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ORIGINAL ARTICLE

Atrial function after percutaneous occluder device and suture-mediated patent fossa ovalis closure

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Abstract

Aims

Suture-mediated patent fossa ovalis (PFO) closure is a recent technique, achieving closure by means of a simple suture. The differences between traditional occluders and suture might have different impacts on atrial function. The aim of this study was to evaluate atrial function after PFO closure by direct suture and traditional occluders.

Methods and results

We prospectively studied 40 patients, 20 undergoing PFO closure by occluder and 20 by suture. Trans-thoracic echocardiography was carried out the day before and 1 year after the procedure. Left atrial (LA) and right atrial (RA) function was evaluated by using speckle-tracking analysis assessing the strain values of the reservoir (st-RES), conduit (st-CD), and contraction phase (st-CT). Compared with values baseline PFO closure, at 1-year follow-up, patients with occluder implantation had significantly worse indices of LA and RA reservoir (LA st-RES $P < 0.001$; RA st-RES $P < 0.001$), conduit (LA st-CD $P < 0.001$; RA st-CD $P < 0.001$), and contraction function (LA st-CT $P < 0.05$; RA st-CT $P < 0.05$). In patients with suture-mediated PFO closure, no significant differences were observed in the same indices of reservoir (LA st-RES $P = 0.848$; RA st-RES $P = 0.183$), conduit (LA st-CD $P = 0.156$; RA st-CD $P = 0.419$), and contraction function (LA st-CT $P = 0.193$; RA st-CT $P = 0.375$).

Conclusion

Suture-mediated PFO closure does not alter atrial function. Conversely, PFO closure by metallic occluders is associated with a deterioration of atrial function. This detrimental effect on atrial function could favour the development of atrial arrhythmias.

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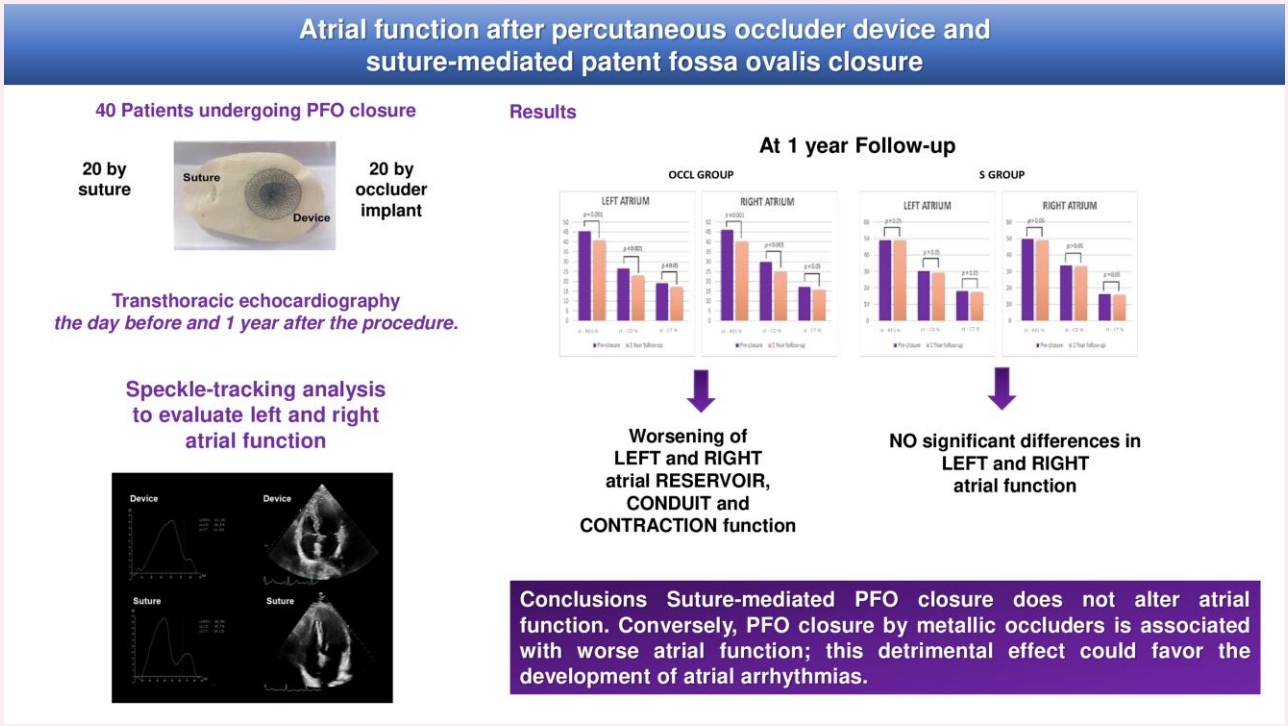
Graphical Abstract



Keywords atrial function • occluder device • patent fossa ovalis • suture

Introduction

Atrial function modulates ventricular filling and performance, by functioning as a reservoir and conduit for venous return and as a booster pump that augments ventricular filling. Atrial dysfunction impairs heart performance; the loss of atrial function coincides with the appearance of atrial arrhythmias and atrial fibrillation and is associated with an increase in cardiovascular morbidity and mortality.[1,2]

Trans-catheter percutaneous closure of patent fossa ovalis (PFO) with an occluder device is followed by the development of supraventricular arrhythmias or atrial fibrillation with an incidence ranging from 1.7% to 7.4%[3–8] up to the 20–37% of patients in recent reports using loop recorder monitoring.[4,9] Indeed, a rigid atrial septal closure device could alter atrial structure and geometry, causing impairment of its electrical stability and function.[10,11] Suture-mediated PFO closure is a new technique, achieving closure of the PFO by means of a polypropylene suture.[12–14] The technical differences between a suture and a prosthetic metallic occluder device may have different impacts on atrial structure and function. The aim of the present study was to analyse prospectively bi-atrial function in patients undergoing PFO closure using the suture-based technique or occluder device implant, in order to assess the different impacts of the two techniques on the atrial function.

