Key Event Rates After 900 Patient-Years in PROTECT AF

	Watchman	Controls	Relative Risk
Hemorrhagic stroke	0.2%	1.9%	–91%
All stroke	2.6%	3.5%	–26%
Primary efficacy end point (all stroke plus cardiovascular death)	3.4%	5.0%	–32%
Primary safety end point (device embolization, pericardial effusion, cranial or other bleeding)	8.7%	4.2%	+102%

Note: Based on data from 707 patients.
Source: Dr. Holmes

Watchman Heart Device Lowers Stroke Risk in Atrial Fibrillation Patients

BY BRUCE JANCIN

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ORLANDO — A left atrial appendage occlusion device called the Watchman strikingly outperformed warfarin in preventing hemorrhagic strokes in patients with atrial fibrillation in a pivotal phase III clinical trial.

On other key efficacy end points, the device showed statistical noninferiority to warfarin through 900 patient-years of follow-up, but with a strong and consistent trend for lower event rates compared with the venerable antithrombotic agent, including a 32% relative risk reduction in the combined primary end point of all forms of stroke and cardiovascular death, Dr. David R. Holmes Jr. reported at the annual meeting of the American College of Cardiology.

Watchman recipients had a 91% relative risk reduction in hemorrhagic stroke, a 26% lower total stroke rate, and 39% lower mortality than did patients who were on warfarin.

The safety analysis showed a twofold greater complication rate in the Watchman group. However, most of these complications consisted of pericardial effusion sustained during implantation.

With the improved training of participating cardiologists, along with a slight modification in device design, the pericardial effusion rate dropped from 6.5% in the trial's early days to just 1.1% at the most recent look, according to Dr. Holmes, professor of medicine at the Mayo Clinic, Rochester, Minn.

Could the still-investigational Watchman herald the dethroning of warfarin as the long-time preferred therapy for stroke prevention in patients with atrial fibrillation (AF)?

Dr. Holmes said he believes so. On the basis of the favorable results that he presented from PROTECT AF (Prospective, Multicenter Randomized Trial of Percutaneous Left Atrial Appendage Occlusion Versus Long-Term Warfarin Therapy in Patients with Nonvalvular Atrial Fibrillation), he sees the Watchman as a safe and effective alternative to the anticoagulant in those patients with nonvalvular AF whose stroke risk score makes them eligible for warfarin therapy.

The Watchman occlusion device is a fabric-covered expandable nitinol cage. It is permanently placed just distal to the ostium of the left atrial appendage in a percutaneous procedure using a transseptal approach. The goal is to seal off the appendage, the source of more than 90% of thrombi in patients with AF.

In PROTECT AF, 707 patients were randomized 2:1 to the device or to long-term warfarin at 59 centers. Watchman recipients stayed on warfarin for the first 45 days while reepithelialization occurred, after which 87% of them were able to permanently discontinue the anticoagulant. In the other 13%, the device didn't completely seal off the appendage, so they remained on warfarin long term.

During 900 patient-years of follow-up, there was a single hemorrhagic stroke in the Watchman group at 15 days post implant, compared with six hemorrhagic strokes—four of them fatal—in the warfarin group. In addition to the 91% relative risk reduction in hemorrhagic stroke, Watchman recipients had a 26% lower total stroke rate and 39% lower mortality than did controls who were on warfarin. (See box.)

It is already well established that warfarin reduces stroke risk in patients with AF by 60%-70% compared with no treatment, and by 30%-40% compared with aspirin, the cardiologist noted.

"I think this is clearly a landmark study," declared discussant Dr. Horst Sievert, director of the cardiovascular center at St. Katharinen Hospital, Frankfurt.

If the Watchman gets the green light from regulatory authorities, though, he sees its initial role in daily practice as being largely confined to patients who can't take warfarin, rather than the sort of subjects enrolled in PROTECT AF.

"Only later, after we see how well this really works, will we place the device in patients who can take warfarin," he predicted.

Another discussant, Dr. A. John Camm of the University of London, noted that several other left atrial appendage occluders are in development.

A limitation shared by all is that other sources of thrombi exist in patients with AF, especially in those with atherosclerotic aortic or carotid disease.

He added that the drug development pipeline holds a host of novel antithrombotic agents that promise to be easier to use and perhaps safer than warfarin.

They are being evaluated in clinical trials that are often 10 times larger than PROTECT AF. And once those are available, a permanent intracardiac device requiring a transseptal approach may lose its luster.

Although a further 4 years of patient follow-up are planned for PROTECT AF, study sponsor Atritech Inc. will present its case for device-marketing approval to a Food and Drug Administration advisory panel in late April.

Dr. Holmes reported having no financial conflicts of interest with regard to the study. ■