Watchman LAA Closure Device in Patients With AF

Written by Toni Rizzo

Vivek Y. Reddy, MD, Mount Sinai Hospital, New York, New York, USA, presented the results from the Watchman Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation trial [PROTECT AF; NCT00129545] that compared the Watchman left atrial appendage (LAA) device with warfarin therapy for patients with atrial fibrillation (AF).

The PROTECT AF trial randomly assigned 707 patients with AF to Watchman implantation (n=463) or warfarin (n=244). The primary efficacy end point was the composite of stroke, systemic embolism, or cardiovascular death. Patients treated with the Watchman device were also treated with warfarin and aspirin for 6 weeks after implant, clopidogrel and aspirin from 6 weeks to 6 months, and aspirin alone after 6 months. Analyses were performed at 600 patient-years and every 150 patient-years thereafter until 1500 patient-years.

After 3.8 years of follow-up, the primary efficacy event rates were 2.3 per 100 patient-years in the Watchman group versus 3.8 in the control group (rate ratio [RR], 0.60; 95% CI, 0.41 to 1.05; noninferiority p>0.999; superiority p=0.960) [Reddy VY et al. HRS 2013 (abstr LBA01-03)]. Table 1 shows the results for the components of the primary efficacy endpoint.

The stroke rates were 1.5 per 100 patient-years in the Watchman group versus 2.2 in the control group (RR, 0.68; 95% CI, 0.42 to 1.37; noninferiority p=0.999; superiority p=0.825). Ischemic strokes were increased in the Watchman group (1.4/patient-year) versus the control group (1.1/patient-year). It appears that the excess strokes were largely procedure related (Figure 1)—thereby confirming that LAA closure has the same benefit in preventing ischemic strokes as systemic oral anticoagulation.

The impact of stroke as measured by Modified Rankin Scores (MRS) was MRS 1.9 in the Watchman group versus 3.6 in the control group (p=0.031). Disabling strokes occurred at 0.5 per 100 patient-years in the Watchman group versus 1.2 per 100 patient-years in the control group.

In a prespecified analysis that analyzed the per-protocol population (which included device patients who stopped warfarin), results were 1.8 per 100 patient-years in the Watchman group versus 3.7 in the control group (RR, 0.50; 95% CI, 0.34 to 0.91; noninferiority p>0.999; superiority

Table 1. PROTECT AF: Components of the Primary Efficacy End Point

	Event Rate (per 100 Patient-Years)			Posterior Probabilities	
	Watchman (n=463)	Control (n=244)	Rate Ratio (95% CI)	Noninferiority	Superiority
Primary efficacy	2.3	3.8	0.60 (0.41, 1.05)	>0.999	0.960
Stroke (all)	1.5	2.2	0.68 (0.42, 1.37)	0.999	0.825
Ischemic	1.4	1.1	1.26 (0.72, 3.28)	0.779	0.147
Hemorrhagic	0.2	1.1	0.15 (0.03, 0.49)	0.999	0.999
Systemic embolization	0.2	0.0	NA	NA	NA
Death (CV and unexplained)	1.0*	2.4	0.40 (023, 0.82)	>0.999	0.995

CV=cardiovascular; NA=not applicable.

*On November 12, 2014, this was changed from 0.1 to 1.0.

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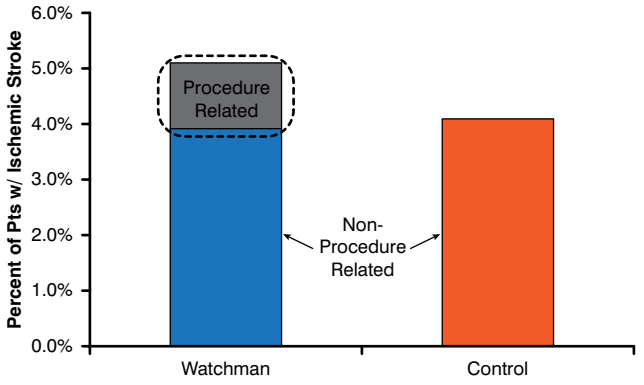
Figure 1. Left Atrial Appendage Closure: Mechanism of Effect



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p=0.990). The rate of events in the post-hoc cohort of patients from the late-therapy analysis (including device patients following the discontinuation of clopidogrel) was 1.8 per 100 patient-years in the Watchman group versus 3.7 in the control group (RR, 0.50; 95% CI, 0.32 to 0.94; noninferiority p>0.999; superiority p=0.985). Intention-to-treat all-cause mortality was significantly lower in the Watchman group versus the control group (HR, 0.66; 95% CI, 0.45 to 0.98; p=0.0379).

