Case reports

Percutaneous occlusion of the left atrial appendage for systemic embolism prevention in patients with atrial fibrillation: state of the art and report of two cases

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Atrial fibrillation is a benign arrhythmia but it is associated with an elevated thromboembolic risk. The treatment of choice is oral anticoagulation. However not all the patients can benefit from oral anticoagulation, due to bleeding risk or other contraindications. Considering that the most common embolic source in patients with atrial fibrillation is the left atrial appendage, different surgical techniques have been suggested for its closure. For patients at high risk, since August 2001 a device is available for percutaneous occlusion of the left atrial appendage (PLAATO). The PLAATO™ device consists of a self-expandable nitinol cage with small anchors on its surface to avoid systemic migration. The implantation procedure is performed with local anesthesia. It requires transseptal puncture and the device is delivered to the appendage through a specially designed sheath. The maneuver is performed under transesophageal and fluoroscopic guidance. At present more than 250 patients have been implanted, and the results, as far as the safety and the effectiveness are concerned, are really promising. We report 2 cases of recently successfully implanted at our Center.

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Introduction

Atrial fibrillation (AF) is a common cardiac arrhythmia. The prevalence increases with age and is up to 9% in the population > 80 years[1,2]. In Italy it has been estimated that about 500 000 patients suffer AF, with an incidence of 60 000 new cases/year. AF is associated with a relevant thromboembolic risk, being related to almost 50% of cardioembolic stroke[2,3]. In patients with AF the thromboembolic risk is estimated to be about 4.5% per year; it can vary from 0.4 to 12% per year depending on patient clinical features[3-7]. Several clinical factors, analyzed in large randomized trials[5-7], identified different patient groups with different thromboembolic risk. The international guidelines recognize as major risk factors: age > 75 years, hypertension, previous stroke or systemic embolism, heart failure; as minor risk factors: age 65-75 years, coronary artery disease, diabetes mellitus[3]. It is noteworthy that a previous stroke, *per se*, increases the risk to 12% per year[4].

Oral anticoagulation (OAC) is the treatment of choice in order to significantly reduce the thromboembolic risk. However, in some cases the use of oral anticoagulants can be contraindicated because of the presence of serious bleeding risk, intolerance or poor compliance and it is estimated that almost 30% of patients cannot benefit from this protection[5-8].

The left atrial appendage (LAA) is a trabeculated structure, with peculiar anatomic and physiological characteristics that render it the ideal place for thrombus formation during low-flow AF conditions[9,10]. A meta-analysis of 23 studies, based on transesophageal echocardiography (TEE), autopsy or intraoperative inspection, identifies the LAA as the preferred location of thrombus (90% of cases in non-valvular AF, 57% of cases of AF associated with valvular disease)[11].

The occlusion of LAA has been proposed as an alternative to OAC. The surgical occlusion is performed routinely during the Maze operation for the treatment of refractory AF and available data strongly recommend this procedure in every patient undergoing valvular cardiac surgery[12]. In this setting a clinical randomized pilot trial (Left Atrial Appendage Occlusion Study-LAAOS) in patients undergoing coronary artery bypass, is still ongoing[13]. Moreover a

single thoracoscopic approach was suggested as an additional tool for stroke prevention[14]. It must be emphasized that even if the surgical approach appears effective in preventing systemic embolism, the procedure is probably too invasive to be widely adopted.

Percutaneous left atrial appendage occlusion

Percutaneous LAA antithrombotic transcatheter occlusion (PLAATO) was first proposed as an experimental option in a canine model in 2002 and in the same year the results of the early clinical experience (15 cases) were published[15,16]. The PLAATO system (*ev3*) consists of an implant and a delivery catheter. The device (Fig. 1) is a self-expanding nitinol cage (range of diameters from 15 to 32 mm) covered with an occlusive expanded polytetrafluoroethylene membrane. The purpose of the membrane is both to occlude the orifice of the LAA and to allow surface endothelialization. Small anchors along the struts help the device to get engaged in LAA walls. The device is delivered through a preformed 14F transseptal sheath curved to aim at the LAA.

