CLINICAL RESEARCH

Percutaneous left atrial appendage closure followed by single antiplatelet therapy: Short- and mid-term outcomes

Fermeture percutanée de l’auricule gauche suivie d’une monothérapie antiaggrégante plaquettaire : devenir à court et moyen terme

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KEYWORDS
Left atrial appendage; Percutaneous closure; Stroke; Atrial fibrillation

Summary
Background. — After left atrial appendage closure (LAAC), various antithrombotic protocols have been suggested, but the optimal post-procedural antithrombotic strategy is still under debate.
Aims. — To investigate the efficacy and safety of LAAC with an AMPLATZER™ Cardiac Plug (ACP) device (St. Jude Medical, Minneapolis, MN, USA) followed by single antiplatelet therapy.
Methods. — Consecutive patients with non-valvular atrial fibrillation and a contraindication for oral anticoagulants who underwent LAAC with an ACP device between 2012 and 2014 in two French centres were included. Follow-up included clinical evaluation at 1, 3, 6 and 12 months, and yearly thereafter, and a cardiac computed tomography scan at 3 months to assess device

Abbreviations: ACP, AMPLATZER™ cardiac plug; AF, Atrial fibrillation; CT, Computed tomography; DAPT, Dual antiplatelet therapy; LAA, Left atrial appendage; LAAC, left atrial appendage closure; OAC, oral anticoagulation; TIA, Transient ischaemic attack; TOE, Transoesophageal echocardiography; TTE, Transthoracic echocardiography.

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Background

Atrial fibrillation (AF) is the most common sustained arrhythmia, and increases the risk of ischaemic stroke [1,2]. Although oral anticoagulation (OAC) is recommended in patients with a CHA2DS2-VASc score ≥ 1, this medication is associated with severe haemorrhagic complications, and a large proportion of patients discontinue OAC after treatment initiation [3]. The PROTECT AF trial showed that percutaneous left atrial appendage closure (LAAC) with the WATCHMAN™ device (Boston Scientific, Natick, MA, USA) was non-inferior, but also superior, to warfarin in preventing the combined outcome of stroke, systemic embolism and cardiovascular death [4–6]. Published results of multicentre studies with the AMPLATZER™ Cardiac Plug (ACP) device (St. Jude Medical, Minneapolis, MN, USA) showed that the annualized rates of major bleeding and stroke were less frequent after LAAC than expected from the CHA2DS2-VASc and HAS-BLED (hypertension, abnormal liver/renal function, stroke, bleeding, labile international normalized ratio, elderly [age ≥ 65 years], drugs/alcohol) scores [7,8]. Therefore, LAAC has become an integral part of the treatment algorithm for patients with AF and a CHA2DS2-VASc score ≥ 2.

Results.— A total of 76 patients underwent successful LAAC (mean age: 73 years; 59% men; mean CHA2DS2-VASc score 4.4 ± 1.3; mean HAS-BLED score 3.4 ± 0.9). Three major complications occurred during the periprocedural period (one cardiac tamponade and two access site haematomas). Device thrombosis was observed at 3 months in five (6.8%) patients who remained asymptomatic. After a mean follow-up of 13 months, the rates of death, stroke and major bleeding were 2.6%, 4.0% and 1.3%, respectively. Embolic and bleeding events were less frequent than expected from CHA2DS2-VASc (4.0% vs 9.9%; P < 0.001) and HAS-BLED (1.3% vs 4.3%; P < 0.001) risk scores.

Conclusions.— LAAC using an ACP device followed by single antiplatelet therapy could be a reasonable alternative for stroke prevention.

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Résumé

Contexte.— Après la fermeture percutanée de l’auricule gauche (FPAG), plusieurs protocoles antithrombotiques ont été suggérés mais la stratégie optimale de traitement antithrombotique reste débattue.

Objectifs.— Évaluer l’efficacité et l’innocuité de la FPAG avec les dispositifs Amplatz Cardiac Plug (St. Jude Medical, Minneapolis, Minnesota) (ACP) suivie d’une monothérapie antiagrégante plaquettaire.

Méthodes.— Les patients consécutifs ayant une fibraison atriale non-valvulaire et une contre-indication aux anticoagulants oraux et ayant bénéficié d’une FPAG avec un dispositif ACP entre 2012 et 2014 dans 2 centres français étaient inclus. Le suivi comportait une évaluation clinique à 1, 3, 6 et 12 mois, puis de manière annuelle ainsi qu’une tomodensitométrie cardiaque à 3 mois pour évaluer la position de la prothèse, la présence d’un éventuel thrombus ou une fuite résiduelle. Une monothérapie antiagrégante était prescrite après la procédure pour au moins 12 mois.

