Retrospective Comparison of Device Versus Suture for Patent Foramen Ovale Closure

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Background: The use of an implantable closure device with medical therapy to prevent recurrent stroke in patent foramen ovale (PFO)-associated stroke has been shown to be superior to medical therapy alone. Recently, an alternative, suture-based method also has shown promise for effective PFO closure. There has been little published data comparing the outcomes of these two technologies. **Methods:** This retrospective study explores the safety and efficacy outcomes of device-based versus suture-based percutaneous PFO intervention. The occurrence of post-procedural atrial fibrillation was of primary interest. Data from 55 single-institution, single-operator PFO closure cases between 1 January 2021 and 8 April 2022 were analyzed. Closure occurred via one of two Food and Drug Administration (FDA)-approved occluders or the NobleStitch™ EL suture-based approach. Data were transcribed into a registered REDCap database for descriptive analysis. Demographics, medical history, imaging, procedural and post-procedural outcomes were the variables collected for each participant. **Results:** All patients had successful PFO closure without major adverse outcomes. Overall efficacy was similar between the two groups. No patient had a residual shunt greater than grade 1. Several suture-group patients required multiple sutures for satisfactory closure. Those who had multiple sutures had no anomalous anatomic PFO features. Three patients (5%), all from the device group, developed atrial fibrillation after PFO closure. **Conclusions:** This study supports the safety and efficacy of device- and suture-based approaches in PFO closure. Suture-based closure would seem a reasonable option where device-based closure raises concerns. Future studies could further explore the observed disparity of atrial fibrillation occurrence between the two PFO closure strategies.

Keywords

Catheterization, neurocardiology, NobleStitch, occluders, percutaneous, stroke

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Data availability: The datasets generated and/or analyzed during the current study are not publicly available due to their collection via a secure, private electronic data capture program, but are available from the corresponding author on request.

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The foramen ovale, an obligatory channel, allows placental oxygenated blood to directly reach the fetal arterial circulation and remains patent in 25% of the adult population.[1] Patency provides a potential gateway for venous emboli to reach the arterial circulation, potentially resulting in systemic embolus or stroke (now termed 'patent foramen ovale [PFO]-associated stroke').[2] Preventive strategies for recurrent PFO-associated stroke have been investigated extensively.[3–8] Percutaneous PFO closure in combination with medical therapy is now convincingly superior to medical therapy alone.[9–12] Two FDA-approved closure devices are available in the USA — the Gore Cardioform Septal Occluder (W.L. Gore & Associates, Newark, DE, USA) and the Amplatzer PFO Occluder (Abbott Cardiovascular, Plymouth, MN, USA).[13] Both devices use deformable nitinol and fabric in the form of a double disc with a connecting bridge. The elongated device traverses a catheter positioned through the PFO and in the left atrium. Catheter retraction allows the device to return to its original shape with a disc on either atrial side of the foramen, thus pinning the PFO in the closed position. The device is then released and the delivery system is withdrawn.

The safety and efficacy of device closure have been well established.[14] As the procedure has become more widespread, several areas of concern have emerged in for which device closure might be less optimal. Among these are patients with thrombophilia, nickel allergy or hypersensitivity and those more prone to post-implant atrial fibrillation, which is the most common procedural complication.[13,15–19]

The NobleStitch™ EL intervention – CE marked for PFO closure and cardiovascular suturing in the European Union in 2012 and FDA cleared for vascular and cardiovascular procedures in 2017 – allows percutaneous, suture-based closure of the PFO without the use of an implanted device.[20,21] As such, it offers a potential advantage for the aforementioned patient subsets. Additionally, for patients who might need transseptal-mediated cardiac procedures in the future, the

intra-atrial septum remains unobstructed with suture-based closure. In this technique, sequential catheters with a proprietary suture delivery system are introduced and a stitch is delivered first to the septum secundum and then to the septum primum. Each suture is pulled through, leaving four tails exteriorized. Over these four suture tails, a 'quickknot' cylinder slides and tightens the sutures, tightly fastening them together. The quickknot is then designed to twist and cut the residual long tails, leaving the sutured PFO and the cylinder behind on the right side of the septum.

To date, there have been a few studies comparing the two PFO closure strategies.[22,23] As both device-mediated and suture-mediated PFO closures have been performed at our institution, almost entirely by the same operator, we conducted an exploratory retrospective study to compare patient outcomes between interventions. The primary outcome of interest was the occurrence of post-procedural atrial fibrillation. Secondary outcomes included a comparison of patient clinical characteristics and the occurrence of post-procedural complications.

Methods

Setting and population

All cases in this study (DeviceStitch 1) were patients in our institution's interdisciplinary neurocardiology clinic who were undergoing a PFO closure procedure. The closure occurred using one of the two US FDA-approved occluders or the NobleStitch™ EL suture-based approach. The first suture-mediated PFO closure at this institution occurred in the spring of 2020, following sufficient training and experience with NobleStitch™ EL technology by the principal investigator of this study.

