Percutaneous left atrial appendage closure for stroke prevention

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ABSTRACT

INTRODUCTION: In atrial fibrillation (AF) patients with an increased stroke risk, oral anticoagulation (OAC) is the standard treatment for stroke prevention. However, this therapy carries a high risk of major bleeding. Percutaneous closure of the left atrial appendage (LAA) is suggested as an alternative option for stroke prevention in AF patients with contraindication(s) for OAC treatment.

MATERIAL AND METHODS: A total of 42 patients underwent percutaneous LAA closure. In this report, we describe our experience with this procedure.

RESULTS: The patients treated were AF patients with a high stroke risk (CHADS-VASc 4.5 ± 1.4) and contra-indication(s) for OAC and/or a high bleeding risk (HAS-BLED 3.7 ± 0.9). A history of intracerebral bleeding was the most common reason for LAA closure. Successful implantation was obtained in 41 of 42 patients. One major peri-procedural complication occurred; a major gastrointestinal bleeding immediately after the procedure. The mean duration of follow-up was 12.6 months. Both ischaemic stroke and bleeding occurred in one patient, resulting in an observed annual stroke and bleeding rate of 2.3%. This rate was lower than expected based on the CHADS-VASc (5.6%/year) and HAS-BLED (7.6%/year) for the patient cohort. At echo follow-up, incomplete LAA closure was seen in one case; device thrombosis was not observed.

CONCLUSION: Our data confirm that percutaneous LAA closure can be a safe and effective strategy for stroke prevention in AF patients with an increased stroke and bleeding risk. However, long-term follow-up studies are needed before this procedure can be recommended for routine clinical use.

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TRIAL REGISTRATION: not relevant.

Atrial fibrillation (AF) is the most common cardiac arrhythmia encountered in clinical practice, and it is known to be associated with substantial mortality and morbidity, particularly due to fatal or disabling stroke. In AF patients at increased risk for stroke, oral anticoagulation has proven to effectively prevent thromboembolic strokes, but the increased risk of serious bleeding prevents many patients from taking this therapy. Therefore, there is a need for alternative treatment options for stroke prevention in AF patients with an increased stroke risk – which do not increase the risk of bleeding [1-3].

As the left atrial appendage (LAA) is the primary site of thrombus formation in AF patients, LAA closure has been suggested as a possible alternative strategy for stroke prevention in these patients. In this report, we describe our experience with percutaneous LAA closure at the Rigshospitalet, Copenhagen, Denmark.

MATERIAL AND METHODS

Between July 2011 and December 2013, a total of 42 patients were treated with percutaneous LAA closure at Rigshospitalet. The selected patients for this procedure were typically AF patients with a high risk of stroke (CHADS-VASc ≥ 3) and contraindication(s) for oral anticoagulation (OAC) and/or high bleeding risk (HAS-BLED ≥ 3). Transoesophageal echocardiography (TOE) was performed before the procedure in all patients in order to evaluate LAA morphology/dimensions and to exclude thrombus in the LAA. In 17 patients, this was supplemented by pre-procedural computed tomography. The percutaneous LAA closure intervention was performed under general anaesthesia, with antibiotic prophylaxis, and with fluoroscopic and TOE guidance. In some cases (n = 12), intra-cardiac echocardiography was used as an extra imaging modality during LAA closure. Vascular access was obtained through the right femoral vein and the left atrium was accessed by transseptal puncture. After the puncture, a bolus of unfractionated heparin was injected to achieve an activated clotting time (ACT) > 250 seconds.

Based on the LAA dimensions measured by TOE and angiography, the correct LAA device size was chosen. The device was placed using a 9-13 Fr delivery catheter. Correct positioning was controlled by TOE and fluoroscopy. Complete sealing was verified with Doppler (Nyquist ~ 40 cm/s). If the result was satisfying, the device was released from the delivery cable. Before discharge, the patients had a chest X-ray and transthoracic echocardiography to rule out device embolisation and pericardial effusion.