Résultats.— Au total, 76 patients ont bénéficié d’une FPAG avec succès (âge : 73 ans, 59 % d’hommes, CHA2DS2-VASc score moyen 4,4 ± 1,3, HAS-BLED score moyen 3,4 ± 0,9). Trois complications majeures sont survenues durant la période periprocédurale (1 tamponnade et 2 complications hémorragiques au point de ponction). Un thrombus sur le dispositif été observé à 3 mois chez 5 patients (6,8 %) par ailleurs asymptomatiques. Après un suivi moyen de 13 mois, les taux de décès, d’accidents emboliques et hémorragiques étaient de 2,6 %, 4,0 % et 1,3 %, respectivement. Les événements emboliques et hémorragiques étaient moins fréquents que le prédisaient les scores de CHA2DS2-VASc (4,0 % vs 9,9 % ; p < 0,001) et HAS-BLED (1,3 % vs 4,3 % ; p < 0,001).

Conclusions.— La fermeture percutanée de l’auricule gauche avec les dispositifs ACP suivie d’une monothérapie antiagrégante peut constituer une alternative raisonnable pour la prévention des accidents emboliques.

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of treatment guidelines in AF patients (grade IIb, level B) [9].

Post-procedural management of antithrombotic therapy in these patients remains, however, a challenge, as the bleeding risk needs to be balanced against the risk of thrombus formation on the device and thromboembolic complications [10]. After LAAC, various antithrombotic protocols have been proposed by different teams, but the optimal postprocedural antithrombotic medication and its duration are still under debate (whether with the WATCHMANTM device or the ACP device). In the PROTECT AF trial, warfarin was prescribed for the first 45 days, followed by dual antiplatelet therapy (DAPT) between 45 days and 6 months after implantation, and aspirin indefinitely [5]. Other antithrombotic protocols included DAPT for 3 months, followed by a further 3 months with aspirin alone [11,12], or DAPT for only 6 weeks, followed by lifelong aspirin treatment [13]. In the ASAP study, DAPT was administered for 6 months, followed by lifelong aspirin [14]. In clinical practice, the anticoagulation protocol of the PROTECT AF trial (OAC for 6 weeks, DAPT for 6 months and lifelong aspirin) is recommended in the WATCHMANTM device instructions for use. After ACP device implantation, an antiplatelet agent (aspirin or clopidogrel) is recommended for at least 6 months.

The aim of this prospective registry was to investigate the efficacy and safety of LAAC using an ACP device, followed by a lightened antithrombotic protocol, including single antiplatelet therapy.

Methods

This prospective registry included consecutive patients with non-valvular AF who underwent LAAC in two French centres (university hospital of Bordeaux and Pasteur Clinic, Toulouse) between January 2012 and December 2014. During this period, LAAC was performed in 76 patients using ACP devices, and in eight patients using WATCHMANTM occluders. Therefore, to have a homogeneous population, and to avoid bias resulting from the small proportion of WATCHMANTM patients, we decided to exclude them from the analysis and focus on the results with ACP devices.

Data were collected prospectively from each centre. Inclusion criteria were age >18 years, documented nonvalvular AF and one or more of the following conditions: severe bleeding or history of disease that contraindicates OAC therapy; repeated failure to adequately control international normalized ratio; high risk of falls. The definitive contraindication for anticoagulation was discussed for each patient during a monthly multidisciplinary meeting. The study protocol conformed with the ethical guidelines of the 1975 Declaration of Helsinki, and was approved by the ethics committees of contributing hospitals. All patients gave informed consent before procedures.

Device implantation

The LAAC procedure and the specific features of the ACP devices have been described in detail [15,16]. All procedures were performed under general anaesthesia and femoral venous access. Real-time three-dimensional transoesophageal echocardiography (TOE) guidance was performed to determine left trial appendage (LAA) size (mm) and to rule out the presence of LAA thrombi. Patients received up to 100 IU/kg of unfractionated heparin intravenously to achieve an activated clotting time of >250 seconds. After transseptal puncture, the LAA was engaged, and angiography was performed to define the LAA anatomy in standard angulations. The appropriate device size was then chosen according to the manufacturer’s recommendations. Appropriate device positioning and stability was assessed by TOE and fluoroscopy before releasing each device. Procedural success was defined as successful implantation of the device in the LAA with no residual leak >3 mm on a colour Doppler ultrasound scan.