The neurocardiology clinic visitation ensured agreement between stroke neurology and interventional cardiology specialists that patients were suitable candidates for PFO closure. In addition to patient interview and examination, all neuro-imaging was reviewed. Transesophageal echocardiogram (TEE) images, previously performed on all patients, were evaluated. In this patient cohort, there were no cardiac imaging features that precluded the suture approach (e.g. large or multiple fenestrations of the intra-arterial septum). Neurocardiology clinic determination of non-stroke indications paralleled Society for Cardiovascular Angiography & Interventions (SCAI) guidelines published in 2022.[14] Patients were given a full description of PFO anatomy, PFO-mediated stroke pathology, the different methods of PFO closure (device versus suture) and the current data available related to both techniques during their in-office evaluation to accomplish shared decision making. For patients who underwent device-mediated closure, the device type was determined by the date of the procedure. There were no patient or device characteristics that favoured using one device over the other.

Study oversight

The DeviceStitch 1 study was a hypothesis-generating retrospective chart review study examining safety and efficacy outcomes of patients who underwent PFO closure performed by a single operator at a single institution. Ethical review of the protocol and approval for the study were provided by the health network's institutional review board prior to the initiation of data collection and analysis. The study was not funded, but it did receive statistical support from the health network's central research office.

Sample and data collection

The sample analyzed for this study included all patients who underwent percutaneous PFO closure between 1 January 2021 and 8 April 8 2022. The list of eligible patients was obtained by querying the cardiac catheterization lab scheduling system for the specified dates. Follow-up data were collected through 31 December 31 2022 to ensure that at least 6 months of post-procedure data were available. Clinical data were extracted from the hospital electronic medical record. No cases were excluded.

The primary outcome of interest was the success of procedure and post-procedural occurrence of atrial fibrillation for 180 days following closure. Success was determined using multiple intra-procedural and post-procedural outcomes, such as insertion of the device/execution of the suture on the first attempt and minimal or low-grade (0-1) residual 'leak' (i.e. shunt), as described below and detailed in *Tables 1–3*.

The PFO indications and characteristics (prior to closure) analyzed are listed in *Table 1*. PFO identification, flow through the PFO, septal risk, septal risk type and PFO tunnel length were all based upon the investigator review of the patient's last echocardiogram (transthoracic and transesophageal) or transcranial Doppler prior to PFO closure.

A list of the PFO closure procedural data points collected is provided in *Table 2*. If cerebrovascular accident was the primary indication for PFO closure, then the number of days between the index event and closure procedure was recorded.

Post-procedural and long-term outcome data were obtained from a review of each patient's chart at least 6 months following PFO closure, and the data are summarized in *Table 3*. All-cause mortality was collected for each patient. The onset of atrial fibrillation and its subsequent need for anticoagulation were measured for each patient immediately following the PFO closure procedure through at least 6 months, and the duration between PFO closure and atrial fibrillation detection was measured in days. Post-procedure intra-cardiac echocardiogram was performed in the cardiac catheterization lab ("Post-Echo w/ bubbles result"), and follow-up transthoracic and/or transesophageal echocardiogram was performed after the patient left the cardiac catheterization lab ('follow-up echo w/ bubbles result' and 'follow-up color flow Doppler result'), and data were collected from standard of care echocardiogram reports. All-cause post-procedural events — including haemorrhages requiring treatment, emergency Ddpartment visits and hospital admissions — were also pulled from the medical record as secondary outcomes of interest to detect differences between device and suture groups.

Statistical analysis

Study data were collected and managed using Research Electronic Data Capture (REDCap) tools hosted by our health network.[24,25] REDCap is a secure, web-based software platform designed to support data capture for research studies, providing the following:

- an intuitive interface for validated data capture,
- audit trails for tracking data manipulation and export procedures,
- automated export procedures for seamless data downloads to common statistical packages and
- procedures for data integration and interoperability with external sources.[24,25]

Descriptive statistics were generated for all variables to describe the sample as a whole and to compare subgroups based on the type of closure (device or suture). Patient characteristics are summarized in *Table 4* and illustrated in *Figure 1*. All demographic and past medical history data were derived from the electronic medical record.