Material and methods

Study population

Fifty patients who have undergone percutaneous PFO closure at Sant'Eugenio Hospital in Rome, between May 2020 and February 2021, were prospectively studied: 25 patients underwent occluder device implantation (OCCL group) and 25 patients underwent suture-mediated PFO closure (HeartStitch, Fountain Valley, CA, USA) (S group).

All patients had PFO closure because of cryptogenic stroke or recurrent transient ischaemic attack associated with positive brain magnetic resonance and grade ≥2 (scale 0–3) atrial right-to-left shunt (RLS) at trans-thoracic and/or trans-oesophageal echocardiography (TTE and TEE). All patients had complete neurological and cardiological examination, pre-procedural 48-h Holter electrocardiogram (ECG) monitoring, supra-aortic vessels Doppler ultrasound, and RoPE score evaluation. Patients were excluded from percutaneous PFO closure in case of even minimal aortic and/or carotid artery disease at carotid Doppler scan, left-sided cardiac, or aortic potential source of peripheral embolism and/or evidence of repetitive supraventricular/ventricular rhythm disturbances at Holter monitoring. Patients with systemic hypertension, valvular heart disease, coronary artery disease, congenital heart disease, arrhythmias, heart failure, cardiomyopathy, obesity, parenchymal lung disease, kidney, endocrine, liver, or neoplastic diseases were excluded from the study; seven patients in the S group and six patients in the OCCL group had frequent migraine episodes (>4 episodes/month).

Patients enrolled in the study underwent a TEE with which the diagnosis of PFO was confirmed and its anatomical characteristics were studied. The mid-oesophageal short-axis view and the bi-caval view were performed and the following measures were taken: PFO diameter, as the maximum separation between septum primum and septum secundum; PFO length, as the maximum overlap between septum primum and septum secundum; and the maximum excursion made by the

inter-atrial septum. Each measurement is taken three times and the measurements are averaged.

To study the RLS, we used a mixture of 9 mL physiological saline, 1 mL blood, and 0.5 mL air, injected via an antecubital vein. The study did not begin until adequate filling of the right atrium was achieved. At least two injections were administered at baseline and up to two injections with the Valsalva manoeuvre.

RLS was semi-quantitatively graded according to the number of micro-bubbles detected in the left atrium (LA) after crossing the inter-atrial septum on a still frame within the first three cardiac cycles of contrast entering the right atrium. Grading was as follows: Grade 0 = none; Grade 1 (minimal) = 1–10 bubbles; Grade 2 (moderate) = 10–20 bubbles; and Grade 3 (severe) ≥ 20 bubbles. Maximal RLS severity (occurring spontaneously or after Valsalva manoeuvre) was considered.

Patients with atrial septal defects and atrial septal aneurysms (defined as mobility of the atrial septum greater than 10 mm) were excluded, in order to obtain study populations with homogeneous echocardiographic characteristics, avoiding different features that could influence atrial function itself. Only patients with an adequate acoustic window that allowed optimal images and cine-loop were included. The patients who met the aforementioned inclusion criteria were enrolled in the study between May 2020 and February 2021, consecutively.

Only patients with no residual RLS, assessed by contrast-enhanced TTE and TEE at 12-month follow-up, were included in the study, in order to rule out any factors, other than the closure technique, that could influence atrial function. A Holter ECG monitoring lasting 48 h was performed in all patients 1 month after the procedure and repeated at 3, 6, and 12 months. Because the suture system for percutaneous PFO closure has been approved in Europe (with its CE mark last renewed in 2018), and the study had a prospective observational design with routine pre- and post-procedural evaluation by protocol, local ethical committee approval and Institutional Review Board approval were not required. All patients provided informed consent for the diagnostic and therapeutic procedures, as well as for the use of their personal data for research purposes.

PFO closure procedure

Both procedures were performed in the Cath Laboratory of our centre by an experienced interventional cardiologist. The right femoral vein was used as venous access for all patients.

Fluoroscopic and TEE guidance were used throughout the procedure for placement and assessment of the septal occluder. A 0032″ wire was advanced across the PFO and, in most cases, into the left upper pulmonary vein. Sizing balloon interrogation of the PFO was performed to determine the anatomy of the septum secundum and septum primum during contrast injection. The occluder device consists of two discs linked together by a short connecting waist. It was advanced along the wire, and, once in position, it was opened so that the atrial septum was located between the two discs obtaining PFO occlusion. After observation and testing of its correct positioning and stability, it was left in place.

The direct suture PFO closure was performed under fluoroscopic guidance. After positioning the 0.032″ wire as above, a 0.018″ wire was advanced into the distal superior vena cava or subclavian vein. A sizing balloon was used to measure PFO and study the septa as above.[12–14]

The direct suture was performed using two dedicated suture delivery catheters to capture and suture the septum secundum and the septum primum using a 4–0 polypropylene suture that produces an 'S' shape closure of the PFO. The distal end of each catheter has a suture-carrying arm that opens inside the heart to engage the septum and an internal needle that pierces through the septum tissue picking the suture up in the opened carrying arm. A third catheter was advanced over the septum secundum and septum primum sutures to approximate both septa to achieve closure by releasing a radiopaque polypropylene knot on the right side of the inter-atrial septum and to cut the excess suture material.

The enrolled patients underwent only PFO closure and not other cardiovascular procedures.