The PREVAIL [NCT01182441] trial missed one of two efficacy end points, but it had a small number of events. The CAP registry data confirmed the PROTECT AF data demonstrating the superiority of the Watchman to warfarin. Safety event rates in all three trials were 9.9% in the first half and 4.8% in the second half of PROTECT AF, 4.1% in CAP, and 4.2% in PREVAIL.

Dr. Reddy concluded that interventional therapies for the prevention of stroke for patients with atrial fibrillation such as LAA closure are feasible and may become alternatives to warfarin. Despite the early risk of events in the periprocedural period, the overall safety event rates with the Watchman were similar to those with warfarin.

High Procedural Success With ACP

Written by Toni Rizzo

The Amplatzer cardiac plug (ACP) is a self-expanding device designed to close the orifice of the left atrial appendage (LAA) to prevent clot formation. Reda Ibrahim, MD, University of Montreal, Montreal, Quebec, Canada, presented data from trials and registries of ACP implantation in patients with atrial fibrillation (AF).

A European retrospective, multicenter data analysis of 143 patients scheduled for transcatheter ACP implantation focused on periprocedural technical and safety issues [Park JW et al. *Catheter Cardiovasc Interv* 2011]. ACP implantation was attempted in 137 of the patients and was successful in 132 patients (96.4%). Ten procedural safety events (7%) were reported: stroke (n=3; 2.1%), serious pericardial effusion (n=5; 3.5%), and device embolization (n=2; 1.4%).

An EU prospective observational study with 6-month follow-up enrolled 204 patients with a history of AF [Walsh K et al. EuroPCR 2012]. The ACP was successfully implanted in 197 of the patients (96.6%). The closure rate was 99.5% at implant and 98.9% at 6 months. Residual flow >3 mm was observed in 0.5% of patients at implant and 1.1% at 6 months. At 6 months, the stroke rate was 1.98%, a 65% reduction from the expected stroke rate (based on the $CHADS_2$ score) of 5.6%. Six safety events (2.9%) were reported: serious pericardial effusion (n=3; 1.5%) and device embolization (n=3; 1.5%).

The Canadian registry implanted 52 patients and had a 98.1% procedural success rate. Complications included one embolization, one pericardial effusion, and one in-hospital transient ischemic attack [Urena M et al. *J Am Coll Cardiol* 2013]. At a mean follow-up of 20±5 months, there was a 65% reduction in the expected stroke rate from 8.6% to 1.1% (p<0.001). Thromboembolic events (3.4%) and major bleeding (3.4%) were significantly reduced from expected rates (p<0.001 for both).

A prospective Italian registry reported that in 134 patients with nonvalvular AF at high risk of stroke and bleeding, ACP implantation was successful in 118 patients (88.1%), with major complications in 1.5% [Stolcova M et al. *J Am Coll Cardiol* 2013 (abstr TCT-97)]. At a median follow-up of 22.8 months, stroke was reduced by 82% (p<0.01) and bleeding by 35% from the expected rates.

A multicenter study attempted ACP implantation in 1047 patients [Tzikas A et al. TCT 2013 (abstr)]. The device was successfully implanted in 1019 patients (97.3%).

Major periprocedural complications were death (n=8; 0.76%), pericardial tamponade (n=13; 1.24%), major bleeding (n=13; 1.24%), stroke (n=9; 0.86%), device embolization (n=1; 0.10%), and myocardial infarction (n=1; 0.10%). At 1349 patient-years, stroke was reduced 59% from the expected rate of 5.62% to 2.30%; bleeding was reduced 61% from the expected 5.34% to 2.08%.

A single-center prospective trial of 80 patients with AF compared the Watchman (n=40) and ACP (n=40) devices [Chun KRJ et al. *Heart Rhythm* 2013]. Watchman implantation was successful in 38 patients (95%) compared with successful ACP implantation in all 40 patients (100%).