Table 1: Pre-procedure patent foramen ovale indication and characteristics, overall and by procedure group

Characteristic	All patients (n=55)	Suture closure (n=27)	Device closure (n=28)	p-value
PFO indication *n (%)**	–	–	–	0.07[a]
CVA	46 (83.64)	21 (77.78)	25 (89.29)	–
Peripheral embolism	4 (7.27)	4 (14.81)	0	–
Hypoxia	1 (1.82)	1 (3.70)	0	–
TIA	4 (7.27)	1 (3.70)	3 (10.71)	–
RoPE score *mean ± SD*	6.31 ± 1.81	6.48 ± 1.70	6.14 ± 1.94	0.49[b]
PASCAL Score (n=51)	–	–	–	–
Likely	24	12	12	–
Possible	26	12	14	–
Unlikely	1	0	1	–
Septum risk *n(%)*	–	–	–	0.61[a]
No	3 (5.45)	2 (7.41)	1 (3.57)	–
Yes	52 (94.55)	25 (92.59)	27 (96.43)	–
Septum risk type *n (%)* (n=52)	–	–	–	–
Atrial septal aneurism	42 (80.77)	18 (72)	24 (88.89)	0.17[a]
Wide (>2 mm) separation primum and secundum septum	20 (38.46)	9 (36)	11 (40.74)	0.73[c]
Hypermobility	32 (61.54)	15 (60)	17 (62.96)	0.83[c]
Prominent Eustachian ridge	35 (67.31)	14 (56)	21 (77.78)	0.09[c]
Jump Rope	2 (3.85)	0	2 (7.41)	0.49[a]
TCD *n (%)*	–	–	–	0.50[c]
No	28 (50.91)	15 (55.56)	13 (46.43)	–
Yes	27 (49.09)	12 (44.44)	15 (53.57)	–
TCD result *n (%)* (n=27)	–	–	–	NA
Positive for bubbles	27 (100)	12 (100)	15 (100)	–
Echo w/ bubbles *n(%)*	–	–	–	0.49[a]
No	1 (1.82)	1 (3.70)	0	–
Yes	54 (98.18)	26 (96.30)	28 (100)	–
Echo w/ bubbles result *n (%)* (n=54)		–	–	**0.03**[a]
No bubbles	6 (11.11)	0	6 (21.43)	–
Grade 1 (1–9)	9 (16.67)	3 (11.54)	6 (21.43)	–
Grade 2 (10–20)	6 (11.11)	4 (15.38)	2 (7.14)	–
Grade 3 (20+)	33 (61.11)	19 (73.08)	14 (50)	–
Tunnel length, mm *mean ± SD* (n=54)	13.57 ± 4.73	12.85 ± 4.16	14.25 ± 5.19	0.28[b]
Source of hypercoagulable state *n (%)*		–	–	–
Panel not performed	13 (23.64)	7 (25.93)	6 (21.43)	0.69[c]
Panel negative	31 (56.36)	13 (48.15)	18 (64.29)	0.23[c]
Factor V Leiden positive	2 (3.64)	2 (7.41)	0	0.24[a]
Prothrombin 20210 G positive	2 (3.64)	1 (3.70)	1 (3.57)	1.00[a]
APLA positive	1 (1.82)	1 (3.70)	0	0.49[a]
Lupus anticoagulant	–	–	–	NA
Protein C positive	2 (3.64)	1 (3.70)	1 (3.57)	1.00[a]
Protein S positive	1 (1.82)	1 (3.70)	0	0.49[a]
Other	5 (9.09)	2 (7.41)	3 (10.71)	1.00[a]
Cardiac monitor *n (%)*	–	–	–	0.94[c]
No	12 (21.82)	6 (22.22)	6 (21.43)	–
Yes	43 (78.18)	21 (77.78)	22 (78.57)	–
Cardiac monitor time *n (%)* (n=43)	–	–	–	0.09[a]
2 weeks non-implanted	25 (58.14)	16 (76.19)	9 (40.91)	–
4 weeks non-implanted	8 (18.60)	2 (9.52)	6 (27.27)	–

Continued

Table 1: Continued

Characteristic	All patients (n=55)	Suture closure (n=27)	Device closure (n=28)	p-value
>4 weeks non-implanted	2 (4.65)	0	2 (9.09)	–
Loop recorder	8 (18.60)	3 (14.29)	5 (22.73)	–

Numbers shown represent column totals. Total n is presented in the column header unless indicated next to the variable name. The RopE score was collected prior to the procedure date. Septum risk refers to any septal characteristics associated with a higher risk PFO. All TCD and echo-related variables are for studies that were done prior to the PFO procedure. The p-value is for comparison of suture versus device procedures. The p-value could not be calculated for the TCD result, lupus anticoagulant and neurocardio plan because there were fewer than two non-missing levels for each of these variables. Statistically significant p-values are marked in bold.
[a]p-value generated using Fisher's exact test.
[b]p-value generated using the independent samples t-test.
[c]p-value generated using the chi-square test of independence.
APLA = antiphospholipid antibody; cardio = cardiologist; CVA = cerebrovascular accident; Echo = echocardiogram; IQR = interquartile range; MI = myocardial infarction; mm = millimeters; NA = not available; neuro = neurologist; PFO = patent foramen ovale; RoPE = Risk of Paradoxical Embolism; TCD = transcranial Doppler; TIA = transient ischemic attack; w/ = with.

