CLINICAL RESEARCH

Extending percutaneous left atrial appendage closure indications using the AMPLATZER™ Cardiac Plug device in patients with persistent left atrial appendage thrombus: The thrombus trapping technique

Étendre les indications de la fermeture percutanée de l’auricule gauche en utilisant le dispositif AMPLATZER™ Cardiac Plug chez les patients avec thrombus persistant de l’auricule : la technique du piégeage du thrombus

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Summary

Background. — Percutaneous left atrial appendage (LAA) closure has emerged as an alternative therapeutic option for the prevention of embolic stroke in high-risk patients with non-valvular

Keywords

Left atrial appendage;
Percutaneous closure; Thrombus; Atrial fibrillation

atrial fibrillation. The presence of thrombus in the LAA is currently a contraindication to the procedure.

Aim. — To describe a modified LAA closure technique that allows a safe procedure in patients with LAA thrombus.

Methods. — Between May 2013 and October 2014, LAA closure was performed in three patients with LAA thrombus (mean age 73.6 ± 14 years; two men), using a modified technique that avoids manipulation of catheters or angiography in the LAA.

Results. — Two patients had persistent thrombus despite appropriate antithrombotic therapy, while the other patient had a contraindication to systemic anticoagulation. The procedure was successful using the modified implantation technique in all patients. The implanted device was the AMPLATZER™ Cardiac Plug (St. Jude Medical, Minneapolis, MN, USA) in one patient and the Amulet™ (St. Jude Medical, Minneapolis, MN, USA) in two patients. No periprocedural complications occurred. After a mean follow-up of 8 ± 2 months, no deaths or late complications were observed.

Conclusions. — Thrombus trapping is a feasible and effective technique for performing LAA occlusion in patients with thrombus within the LAA. This modification of the implantation technique may allow LAA closure indications to be extended to include patients with LAA thrombus, who were formerly considered unsuitable.

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Background

Embolic stroke is the main complication that occurs in patients with atrial fibrillation (AF), with an annualized incidence ranging from 1.9% to 18.2% [1]. Oral anticoagulation (OAC), using either vitamin K antagonists or the more recently introduced factor II/Xa inhibitors, is recommended in patients with a Cardiac failure, Hypertension, Age ≥ 75 years (Doubled), Diabetes, Stroke (Doubled) — Vascular disease, age 65—74 years and Sex category (Female) (CHA2DS2-VASc score ≥ 1, to reduce stroke risk in these patients. However, OAC is associated with severe haemorrhagic complications, and many patients discontinue this therapy a few years after treatment initiation [2,3].

Based on the concept that up to 90% of emboli from non-valvular AF originate in the left atrial appendage (LAA), percutaneous LAA closure has emerged as an alternative therapeutic option to OAC, for the prevention of embolic
stroke in high-risk patients [4–6]. Indeed, after exclusion of the LAA embolic source, the remaining risk is too small to warrant OAC, with its inherent bleeding risk. Indications for LAA closure are expanding widely, but these procedures remain contraindicated in several settings, including presence of thrombus in the LAA [7,8]. During the LAA occlusion procedure, thrombus dislodgement may occur with the manipulation of sheaths or guidewires in the LAA. The presence of LAA thrombus despite appropriate antithrombotic therapy or in patients with a contraindication to systemic OAC is a major concern, as these patients are at high-risk of embolic complications.

Some authors have published brief reports of percutaneous LAA occlusion in patients with known thrombus within the LAA [9,10]. In this article, we report procedural and short-term outcomes in a series of three patients with LAA thrombus in whom a modified technique was used to avoid manipulation of sheaths and catheters in the LAA, allowing a successful percutaneous closure procedure.

Methods

Patient selection

Between January 2011 and October 2014, we identified patients with LAA thrombus in whom LAA closure was attempted using a modified and simplified implantation technique.

Patients’ demographic data were analysed from medical records. CHA2DS2-VASC and Hypertension, Abnormal liver/renal function, Stroke, Bleeding, Labile international normalized ratio, Elderly (age > 65 years), Drugs/alcohol (HAS-BLED) scores were calculated. All patients gave written informed consent before the procedure.

Preprocedural management

All patients had cardiac computed tomography (CT) for the detection of LAA thrombus before the procedure, and for LAA anatomical assessment. In case of high suspicion of LAA thrombus on CT, the diagnosis was confirmed by transoesophageal echocardiography (TOE). Patients with LAA thrombus were treated with OAC or low-molecular-weight heparin for approximately 4 weeks, combined with single antiplatelet therapy (aspirin 160 mg/day), according to the patient’s status regarding contraindication to antithrombotic treatment. In case of OAC ineligibility or thrombus persistence despite appropriate therapy, LAA occlusion was considered using a modified implantation technique (see below). Patients with left atrial or left ventricular thrombus were excluded.