Antithrombotic therapy

No anticoagulation therapy was administered after the procedure. Single antiplatelet therapy, consisting of aspirin (80–325 mg/day) or clopidogrel (75 mg/day) alone, was started on the first day, and was given for at least 12 months after the procedure. Lifelong aspirin was given thereafter, in case of high cardiovascular risk, defined by: 10-year risk of fatal cardiovascular disease > 5% and/or diabetes mellitus and/or vascular disease (coronary artery disease, obliterator peripheral arteriopathy). This institutional antithrombotic protocol was chosen before initiating the LAAC programme, because a large majority of patients had an OAC contraindication with an increased risk of bleeding and, therefore, in cooperation with neurological and gastroenterology teams, we did not want to treat them with DAPT or OAC to decrease their haemorrhagic risk. In some cases, the choice and duration of single antiplatelet therapy were individualized depending on patient history and physician preference.

As there was no control group in this study, the efficacy of this antithrombotic strategy was evaluated by comparing the actual rate of embolic and bleeding events at follow-up with the event rate predicted by the patients’ CHA2DS2-VASc and HAS-BLED scores, respectively [17].

Follow-up

Transthoracic echocardiography (TTE) was performed 24 hours after the procedure in all patients. Follow-up was performed via clinical visits at 1, 3, 6 and 12 months, and yearly thereafter. TTE was performed at 1 month to evaluate device position. Control cardiac computed tomography (CT) was performed at 3 months to evaluate device position and device-related thrombi, and to assess residual perdevice leak. In case of an abnormal CT scan, TOE was performed to confirm the suspected diagnosis (i.e. thrombus or device-related leak). If device-related thrombus was confirmed, subcutaneous low-molecular-weight heparin at a therapeutic dose or a second antiplatelet agent was considered, depending on the patient’s individual bleeding risk.

Adverse events

Major complications occurring during the periprocedural and follow-up periods were defined according to valve academic research consortium-2 criteria [18], and included...
death, stroke, transient ischaemic attack (TIA), myocardial infarction, systemic embolization, device embolization, significant pericardial effusion or cardiac tamponade, major bleeding (requiring surgery or transfusion) and device-related complications requiring surgery.

Minor complications were defined as minor bleeding or vascular complications without the need for intervention.

Statistical analysis

Values are expressed as mean ± standard deviation or median [range] for continuous variables, and as numbers and percentages for categorical variables. The expected incidence of thromboembolic or bleeding events in the studied population was calculated as the mean of the individual risk of each patient, according to their CHA2DS2-VASc and HAS-BLED scores [17]. The observed incidence of events was calculated per patient and year of follow-up (number of patients multiplied by the mean time of follow-up of those patients expressed in years). Comparisons between observed and expected rates of thromboembolic and bleeding events were assessed using binomial tests. A P-value < 0.05 was considered significant. Data analysis was performed using STATA® software, (StataCorp LP, College Station, TX, USA).

Results

Population characteristics

A total of 76 patients were prospectively included in this study (mean age 73 ± 8 years; 59% men). Permanent AF was present in 42 (55%) patients. The mean CHA2DS2-VASc score was 4.4 ± 1.3. The mean HAS-BLED score was 3.4 ± 0.9, with a score ≥ 3 present in 66 (87%) patients. The main indication for LAAC was OAC contraindication (86%), mostly because of a neurological complication (66%). Baseline characteristics of the study population and LAAC indications are shown in Table 1 and Table 2, respectively.

<table>
<thead>
<tr>
<th>Table 1 Population baseline characteristics (n=76).</th>
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<tbody>
<tr>
<td><strong>Age (years)</strong></td>
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<tr>
<td><strong>Men</strong></td>
</tr>
<tr>
<td><strong>Atrial fibrillation</strong></td>
</tr>
<tr>
<td>Paroxysmal/persistent</td>
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<tr>
<td>Permanant</td>
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<td><strong>Congestive heart failure</strong></td>
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<td><strong>Arterial hypertension</strong></td>
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<td><strong>Diabetes mellitus</strong></td>
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<tr>
<td><strong>Coronary artery/vascular disease</strong></td>
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<tr>
<td><strong>Previous stroke/TIA</strong></td>
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<tr>
<td><strong>CHA2DS2-VASc score</strong></td>
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<tr>
<td><strong>HAS-BLED score</strong></td>
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<tr>
<td><strong>Annual risk of thromboembolism (%)</strong></td>
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<tr>
<td><strong>Annual risk of major bleeding (%)</strong></td>
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Data are expressed as mean ± standard deviation or number (%). TIA: transient ischaemic attack.

