, Mono et al. recently described that concurrent etiologies, apart from PFO, were observed in more than one third of recurrent ischemic events in 308 patients with cryptogenic ischemic stroke who received medical therapy or underwent percutaneous PFO closure [4].

Conclusions

Our data regard early results from Italian Patent Foramen Ovale Survey and we need a longer follow-up in order to assess a comprehensive and conclusive evaluation of all clinical and technical characteristics correlated with a population who underwent percutaneous PFO closure.

Our study would confirm that percutaneous PFO closure is a safe procedure, pointing out that early complications and those during follow-up are not uncommon and are mostly related to cardiac arrhythmias.

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Appendix A.

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