Echocardiographic evaluation of atrial function

2D Echocardiography

The study was designed using patients as self-control before and after the procedure. All patients underwent TTE examination the day before and 1 year after the procedure, using an EPIQ CVx scanner (Philips Healthcare Italy, Milan, Italy). The echocardiographic analysis was conducted by two expert echocardiographers. All measurements and videos were validated with common consent by two other expert operators not involved in the study. Measurements of cardiac chambers were performed according to established criteria.[15] Using a modified Simpson biplane method, left ventricle (LV) end-diastolic volume (EDV) and end-systolic volume (ESV) were measured from apical four-chamber and two-chamber views and were indexed to body surface area. The LV ejection fraction (LV EF) was calculated from EDV and ESV estimates. Pulsed-wave Doppler of trans-mitral flow was obtained, and peak A-wave velocity and the *E*/*A* ratio were measured. Colour tissue Doppler imaging analysis, either from the septal or from lateral mitral annulus, was performed and measurements of *A*′-wave velocities and the *E*/*E*′ ratio were obtained. From a right ventricle (RV)-focused apical four-chamber view, RV end-diastolic area and end-systolic area were estimated and indexed to body surface area. Fractional area change was obtained from these measures. Pulsed-wave Doppler of tricuspid flow was obtained, and *A*-wave velocity was measured. Peak *A*′-wave velocity and the *E*/*E*′ ratio, by colour tissue Doppler from tricuspid lateral annulus, were obtained. Tricuspid annular plane systolic excursion was obtained by M-mode echocardiography. Pulmonary artery systolic pressure was measured from the tricuspid regurgitation peak velocity and evaluation of the inferior vena cava in the subcostal view. LA maximal volume (LAV_{max}), at the end of LV systole just before mitral valve opening, and minimal volume (LAV_{min}), at the end of LV diastole at mitral valve closure, were measured from apical four-chamber and two-chamber views, using a modified Simpson bi-plane method, and were indexed to body surface area. LA total emptying fraction ($LA\text{-}TE_{mtp}F$) was calculated as $[(LA\text{-}V_{max} - LA\text{-}V_{min})/LA\text{-}V_{max}] \times 100$. Right atrial (RA) maximal volume (RAV_{max}) and minimal volume (RAV_{min}) were measured from the apical four-chamber view and were indexed to body surface area. RA total emptying fraction ($RA\text{-}TE_{mtp}F$) was measured as above. Three measurements for each index were averaged and used for analysis.

2D speckle tracking echocardiography

For 2D speckle tracking echocardiography (2D-STE), echocardiographic cine-loop was recorded with a length of 3 beats in an apical four-chamber view optimized for atrial function and with a frame rate set of 50 Hz for all patients. Loops analysis was obtained using QLAB software (Philips Healthcare) with the latest version 15.0 'AutoStrain LA' (*Figure 1*). This software package allows specific LA strain analysis and overcomes the limitations of previous software where atrial speckle tracking was obtained manually by adapting ventricular track on the atria. It improves accuracy and takes specific factors into account, such as the thin thickness of atrial wall that does not make an adequate subdivision into segments. Therefore, the software produces a global, and not a segmental, strain analysis, following the strain task force standardization document.[16] The AutoStrain application uses two automation technologies: *Auto View Recognition* to identify automatically the apical four-chamber and

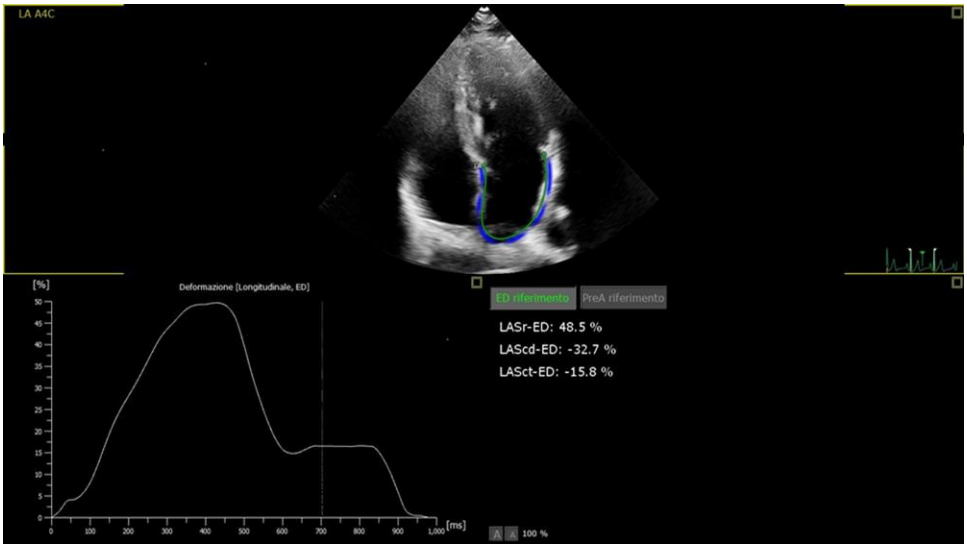


Figure 1 LA speckle tracking analysis using Philips QLAB with the latest software version 15.0 'Autostrain LA'. The atrial speckle tracking curve represents the change in length of the atrial myocardium over time. Three strain values, of the three phases of atrial cycle, are obtained: st-RES (reservoir phase), st-CD (conduit phase), and st-CT (contraction phase).