Table 2 Left atrial appendage closure indications (n=76).

| **Bleeding**                                      | 65 (86) |
| **Intracranial haemorrhage**                      | 50 (66) |
| **Gastrointestinal haemorrhage**                  | 13 (17) |
| **Other**                                         | 2 (2.6) |
| **High risk of fall/dementia**                    | 4 (5.2) |
| **International normalized ratio liability**      | 3 (4)   |
| **Other**                                         | 4 (5.2) |

Data are expressed as number (%).

Periprocedural results

Procedure-associated findings are displayed in Table 3. The rate of successful implantation was 100%. Mean device sizes were 24.2 ± 3.8 mm for the ACP device (n=61) and 22.4 ± 3.6 mm for the Amulet device (n=15). Other than LAAC, no additional intervention was performed during the procedures. All but two patients received single antiplatelet therapy after the procedure: either aspirin (n=71, 93%) or clopidogrel (n=3, 4.0%). One patient with severe congenital thrombocytopenia presented with a contraindication to antiplatelet agent, and therefore received a non-vitamin K antagonist OAC for 3 months. One patient presented a periprocedural thrombus on the right side of the interatrial septum, and therefore received aspirin and OAC for 1 month, after which a control TOE showed complete thrombus disappearance; he then received lifelong treatment

<table>
<thead>
<tr>
<th>Table 3 Procedure-associated characteristics (n=76).</th>
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<tr>
<td><strong>Device size (mm)</strong></td>
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<tr>
<td><strong>ACP</strong></td>
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<tr>
<td><strong>Amulet</strong></td>
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<td><strong>Combined procedure</strong></td>
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<tr>
<td><strong>Successful implantation</strong></td>
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<td><strong>In-hospital outcomes</strong></td>
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<tr>
<td>Death</td>
</tr>
<tr>
<td>Stroke/TIA</td>
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<tr>
<td>Cardiac tamponade</td>
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<tr>
<td>Device embolization</td>
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<tr>
<td>Major bleeding</td>
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<tr>
<td><strong>Myocardial infarction</strong></td>
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<tr>
<td><strong>Systemic embolism</strong></td>
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<tr>
<td>Need for surgery</td>
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<tr>
<td>Minor bleeding</td>
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<tr>
<td><strong>Post-procedural antithrombotic therapy</strong></td>
</tr>
<tr>
<td>Aspirin</td>
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<tr>
<td>Cloridogrel</td>
</tr>
<tr>
<td>Aspirin + OAC</td>
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<tr>
<td>OAC</td>
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<tr>
<td><strong>Duration of hospitalization (days)</strong></td>
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</table>

Data are expressed as mean ± standard deviation or number (%). ACP: AMPLATZER™ cardiac plug; OAC: oral anticoagulation; TIA: transient ischaemic attack.
with aspirin. These two patients were excluded from subsequent analyses. The mean duration of hospitalization was 3.9 ± 1.7 days.

Three major complications (3.9%) were reported during the periprocedural period. One patient had cardiac tamponade, which resolved with pericardial puncture. Two patients had major bleeding while receiving aspirin therapy because an access site haematoma caused a fall in the haemoglobin level, leading to transfusion. No periprocedural death or embolic complication occurred.

**Follow-up**

Clinical follow-up was completed in 73/74 (98.6%) of the remaining patients. The mean duration of follow-up was 13 ± 3 months, giving a follow-up rate of 75 patients/year.

There were two deaths. One patient presented a left ventricular device embolization, diagnosed 1 month after the procedure (LAA device position was correct on immediate post-procedural TTE). As the device was trapped by papillary muscles and trabeculations, he underwent hybrid surgical transapical retrieval of the device, but died subsequently because of multiorgan failure. The second patient presented a massive intracranial haemorrhage, 6 months after LAAC, while receiving aspirin, and died subsequently. One-year all-cause mortality was 2.6%.