Implantation technique

All procedures were performed under general anaesthesia, fluoroscopy and real-time three-dimensional (3D) TOE guidance. Patients received unfractionated heparin intravenously to achieve an activated clotting time > 250 seconds. Baseline LAA measurements of the landing zone were obtained by TOE. Femoral venous access was obtained, and transseptal puncture was then performed under fluoroscopic and TOE guidance in the inferioposterior part of the fossa ovalis. To prevent thrombus dislodgement during the procedure, any contrast injection or guidewire or catheter manipulation in the LAA was avoided. The transseptal sheath was advanced in the upper left pulmonary vein and an over-the-guide exchange was performed with the delivery sheath, using a 260-cm Amplatz Super Stiff™ J Guidewire (Boston Scientific, Marlborough, MA, USA). The wire and sheath were advanced carefully using TOE guidance, to avoid inadvertently entering the LAA. The delivery sheath was then pulled back gently from the vein and moved forward towards the LAA ostium, without engaging the latter. The operator took care to avoid entering the LAA with the sheath.

Optimal device sizing was achieved using 3D multimodality imaging, including preprocedural CT and two-dimensional/3D periprocedural TOE. The device size was chosen to be 10–20% larger than the measured landing zone diameter (using the usual anatomical landmarks, i.e. the left circumflex coronary artery and the LAA roof 1 cm inward from the tip of the ridge separating the LAA and the left upper pulmonary vein) [7]. Device preparation was performed according to the manufacturer’s recommendations. After purging, the device was advanced to the distal end of the access sheath. Usually, a counterclockwise rotation of the sheath was performed to orientate it parallel to the LAA neck. For the AMPLATZER™ Cardiac Plug (St. Jude Medical, Minneapolis, MN, USA) and Amulet™ (St. Jude Medical, Minneapolis, MN, USA) prosthesis, the first half of the device (lobe) was delivered by sheath retraction, and the second half by pushing it forward. Then, the disc was deployed by further retracting the sheath while the operator pushed gently on the device. After confirming proper positioning using TOE and fluoroscopy and a sustained tug test, the device was released. Regarding device selection, the first implantations were performed with the AMPLATZER™ Cardiac Plug; a switch was made to the Amulet™ when it became available in France.

Follow-up

Transthoracic echocardiography (TTE) was performed 24 hours after the procedure in all patients. After device implantation, antithrombotic therapy was given according to LAA closure indication: patients with OAC contraindication received lifelong single antiplatelet therapy consisting of aspirin (160 mg/day) or clopidogrel (75 mg/day); patients with persistent LAA thrombus despite appropriate OAC treatment continued OAC after LAA closure. Follow-up was performed at clinical visits at 1, 3, 6, and 12 months, and yearly thereafter. TTE was performed at 1 month to evaluate device position. Control cardiac CT was performed at 3 months to evaluate device position and device-related thrombus, and to assess residual peridevice leak. In case of abnormal CT, TOE was performed to confirm the suspected diagnosis (i.e. thrombus or residual leak), according to our institutional protocol.

Major non-fatal complications were defined as embolic events (stroke, transient ischaemic attack, cardiac embolism), the need for emergency surgical intervention, life-threatening arrhythmias and pericardial tamponade.
Minor complications were defined as minor bleeding or vascular complications without need for intervention.

**Statistical analysis**

Data are expressed as mean ± standard deviation or median (range) for continuous variables, and as number (percentage) for categorical variables. No statistical analysis was performed.

**Results**

During the study period, LAA closure was performed in three patients with echocardiographic contrast LAA thrombus in the University Hospital of Bordeaux. Patients were aged between 57 and 82 years at the time of intervention (mean age 74 ± 14 years old; two men) and had a high bleeding risk (mean HAS-BLED score 3 ± 0) as well as a high thromboembolic risk profile (mean CHA₂DS₂-VASC score 4.3 ± 0.5). Patient 1 had non-valvular AF with a mild valvular disease: moderate mitral regurgitation without stenosis and mild aortic stenosis (Doppler maximal peak velocity of 2.6 m/s without associated leak). Patients 1 and 2 had chronic AF, while patient 3 had paroxysmal atrial fibrillation. The LAA closure indication was OAC contraindication because of intracranial haemorrhage in patient 2, and persistent LAA thrombus despite appropriate antithrombotic therapy in patients 1 and 3. Patient 1 presented with multiple systemic embolisms despite optimal OAC. The mean baseline left ventricular ejection fraction was 53 ± 11%. The patients’ baseline demographic data are displayed in Table 1.

