Left Atrial Appendage Closure and Stroke Prevention

Written by Mary Mosley

Left atrial appendage closure (LAAC) is an alternative to oral anticoagulation (OAC) therapy that can be used to reduce the risk of stroke in patients with nonvalvular atrial fibrillation (NVAF), according to Ramon Quesada, MD, Miami Cardiac and Vascular Institute, Miami, Florida, USA. Evidence reviewed in this session showed that stroke reduction with the Lariat and Watchman devices is at least similar to that with OAC, but no closure device has been approved for use in patients not eligible for OAC. The procedure-related complications are being reduced through increased operator experience and improved design in next-generation devices that are being developed or entering clinical trials.

LAA ANATOMY AND STROKE RISK

A correlation between the morphology of the left atrial appendage (LAA) and the risk of stroke was found in a study of 932 patients with NVAF undergoing catheter ablation [Di Biase L et al. *J Am Coll Cardiol*. 2012]. Using computed tomography or magnetic resonance imaging, the morphologies were categorized as chicken wing in 48% of patients, cactus in 30%, windsock in 19%, and cauliflower in 3%. In the 78 (8%) patients who had experienced a stroke or transient ischemic attack, the least prevalent morphology was chicken wing at 4%, while the prevalence was 12%, 10%, and 18% for the cactus, windsock, and cauliflower morphologies, respectively ($P = .003$).

Compared with the chicken wing, the adjusted stroke risk was 8 times higher with the cauliflower type ($P = .056$), and with the windsock and cactus types it was 4.5 and 4.1 times higher ($P = .038$ and $P = .046$, respectively) in this study. Overall, the stroke rate was 12% for the non–chicken wing types and 4% for the chicken wing type. In patients with a $CHADS_2$ score of 0 or 1, the risk of a history of stroke was higher with the non–chicken wing types (OR, 10.1; 95% CI, 1.25 to 79.7; $P = .019$).

EVIDENCE FOR THE LARIAT AND WATCHMAN DEVICES

The 5 nonrandomized clinical studies that comprise the evidence base for the Lariat device were primarily feasibility studies or single-operator experiences that showed the device provided complete LAAC with complication rates for death, stroke, and major bleeding that were considered acceptably low, stated Steven J. Yakubov, MD, OhioHealth Research Foundation, Columbus, Ohio, USA. The largest of these studies was conducted by Sievert and colleagues in 143 patients with NVAF ineligible for OAC, which is the most common subgroup. The mean age was 67.4 years, the $CHADS_2$ score was 2.4, and the HAS-BLED score was 2.8. The device was not implanted in 4 patients because of pericardial adhesions, which is the most frequent reason across studies. Postprocedure therapy varied, with some patients receiving no antiplatelet therapy while others received aspirin with or without clopidogrel. Patients treated with the Lariat had an annual event rate of 1.3% for stroke and systemic embolism and 3.3% for combined stroke, systemic embolism, and death over 300 patient-years of follow-up.

The annual stroke event rate in the Sievert study was comparable with the annual stroke rate seen with the non–vitamin K antagonist oral anticoagulants (NOACs), stated Dr Yakubov. In the ARISTOTLE study, it was 1.27% and 1.6% with apixaban and warfarin, respectively [Granger CB et al. *N Engl J Med*. 2011], and it was 1.6% and 3.7% with apixaban and aspirin, respectively, in the AVERROES study [Connolly SJ et al. *N Engl J Med*. 2011].

The bleeding rates with the Lariat procedure were considerable, stated Dr Yakubov. One study showed that major bleeding (BARC ≥3A) occurred in 14 (9.1%) of 154 patients [Price MJ et al. *J Am Coll Cardiol*. 2014]. Seven (4.5%) patients required a transfusion, which was higher than with the Watchman device.

A comparison of the Lariat and Watchman devices showed that the rate of periprocedural complications was fairly low in experienced hands, but tamponade was more frequent with the Lariat (4 of 259 patients vs none with the Watchman) [Pillarisetti J et al. *Heart Rhythm*. 2015]. However,

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Table 1. PROTECT AF: Outcomes at 4 Years

