Percutaneous Left Atrial Appendage Transcatheter Occlusion to Prevent Stroke in High-Risk Patients With Atrial Fibrillation : Early Clinical Experience

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Early Clinical Experience

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Background—Thromboembolism due to atrial fibrillation (AF) is a frequent cause of stroke. More than 90% of thrombi in AF form in the left atrial appendage (LAA). Obliteration of the appendage may prevent embolic complications.

Methods and Results—We evaluated the feasibility and safety of implanting a novel device for percutaneous left atrial appendage transcatheter occlusion (PLAATO). LAA occlusion using the PLAATO system was attempted in 15 patients with chronic AF at high risk for stroke, who are poor candidates for long-term warfarin therapy. The implant consists of a self-expanding nitinol cage covered with a polymeric membrane (ePTFE). The LAA was successfully occluded in 15/15 patients (100%). Angiography and transesophageal echocardiography (TEE) during the procedure showed that the device was well-seated in all patients and that there was no evidence of perforation, device embolization, or interference with surrounding structures. In 1 patient, the first procedure was complicated by a hemopericardium, which occurred during LAA access. A second attempt 30 days later was successful with no untoward sequela. No other complications occurred. At 1-month follow-up, chest fluoroscopy and TEE revealed continued stable implant position with smooth atrial-facing surface and no evidence of thrombus.

Conclusions—Thus, transcatheter closure of the LAA is feasible in humans. This novel implant technology may be appropriate for patients with AF who are not suitable candidates for anticoagulation therapy. Further trials are needed to show the long-term safety and its efficacy in reducing stroke. **(*Circulation*. 2002;105:1887-1889.)**

Key Words: atrial flutter ■ embolism ■ stroke ■ thrombus ■ atrium

Patients with atrial fibrillation (AF) are at high risk of thromboembolic stroke. Anticoagulation treatment with warfarin is effective, but it is difficult to manage in clinical practice. Several echocardiographic, surgical, and postmortem studies have demonstrated that, in nonrheumatic AF, 90% to 100% of the thrombi form in the left atrial appendage (LAA).[1–4] Occluding the LAA may therefore prevent thromboembolism in these patients.

A new device has been developed that allows percutaneous left atrial appendage transcatheter occlusion (PLAATO) via transseptal catheterization. Studies in dogs demonstrated the ability of the device to seal the LAA.[5] We report our initial experience in humans.

Methods

Patient Selection

Patients with nonrheumatic AF and contraindications to long-term warfarin therapy, who were identified as high risk for thromboembolism based on the presence of congestive heart failure, diabetes mellitus, hypertension, history of transient ischemic attack/stroke, or spontaneous echo contrast in the LAA on transesophageal echocardiography (TEE), were recruited into the study.

PLAATO Device and Procedure

The PLAATO system (Appriva Medical), consists of an implant and a delivery catheter. The implant (Figure 1) is a self-expanding nitinol cage (range of diameters from 15 to 32 mm) covered with an occlusive expanded polytetrafluoroethylene (ePTFE) membrane, which is laminated directly to the frame structure so that the perimeter has intimate contact with the inner wall of the appendage. The purpose of the membrane is both to occlude the orifice of the left atrial appendage and to allow tissue incorporation into the device. Small anchors along the struts and passing through the occlusive membrane assist with device anchoring and encourage healing response. The device is delivered through a custom 14Fr transseptal sheath curved to point at the LAA.

