

# Clinical and brain magnetic resonance imaging long-term follow-up in patients with cryptogenic stroke undergoing PFO closure with the NobleStitch EL system. A single-centre experience

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## Introduction

The NobleStitch EL system has recently been proposed as a safe and effective technique for percutaneous closure of patent fossa ovalis (PFO) in patients with cryptogenic stroke and evidence of paradoxical embolism [1]. Data on its long-term efficacy are, to date, quite scarce and limited to recurrences of clinically relevant neurological events [2]. It is unknown whether such a procedure confers protection against novel asymptomatic ischaemic lesions evaluated through appropriate brain imaging.

## Aim

The present study aims to report initial results from a cohort of subjects treated with suture-mediated PFO closure for cryptogenic stroke, undergoing longitudinal clinical and instrumental follow-up by brain magnetic resonance imaging (MRI).

## Material and methods

We initially screened all patients with cryptogenic stroke and PFO evaluated at the Unit of Interventional Cardiology, “Santa Maria” University Hospital, Terni, Italy, during the period between January 2018 and December 2020, who satisfied criteria for percutaneous closure. Patients with carotid or aortic atherosclerotic plaques, left-sided cardiac embolic sources, repetitive supraventricular or ventricular arrhythmias at ECG-Holter monitoring, or multi-fenestrated septum at initial echocardiography screening were excluded from the study. All the

remaining patients were treated with the NobleStitch EL system and subsequently followed up. The period of observation started immediately after the percutaneous interventional procedure. Baseline pre-procedural clinical, contrast echocardiographic (LV ejection fraction, right-to-left shunt, PFO length and width, presence of atrial-septal aneurysm), and neuroimaging (brain MRI) data were collected. Echocardiographic images were acquired only in 2D modality. We used the echo-contrast mode with microbubbles to identify and quantify the right-to-left shunt before and after the intervention. All PFO closure procedures were performed by 2 operators experienced in interventional cardiology, all under local anaesthesia, through right femoral venous access, under fluoroscopic guidance. We employed iodinated contrast medium administration for a correct intra-procedural PFO anatomy evaluation and subsequent closure of the same. Following the operation, the standard of care pharmacological treatment, consisting in a single antiplatelet agent (acetylsalicylic acid or clopidogrel) was prescribed according to current position statements [3]. Longitudinal follow-up visits were planned for each patient every 6 months from the day of procedure. After at least 1 year, all patients repeated contrast echocardiography and brain MRI in a day hospital regime. Such procedures were performed by the same physicians who carried out the baseline examination. Both exams (echocardiography and brain MRI) were performed at the same follow-up visit. All enrolled patients signed informed consent to participate in this investigation; the study was prospective observational,

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**Table I.** Demographic, clinical, and echocardiographic characteristics of the study sample

Parameter	No residual shunt	Residual shunt	P-value
N (%)	20 (87)	3 (13)	
Age [years]	56 (8)	53 (12)	0.51
Male sex, n (%)	9 (45)	3 (100)	0.08
Hypertension, n (%)	8 (40)	1 (33)	0.84
Follow-up length [months]	23 (16)	16 (9)	0.42
Ejection fraction, n (%)	62 (5)	63 (5)	0.75
PFO length [mm]	13 (5)	24 (6)	0.04
PFO width [mm]	3 (1)	4 (1)	0.24
PFO (length × width) [mm <sup>2</sup> ]	43 (24)	82 (62)	0.04
ASA at follow-up, n (%)	2 (10)	1 (33)	0.28

PFO – patent fossa ovalis, ASA – atrial septal aneurysm.

spontaneous, not for profit, and did not have any external funding source. It was approved by the Institutional Ethics Committee (CER N.: 4040/19). Given an expected annual incidence rate of clinically relevant and silent events of 20% [4] and the sample size of our study, a type II error could be avoided with a power of > 75%.

### Statistical analysis

The assumption of satisfactory normal distribution was tested for all the examined variables by the Kolmogorov-Smirnov Z test. Continuous variables were expressed as mean ± standard deviation (SD) if normally distributed, or as median and interquartile range (IQR) if non-normally distributed. Categorical variables were expressed by their relative (%) frequencies. The significance of the difference between baseline and follow-up parameters was assessed via *t*-test for paired data. Analyses were performed using SPSS software for Windows (version 22.0; IBM corp., Armonk, NY), with significance set at a 2-sided *p* < 0.05.