The mean and standard deviation were reported for normally distributed continuous variables, while the median and interquartile range were used for those that were not normally distributed. Frequencies and percentage were reported for categorical variables. All analyses were conducted by a biostatistician in our health network's central research office using SAS software version 9.4.(©2016 SAS Institute Inc., Cary, NC, USA.) To assist with hypothesis generation, p-values were generated for comparative analysis; a p-value <0.05 was considered statistically significant unless otherwise stated.

Results

The 55 patients who underwent PFO closure during the study time period were included. Of those, 28 procedures used an FDA-approved PFO occluder device, while 27 were completed using a suture-based technique.

Demographics

The average age of the overall sample was 52 years old, with the majority being (62%) male and White (89%). Approximately 50% of patients had hypertension and 50% had hyperlipidaemia. No significant differences existed between procedure groups.

Pre-procedural characteristics

A majority (84%) of patients had a cerebrovascular accident as the index event prior to PFO closure, while four (7%) had a peripheral embolus, four (7%) had TIA and one (2%) had hypoxia. The mean Risk of Paradoxical Embolism (RoPE) score was 6.3, and PFO-Associated Stroke Causal Likelihood (PASCAL) classifications were as follows: 10% unlikely, 75% possible and 15% probable. Most (95%) patients had at least one high-risk septal feature, and 60% had two or more high-risk septal features.

Table 2: Patent foramen ovale procedural information, overall and by procedure group

Characteristic	All patients (n=55)	Suture closure (n=27)	Device closure (n=28)	p-value
Days from CVA to PFO closure *median (IQR)* (n=46)	132 (76–228)	158 (94–228)	99 (72–216)	0.36[a]
Closure method *n (%)*	–	–	–	NA
Suture	27 (49.09)	27 (100)	0	–
Device	28 (50.91)	0	28 (100)	–
Device type *n (%)* (n=28)	–	–	–	NA
Gore cardioform septal occluder	14 (50)	0	14 (50)	–
Amplatzer PFO occluder	14 (50)	0	14 (50)	–
Successful procedure *n (%)*	–	–	–	NA
Yes	55 (100)	27 (100)	28 (100)	–
Multiple attempts *n (%)*	–	–	–	0.30[b]
No	42 (76.36)	19 (70.37)	23 (82.14)	–
Yes	13 (23.64)	8 (29.63)	5 (17.86)	–
Attempts *n (%)*	–	–	–	–
Two devices/stitches used	12 (21.82)	8 (29.63)	4 (14.29)	0.17[b]
Three devices/stitches used	1 (1.82)	0	1 (3.57)	1.00[c]
Crossover to other methods	–	–	–	NA
Procedural comps *n (%)*	–	–	–	NA
No	55 (100)	27 (100)	28 (100)	–

Numbers shown represent the column totals. Total n is presented in the column header unless indicated next to the variable name. The procedure was determined to be successful if the device/stitch was successfully deployed and the residual shunt was grade 0–1. Total n for the number of days from CVA to PFO is only 42 because it applies only to those whose PFO indication was listed as CVA. The p-value is for comparison of suture versus device procedures. p-values for successful procedures, crossover to other methods and procedural complications (y/n) cannot be computed because there are fewer than two non-missing levels.
[a]p-value generated using the Mann–Whitney U-test.
[b]p-value generated using the chi-square test of independence.
[c]p-value generated using Fisher's exact test.
btw = between; Comps = complications; CVA = cerebrovascular accident; IQR = interquartile range; NA = not available; Num = number; PFO = patent foramen ovale.

Table 3: Patent foramen ovale post-procedure outcomes, overall and by procedure group