**Procedural results**

The procedure was successful using the simplified implantation technique in all patients (Figs. 1, 2 and 3). The implanted device was the AMPLATZER™ Cardiac Plug in patient 2 and the Amulet™ in patients 1 and 3. Patient 1 had a mild perdevice leak (< 2 mm) after device release.

The mean procedural duration was 51 ± 15 minutes. No complication occurred during the procedures. Post-procedural TTE showed that the devices were safely anchored in the LAA without pericardial effusion. There were no complications during the hospitalization period. The main procedural results are shown in Table 2.

**Follow-up**

After a mean follow-up of 8 ± 2 months, no deaths or complications were observed. TTE and CT evaluations showed that device was still safely anchored in the LAA in all examined patients, without thrombus. Patient 1 had mild residual flow within the LAA that had already been noticed during the implantation procedure. Follow-up results are displayed in Table 2.

**Discussion**

We report a case series of three patients known to have thrombus within the LAA, in whom successful percutaneous LAA closure was performed using a simplified implantation technique. No early procedural-related complications occurred in these patients. To the best of our knowledge, this is the first reported series of percutaneous LAA closure in patients with known LAA thrombus.

**Extending LAA closure indications**

The goal of percutaneous LAA closure is the prevention of embolic stroke in high-risk patients. It has been reported that the incidence of LAA thrombus on TOE among patients scheduled for AF ablation who have been adequately anticoagulated is up to 11% in patients with a Cardiac failure, Hypertension, Age, Diabetes, Stroke (Doubled) (CHA₂DS₂) score of 4–6 [8]. Therefore, the prevalence of LAA thrombus may be higher in patients referred for LAA closure indication, as they have a high CHA₂DS₂-VASC score and cannot be treated with OAC. In this growing population, there is a need for an alternative treatment for the prevention of thrombus-related embolic stroke [7].

The presence of a thrombus in the LAA is considered as a contraindication to percutaneous LAA occlusion, as manipulation of catheters, guidewires, sheaths or devices in the LAA may lead to systemic embolization. The recently

### Table 1 Patients’ preprocedural clinical characteristics.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Sex</th>
<th>AF type</th>
<th>CHA₂DS₂-VASC score</th>
<th>HAS-BLED score</th>
<th>Baseline antithrombotic therapy</th>
<th>LAAC indication</th>
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<tr>
<td>1</td>
<td>57</td>
<td>Male</td>
<td>Chronic</td>
<td>4</td>
<td>3</td>
<td>Aspirin + LMWH</td>
<td>Persistent thrombus despite OAC</td>
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<tr>
<td>2</td>
<td>82</td>
<td>Female</td>
<td>Chronic</td>
<td>5</td>
<td>3</td>
<td>Aspirin</td>
<td>OAC contraindication</td>
</tr>
<tr>
<td>3</td>
<td>82</td>
<td>Male</td>
<td>Paroxysmal</td>
<td>4</td>
<td>3</td>
<td>OAC</td>
<td>Persistent thrombus despite OAC</td>
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</table>

AF: atrial fibrillation; CHA₂DS₂-VASC: Cardiac failure, Hypertension, Age ≥ 75 years (Doubled), Diabetes, Stroke (Doubled), Vascular disease, age 65–74 years and Sex category (Female); HAS-BLED: Hypertension, Abnormal liver/renal function, Stroke, Bleeding, Labile international normalized ratio, Elderly (age > 65 years), Drugs/alcohol; LAAC: left atrial appendage closure; LMWH: low-molecular-weight heparin; OAC: oral anticoagulation.
Figure 1. Patient 2. A—B. Preprocedural cardiac computed tomography (CT) (A) and perprocedural transoesophageal echocardiography (TOE) (B) showing distal left atrial appendage (LAA) thrombus (red arrow); the green line shows the planified landing zone. C. X-plane TOE after device release showing good device position compared with the planified landing zone (see panel B); the red arrow indicates thrombus trapping. D. Cardiac CT volume rendering technique showing 28-mm AMPLATZER™ Cardiac Plug (St. Jude Medical, Minneapolis, MN, USA) with complete occlusion of the LAA (no contrast medium seen in the distal LAA beyond the device); the green circle shows the planified landing zone based on preprocedural CT (3mensio Medical Imaging BV, Bilthoven, Netherlands).

