Stroke Prevention in Non-valvular Atrial Fibrillation: Long-Term Results after 6 Years of the WATCHMAN Left Atrial Appendage Closure Pilot Study

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Abstract

Background: Patients with non-valvular atrial fibrillation (NVAF) are at enhanced risk of embolic stroke; it has been reported that up to 90% of left atrial thrombus in NVAF patients are found in the left atrial appendage (LAA).

Methods: The WATCHMAN® LAA Closure device (Boston Scientific/Atritech, Plymouth, MN) is made of nitinol, incorporates fixation anchors around its perimeter and has a porous membrane on its atrial surface. A multi-center pilot study was initiated in August 2002. Patients were assessed at 45 days, 6 months and one year with transesophageal echo (TEE) and clinically assessed annually.

Results: Of 75 patients enrolled, the device was implanted successfully in 66. Anatomic limitations in 7, failure of venous access and an earlier generation delivery cable problem resulted in the other 2 unsuccessful implants. Mean follow-up was 67.5 months for all patients and 68.5 months for patients still actively followed. Mean age was 66.5±8 years at enrollment. The acute results have been published previously. After 6 months, 92% had discontinued warfarin therapy and at the present time, 91% remain off warfarin therapy. On routine 6 month TEE follow-up, 4 patients were noted to have a thrombus layer along the atrial face of the implant, one of whom developed a transient ischemic attack (TIA). Warfarin was restarted in those patients for 3 months without further evidence of thrombus. Two patients had an atrial ablation; one at 2 months and one at 39 months in the setting of severe concurrent cardiac disease. These data reflect an actual stroke rate of 0.3% (2 events in 688 patient years); the expected stroke rate, given a mean CHADS2 Score of 1.8±1.1 would have been 5.75%. Fourteen patients have died (mean 47±20 months), of death 45 days, 4 months and 6 years were non-device and non-procedure related.

Conclusions: The data suggest that the WATCHMAN® procedure is safe and feasible, with two embolic strokes through more than 6 years of active follow-up. An 800 patient 2:1 randomized study comparing the WATCHMAN Device to warfarin therapy was completed (PROTECT AF Study) and demonstrated non-inferiority of the WATCHMAN Device to warfarin therapy for the composite endpoint of stroke, systemic embolism and CV death. Additional studies are ongoing comparing the device in the NVAF population.

Introduction

To characterize the rates of ischemic stroke, systemic embolism and major bleeding complications in patients with non-valvular atrial fibrillation (NVAF) who have an indication for anticoagulation therapy due to the CHADS2-Score.

Inclusion criteria:
- Chronic or paroxysmal non-valvular atrial fibrillation
- History of transient ischemic attack with no neurologic residuals
- 45 day anticoagulation with warfarin must be possible

Methods

Device implantation with angiographic and TEE measurements at baseline
- Chest x-ray immediately post implant
- TEE plus chest x-ray at 45 days & 6 months
- Anticoagulation therapy post-procedure warfarin & aspirin 45 days, then adult aspirin only
- Follow-up at 45 days, 6, 12 months and yearly thereafter

Demographics
- First human implant (Germany) – August 22, 2002
- First US implant – October 31, 2003
- 75 patients enrolled,
- 66 implanted patients (anatomic limitations in 7, failure of venous access and delivery catheter problem)
- 368 cumulative implant years
- Includes 56 patients with ≤ 1 year follow-up
- 67 ± 21 months average follow-up

Results

Adverse Events (16)
- 2 device embolizations early in study
- Recaptured percutaneously – patients doing fine
- Device anchors enhanced, no further issues
- 1 delivery system issue
- Requiring surgical intervention
- Delivery system enhanced, no further issues
- 2 pericardial effusions with tamponade
- 3 pericardial effusions without tamponade
- 14 deaths (mean follow up 47±20 months) all non-device related
- 1 Rupture of aortic aneurysm
- 1 Multi-organ failure after bowel operation
- 1 Lung cancer
- 3 Pneumonias/respiratory failure
- 1 Sepsis
- 3 Unknown

Procedural Events (3)
- 2 hematoma requiring transfusion
- 1 air embolism

Safety Endpoints
- 4 patients with thrombus formation at 6 months, one of them with a TIA (Warfarin restarted for 3 months, no further evidence of thrombus)
- 2 embolic strokes (one at 2 months, one at 39 months in setting of severe carotid disease)
- Annual stroke rate 0.5% (2 events in 368 patient years)
- 92% warfarin cessation at 6 months; 91% warfarin cessation at long term follow-up

Conclusions

A device based solution such as the WATCHMAN® may become an alternative to standard anticoagulation therapy.

The annual stroke rate was much lower than the expected stroke rate according to the CHADS2-Score in patients without anticoagulation therapy.

Implantation of second generation devices was demonstrated to be safe. There were no procedure related deaths after implantation and delivery issues were solved.

Antiplaquet therapy should include Clopidogrel up to 6 months to avoid thrombus formation on top of the device after implantation.

An 800 patient 2:1 randomized study comparing the WATCHMAN Device to warfarin therapy was completed (PROTECT AF Study) and demonstrated non-inferiority of the WATCHMAN Device to warfarin therapy for the composite endpoint of stroke, systemic embolism and CV death. Additional studies are ongoing comparing the device in the NVAF population.

Disclosures: Study was sponsored by Boston Scientific/Atritech Company, Minnesota, USA by an unrestricted grant. Personal disclosures are honorary fees for lectures and training courses for the device.