At 45-90 days after the procedure, all patients had a control TOE in order to ensure complete sealing of the LAA and exclude thrombus formation on the device. The

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ABBREVIATIONS

ACP = Amplatzer Cardiac Plug
ACT = activated clotting time
AF = atrial fibrillation
DAPT = dual anti-platelet therapy
FDA = Food and Drug Administration
GI = gastrointestinal
LAA = left atrial appendage
NOAC = new oral anticoagulation
OAC = oral anticoagulation
PCI = percutaneous coronary intervention
RCT = randomised controlled trial
TOE = transoesophageal echocardiography

post-procedural anti-thrombotic regime was adapted to the patient's characteristics.

Trial registration: not relevant.

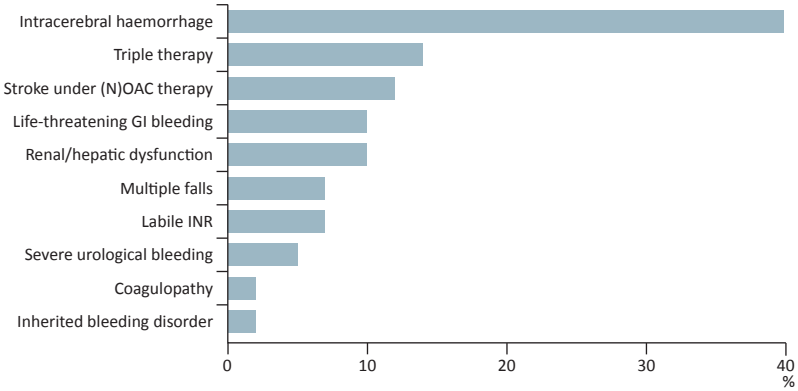
RESULTS

Baseline characteristics

The mean age of our cohort was 74.6 ± 8.2 years and 62% were male. About half of the patients (52.4%) were known with permanent AF, the remaining patients with paroxysmal/persistent AF. The average stroke risk (CHADS-VASc score) of our cohort was 4.5 ± 1.4, and the average bleeding risk (HAS-BLED score) was 3.7 ± 0.9. About half of the referred patients were AF patients with previous intra-cerebral haemorrhage or life-threatening gastrointestinal (GI) bleeding under intake of new (N) OAC. Another 10-15% were AF patients needing triple therapy – i.e. dual anti-platelet therapy (DAPT) and OAC – after percutaneous coronary intervention (PCI) with stent implantation; and about 1/10 of the referred patients were previously admitted with a stroke under (N)OAC therapy (**Figure 1**).

FIGURE 1

Indications for percutaneous left atrial appendage closure in our cohort, expressed as % of all patients.



GI = gastrointestinal; INR = international normalised ratio; (N)OAC = (new) oral anticoagulation.

Procedural outcome

Successful device implantation was achieved in 41/42 patients (97.6%); in one patient, the LAA anatomy made it impossible to implant the device. All three commercially available LAA closure devices were used – most experience has been established with the Amplatzer Cardiac Plug (ACP) device (n = 22; St Jude Medical, USA, **Figure 2**). Moreover, we have used the Watchman device (n = 9; Boston Scientific, USA), and our centre also participated in the initial studies with the WaveCrest LAA closure device (n = 10; Coherex, USA).

As a major peri-procedural complication, we report one patient with a major GI bleeding immediately after the procedure (when ACT was still > 250). Two minor complications were registered – one patient had a minor bleeding in relation to the puncture site, another patient had a minor pericardial effusion that was treated conservatively.