Figure 2. Patient 1. A—B. Preprocedural cardiac computed tomography (CT) (A) and perprocedural transoesophageal echocardiography (TOE) (B) showing distal left atrial appendage (LAA) thrombus (red arrow); the green line shows the planified landing zone; the black arrow shows the circumflex artery. C. TOE after device deployment during tug test showing good device position compared with the planified landing zone (see panel B); the red arrow indicates thrombus trapping. D. Cardiac CT showing 22-mm Amulet™ device (St. Jude Medical, Minneapolis, MN, USA) with complete occlusion of the LAA.
published French National Authority for Health guidelines state that LAA closure might be considered in patients with formal OAC contraindication, but did not mention patients with persistent LAA thrombus despite appropriate antithrombotic therapy. In case of contraindication to OAC, there is no alternative option for decreasing the high-risk of an embolic event. The prevalence of LAA thrombus in patients with an LAA closure indication is difficult to evaluate, as LAA thrombus or dense spontaneous contrast on TOE are considered as exclusion criteria in the majority of studies.

Brief reports of percutaneous LAA occlusion in patients with known LAA thrombus have been published [9,10]. Bokhari et al. [9] described the case of a 76-year-old woman who was found to have LAA thrombus persistence despite dabigatran anticoagulation; she underwent LAA mechanical thrombectomy using an AngioJet™ catheter (MEDRAD Inc., Warrendale, PA, USA), with subsequent successful LAA closure using a 20-mm atrial septal defect occlusion device (St. Jude Medical, Minneapolis, MN, USA). As the patient was at very high-risk of embolic stroke, operators used bilateral embolic neuroprotection, employing the Mo.Ma® device (Invatec Inc./Medtronic, Bethlehem, PA, USA) on the right, and the SpiderFX™ filter device (ev3 Endovascular, Inc., Plymouth, MN, USA) in the left carotid artery. No major complication occurred, except transient bradycardia during the procedure, which required a temporary pacemaker.

More recently, Meincke et al. [10] published two cases of successful LAA occlusion using the WATCHMAN™ device (Boston Scientific, Marlborough, MA, USA) and similar cerebral protection systems in patients with known thrombus within the LAA.

Although the use of cerebral protection systems is relevant in this context, we did not use this type of device in our patients for several reasons. Firstly, the use of such devices needs arterial vascular access and catheter and device manipulation in the aortic arch, and extends the duration of the procedure, which may increase the risk of periprocedural complications in such fragile patients. Secondly, embolic events can occur despite the use of these devices [11,12]. We used a simplified implantation technique, avoiding any manipulation of catheters and wires or injection of contrast medium in the LAA, unlike the above-mentioned authors who performed LAA thrombectomy [9].

In our series, no periprocedural complications occurred – especially clinically apparent embolic events. After a mean follow-up of 8 ± 2 months, no deaths or complications were observed in patients.

<table>
<thead>
<tr>
<th>Case</th>
<th>Procedure/fluoroscopy time (minutes)</th>
<th>Implanted device</th>
<th>Device size (mm)</th>
<th>Early complications</th>
<th>Follow-up duration (months)</th>
<th>Follow-up complications</th>
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<tr>
<td>4</td>
<td>40/13</td>
<td>Cardiac Plug™</td>
<td>20</td>
<td>0</td>
<td>8</td>
<td>0</td>
</tr>
</tbody>
</table>

* St. Jude Medical, Minneapolis, MN, USA.
Technical features

Periprocedural imaging

Currently, TOE is considered as the gold-standard technique for the detection of thrombus in the LAA [13]. In our unit, the policy is to perform a cardiac CT scan for LAA or cardiac thrombus detection before the procedure. The diagnostic performance of cardiac CT examination for LAA thrombus detection has been studied in patients with stroke [14]. The overall sensitivity and specificity of CT for the detection of thrombus in the LAA were 96% and 100%, respectively. Pre-procedural CT assessment also helps with characterization of the LAA shape and the presence of multiple lobes and, above all, allows specific measurements to be made of the landing zone, which is mandatory for device size selection. The spatial relationship between the landing zone and the thrombus can also be evaluated before the procedure. In our study, all patients with high suspicion of LAA thrombus on CT underwent TOE during the 24 hours after the CT, to confirm the diagnosis.

Adequate use of various imaging modalities is essential for performing a safe and successful standard LAA occlusion procedure; this is even more important for the "thrombus trapping" procedure, where the use of contrast injection to delineate LAA anatomy is avoided. Therefore, non-invasive sizing and procedure planning based on CT and TOE must be performed in all cases to make the procedure safer and faster.

The TOE operator needs to be familiar with the standard implantation technique and the device characteristics; their role is crucial in this modified technique as no LAA angiography is performed, making TOE guidance the only means of achieving accurate LAA anatomical assessment and device positioning during the procedure.