All procedures were performed under TEE guidance. After transseptal access, angiography was performed to assess the size and

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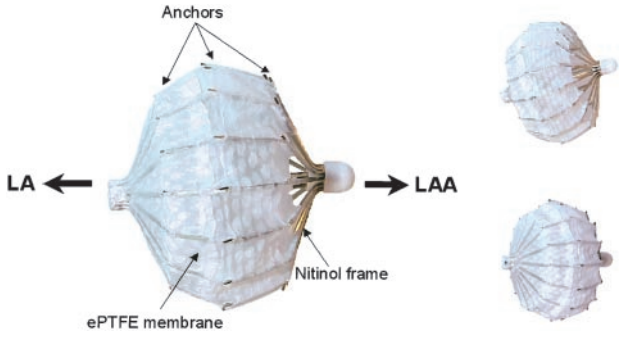

Figure 1. The implant is constructed of a nitinol frame and an implant occlusion membrane consisting of a laminated ePTFE. Small anchors along the frame and passing through the occlusive membrane assist with device anchoring.

shape of the appendage (Figure 2a). An initial device was chosen that had a diameter 20% to 40% larger than the diameter of the LAA ostium. Patients were given heparin (after transseptal puncture) in order to keep activated clotting time (ACT) >250 seconds. The delivery catheter and transseptal sheath were withdrawn, revealing the implant, which was allowed to expand, filling the appendage. Radiocontrast was injected both distal (through a special lumen in the device; Figure 2b) and proximal (ie, in the left atrium [LA]) to assess for leaks and positioning. If sealing was not adequate, the device was collapsed, repositioned, and re-expanded, or completely removed while transseptal access was maintained and replaced with a device of different diameter. Until final release, devices were completely retrievable. Final seal was evaluated via contrast fluoroscopy in the LA once the device had been completely released (Figure 2c).

Follow-Up Evaluation

All patients were placed on aspirin, 300 mg per day indefinitely, and clopidogrel, 75 mg per day for 6 months after the procedure. Patients were assessed with sequential chest fluoroscopy, transthoracic echocardiography, and clinical examination. TEE with color Doppler was performed 1 month after the procedure.

Results

LAA occlusion was attempted in 15 patients (59 to 78, 69±5 years) with chronic AF. The contraindications to warfarin included cerebral hemorrhage in 1, gastrointestinal bleeding in 9, unstable INR in 2, and severe chronic liver disease in 1 patient. Three patients had a thromboembolic event while on warfarin treatment. Risk factors for stroke[6] included older age >75 years in 3, hypertension in 12, diabetes mellitus in 3, and a history of stroke in 2. Abnormalities of the atrial septum and LAA clots were excluded by TEE just before the procedure in all. No patient had significant mitral or aortic valve disease. TEE showed spontaneous echo contrast in the LAA or LA in 4, and LAA emptying velocity <20cm/s in 3.

The LAA was successfully occluded in 15/15 patients. The mean orifice diameter of the LAA was 20.1±4.3 mm and the median size of the final implanted device was 26 mm (range 18 to 32 mm). Mean procedure time from initial groin puncture to removal of all sheaths was 92.7±43.3 minutes.

In 1 patient, the initial procedure was complicated by hemopericardium associated with LAA access before device implantation and diagnosed with intraprocedure TEE. The procedure was halted and pericardiocentesis performed without sequelae. The appendage was successfully occluded 4 weeks later.

The implant was removed and exchanged for a new size in patient Nos. 3, 4, 5, and 8 with no problems. The series of device changes in these 4 patients was 26 to 29 to 18 mm, 29 to 32 mm, 29 to 26 to 23 to 32 mm, and 32 to 32 mm. In 11/15 patients, the first device selected was implanted without need for exchange. At 1-month follow-up in all patients, chest X-ray and TEE revealed stable implant position, no evidence of migration, erosion, or encroachment on surrounding structures, and smooth healing on the LA-facing surface with no thrombi and no remaining atrial shunt after transseptal puncture. There have been no late complications or embolic events during follow-up.

Discussion

AF is responsible for 20% of all strokes.[7–9] Several large trials have demonstrated the efficacy of anticoagulation with warfarin in reducing the annual stroke rate in patients with AF. However, warfarin can be a difficult medication to administer or to take. Its use is associated with an increased risk of major (1% to 2%/year) and minor (5% to 10%/year) hemorrhagic complications.[10] The effectiveness of warfarin is affected by a number of drug and dietary interactions, which can be difficult to manage. Frequent blood tests to monitor INR are required, at some cost and patient inconvenience.