Characteristic	All patients (n=55)	Suture closure (n=27)	Device closure (n=28)	p-value
Mortality *n (%)*	–	–	–	NA
Alive	55 (100)	27 (100)	28 (100)	–
MI *n (%)*	–	–	–	NA
No	55 (100)	27 (100)	28 (100)	–
Atrial fibrillation* *n (%)*	–	–	–	0.24[a]
No	52 (94.55)	27 (100)	25 (89.29)	–
Yes	3 (5.45)	0	3 (10.71)	–
Anticoagulation for atrial fibrillation *n (%)* (n=3)		–	–	NA
Yes	3 (100)	0	3 (100)	–
Days from procedure to atrial fibrillation *median (IQR)* (n=3)	25 (21–37)	–	25 (21–37)	NA
Days btw procedure and DC *median (IQR)*	0 (0–1)	0 (0–1)	0 (0–1)	0.37[b]
DC delayed *n (%)*	–	–	–	1.00[a]
No	53 (96.36)	26 (96.30)	27 (96.43)	–
Yes**	2 (3.64)	1 (3.70)	1 (3.57)	–
Post echo w/ bubbles result *n (%)*		–	–	0.11[a]
No bubbles	52 (94.55)	24 (88.89)	28 (100)	–
Grade 1 (1–9)	3 (5.45)	3 (11.11)	0	–
Grade 2 (10–20)	–	–	–	–
Grade 3 (>20)	–	–	–	–
Follow-up echo *n (%)*	–	–	–	0.49[a]
No	1 (1.82)	1 (3.70)	0	–
Yes	54 (98.18)	26 (96.30)	28 (100)	–
Type of follow-up echo *n (%)* (n=54)		–	–	0.85[c]
Echo w/ bubbles	18 (33.33)	9 (34.62)	9 (32.14)	–
Colour flow Doppler	36 (66.67)	17 (65.38)	19 (67.86)	–
Follow-up echo w/ bubbles result *n (%)* (n=18)		–	–	NA
No bubbles	18 (100)	9 (100)	9 (100)	–
Grade 1 (1–9)	–	–	–	–
Grade 2 (10–20)	–	–	–	–
Grade 3 (>20)	–	–	–	–
Follow-up colour flow Doppler result *n (%)* (n=36)		–	–	1.00[a]
No blood flow across septum	35 (97.22)	17 (100)	18 (94.74)	–
Yes, blood flow across septum	1 (2.78)	0	1 (5.26)	–
Procedure to follow-up echo, days *median (IQR)* (n=54)	1 (0–171)	1 (0–122)	41 (0–229)	0.19[b]
Bleeding event *n (%)*	–	–	–	0.24[a]
No	52 (94.55)	27 (100)	25 (89.29)	–
Yes	3 (5.45)	0	3 (10.71)	–
Treatment for bleed *n (%)* (n=3)		–	–	–
None	3 (100)	0	3 (100)	NA
Transfusion	–	–	–	NA
Days btw procedure and bleed *median (IQR)* (n=3)	4 (0–4)	–	4 (0–4)	NA
ED post-procedure *n (%)*	–	–	–	**0.03**[c]
No	42 (76.36)	24 (88.89)	18 (64.29)	–
Yes	13 (23.64)	3 (11.11)	10 (35.71)	–
ED reason *n (%)*	–	–	–	–
Ischaemic stroke	–	–	–	NA
Haemorrhagic stroke	–	–	–	NA
TIA	–	–	–	NA
Migraine (w/ or w/o aura)	1 (1.82)	0	1 (3.57)	1.00[a]
Bleeding	1 (1.82)	0	1 (3.57)	1.00[a]

Continued

Table 3: Continued

Characteristic	All patients (n=55)	Suture closure (n=27)	Device closure (n=28)	p-value
Arrhythmia	2 (3.64)	0	2 (7.14)	0.49[a]
Groin issue	–	–	–	NA
Other unrelated	9 (16.36)	3 (11.11)	6 (21.43)	0.47[a]
Days btw procedure and ED *median (IQR)* (n=13)	74 (21–182)	74 (19–138)	80 (21–196)	0.80[b]
Hospital readmission *n (%)*	–	–	–	0.11[a]
No	51 (92.73)	27 (100)	24 (85.71)	–
Yes	4 (7.27)	0	4 (14.29)	–
Readmission reason *n (%)*	–	–	–	–
Ischaemic stroke	–	–	–	NA
Haemorrhagic stroke	–	–	–	NA
TIA	–	–	–	NA
Migraine (w/ or w/o aura)	1 (1.82)	0	1 (3.57)	1.00[a]
Bleeding	–	–	–	NA
Arrhythmia	2 (3.64)	0	2 (7.14)	0.49[a]
Groin issue	–	–	–	NA
Pulmonary embolism	1 (1.82)	0	1 (3.57)	1.00[a]
Days btw procedure and readmission *mean ± SD* (n=4)	166.25 ± 170.43	–	166.25 ± 170.43	NA

*Numbers shown represent column totals. *Atrial fibrillation must have occurred within 180 days of PFO closure to count (there was one additional patient who had atrial fibrillation, but it was 630 days after PFO closure). **None of the discharge delays was due to factors associated with the PFO procedure. Follow-up echo with bubbles was performed in the cardiac catheterization lab via intracardiac echo. Follow-up echo was performed after the patient left the cardiac catheterization lab. The bleeding event must have occurred within 2 weeks of PFO closure to count. Treatment for bleed, reason for ED visit and reason for hospitalization may not add up to 100%. The p-value is for comparison of suture versus device procedures. Statistically significant p-values are marked in bold.*
[a]p-value generated using the Fisher's exact test.
[b]p-value generated using the Mann–Whitney U test.
[c]p-value generated using the chi-square test of independence.
btw = between; CVA = cerebrovascular accident; DC = discharge; Echo = echocardiogram; ED = emergency department; IQR = interquartile range; LTF = lost to follow-up; MI = myocardial infarction; NA = not available; Num = number; PFO = patent foramen ovale; TIA = transient ischaemic attack; w/ = with; w/o = without.