Follow-up results

The total follow-up period was 530 months (range 1-31 months), which gave a mean follow-up period of 12.6 ± 10.4 months per patient. At the control TOE within 45-90 days after the procedure, an incomplete LAA closure was observed in one patient. This resulted in continuation of NOAC treatment. Device thrombus formation was not observed. In the total follow-up period of 530 months, one patient was diagnosed with a new stroke. This corresponds to an observed annual stroke rate of 2.3%; whereas with a CHADS-VASc stroke risk score of 4.5, the expected annual stroke rate of our cohort was estimated to be 5.6% (**Figure 3**A). In addition, we registered a major bleeding in one patient in this same follow-up period. This patient was advised to continue low-dose NOAC after LAA closure because of a prior stroke under OAC therapy. This observation yields an annual observed bleeding rate of 2.3% in our cohort compared with an expected annual bleeding risk of 7.6% based on the HAS-BLED score of 3.7 (Figure 3B).

Figure 4 shows the change in our patients' anti-thrombotic and anti-coagulation therapy after percutaneous LAA closure – at referral and after LAA closure, before and after TOE control, respectively.

DISCUSSION

As percutaneous LAA closure is a procedure for stroke "prevention" in AF patients, procedural safety is paramount before this procedure can be considered in routine clinical practice. The PROTECT AF trial, an early randomised controlled trial (RCT) published in 2009, reported a complication rate of 7.4% of which > 50% were pericardial effusions [4]. In comparison, more recent data from the PREVAIL study [5] and large registries (> 500 patients, both the Watchman [6] and the ACP device

[7]) have shown improved procedural safety with a complication rate of about 4% – encompassing primarily pericardial effusion and bleeding that can be managed conservatively [8-10]. These lower complication rates can probably be ascribed to a better understanding of the procedure and an operator learning curve effect. In this context, the results described in this paper show that percutaneous LAA closure can be performed safely in a centre with large experience in structural heart disease interventions. Based on the latest data, the Watchman device also received substantial endorsement from a Food and Drug Administration (FDA) advisory panel in December 2013. A definitive FDA approval is expected later this year.

Although the two RCTs available to date (PROTECT-AF and PREVAIL) included only patients who were eligible for OAC therapy [4, 5], we believe that current data only justify the use of this therapeutic option in patients with contraindications to OAC therapy. Patients with AF who have no contraindication(s) for OAC should have LAA occlusion only in exceptional cases. Accordingly, the updated European Society of Cardiology (ESC) guidelines recommend LAA occlusion in patients with AF who are at a high risk of stroke and have contraindications to long-term OAC therapy (Class IIb, level of evidence B) [11]. In our cohort, the primary reason for referral was previous intracerebral haemorrhage under (N)OAC therapy. Other reasons for referral to LAA closure were previous major GI bleeding, the need for triple therapy, and prior stroke under (N)OAC therapy. As shown in Figure 4, only 55% of the 42 patients were taking OAC therapy at the time of referral (29% OAC, 26% NOAC). These results support other data indicating that there is a large group of AF patients at high risk of stroke who are not receiving any thromboembolic protection [12-14].

Finally, we want to discuss the anti-thrombotic regime after LAA closure in our patients. This topic is frequently discussed in the literature; however, so far, there is no specific guideline available. Based on Figure 4, we would like to emphasize the following points: 1) (N)OAC therapy was terminated in most cases immediately after LAA closure, 2) most patients were prescribed DAPT the first 45-90 days until control TOE was performed, 3) in five patients, typically patients with prior stroke under (N)OAC therapy, the decision was taken to continue OAC (n = 1) or low-dose NOAC (n = 4) treatment. Unfortunately, it was a patient who continued NOAC therapy who presented with a major bleeding in the follow-up period.

Although recent studies report that the use of DAPT for 1-3 months after LAA closure would be sufficient, we believe that a post-procedural anti-thrombotic therapy tailored to the specific individual thrombotic and bleeding risk profile may be warranted.

FIGURE 2

The Amplatzer Cardiac Plug device. **A** + **B.** The device consists of a lobe and a disk connected by a short, flexible waist. The lobe is implanted within the neck of the left atrial appendage (the so-called "landing zone"), and achieves device stabilisation and retention by means of a number of stabilisation wires. **C.** Implantation of a device in the regular way. **D.** Implantation using the "sandwich technique" when confronted with a chicken wing left atrial appendage with a short neck.