Overall, three patients presented thromboembolic events. The first patient had an occlusion of the central retinal artery after 2 months of follow-up; the second patient had a lacunar stroke 18 months after the procedure, with complete recovery and no sequelae; the last patient had a TIA after 22 months of follow-up. All three strokes were non-disabling. These patients were receiving aspirin at the time of the event and, after the event, TOE showed the absence of cardiac thrombi and complete LAA sealing for each of them. There was no evidence of extracardiac origin of stroke, except for the third patient, who had atherosclerotic plaques on the aorta.

Control cardiac CT was performed in 66/73 patients after a median period of 12 weeks. Six patients did not have a CT control: one patient was lost to follow-up; one patient died 1 month after the procedure; and four patients had renal failure, which contraindicated contrast injection, and underwent TOE, which was normal.

Among the patients who underwent cardiac CT, device thrombosis was suspected and confirmed by subsequent TOE in five (6.8%) patients. These five patients had a high bleeding risk (amyloid angiopathy, n = 3; cerebral haemorrhage, n = 2), and, after a multidisciplinary meeting, were considered as formally contraindicated to both heparin and DAPT. Therefore, these patients continued with single antiplatelet therapy. Of note, neither stroke nor TIA was observed in these patients during follow-up.

A total of 24 (38%) patients had peri-device leak, as determined by CT (ACP, n = 20; Amulet, n = 4). The leak was trivial or mild in 16 patients, and significant in eight patients. Among patients with a significant leak, control TOE showed a leak size of < 5 mm. Patients with peri-device leak were still treated with the same antiplatelet agent. Device leaks did not correlate with thromboembolic events. Indeed, no stroke or TIA was observed in patients with incomplete closure at follow-up.

![Figure 1. Effectiveness of left atrial appendage closure using AMPLATZER™ cardiac plug devices in the reduction of thromboembolic and bleeding events, based on annual rates predicted by the CHA_2DS_2-VASc score and the HAS-BLED score, respectively.](image)

**Comparison with expected annual embolic/bleeding risk**

The mean CHA_2DS_2-VASc score for patients with complete follow-up was 4.4 ± 1.3 (annual risk of thromboembolism: 9.9 ± 4.2%). The annual rate of systemic thromboembolism in the study was 4.0% (3/75 patient-years), which was significantly lower than the predicted rate (P < 0.001). The mean HAS-BLED score of implanted patients was 3.4 ± 1.0 (annual risk of bleeding 4.3 ± 2.4%). The annual rate of major bleeding during study follow-up was 1.3% (1/75 patient-years) — again, significantly lower than the predicted rate (P < 0.001).

The annual rates of observed versus expected events are shown in Fig. 1.

**Discussion**

In this article, we report on a series of 76 patients who underwent LAAC using ACP devices followed by single antiplatelet therapy. To the best of our knowledge, this is the first study evaluating the safety of this lightened antithrombotic protocol in such a large cohort of patients. This strategy showed a favourable outcome in terms of prevention of thromboembolic and bleeding events.

**Safety and efficacy of single antiplatelet strategy**

Based on our local unit protocols, LAAC was followed by single antiplatelet treatment, provided that patients had no contraindications for antiplatelet agents. This strategy may be controversial. Indeed, the post-procedural management of antithrombotic therapy in these patients is based on a
balance between thromboembolic risk, caused by thrombus formation on the device, and bleeding risk; this is particularly critical during the healing process, until complete endocardialization of the device. Preclinical canine studies showed that the WATCHMAN™ device was completely incorporated after 28 days, with organized neocapillary growth and fibrin deposition, with an antithrombotic treatment consisting of warfarin and aspirin [19,20]. A report on the ACP device implanted in 10 dogs treated only with aspirin also demonstrated that the atrial aspect of the device was covered by a stable mature neo-intima 90 days after implantation, with no thrombus formed on the LAA disc, except for one animal that had the end screw of the device in contact with the left atrial wall because of a small canine left atrium [21].

For clinical practice, after ACP device implantation, an antiplatelet agent (aspirin or clopidogrel) is recommended by the manufacturer for at least 6 months, but without further details. The anticoagulation protocol of the PROTECT AF trial (OAC for 6 weeks, DAPT for 6 months and lifelong aspirin) is recommended in the WATCHMAN™ device instructions for use. However, in the PROTECT AF trial, one of the main inclusion criteria was eligibility for warfarin therapy, whereas in real-life clinical practice, most patients are contraindicated to OAC, making this antithrombotic protocol inapplicable. Moreover, the recently published French National Authority for Health and expert consensus guidelines state that LAAC might be considered in patients with a formal OAC contraindication, showing that this population is clearly at high risk of bleeding [22,23].