External cardiac monitors were placed in 80% of patients prior to PFO closure, with 2 weeks being the most common length of monitoring. The mean number of days between the index event and PFO closure was 132, ranging from 76 to 228.

Intra-procedural metrics

There were no intra-procedural complications or mortalities in either group. Within the device group, 14 (50%) patients received the Gore device and 14 received the Amplatzer device. Device use was based entirely on scheduling day. More than 70% of patients in both groups exhibited the lowest-level residual 'leak' (grade 0–1) after the first attempt at device implantation or suturing. Eight patients in the suture group required an additional suture to achieve successful closure, but none was due to any identifiable anatomical features. No patients in the device arm required multiple devices to achieve successful closure; however, five patients required an alternate-sized device to achieve this outcome. Three patients (all from the suture group) had a grade 1 residual leak following closure, but all three were measured as grade 0 on pre-discharge TTE in the holding area. The majority (96%) of patients were discharged within 1 day after the procedure. Two patients (one from each group) with delayed discharges were not held in the hospital for reasons related to the PFO closure procedure.

Follow-up metrics

Post-procedural atrial fibrillation occurred in three patients, all in the device arm. All were subsequently anticoagulated for 6 months. None had a stroke or neurologic events related to the atrial fibrillation. All but one patient was seen for follow-up visits at 3 and 6 months, with at least one post-procedural echocardiogram. The time to follow-up echo ranged from 0 to 129 days. Patients in the device arm who had an intra-procedural grade 1 shunt all had a grade 0 shunt on follow-up echocardiograms. One patient in the device arm had a grade 1 residual shunt. There were three patients (all in the device arm) who had bleeding events attributable to post-procedural medications. No patients received transfusions. No patients presented with recurrent stroke.

Discussion

There was an important numerical difference in the occurrence of post-implant atrial fibrillation between our two groups. While this study was not powered to declare the statistical significance of this difference, the absence of atrial fibrillation in the suture group is clinically noteworthy.

Recent data suggest that implantable monitoring detects increased atrial arrhythmia at a much higher frequency and for a far longer period than the traditionally quoted 90-day vulnerable period among patients who underwent device-mediated percutaneous PFO closure.[26] The actual occurrence of atrial fibrillation in these patients is somewhat unclear and may depend on patient characteristics, the type of device implanted and, perhaps most importantly, the method used to detect post-implant atrial fibrillation.[9,12] If further study supports our findings that suture-based closure provides similar efficacy with a lower incidence of atrial fibrillation, the discussion regarding PFO closure would certainly change.

PFO has, in addition, been associated with other conditions including migraine with aura, decompression illness and platypnea orthodeoxia syndrome.[27–29] As PFO closure is contemplated in these areas, a

Table 4: Patient demographics and past medical history, overall and by procedure group

Characteristic	All patients (n=55)	Suture closure (n=27)	Device closure (n=28)	p-value
Age (years) *mean ± SD*	52.05 ± 14.11	51.81 ± 14.62	52.29 ± 13.87	0.90[a]
Gender *n (%)*	–	–	–	0.47[b]
Male	34 (61.82)	18 (66.67)	16 (57.14)	–
Female	21 (38.18)	9 (33.33)	12 (42.86)	–
Race *n (%)*	–	–	–	0.14[c]
White	49 (89.09)	22 (81.48)	27 (96.43)	–
Black or African American	2 (3.64)	1 (3.70)	1 (3.57)	–
Multiracial	1 (1.82)	1 (3.70)	0	–
Other	3 (5.45)	3 (11.11)	0	–
Ethnicity *n (%)*	–	–	–	0.19[c]
Hispanic or Latino	5 (9.09)	4 (14.81)	1 (3.57)	–
Not Hispanic or Latino	50 (90.91)	23 (85.19)	27 (96.43)	–
Height (inches) *mean ± SD*	67.98 ± 4.21	68.15 ± 4.31	67.82 ± 4.18	0.78[a]
Weight (pounds), *median (IQR)*	195 (179–225)	198 (179–226)	192.50 (177–207)	0.77[d]
Relevant medical history *n (%)*	–	–	–	0.67[c]
No	5 (9.09)	3 (11.11)	2 (7.14)	–
Yes	50 (90.91)	24 (88.89)	26 (92.86)	–
Relevant medical history *n (%)*	–	–	–	–
Hyperlipidaemia	28 (50.91)	12 (44.44)	16 (57.14)	0.35[b]
HTN	26 (47.27)	9 (33.33)	17 (60.71)	**0.04[b]**
DM	4 (7.27)	1 (3.70)	3 (10.71)	0.61[c]
COPD	1 (1.82)	0	1 (3.57)	1.00[c]
Renal insufficiency	4 (7.27)	2 (7.41)	2 (7.14)	1.00[c]
Sleep apnea	12 (21.82)	7 (25.93)	5 (17.86)	0.47[b]
Cancer	3 (5.45)	2 (7.41)	1 (3.57)	0.61[c]
MI	–	–	–	NA
CAD	2 (3.64)	0	2 (7.14)	0.49[c]
CHF	1 (1.82)	1 (3.70)	0	0.49[c]
Valvular heart disease	1 (1.82)	1 (3.70)	0	0.49[c]
Cardiac arrhythmia	2 (3.64)	1 (3.70)	1 (3.57)	1.00[c]
PVD	1 (1.82)	0	1 (3.57)	1.00[c]
Peripheral TEE	5 (9.09)	4 (14.81)	1 (3.57)	0.19[c]
Headache	12 (21.82)	4 (14.81)	8 (28.57)	0.22[b]
Migraine with aura	10 (18.18)	4 (14.81)	6 (21.43)	0.73[c]
Migraine without aura	3 5.45)	2 (7.41)	1 (3.57)	0.61[c]
Ischaemic stroke	13 (23.64)	9 (33.33)	4 (14.29)	0.097[b]
Haemorrhagic stroke	2 (3.64)	1 (3.70)	1 (3.57)	1.00[c]
TIA	1 (1.82)	1 (3.70)	0	0.49[c]
Smoker	14 (25.45)	7 (25.93)	7 (25)	0.94[b]