Auto Contour Placement to anchor automatically three reference points: one point located on the roof of the atrial chamber and two points located on the atrioventricular annulus, septal and lateral. Echocardiographers verify adequate tracking and corrected it manually if needed. The atrial speckle tracking diagram representing the change in length of the atrial myocardium over time is produced. The curve is obtained using R-wave onset of the ECG, corresponding to the end of diastole, as a reference point.[16,17]

The first peak of the curve corresponds to the maximum LA wall lengthening, at ventricular end-systole, and the second late peak is just before the active atrial contractile phase begins, at the onset of the P wave on the ECG. The st-RES is the strain during the reservoir phase, measured as the difference of the strain value at mitral valve opening minus ventricular end-diastole (positive value). The st-CD is the strain during the conduit phase, measured as the difference of the strain value at the onset of atrial contraction minus mitral valve opening (negative value). The st-CT is the strain during the contraction phase, measured as the difference of the strain value at ventricular end-diastole minus the onset of atrial contraction (negative value).[18–20] The software is specific only for the LA. So, the software produced an automatic LA trace that was usually correct and no or minimal corrections were made by the operators. Instead the right atrium automatic trace was corrected by the operators for all patients, but the corrections consisted of repositioning the three reference points never more than 2 mm.

Statistics

For each continuous variable, we verified the normal distribution by the Shapiro–Wilk test. Normally distributed variables were described as mean ± standard deviation, whereas non-normally distributed ones were described as median (interquartile range). The comparisons between the groups were performed by *t*-tests or Wilcoxon rank sum tests, as appropriate. The categorical variables were described as frequencies (percentages) and compared by chi-squared test or McNemar test, as appropriate. We assessed the reliability using inter-class correlation coefficient (ICC) on a randomly selected sample of 20 patients, with 10 patients per group. Inter-rater reliability was obtained by two trained readers independently assessing TTE anatomical and functional parameters, while intra-rater reliability was assessed by one same reader re-evaluating the same parameters 2 weeks apart. Two-sided $P < 0.05$ was required for statistical significance. Data were analysed with R version 4.1.2 software (R Foundation for Statistical Computing, Vienna, Austria).

Results

Patients

A total of 50 patients were enrolled in this study, with 25 patients assigned to each group. After 1 year, two patients in the OCCL group and four patients in the S group still had a residual RLS > 1. The percentage of patients without any residual RLS was 92% (23 patients) in the OCCL group and 84% (21 patients) in the S group. In the OCCL group, two patients did not complete the follow-up, and one patient was excluded because she was pregnant. In the S group, one patient did not complete the follow-up, resulting in 20 patients for each group being included in the final analysis.

The two patient groups were comparable in demographic and clinical characteristics (*Table 1*). Before the procedure, the maximum RLS recorded was moderate (Grade 2) in eight patients of the S group (40%) and in six patients of the OCCL group (30%), while it was severe (Grade 3) in 12 S patients (60%) and in 14 OCCL patients (70%), without significant differences between the two groups ($P = 0.13$). Only patients with similar PFO characteristics were enrolled (*Table 1*). The choice of using the occluder or the direct suture did not depend on the different anatomical PFO characteristics but on the operator's expertise. In the OCCL group, PFO closure was achieved using Amplatzer septal occluder device (St. Jude Medical, St. Paul, MN, USA; Amplatzer). Amplatzer™ Cribriform Multi-Fenestrated Septal Occluder 25 mm was used in 17 patients and Amplatzer™ PFO Occluder 25/18 mm in three patients. Only one suture was used in the S group. All patients were in sinus rhythm at baseline and 1 year after PFO closure. One patient in the OCCL group had two short

Table 1 Baseline characteristics of study population

Variable	NobleStitch ($n = 20$)	Occluder ($n = 20$)	P
Age, y	47.1 ± 8.6	48.1 ± 11.8	0.761
Gender M	12 (60%)	7 (35%)	0.103
Ethnicity	Caucasian (100%)	Caucasian (100%)	—
Body surface area, m^2	1.83 ± 0.21	1.78 ± 0.21	0.402
BMI, kg/m^2	23.0 ± 3.5	23.2 ± 3.3	0.849
Heart rate, bpm	70 ± 9	71 ± 11	0.751
Systolic BP, mmHg	115 ± 10	114 ± 12	0.679
Diastolic BP, mmHg	70 ± 9	72 ± 9	0.617
TIA	12 (60%)	8 (40%)	0.999
Ischaemic stroke	11 (55%)	9 (45%)	0.999
RoPE SCORE	7.35 ± 1.0	7.4 ± 1.1	0.885
PFO			
Length (mm)	8.3 ± 1.3	8.2 ± 1.4	0.860
Diameter (mm)	3.6 ± 0.6	3.6 ± 0.5	0.868
Inter-atrial Septum			
Excursion (mm)	4.7 ± 1.6	4.7 ± 1.9	0.992
Maximum RLS			
Grade 2	8 (40%)	6 (30%)	0.137
Grade 3	12 (60%)	14 (70%)	

The two patient groups did not show significant differences in demographic and clinical characteristics.
BP, blood pressure; PFO, patent fossa ovalis; RLS, right-to-left shunt; TIA, transient ischaemic attack.

asymptomatic periods of atrial fibrillation (<60 s) and two patients had repetitive symptomatic supraventricular ectopic beats at the Holter monitoring carried out 1 and 3 months after the procedure. One of these two patients had still symptomatic supraventricular ectopic beats at the Holter monitoring at 6- and 12-month Holter monitoring. No patients showed arrhythmias in the S group.

Echocardiographic evaluation

Ventricular echocardiographic data are reported in *Table 2*. In the S group, no significant differences were observed in volumetric, systolic, and diastolic values before and after PFO closure. Volumetric and systolic indices showed no significant differences in the OCCL group too. However, 1 year after the procedure, Doppler analysis showed significant worsening in mitral *A* velocity ($P < 0.001$), *A′* septal mitral annulus velocity ($P < 0.05$), *A′* lateral mitral annulus velocity ($P < 0.05$), tricuspid *A* velocity ($P < 0.05$), and *A′* tricuspid annulus velocity ($P < 0.05$).