Event	Device Group (n = 463)		Warfarin Group (n = 244)		Device/ Warfarin Rate Ratio (95% Credible Interval)	Posterior Probabilities, %	
	Events/ Patient-Years	Observed Rate[a]	Events/ Patient-Years	Observed Rate[a]		Noninferiority	Superiority
Primary efficacy end point[b]	39/1720.2	2.3 (1.7-3.2)	34/900.8	3.8 (2.5-4.9)	0.60 (0.41-1.05)	>99	96
Stroke	26/1720.7	1.5 (1.0-2.2)	20/900.9	2.2 (1.3-3.1)	0.68 (0.42-1.37)	>99	83
Ischemic	24/1720.8	1.4 (0.9-2.1)	10/904.2	1.1 (0.5-1.7)	1.26 (0.72-3.28)	78	15
Hemorrhagic	3/1774.2	0.2 (0.0-0.4)	10/916.2	1.1 (0.5-1.8)	0.15 (0.03-0.49)	>99	99
Disabling[c]	8/1771.3	0.5 (0.2-0.8)	11/912.7	1.2 (0.6-1.9)	0.37 (0.15-1.00)	>99	98
Nondisabling[c]	18/1723.7	1.0 (0.7-1.7)	9/907.7	1.0 (0.4-1.7)	1.05 (0.54-2.80)	89	34
Systemic embolization	3/1773.6	0.2 (0.0-0.4)	0/919.5	0	NA		
Cardiovascular or unexplained death	17/1774.3	1.0 (0.6-1.5)	22/919.4	2.4 (1.4-3.4)	0.40 (0.23-0.82)	>99	99
Primary safety end point[d]	60/1666.2	3.6 (2.8-4.6)	27/878.2	3.1 (2.0-4.3)	1.17 (0.78-1.95)	98	20

Abbreviation: NA, not applicable.

[a]Events per 100 patient-years (95% credible interval).

[b]Primary efficacy defined as composite of stroke, systemic embolization, or cardiovascular/unexplained death.

[c]Disabling or fatal strokes were those with a Modified Rankin Score of 3-6 after the stroke. Nondisabling strokes were those with Modified Rankin Scores of 0-2 after the stroke.

[d]Safety defined as procedure-related events (pericardial effusion requiring intervention or prolonged hospitalization, procedure-related stroke, or device embolization) and major bleeding (intracranial or bleeding requiring transfusion).

the micropuncture technique for pericardial access for the Lariat device appears to reduce the incidence of tamponade.

A recent systematic review highlighted the risk of adverse events with off-label use of the Lariat device and there was a lack of randomized data despite the approval of the device for use in clinical practice [Chatterjee S et al. *JAMA Intern Med*. 2015]. Dr Yakubov stated that device improvements and improved operator experience will make the procedure safer and more effective, so it is still early to determine which device is the best tool for LAAC.

DATA REVIEW OF THE WATCHMAN DEVICE

Zoltan G. Turi, MD, Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey, USA, reviewed data for the Watchman device from the randomized PROTECT AF [Holmes DR et al. *Lancet*. 2009] and PREVAIL [Holmes DR Jr et al. *J Am Coll Cardiol*. 2014] studies.

PROTECT AF showed that Watchman was noninferior to warfarin (Table 1) for the primary efficacy outcome of combined stroke, cardiovascular death, and systemic embolism over the 4-year follow-up. The primary safety outcome of major bleeding, pericardial effusion, and device embolization was higher with the Watchman device than the control initially although the difference narrowed with time; there was a significant learning curve in the early period, stated Dr Turi. The 707 patients had NVAF, and their mean age was 72 years and their mean $CHADS_2$ score was 2.2. The 4-year follow-up data from PROTECT AF showed that the rates of disabling stroke and cardiovascular death were lower with Watchman than with warfarin, but they were similar for ischemic stroke (Table 1) [Reddy VY et al. *JAMA*. 2014].

The PREVAIL study of 407 patients with a $CHADS_2$ score of 2.6 failed to show noninferiority of the Watchman to warfarin for either primary efficacy outcomes of stroke, systemic embolism, and cardiovascular or unexplained death at 18 months (0.064 and 0.063 event rate, respectively), or the late primary efficacy outcomes occurring >7 days after procedure (risk difference 0.0053). The primary safety outcome met its criteria for success, with an event rate of 2.2% at 7 days in the Watchman group. The ischemic stroke rate was 2.7% with Watchman and 1.0% with warfarin, but the Watchman data matched the expected rate for this population, stated Dr Turi.

In conclusion, it is anticipated that refinements in the next generation of LAAC devices will provide better reductions in stroke and clinical event rates in patients with NVAF with a better overall safety profile. Long-term outcomes with the devices are needed, along with comparisons between devices and with NOACs, and a determination of the economic benefits.