Numbers shown represent column totals. Total n is presented in the column header unless indicated next to the variable name. Relevant medical history included conditions that could be related to stroke risk and general health up to and including the date of the index event. It was a check-all-that-apply field so column totals may not add up to 100%. Age, height and weight were collected at the time of PFO/admission. The p-value is for comparison of suture versus device procedures. The p-value could not be calculated for MI, as no one in either group had a history of MI. Statistically significant p-values are marked in bold.

[a]*p-value generated using the independent samples t-test.*

[b]*p-value generated using the chi-square test of independence.*

[c]*p-value generated using Fisher's exact test.*

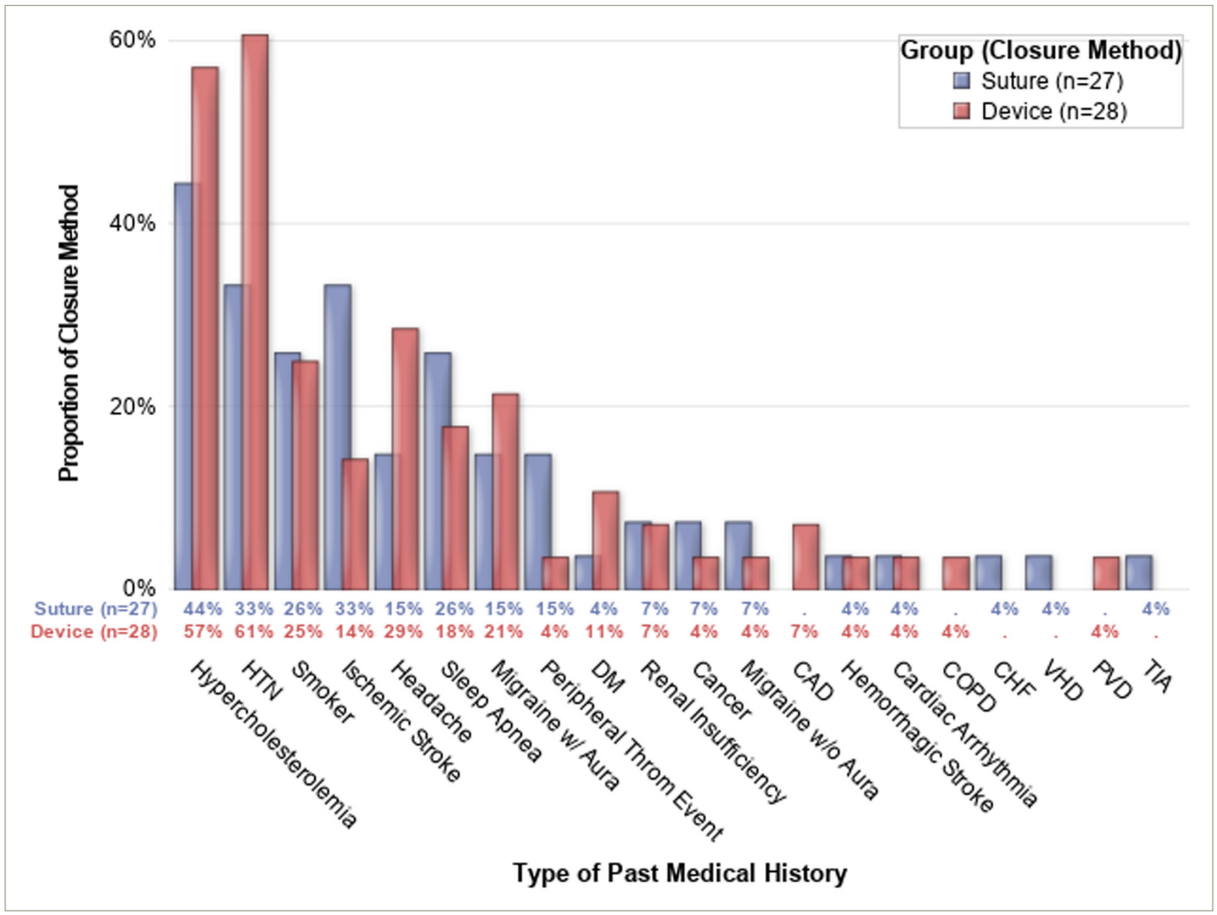
[d]*p-value generated using the Mann–Whitney U test.*