In both groups, left and right maximal atrial volumes (LAV_{max} – RAV_{max}) did not significantly change at 1-year follow-up compared with baseline. Minimal volumes (LAV_{min} – RAV_{min}) and total emptying fraction values (LA-TE_{mtp}F and RA-TE_{mtp}F) were significantly different in OCCL group, but not in S group, at 1-year follow-up compared with baseline (*Table 3*).

Atrial strain parameters are reported in *Table 3*. Compared with values baseline PFO closure, at 1-year follow-up, patients who underwent occluder implantation had significantly worst indices of LA and RA reservoir function (LA st-RES $P < 0.001$; RA st-RES $P < 0.001$), conduit function (LA st-CD $P < 0.001$; RA st-CD $P < 0.001$), and contraction function (LA st-CT $P < 0.05$; RA st-CT $P < 0.05$) (*Figure 2*). In patients who underwent suture-mediated PFO closure, no significant differences were observed in the same indices of reservoir (LA st-RES $P = 0.848$; RA st-RES $P = 0.183$), conduit (LA st-CD $P = 0.156$; RA st-CD $P = 0.419$), and contraction function (LA st-CT $P = 0.193$; RA st-CT $P = 0.375$) (*Figure 3*). Inter-rater reliability was good (ICC > 0.60) while the intra-rater reliability was excellent (ICC > 0.80) for all TTE anatomical and functional parameters considered. *Table 4* shows the ICC values specifically for atrial volumetric and speckle tracking analysis.

Discussion

The results of this prospective study indicate that PFO closure by a metallic prosthetic device causes detrimental changes in atrial function. On the contrary, the closure of the PFO by direct suture does not cause any modification of the atrial function.

A very limited number of studies investigated the impact of a metallic occluder device on atrial function in patients with PFO.[21,22] Vitarelli *et al.*[21] analysed atrial function after percutaneous occluder implantation in 116 patients. A worse 'time-to-peak strain' value in all segments of the LA and septum compared with the value before the procedure was reported. Vavuranakis *et al.*[22] observed a transient alteration of LA function in 25 patients who had undergone occluder PFO closure. In a previous preliminary study, we retrospectively investigated LA function in patients who underwent occluder implantation and suture-mediated PFO closure.[23] Patients who underwent percutaneous PFO closure with an occluder device implant had LA indices of the reservoir, conduit, and active pump phase worse than healthy subjects. Instead, patients who underwent suture-mediated closure showed no significant differences in LA function values compared with healthy subjects.

Atrial function impairment reduces global heart performance and is associated with an increased risk of developing atrial fibrillation. Hauser *et al.*[1] performed a prospective longitudinal study on 3590 patients from the 'fifth Copenhagen City Heart Study'. During a median follow-up of 5.3 years, patients with reduced atrial strain values of the reservoir and contraction phase have an increased risk of

Table 2 Ventricular echocardiographic analysis before and after PFO closure

	S group			OCCL group		
	Before PFO closure	1-year follow-up	*P*	Before PFO closure	1-year follow-up	*P*
Left ventricle						
LV EDV, mL/m^2	53.3 ± 10.4	52.9 ± 10.1	0.423	56.4 ± 12.1	56.1 ± 12	0.605
LV ESV, mL/m^2	21.1 ± 5.9	20.9 ± 5.6	0.683	22.4 ± 5.8	22.3 ± 6.4	0.743
LV EF %	60.9 ± 4.9	60.8 ± 4.1	0.939	60.4 ± 3.6	60.7 ± 4.4	0.637
LV mass/BSA, g/m^2	66.7 ± 11.1	66.5 ± 11.6	0.571	68.0 ± 12.4	67.8 ± 12.6	0.619
LV wall thickness						
Septal wall, mm	7.1 ± 1.0	7.1 ± 1.1	0.666	7.4 ± 1.0	7.5 ± 1.0	0.649
Posterior wall, mm	7.4 ± 1.1	7.4 ± 0.9	0.804	7.4 ± 1.0	7.3 ± 1.0	0.841
Mitral *A* velocity, cm/s	54.0 ± 12.4	54.2 ± 12.5	0.791	58.0 ± 15.3	55.6 ± 15	**<0.001**
Mitral *E*/*A*	1.27 ± 0.37	1.26 ± 0.36	0.946	1.03 ± 0.3	1.06 ± 0.3	0.491
A′ septal velocity, cm/s	9.05 ± 1.9	9.04 ± 1.7	0.996	9.04 ± 1.4	8.08 ± 1.7	**<0.05**
A′ lateral velocity, cm/s	10 ± 3.23	10.4 ± 2.83	0.363	10.6 ± 2.8	9.5 ± 1.9	**<0.05**
E/*E*′ ratio	5.2 ± 1.1	5.3 ± 1.1	0.625	5.1 ± 1.6	5.0 ± 1.5	0.521
Right ventricle						
RV EDA, cm^2/m^2	10.5 ± 1.5	10.4 ± 1.9	0.637	10.7 ± 2.4	10.6 ± 2.3	0.476
RV ESA, cm^2/m^2	5.6 ± 0.8	5.5 ± 0.9	0.412	5.5 ± 1.3	5.4 ± 1.4	0.937
FAC %	46.5 ± 3.6	47.0 ± 3.9	0.408	48.9 ± 4.04	48.4 ± 6.6	0.715
TAPSE, mm	24 ± 1.8	24.2 ± 1.9	0.704	23.4 ± 1.6	23.6 ± 1.6	0.586
Tricuspid A velocity, cm/s	31 ± 4.8	31.2 ± 4.7	0.692	35.4 ± 7.5	33.3 ± 7.9	**<0.05**
A′ velocity, cm/s	13.7 ± 3.3	13.6 ± 3.2	0.887	12.9 ± 3.6	11.9 ± 2.6	**<0.05**
E/*E*′ ratio	3.6 ± 0.78	3.9 ± 0.79	0.102	4.3 ± 1.5	4.2 ± 1.5	0.896
PAPs, mmHg	22 ± 2.9	21.8 ± 2.5	0.778	21.3 ± 2.7	22.1 ± 2.8	0.307