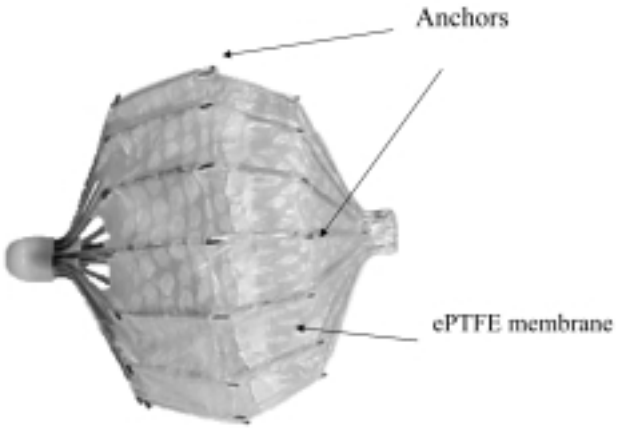

Figure 1. *The PLAATO device. The device is a self-expanding nitinol cage (range diameter from 15 to 32 mm) covered with expanded polytetrafluoroethylene (ePTFE) membrane. Small anchors along the struts fix the device to the left atrial appendage walls.*

The PLAATO obtained the CE approval in 2003 and has been implanted so far in more than 250 patients worldwide. The most important experience is collected in the *ev3* (the company that owns the trademark) registry. The registry collects data from the US (safety and effectiveness primary endpoint) and European Centers (safety and feasibility primary endpoint). The inclusion criteria are AF, at least one major thromboembolic risk factor and the presence of an important contraindication to OAC (not treatable bleeding source, repeated falls, impossibility of maintaining an adequate INR value, psychiatric disorders, serious renal or hepatic disease). Every potential source of embolism outside the LAA has to be excluded and for this reason the presence of relevant aortic or carotid plaques, significant valvular disease (or prosthesis), severely depressed left ventricular function are considered exclusion criteria for PLAATO treatment. Also the presence of LAA thrombosis must be excluded considering the potential embolic risk during implantation. The employment of TEE evaluation is therefore critical in order to perform the procedure.

Before enrollment TEE is necessary to exclude severe aortic disease, to study LAA anatomy, and to evaluate patient probe tolerability.

TEE is the diagnostic modality of choice to visualize the LAA. The study of Veinot et al.[9] defined the morphology of the LAA in 500 normal autopsy specimen hearts. Fifty-four percent of LAAs had two lobes, 23% three-four lobes. Lobes exist in different planes of the heart. Then for an accurate LAA evaluation it is mandatory to obtain a multiplane LAA visualization (0, 45, 90, and 135°), mainly to exclude the presence of thrombosis[9,17,18] and find the best orifice measurement.

During the procedure, TEE may be helpful in locating the fossa ovalis and to assist transseptal puncture, but the most important data to be obtained are the LAA shape and dimensions, that allow, added to fluoroscopic measurement, to choose the proper device size (Fig. 2).

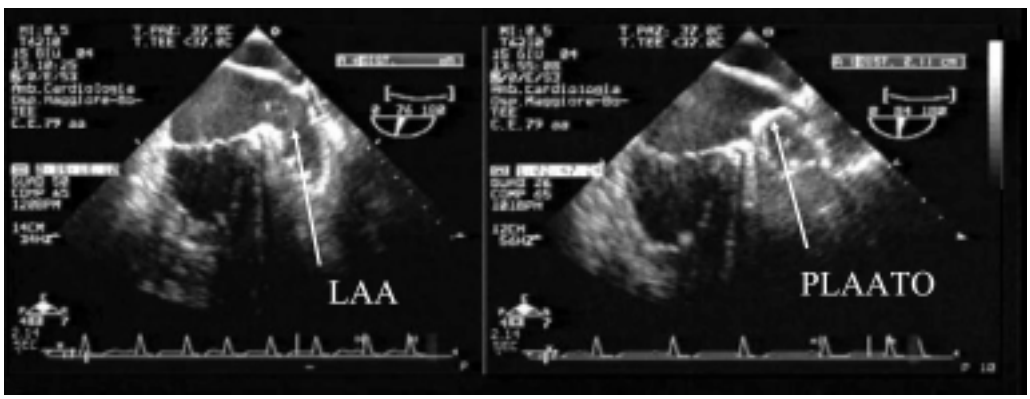

Figure 2. *Transesophageal echocardiographic images, view at about 90°, showing the left atrial appendage (LAA) before, free of every thrombus, and after PLAATO implantation. The appropriate sealing of the LAA is visible.*

Shortly after implantation TEE is necessary again to assess the appropriate device position, to check for relevant leaks and to verify the device wall engagement.