### Results

Twenty-three patients (mean age: 56 ± 8 years, men 56%) were enrolled in the present study. Demographic, clinical, and echocardiographic characteristics of the population at baseline and at follow-up are shown in Table I. Regarding intervention, the total procedural time was 64 ± 21 min, the average fluoroscopy time was 22 ± 7 min, the average radiation dose was 12.249 ± 8241 cGy·cm<sup>2</sup>,

and contrast medium 225 ± 74 ml (Table II). None of the percutaneous suture-mediated closures were complicated by peri-procedural events. The median follow-up duration was 16 months (IQR: 10–28 months). None of the patients reported new-onset neurological signs or symptoms at follow-up, or novel ischaemic lesions at brain MRI. Post-procedural residual grade 2 right-to-left shunt was found at the contrast echocardiography in 3 (13%) patients. The latter showed significantly greater PFO dimensions at baseline (Table I).

### Discussion

Suture-mediated PFO closure with the NobleStitch EL system represents an innovative approach to treat patients with cryptogenic stroke and evidence of paradoxical embolism [5]. The main advantage of this technique is the lack of a permanent closure with a device in the heart, which allows all the limitations related to the presence of an obstacle to the percutaneous left heart access to be overcome [1]. Nowadays, suture-mediated PFO closure is increasingly required due to the implementation of the number and the complexity of the electrophysiological and structural techniques [2, 5–7]. Gaspardone *et al.* demonstrated the feasibility and safety of this approach in the majority of septal anatomies [6], identifying predictors of low probability of complete closure with a single device in a channel width greater than 5 mm and in a spontaneous large right-to-left shunt [1]. Our data confirm overall long-term good efficacy of the procedure, given the low rate of residual shunt persistence (13%), which is in line with previous literature, and also that characteristics of the PFO (tunnel length and area, calculated as the product of length × width) at baseline could predict the long-term risk of residual inter-atrial shunt and should be considered during the screening phase. In our study, a residual grade 2 shunt at the follow-up was not associated with new-onset neurological signs or symptoms at the clinical and neuroimaging evaluation. This result, although limited by the

**Table II.** Angiographic findings related to the suture-mediated PFO closure procedure

Parameter	Value
Total procedural time [min]	64 ± 21
Average fluoroscopy time [min]	22 ± 7
Average radiation dose [cGy·cm <sup>2</sup> ]	12.249 ± 8241
Contrast medium [ml]	225 ± 74

low sample size, highlights the overall effectiveness and safety of this procedure, not only regarding the incidence of new-onset neurological manifestations but also in relation to asymptomatic brain lesions evaluated through neuroimaging. From our experience, we can state that the possible disadvantages of this percutaneous technique, when compared with the classic procedure with an umbrella-like double disk prosthesis, include the following: a longer learning curve with a prolonged procedural time, the exclusive use of fluoroscopic guidance with greater exposure to X-rays, and the employment of a discrete amount of iodinated contrast medium. Additional studies with larger sample sizes are needed to further investigate this innovative interventional technique.

### Conflict of interest

The authors declare no conflict of interest.

### References

1. Gaspardone A, Sgueglia GA, De Santis A, et al. Predictors of residual right-to-left shunt after percutaneous suture-mediated patent fossa ovalis closure. *JACC Cardiovasc Interv* 2020; 13: 2112-20.
2. Gaspardone A, Cinque A, Beggio E, et al. Percutaneous suture-mediated patent fossa ovalis (PFO) closure: two-year clinical follow-up. *Minerva Cardiol Angiol* 2021 Jun 17. doi: 10.23736/S2724-5683.21.05718-5.
3. Pristipino C, Sievert H, D'Ascenzo F, et al.; Evidence Synthesis Team; Eapci Scientific Documents and Initiatives Committee; International Experts. European position paper on the management of patients with patent foramen ovale. General approach and left circulation thromboembolism. *Eur Heart J* 2019; 40: 3182-95.
4. Vigna C, Inchingolo V, Giannatempo G, et al. Clinical and brain magnetic resonance imaging follow-up after percutaneous closure of patent foramen ovale in patients with cryptogenic stroke. *Am J Cardiol* 2008; 101: 1051-5.
5. Gaspardone A, Sgueglia GA. Suture-mediated patent fossa ovalis closure: the NobleStitch technique. In: *Percutaneous Cardiac Interventions Textbook. Tips and Tricks of New Techniques Beyond Stenting*. 2nd edition. Sabatè M, Brugaletta S (eds.). Europa Digital and Publishing, Toulouse, France 2019.
6. Gaspardone A, De Marco F, Sgueglia GA, et al. Novel percutaneous suture-mediated patent fossa ovalis closure technique: early results of the NobleStitch EL Italian Registry. *EuroIntervention* 2018; 14: e272-9.
7. Tarsia C, Gaspardone C, Sgueglia GA, et al. Atrial function analysis after percutaneous umbrella device and suture-mediated patent fossa ovalis closure. *Minerva Cardiol Angiol* 2021 Oct 29. doi: 10.23736/S2724-5683.21.05710-0.