In the S group, no significant differences were observed in volumetric, systolic, and diastolic values before and after PFO closure. Instead 1 year after the procedure, the OCCL group showed significant worsening in mitral *A* velocity, *A*′ septal mitral annulus velocity, *A*′ lateral mitral annulus velocity, tricuspid *A* velocity, and *A*′ tricuspid annulus velocity.
EDA, end-diastolic area; EDV, end-diastolic volume; EF, ejection fraction; ESA end-systolic area; ESV, end-systolic volume; FAC, fractional area change; LV, left ventricle; OCCL, occluder group; PAPs, pulmonary artery systolic pressure; PFO, patent fossa ovalis; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion.

developing atrial fibrillation. Alhakak *et al.*[24] found that reservoir atrial strain provides prognostic information on the long-term risk of atrial fibrillation and ischaemic stroke. Olsen *et al.*[25] found that atrial functional measures predict atrial fibrillation in the general population.

These studies demonstrate that deterioration in atrial function is associated with the development of atrial arrhythmias and that atrial function indices, such as strain values, can predict the future risk of atrial fibrillation onset.

Atrial fibrillation is the most frequent arrhythmia in the general population (3% of the general population) and is associated with an increased risk of cardiovascular morbidity and mortality.[1,2,26] Undiagnosed atrial fibrillation is the cause of 25% of cryptogenic stroke,[26] with significant consequences on the social and economic cost. Knowing conditions that favour atrial function impairment and increase the risk of atrial fibrillation could be useful in reducing atrial fibrillation incidence or allowing its early diagnosis.

Atrial fibrillation is an insidious and undesirable complication after closure of the PFO with a prosthetic device with an incidence in controlled trials ranging from 1.7% to 7.4% within 45 days following the procedure.[3–8] However, this incidence is probably underestimated. More recently, by using loop recorder monitoring for ≥28 days after PFO closure with an occluder, supraventricular arrhythmias were diagnosed in 20% of the patients,[4] confirming previous report carried out in a small study.[27] Additionally, in another recent study, by using loop recorder monitoring for 1 year after PFO closure, atrial fibrillation was reported in 37% of patients.[9]

The mechanisms responsible for the development of supraventricular arrhythmias after implantation of a device remain speculative. Intuitively, it is conceivable that the presence of a rigid metal structure at the level of the inter-atrial septum, which is partly contractile, can cause structural and functional alterations such as electrical dispersion and new atrial re-entry circuits.[10,11,28]

In the present study, we prospectively investigated LA and RA function before and after PFO closure with an occluder device or direct suture, by TTE 2D STE, using the same patient as own control. Moreover, selected patients had similar anatomical and clinical features of the atrial septum in order to avoid bias related to confounding features. At 1-year follow-up, patients undergoing occluder implantation presented maximal atrial volumes comparable with those before the procedure. However, the worst values of atrial minimal volumes and total emptying fraction suggested the worsening of atrial pump function measured by volumetric analysis and this is consistent with the strain analysis results. OCCL patients have a reduction in atrial reservoir, conduit, and contraction function for both LA and RA, as indicated by significantly lower st-RES, st-CD, and st-CT strain values, compared with baseline. Strain measured at the inter-atrial septum is influenced by the presence of the metal device, and it is likely not representative of tissue strain alone, but the deformation measured by the software corresponds to the final effect of the presence on the atrial septum. Intuitively, it can be assumed that a bulky double-disk device reduces tissue deformation. In support of the data obtained from the strain analysis, also the volumetric analysis itself showed a reduction in atrial function in patient who underwent occluder implant. Furthermore, Doppler analysis showed a significant

Table 3 Atrial analysis before and after PFO closure

	S group			OCCL group		
	Before PFO closure	1-year follow-up	*P*	Before PFO closure	1-year follow-up	*P*
LA						
Vol max (mL/m^2)	25.79 ± 4.38	25.51 ± 4.33	0.489	25.32 ± 5.3	25.33 ± 5.2	0.975
Vol min (mL/m^2)	10.05 ± 3.09	10.09 ± 3.48	0.903	10.17 ± 4.13	11.37 ± 4.57	**<0.05**
$TE_{mtp}F$ %	61.32 ± 8.51	60.8 ± 10.42	0.695	60.31 ± 12.01	55.73 ± 12.32	**<0.05**
LA						
st-RES %	48.9 ± 5.3	48.9 ± 5.4	0.848	45.4 ± 6.0	40.8 ± 5.7	**<0.001**
st-CD %	−30.3 ± 6.5	−29.3 ± 5.9	0.156	−26.6 ± 5.9	−22.9 ± 5.7	**<0.001**
st-CT %	−18.1 ± 3.1	−17.5 ± 2.7	0.193	−18.9 ± 4.3	−17.1 ± 4.1	**<0.05**
RA						
Vol max (mL/m^2)	22.82 ± 3.60	22.67 ± 4.06	0.745	22.55 ± 5.67	23.39 ± 4.93	0.106
Vol min (mL/m^2)	10.13 ± 2.41	10.03 ± 2.59	0.704	10.16 ± 2.61	12.06 ± 3.40	**<0.001**
$TE_{mtp}F$ %	56.01 ± 7.89	55.51 ± 8.84	0.693	54.07 ± 9.66	48.11 ± 12.02	**<0.05**
RA						
st-RES %	49.6 ± 5.3	49.1 ± 5.4	0.183	46.2 ± 6.0	40.3 ± 5.7	**<0.001**
st-CD %	−33.6 ± 6.5	−33.1 ± 5.9	0.419	−29.7 ± 7.5	−24.9 ± 7.2	**<0.001**
st-CT %	−16.2 ± 3.9	−15.8 ± 3.4	0.375	−17.1 ± 4.4	−15.8 ± 3.7	**<0.05**