The thrombus trapping technique

We describe here a modification to the standard LAA closure technique (using the AMPLATZER™ Cardiac Plug and Amulet™ devices), specifically for patients with LAA thrombus. This technique aims to jail the thrombus in the distal part of the LAA by implanting the closure device in its regular position, but without any catheter or guidewire manipulation or contrast injection in the LAA. The exchange between the transseptal sheath and the delivery sheath must be performed in the left upper pulmonary vein using a stiff guidewire. The wire and sheath have to be advanced carefully using fluoroscopy and, above all, TOE guidance, to avoid inadvertently entering the LAA. Some of the technical modifications shown here are quite similar to those described in an earlier paper [15]; however, these procedures were performed in patients without thrombus using LAA contrast injection, while TOE guidance and sedation were omitted. Our slight modification allowed us to successfully implant three patients with known thrombus within the LAA, without any periprocedural complications. This technique may also be useful in patients with severe spontaneous contrast within the LAA.

Several potential risks inherent to the LAA closure procedure have to be anticipated and discussed in the specific setting of the thrombus trapping technique. First, the occurrence of incomplete LAA occlusion with perdevice leaks may allow thrombus embolization. Detection of perdevice leaks is challenging, and variable leak frequencies ranging from 8.2% to 62% have been reported after AMPLATZER™ Cardiac Plug implantation using TOE or CT imaging [16,17]. However, residual leak has not been clearly linked with an increased risk of subsequent thromboembolism. There was no perdevice leak in our series; however, if it occurs after using the thrombus trapping technique, OAC treatment should be considered, especially in case of large leaks (> 4 mm). Secondly, the occurrence of periprocedural device embolization has also to be anticipated, but, from our point of view, there is no additional risk using the thrombus trapping technique. Finally, in case of device malposition, one should be as cautious as possible when recapturing the device, never to cross the landing zone with the sheath, to avoid entering the distal LAA, with potentially catastrophic results. These hazards highlight the fact that although feasible, the thrombus trapping technique should still be considered a high-risk, and that careful multimodality imaging is mandatory in this procedure, to allow accurate device sizing, deployment and release by the operator.

Several devices are currently in clinical development for catheter-based LAA occlusion, but none has been designed to be implanted in patients with LAA thrombus [18,19]. The most commonly used devices in Europe at present are the WATCHMAN™ and the AMPLATZER™ Cardiac Plug/Amulet™. However, the thrombus trapping technique is not feasible with the WATCHMAN™. Indeed, the WATCHMAN™ delivery sheath has to be advanced into the LAA until its marker aligns with the ostial plane of the appendage, making the procedure too risky in case of an LAA thrombus. Therefore, the AMPLATZER™ Cardiac Plug/Amulet™ is the most appropriate device to perform the thrombus trapping, as it can be safely implanted without entering the LAA with the delivery sheath.

Provided that careful multimodality imaging (i.e. cardiac CT and TOE) is achieved by trained physicians, performing the thrombus trapping technique is easy and does not extend procedural duration. One of the key points of this technique is the close cooperation required between the TOE and catheterization operators, who have to be used to working together. This simplified technique can also be used for routine LAA closure, and may decrease the LAA perforation risk.

Study limitations

This paper reports results from a small series of three cases, and no general conclusions can be drawn from our findings. Although no strokes occurred during the study period, we cannot confirm the absence of potential thromboembolic complications when using the thrombus trapping technique. The feasibility of the technique is shown in this paper, but the demonstration of its safety requires a cohort of sufficient size to facilitate a statistical comparison. Furthermore, because the follow-up duration was relatively short in most patients, we cannot comment on the long-term complications of LAA occlusion in this patient population. Long-term follow-up is mandatory before conclusive answers can be given. However, as periprocedural and early outcome results were satisfactory, this technique shows real promise.
Conclusion

Thrombus trapping is a feasible and effective technique for performing LAA occlusion in patients with thrombus within the LAA. This high-risk procedure is a modification of the standard LAA closure technique, and aims to jail the thrombus in the distal part of the LAA without any catheter or guidewire manipulation or angiography in the LAA. Thus, the adequate use of various non-invasive imaging modalities is critical before and during the procedure. This modification may extend the indications for LAA closure to patients with LAA thrombus who were formerly considered unsuitable, and may also be useful in patients with severe spontaneous LAA contrast. Further studies with larger series and a longer follow-up are warranted to confirm these preliminary results.

Disclosure of interest

J. B. T., X. I. Proctors for the companies St. Jude Medical and Boston Scientific.

The other authors declare that they have no competing interest.

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