The procedure is performed under local anesthesia with mild sedation, in order to improve probe tolerability (propofol 10-100 mg i.v.). After venous groin access a transseptal procedure is performed under TEE guidance and a transseptal sheath is positioned in the left atrium. In order to optimize the delivery system orientation, the septum should be punctured as inferiorly as possible. Heparin infusion is given to maintain the activated clotting time > 250 s. The transseptal puncture can be performed with a specially designed 14F sheath delivery system or, as an alternative, a conventional transseptal sheath can be employed first and the dedicated system will be inserted using a stiff wire. After advancing the tip of the system into the LAA, dye injection is performed, to exactly measure the ostium diameter (obtained in two angulations: right cranial oblique and antero-posterior) (Fig. 3). Contemporarily TEE is repeated and in order to choose the device size an average of three measurements (right anterior oblique and antero-posterior by fluoroscopy and the best one by TEE) must be obtained.

The device diameter should be about 20-40% larger than the LAA ostium diameter. Then the device is expanded into the LAA ostium. Proximal and distal dye injection (Fig. 4) and little movement under TEE monitoring, allow to verify the good device sealing and engagement in LAA walls.

Only after the complete assessment of its sealing and stability, the PLAATO can be released (Fig. 5). After the definitive release the device cannot be recaptured.

If the tests reveal an incomplete sealing or inadequate engagement, the device must be collapsed and better positioned or, alternatively, retracted inside the system, and replaced with another one of a proper size.

At the moment data on the first 103 patients enrolled (101 treated) are available. Patient characteristics are: average age 71 ± 9 years, median AF duration > 3 years (88% chronic AF, 12% paroxysmal AF), 37% prior stroke.

During implantation or immediately after the procedure 4 cardiac tamponade occurred and one of them was surgically treated. Four cases of pericardial effusion were also observed with only one requiring pericardiocentesis. It is important to underline that this kind of complications are not rare in high-volume catheterization laboratories, and usually they are not associated with permanent damage.

During a 12-month follow-up 3 deaths were documented, none related to the procedure or device implantation, and 2 strokes were verified (2.2%/99.7 patient-year of follow-up). Considering an expected risk of stroke of 4.2% (based on risk score of the population enrolled) it is possible to estimate a risk re-

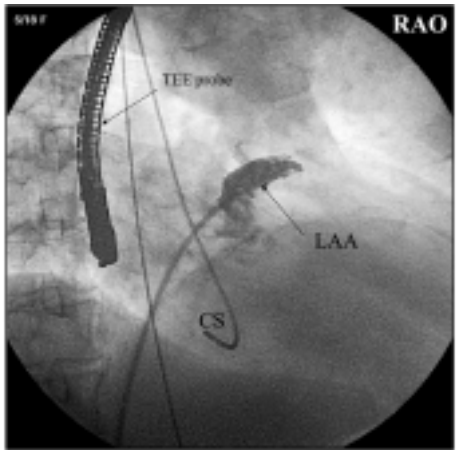

Figure 3. *Fluoroscopic right anterior oblique (RAO) image of left atrial appendage (LAA) angiography. In order to choose the device size an average of three measurements (RAO and antero-posterior angiography and the best one by transesophageal echocardiography-TEE) should be obtained. CS = coronary sinus.*

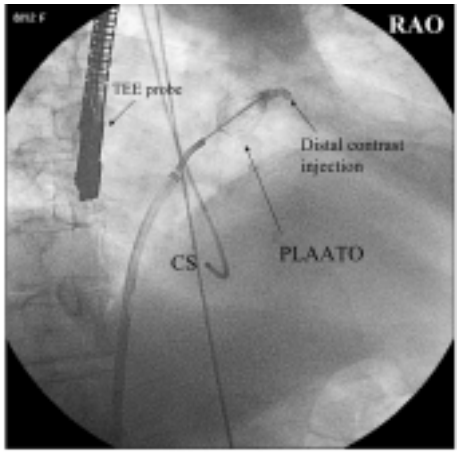

Figure 4. *Fluoroscopic right anterior oblique (RAO) image of dye distal injection after PLAATO implantation. It is clearly visible the absence of leak as the dye is confined beyond the device. This is an objective sign of PLAATO well left atrial appendage sealing. CS = coronary sinus; TEE = transesophageal echocardiography.*

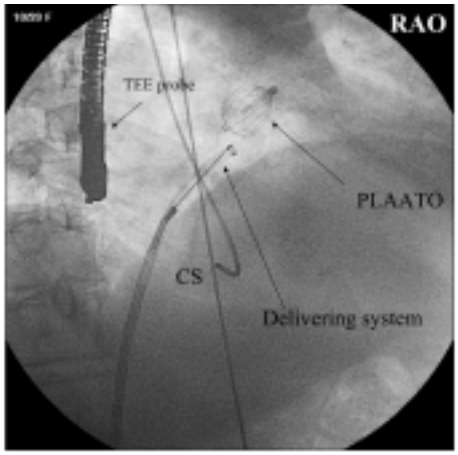

Figure 5. *Fluoroscopic right anterior oblique (RAO) image of PLAATO releasing. It is recognizable the specific delivery system and the device in the left atrial appendage. After this definitive release the device cannot be recaptured. CS = coronary sinus; TEE = transesophageal echocardiography.*

duction of 47.6%. We do not expect an abolishment of stroke recurrence (neither OAC can do it), considering multiple stroke etiology in a so high-risk population.