At 1-year follow-up in the S group, no significant differences were observed in atrial volumetric analysis and in the indices of left and right atrial reservoir, conduit, and contraction function. In the OCCL group, left and right maximal atrial volumes did not significantly change at 1-year follow-up compared with baseline. Instead minimal volumes (LAV_{min} – RAV_{min}) and total emptying fraction values (LA-TEmtpF and RA-TEmtpF) were significantly different at 1-year follow-up compared with baseline. At 1-year follow-up, patients who underwent occluder implantation had significantly worst indices of left and right atrial reservoir, conduit, and contraction function.
LA, left atrium; OCCL, occluder group; RA, right atrium; st-CD, strain value of conduit phase; st-CT, strain value of contraction phase; st-RES, strain value of reservoir phase; $TE_{mtp}F$, total emptying fraction; Vol max, maximal volume; Vol min, minimal volume.

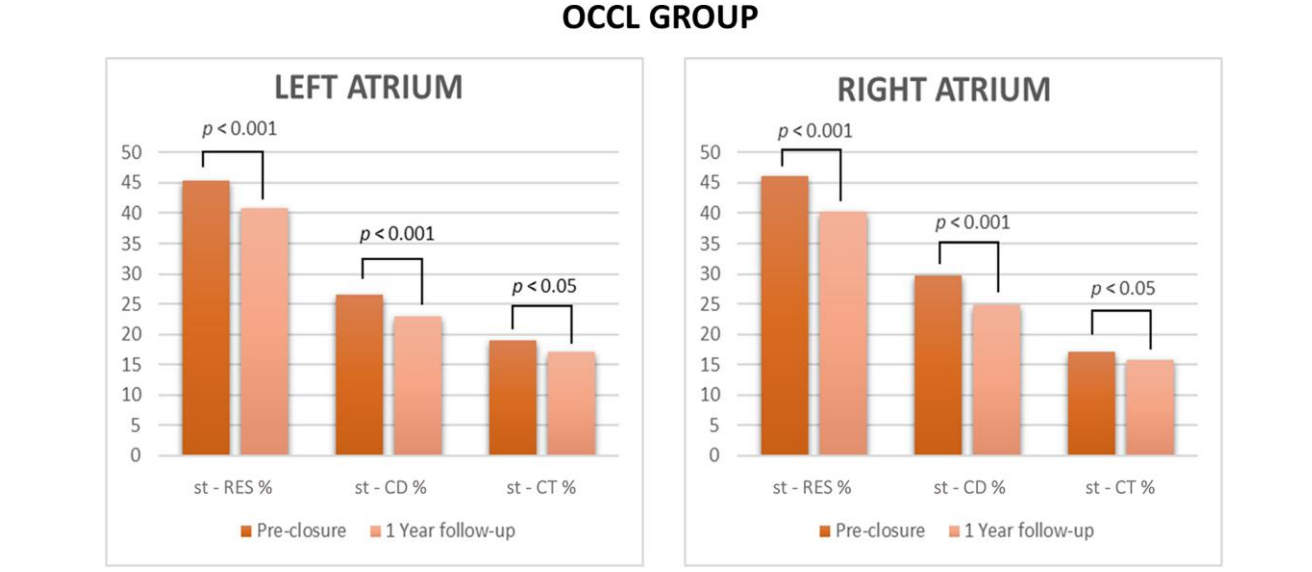


Figure 2 Atrial strain values in the OCCL group. Compared with values baseline PFO closure, at 1-year follow-up, patients with occluder implantation had significantly worst indices of LA and RA reservoir function (LA st-RES $P < 0.001$; RA st-RES $P < 0.001$), conduit function (LA st-CD $P < 0.001$; RA st-CD $P < 0.001$), and contraction function (LA st-CT $P < 0.05$; RA st-CT $P < 0.05$).

reduction in the values of mitral *A* velocity, *A*′ septal and lateral mitral annulus velocities, tricuspid *A* velocity, and *A*′ tricuspid annulus velocity. These results are consistent with the reduction of atrial deformation in the active contraction phase. In contrast, in S patients, strain analysis did not demonstrate any significant changes in LA and RA function indices at 1-year follow-up. These data suggest that patients who underwent