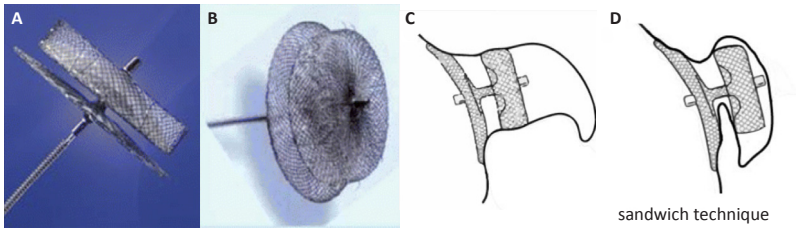
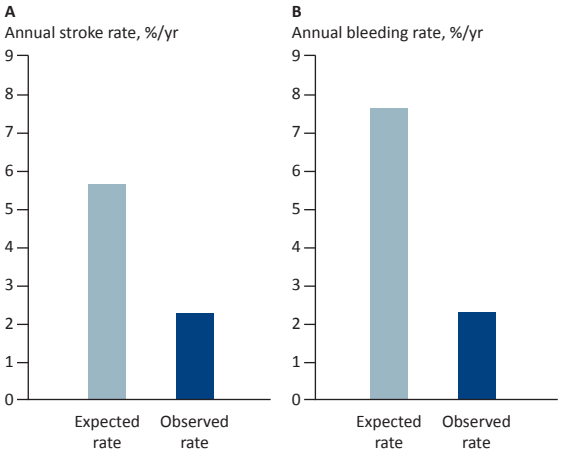
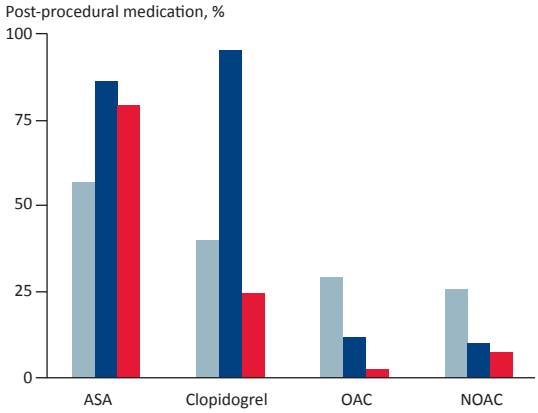


FIGURE 3



A. Effectiveness in stroke reduction based on observed annual stroke rate versus expected annual stroke rate based on a CHADS-VASc stroke risk score of 4.5. **B.** Effectiveness in bleeding reduction based on observed annual bleeding rate versus expected annual stroke rate based on a HAS-BLED bleeding risk score of 3.7.

FIGURE 4



Overview of anti-thrombotic and anti-coagulant medical treatment in our cohort, expressed as percentages of total patients, at three different time points: before LAAO ( ), after LAAO and before echocardiographic control (< 45 days) ( ), and after LAAO and after echocardiographic control (at > 45 days) ( ).

ASA = acetylsalicylic acid; LAAO = left atrial appendage occlusion; NOAC = new oral anticoagulation; OAC = oral anticoagulation.

CONCLUSION

Percutaneous LAA occlusion can be an alternative option

for stroke prevention in AF patients with an increased stroke risk and contraindication(s) for OAC therapy. Our data confirm that this procedure can be performed safely and with a satisfying short-term outcome. Therefore, we believe that percutaneous LAA occlusion offers an alternative to physicians who are facing a complicated risk-benefit analysis in AF patients who should receive OAC therapy based on a high stroke risk score, but who also have a high bleeding risk. However, since these high-risk patients were typically excluded or underrepresented in the available RCTs, additional comparative studies of percutaneous LAA closure versus OAC therapy are needed before this procedure can be recommended for clinical routine use.

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