As summarized in Table 4, various antithrombotic strategies have been proposed by different authors after LAAC [7,8,12,14]. These protocols (usually DAPT for 1–6 months followed by single antiplatelet treatment) led to a significant reduction in the rate of stroke events compared with the score-predicted rate in this specific patient population with most patients contraindicated to OAC. More generally, in AF patients, DAPT including aspirin and clopidogrel was shown to reduce the risk of ischaemic stroke compared with aspirin alone, but at the cost of an increased risk of major bleeding (2.0% vs 1.3% per year) [24]. Tzikas et al. clearly showed that intra-procedural strokes or TIA were more frequent in patients who were taking any antithrombotic treatment other than aspirin (i.e. OAC or DAPT) at last study follow-up, showing a relationship between the antithrombotic treatment and patient outcome [8]. Therefore, we chose this tightened post-procedural protocol that included a single antiplatelet agent before initiating the LAAC programme, because a large proportion of patients had an OAC contraindication with an increased haemorrhagic risk and, therefore, in cooperation with neurological and gastroenterology teams, we did not want to treat them with DAPT or OAC, in order to decrease their bleeding risk.

As shown in Table 4, in comparison with reported results of LAAC with ACP devices in recent studies, our strategy led to a significant reduction in the rate of bleeding events versus the score-predicted rate, without increasing the risk of stroke or device thrombosis. Indeed, in our cohort, the use of single antiplatelet therapy was associated with a lower-than-expected rate of bleeding, with only one serious haemorrhagic event occurring during the follow-up period (1.2% per year). Several studies have demonstrated that the benefit of LAA closure increases with time. In other words, after this procedure, bleeding should be expected during the first months after the procedure, but the bleeding risk decreases significantly thereafter, and the relative stroke reduction is higher for patients with more than 1 year of follow-up [7,8]. In the Iberian registry, the reduced incidence of bleeding became significant between the first and second years after withdrawal of antiplatelet drugs, but was not significant after 1 year of follow-up. In our registry, we found a thromboembolic event rate that was slightly higher than in the other series; this may be partially explained by a shorter follow-up in our series. Indeed, in the Iberian registry, the observed incidence of TIA/stroke decreased from 3.9% at 1 year to 2.4% after 2 years of follow-up [7]. As our follow-up period was relatively short, we can expect that the benefits of LAAC, in terms of embolic or bleeding events, will increase with a longer follow-up.

In our series, strokes/TIAs occurred after a mean of 14 months, clearly beyond the theoretical healing period of 45 days that usually underlies reinforced antithrombotic strategies during the first post-implantation weeks or months. These patients were treated with aspirin when the embolic event occurred, and no embolic event was observed before 45 days, suggesting that single antiplatelet treatment after LAAC may be a safe strategy.

Thrombus formation, peridevice leaks

In our cohort, device-related thrombus was suspected on cardiac CT and confirmed by TOE in five patients (6.8%). Moreover, all patients with an embolic event during follow-up underwent TOE, which showed the absence of cardiac thrombi and complete LAA sealing for each of them. Currently, TOE is considered the gold-standard technique for the detection of thrombi in the LAA [25]. In our unit, the policy is to perform a cardiac CT scan for LAAC or cardiac thrombus detection before the procedure and during follow-up, to avoid the invasiveness of TOE in such fragile patients. The diagnostic performance of a cardiac CT examination for LAAC thrombus detection has been studied in patients with stroke [26]. The overall sensitivity and specificity of CT for the detection of thrombi in the LAA were 96% and 100%, respectively. Our results are in line with studies where the device-related thrombus incidence ranged from 4% to 17%, depending on the TOE-follow-up protocol (i.e. inclusion or exclusion of mural thrombi) [7,8,10–14]. Recently published data using CT assessment showed a lower incidence of device-related thrombus [27,28]. These occurrences are reported predominantly on non-endothelialized device protrusions, such as the proximal end screw with ACP, especially if implants are too deep. Of note, a recent paper showed that two-thirds of a series of 46 patients who had device thrombosis after LAAC with the WATCHMAN™ device were clopidogrel resistant [29]. Nevertheless, consistent with our findings, the reported thromboembolic stroke event rates related to device thrombus are relatively low (from 0.3% to 0.7%).