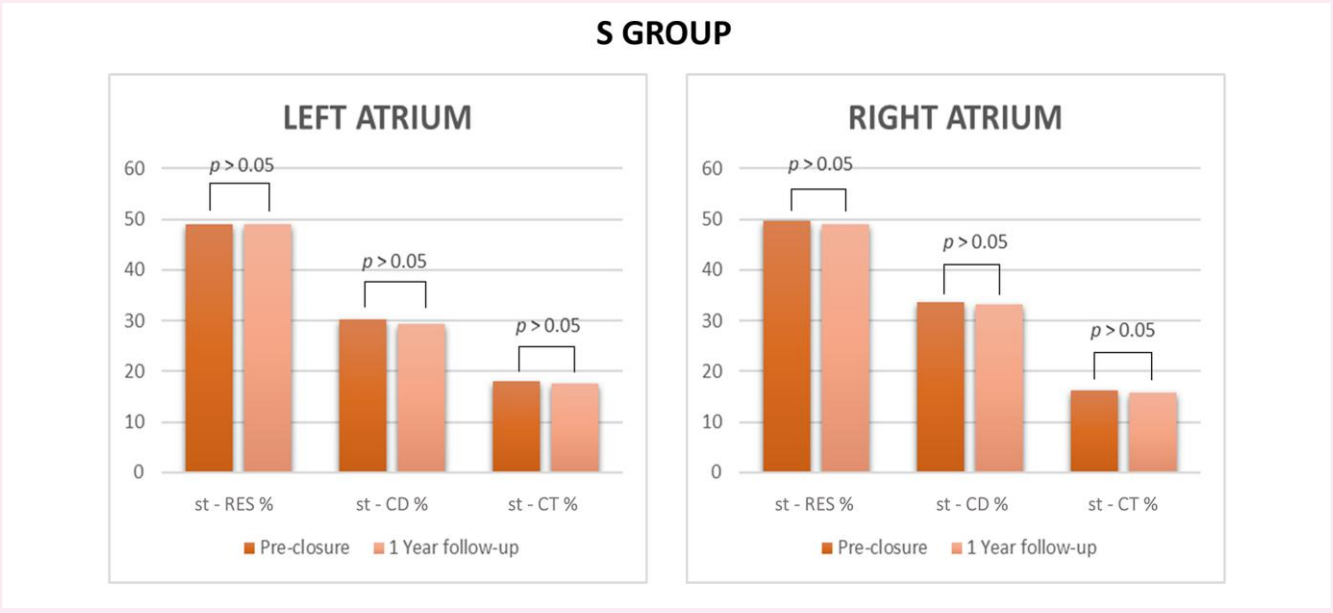


Figure 3 Atrial strain values in the S group. In patients with suture-mediated PFO closure, at 1-year follow-up, no significant differences were observed in the indices of reservoir (LA st-RES $P = 0.848$; RA st-RES $P = 0.183$), conduit (LA st-CD $P = 0.156$; RA st-CD $P = 0.419$), and contraction function (LA st-CT $P = 0.193$; RA st-CT $P = 0.375$) of both atria.

Table 4 ICC values for inter-rater and intra-rater reliability in echocardiographic measurements of left and right atrial parameters

	Inter-rater ICC	Intra-rater ICC
LA		
Vol max (mL/m^2)	0.71	0.83
Vol min (mL/m^2)	0.73	0.86
$TE_{mtp}F$ %	0.73	0.85
LA		
st-RES %	0.81	0.91
st-CD %	0.79	0.88
st-CT %	0.82	0.89
RA		
Vol max (mL/m^2)	0.60	0.79
Vol min (mL/m^2)	0.65	0.82
$TE_{mtp}F$ %	0.64	0.81
RA		
st-RES %	0.69	0.80
st-CD %	0.71	0.83
st-CT %	0.73	0.81

ICC, intra-class correlation coefficient; LA, left atrium; RA, right atrium; st-CD, strain value of conduit phase; st-CT, strain value of contraction phase; st-RES, strain value of reservoir phase; $TE_{mtp}F$, total emptying fraction; Vol max, maximal volume; Vol min, minimal volume.

occluder implantation show a reduction in LA and RA compliance and contractility after device-mediated PFO closure, while suture-mediated PFO closure does not affect atrial function. Alterations found with strain analysis, not related to atrium dilation, probably constitute the early sign of the development of anatomical and functional alterations. At the last follow-up of Holter rhythm monitoring, all patients were in sinus rhythm and without clinical events. However, one patient undergoing device implant had brief episodes of asymptomatic paroxysmal fibrillation 1 year after the procedure. As cardiac rhythm control is not frequently used in clinical practice, this finding indicates that the long-term incidence of atrial arrhythmia is probably underestimated after PFO closure by occluder implant and suggests that closer and more systematic monitoring should be performed routinely in these patients as rhythm disturbances are often asymptomatic.

Clinical perspectives

Direct suturing reduces the risk of deterioration of atrial function. This should be useful even more for patients who are at risk of developing atrial dysfunction or who already have atrial dysfunction, such as patients with diastolic or systolic dysfunction, or patients with mitral or aortic valve disease: in these patients, the occluder device implantation may further worsen atrial function and accelerate the atrial fibrillation development. Also, patients with a higher thromboembolic risk may be better candidates for direct suture rather than occluder implantation.

Routine measurement of atrial strain is time-consuming, so it does not apply to all patients, but certainly, it could be performed in patients who have a greater risk of atrial dysfunction to identify those in which the occluder implantation should be avoided.

Finally, in patients who underwent occluder implant, closer and more systematic monitoring should be performed routinely as rhythm disturbances are often asymptomatic. We propose to perform a Holter monitoring twice a year, after the occluder implant is performed, also in asymptomatic patients. If the Holter ECG shows no alterations, but the patient is symptomatic due to palpitations, a loop recorder could be implanted.

Study limitations

The study was conducted in a single centre and the major limitation is related to the small size of the study population and his non-

randomized nature. One technical limitation is that the software used in the study is dedicated for the LA that is innovative compared with the previous ones, but which is not specific also for the right atrium. So, the right atrial 2D-STE was obtained by manual adaptation of the track on the right chamber, potentially reducing the accuracy of the analysis. Furthermore, the analysis was not carried out by sector; therefore, the function data limited to the septum were not detected in isolation.

Conclusions

Our study demonstrates that PFO closure with the suture system does not alter bi-atrial function. On the contrary, at 1-year follow-up, occluder implantation is associated with significant worsening of LA and RA function values, suggesting that a permanent metallic implant across the inter-atrial septum could alter atrial structure and function and potentially constitutes the anatomical and functional basis for future development of arrhythmias.

Lead author biography

Dr Carmela Tarsia is a cardiology at Sant'Eugenio Hospital, Rome. She completed her MD at the University of Roma Tor Vergata. Her current research interests include echocardiographic imaging, interventional cardiology, and congenital heart disease.

Conflict of interest: None declared.

Data availability

Data are available on request.

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