CAD = coronary artery disease; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; HTN = hypertension; IQR = interquartile range; MI = myocardial infarction; NA = not available; PMH = past medical history; PVD = peripheral vascular disease; SD = standard deviation; TEE = transoesophageal echocardiogram; TIA = transient ischaemic attack.

procedure that minimizes post-implant atrial fibrillation would offer a more favourable alternative.

Anytime technology emerges that is intended to improve existing options for medical treatment, there is a subset of patients for whom the technology works less well. This certainly has been the case with previous and current generations of PFO closure devices. Arguably, these devices have made a demonstrable reduction in recurrent PFO-associated stroke when used as intended and approved.[10–12] However, decisions for patients with nickel allergy, limited capacity for medication compliance,

Figure 1: Past medical history of patients in each procedure group



an inherited or acquired hypercoagulable state, as well as those at the far end of the age spectrum, are often more nuanced. Anticipating post-procedure complications in these individuals complicates the decision to recommend closure. This study suggests that NobleStitch™ EL technology has the potential to provide PFO closure in a manner that is favourable to subset patients such as these.[30,31]

Our patients had overall similar outcomes both procedurally and post-procedurally to an average follow-up time of 6 months. The initial higher incidence of grade 1 bubble flow on intra-cardiac echo among patients who had a suture-based procedure resolved in pre-discharge echocardiography. No patients developed subsequent shunt on follow-up echo.

Within the available literature on NobleStitch™ EL, there has been an element of confusion about the definition of procedural success.[32,33] Residual leak following the placement of a single suture has, in some reports, been defined as an unsuccessful procedure, and in other reports, the number of sutures is not specified clearly. This has led to the impression that NobleStitch™ EL success rate is low relative to device closure or that there are some anatomic features (e.g. tunnel length) that preclude success. Our analysis did not support these impressions. These anatomical features instead more correctly predicted the need for an additional suture, which does not necessarily indicate procedural failure.[34] Specifically, our sample's average tunnel length was long (13.57 mm), and nearly one-third of patients needed a second suture; yet, all achieved complete closure. In addition, the presence of atrial septal aneurysm was high among our patients; yet, complete closure was achieved in all these cases as well.

While the cost of two sutures exceeded the cost of a device, the initial cost of the NobleStitch was several thousand dollars less than either device. Our financial analysis demonstrated that, with a similar payor mix, the cost of NobleStitch PFO closure and device PFO closure, including supplies, was quite similar. That advantage was lost if additional suture components were needed. If an additional suture was required, the advantage was reversed. In the end, the cost was similar, and with fewer technical multiple stitch cases, this was expected to remain similar.

Strengths, limitations and opportunities for future study

The strengths of this study include an even distribution between intervention groups, providing a unique opportunity for appraisal. In addition, the comprehensive neurocardiology clinic demonstrates a collaborative approach to patient selection. All patients were seen in our neurocardiology clinic and had given stroke neurology and interventional cardiology assent on the intervention type prior to the procedure. The weaknesses of the study include sample size and the study's retrospective, non-randomized design. While a single-center, single-operator design has inherent weakness, the number of NobleStitch operators in the USA is somewhat limited. This was an opportunity to share the results of the two techniques. It is noteworthy that the trial period was flanked by pandemic enrollment limitations and an intravenous contrast shortage.

Future areas of investigation might include expanded, multiple-institution and prospective randomized designs, which, if successful, would serve to clarify and confirm these observations.

Conclusion

This retrospective comparison study supports the continued use of suture-based percutaneous PFO closure as an alternative to device-mediated closure, given the similarities in outcomes between the two approaches. Additionally, this study demonstrates the need for future prospective studies with greater power to further discern differences in outcomes (especially in terms of atrial fibrillation rate) between the two PFO closure approaches. ❑

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