Data on a 6-month TEE follow-up have been published, and no problems of the device or contiguous structures have been reported[19].

Case report

We present the first 2 patients implanted by PLAATO at our Center. The first case is a 79-year-old man with chronic AF and hypertension. In 2003 he was hospitalized for a transient ischemic attack. In spite of a high thromboembolic risk he did not receive OAC due to the impossibility of reaching stable INR values. On April 2004 he suffered a cerebral hemorrhage, while on antiplatelet therapy, resulting in left-sided paresthesias and walking troubles. Then he was considered a candidate for PLAATO implantation. TEE revealed a spontaneous echocontrast in the left atrium and a large LAA, without thrombosis, but with a flow velocity < 20 cm/s.

The second case is a 75-year-old man, affected by chronic AF, hypertension and diabetes mellitus. In January and March 2004 he presented, during OAC, with two episodes of severe gastrointestinal bleeding requiring blood transfusion. A severe colonic angiodysplasia was diagnosed and, in spite of the thromboembolic risk, OAC therapy was stopped. Subsequently the patient was sent to our Center. TEE showed the absence of LAA thrombus and the PLAATO implantation was planned.

In the first case, after the device expansion, an inadequate sealing was apparent and the device was repositioned too more proximally inside the appendage.

The two procedures were performed in the same day without any complication. The mean procedure time was 80 min and the mean fluoroscopy time 21 min. Two days after the implant the patients were discharged taking clopidogrel and aspirin in one case and clopidogrel only in the other one, because of serious aspirin intolerance.

After 2 and 6 months of follow-up a TEE examination revealed a stable and correct device position, and a partial thrombosis of the distal LAA portion behind the PLAATO was documented. No thrombus was observed on the proximal side of the device. No residual interatrial defect was noted. The patients' clinical conditions were stable and no neurologic complication was documented.

Discussion

So far more than 250 PLAATO implantations have been performed worldwide and available data show the feasibility and safety of the procedure. The related complications decrease as the operator learning curve improves. The procedure requires well trained interventional cardiologists confident with transseptal puncture. The entire procedure must be performed during TEE guidance and it is mandatory that a dedicated operator takes care of this aspect.

There are some concerns in the literature about the PLAATO procedure because randomized trials are lacking[20]. PLAATO feasibility is based on observational studies with a short follow-up. However it seems unlikely that in the future randomized data will be available considering that at present the PLAATO target is only the high-risk AF subset, not suitable for OAC, for which any proved alternative is lacking. In this AF subset at high thromboembolic risk, the annual risk of stroke, without OAC, can be as high as 12% per year[4], and although rarely considered in the big randomized trials, it constitutes a frequent and troubling problem in clinical practice[2].

The evidence supporting the effectiveness of the PLAATO is at least as great as that supporting other invasive procedures like patent foramen ovale closure, that have been performed worldwide without any randomized trials. Only recently comparative data between patent foramen ovale closure and medical therapy have been reported[20]. We think that at the moment it would be extremely important to organize a national registry in order to collect the experience of all the Centers performing PLAATO procedures.

Some criticism has been expressed regarding the antiplatelet therapy[21]. After PLAATO implantation it is recommended, for at least 6 months, a combined antiplatelet therapy (clopidogrel and aspirin), that could be hazardous considering the frequent high risk of bleeding in the PLAATO population. On the other hand it is noteworthy that at present the indication of this treatment is preventive and not curative. Some of the PLAATO patients (as in our experience) are actually taking only one antiplatelet agent. Available data show that there is no thrombus formation at follow-up with the device[19], probably due to complete endothelialization of atrial surface[15], and it is possible that in the future antiplatelet drug use will be not mandatory.

Follow-up data about embolic risk reduction at the moment are really interesting (47.6% relative risk reduction), but it is important to emphasize once again that so far the device should not be considered as an alternative to OAC treatment. The PLAATO indication, in our opinion, has to be confined to high-risk AF patients not suitable for OAC.

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