Despite clear guidelines, warfarin is not used or used improperly on a large scale.[11–14] In perhaps the largest and most influential survey, Stafford and Singer[14,15] found that in only about a third of outpatients was anticoagulation used.

There is an extensive literature supporting the notion that the LAA is the source of cardioemboli in over 90% of patients with AF, at least in those without rheumatic valve disease.[1] It is logical therefore to hypothesize that closing or obliterating the LAA would be an effective way to prevent most cardioemboli in patients with AF. Techniques for surgical obliter-

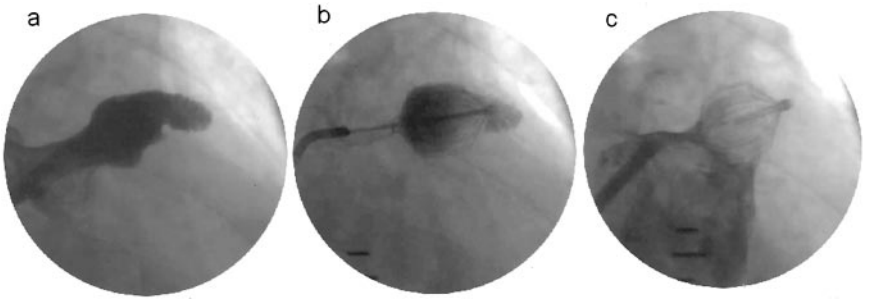

Figure 2. Left atrial angiogram: (a) after transseptal puncture and LAA cannulation, contrast injection outlines LAA from which an ostial diameter can be measured; (b) contrast injection via a lumen through the implant reveals hang up of dye behind the sealing surface, indicating proper position and occlusion; (c) after device release, contrast injection in the LA establishes complete seal.

ation have been described.[16,17] Nonetheless, surgical or thoracoscopic LAA closure, other than as an adjunctive procedure as recommended by ACC guidelines[18] in patients undergoing mitral valve surgery, has not been enthusiastically accepted because of its invasive nature.

PLAATO provides for a less invasive, percutaneous approach to closing the LAA. Previous animal studies of the device with follow-up of up to 1 year have demonstrated occlusion of the LAA with complete healing, absence of erosions, new thrombus formation on the device, or interference with atrial function.[19]

In this initial cohort of 15 patients, occlusion of the LAA was successful in all, as proven by LA angiography. There have been no complications associated with the device, either acutely during the implantation procedure or during follow-up. The only complication during the study was hemopericardium in the first patient attempted, which was not device-related, resulted from LAA access, and should be easily avoided with increased experience. The procedure was successful in a second attempt in this patient.

All patients have done well in follow-up. One theoretical concern is the development of new thrombi on the implant. However, the use of ePTFE on the implant surface results in particularly benign healing.[20] Histological examination in dogs undergoing PLAATO reveal partial endothelialization at 1 month, which is complete by 2 to 3 months. In our patients, TEE at 1 month has shown the surface to be completely smooth and free of mobile thrombi.

Conclusion

This initial study supports the concept that implantation of a mechanical device to occlude the LAA can be done safely and with relative ease. Further studies are needed before PLAATO can be recommended for the large number of patients with AF at risk for stroke. These studies will need to confirm reduction in stroke incidence and longer term safety. The attraction of the procedure, however, resides in its directly addressing the mechanism of stroke in AF and its operational simplicity. It may become a valuable alternative for those patients with chronic nonrheumatic AF in whom standard anticoagulation therapy is contraindicated or poorly tolerated.

Note Added in Proof

Since acceptance of this manuscript, 16 additional patients have been treated. In 1 patient, a hemopericardium occurred during a successful implantation without sequelae. No other complication occurred.

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