Detection of peridevice leaks after LAAC is challenging, and published data have reported a variable leak frequency of between 8.2% and 63% after ACP implantation, using TOE or CT imaging [7,8,25,26]. Based on CT assessment, we found a 36% incidence of peridevice leak, which was
trivial or mild in 18 (24%) patients, and significant in 9 (12%) patients. Patients with significant leak underwent control TOE, which showed a leak size of <5 mm. Patients with peridevice leak were still treated with the same antidevice agent. In the PROTECT AF study, the impact of peridevice leak severity, defined as minor, moderate or major (< 1 mm, 1–3 mm and > 3 mm, respectively), on the composite primary efficacy endpoint (stroke, systemic embolism and cardiovascular death) was not demonstrated. There was no association between small peridevice leaks and increased risk of thromboembolism [30]. This is consistent with our results, as no stroke or TIA was observed in patients with incomplete closure at follow-up in our series.

Study limitations

This was a non-randomized, hypothesis-generating, observational study reporting a prospective dual-centre experience, with no control group. Therefore, we acknowledge that the use of CHA2DS2–VASc and HAS-BLED scores for comparisons was not methodologically perfect, although these scores have been validated previously. Moreover, CT follow-up was not available for all patients, clinical CT and TOE results were self-reported and there was no independent adjudication. These results will therefore have to be confirmed with randomized, controlled trials.

Conclusions

In patients with non-valvular AF at high risk of cardioembolic events and with contraindications for anticoagulation therapy, percutaneous LAAC with an ACP device followed by single antplatelet therapy is associated with a favourable outcome in terms of prevention of thromboembolic and bleeding events. The results of systematic CT/TOE at 3 months did not modify the management strategy, and a simplified follow-up protocol should therefore be discussed in this frail population. Our post-procedural antithrombotic protocol led to a significant reduction in the rate of bleeding events versus the score-predicted rate, without increasing the risk of stroke or the rate of device thrombosis. However, these results do not provide sufficient evidence to enable this tightened antithrombotic protocol to be recommended. Further randomized controlled trials are warranted to confirm these promising preliminary results.

Sources of funding

None.

Disclosure of interest


The other authors declare that they have no competing interest.

References


Table 4  Reported thromboembolic and bleeding events and device thrombosis after left atrial appendage closure with AMPLATZER™ cardiac plug devices in recent studies, and comparison with our results.

<table>
<thead>
<tr>
<th>Reference</th>
<th>n</th>
<th>Device</th>
<th>Antithrombotic therapy</th>
<th>Follow-up (months)</th>
<th>TE events versus predicted (%/year)</th>
<th>Bleeding events versus predicted (%/year)</th>
<th>Device thrombosis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tzikas et al. [8]</td>
<td>1047</td>
<td>ACP</td>
<td>DAPT 1–3 months; ASA 3 months</td>
<td>13 [6–25]</td>
<td>2.3 vs 5.6</td>
<td>2.0 vs 5.3</td>
<td>4.4</td>
</tr>
<tr>
<td>Lopez Minguez et al. [7]</td>
<td>167</td>
<td>ACP</td>
<td>DAPT 3–6 months; ASA 6–12 months</td>
<td>22 ± 8.3</td>
<td>2.4 vs 8.3</td>
<td>3.1 vs 6.6</td>
<td>8.0</td>
</tr>
<tr>
<td>Urena et al. [12]</td>
<td>52</td>
<td>ACP</td>
<td>DAPT 1–6 months or ASA or clopidogrel Single antiplatelet therapy</td>
<td>20 ± 5</td>
<td>3.4 vs 10.0</td>
<td>3.4 vs 8.7</td>
<td>0</td>
</tr>
<tr>
<td>Jalal et al.</td>
<td>73</td>
<td>ACP</td>
<td>Single antiplatelet therapy</td>
<td>13 ± 3</td>
<td>4.0 vs 9.9</td>
<td>1.3 vs 4.3</td>
<td>6.8</td>
</tr>
</tbody>
</table>

ACP: AMPLATZER™ cardiac plug; ASA: aspirin; DAPT: double antiplatelet therapy; TE: thromboembolic events (i.e. stroke, transient ischaemic attack and systemic embolisms).

a Median [range] or mean±standard deviation.


