Dr. Vespa noted that endoscopic surgery for ICH is safe (eg, lower mortality at all time points compared with medical treatment), results in an immediate 70% reduction in ICH volume, and conveys a 15% advantage for a good clinical outcome (mRS score ≤3) after 180 days. Despite some variability in surgical technique—particularly with respect to suction, the procedure is generalizable and reproducible across multiple centers and surgeons.

The EMBRACE Trial: Prolonged Ambulatory Cardiac Monitoring Improves the Detection and Treatment of Atrial Fibrillation in Patients With Cryptogenic Stroke

Written by **Phil Vinall**

Data from the 30-Day Cardiac Event Monitor Belt for Recording Atrial Fibrillation After a Cerebral Ischemic Event trial [EMBRACE; NCT00846924] presented by David J. Gladstone, MD, PhD, University of Toronto, Toronto, Ontario, Canada, showed that prolonged continuous cardiac monitoring to detect poststroke paroxysmal atrial fibrillation (AF) in patients with unexplained strokes is feasible, more effective than standard approaches, and leads to clinically meaningful changes in patient management.

Identification and treatment of AF can prevent second strokes; however, paroxysmal AF can be difficult to detect in patients with stroke or transient ischemic attack (TIA), and the most common screening method, 24-hour Holter monitoring, has a low sensitivity (~5%) for detecting it post stroke. Small observational studies have suggested benefits of longer duration electrocardiogram (ECG) monitoring [Stahrenberg R et al. *Stroke* 2010; Sobocinski PD et al. *Europace* 2012; Flint AC et al. *Stroke* 2012]. The objective of the EMBRACE study, funded by the Canadian Stroke Network, was to determine the diagnostic yield of 30 days of home-based cardiac monitoring compared with repeat 24-hour Holter monitoring for detecting paroxysmal AF in patients with a recent diagnosis of cryptogenic ischemic stroke or TIA following a routine diagnostic stroke workup that included a negative Holter monitor. Secondary outcomes included monitoring adherence and anticoagulation status.

To be eligible for the study, patients had to be aged ≥55 years without previously documented AF, with a recent (≤6 months) diagnosis of a presumed embolic acute arterial ischemic stroke (confirmed by neuroimaging) or TIA of etiology (or suspected cardioembolic etiology but without proven AF). Subjects were required to have negative results on baseline tests that included ECG, Holter monitor, vascular imaging with computed tomography angiography or magnetic resonance angiography, and echocardiography. The primary study outcome was detection of ≥1 episode of AF or atrial flutter of ≥30 seconds within 90 days of randomization, confirmed by central adjudication. The study included 572 subjects (mean age, 73 years; ~45% women). Sixty-three percent of the subjects had an ischemic stroke and 37% had a TIA. Baseline anticoagulant use was 5%. Over 90% of participants had a modified Rankin score of 0 to 2, indicating functional independence. Subjects were randomly assigned to repeat 24-hour Holter monitoring (n=285) or 30-day cardiac monitoring (n=287). In the 30-day group, subjects wore an event-triggered loop recorder (attached to a nonadhesive chest electrode belt) that was programmed to automatically record AF. They were instructed to wear this recorder for as much of the day as possible for up to 30 days or until AF was detected. The median number of days from the index event to randomization was about 70 (range, 45 to 103).

New AF was detected in significantly more patients in the 30-day group (16%) compared with the repeat Holter group (3%; p<0.001; Table 1). In the 30-day group, 82% of all participants wore their monitor for ≥3 weeks. Most AF events were captured within the first 2 weeks, with an incremental yield up to 30 days (Figure 1). Most patients with newly detected AF (72%) were placed on anticoagulants. Anticoagulant use increased by 90 days and was significantly greater in the 30-day group (18%) compared with the repeat Holter group (10%; p=0.01; Table 2).

Figure 1. Time to First Atrial Fibrillation Detection

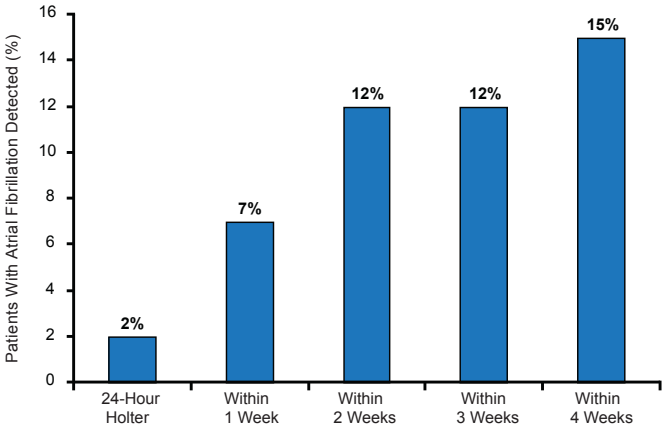

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Table 1. Between-Group Comparison of Atrial Fibrillation Detection

	Repeat Holter (n=285)	30-Day Monitor (n=287)	p Value	Absolute Detection Difference (95% CI)	NNS
Primary Outcome					
AF ≥30 seconds (within 90 days)	3%	16%	<0.001	13% (9%, 18%)	8
AF ≥30 seconds (study monitors only)	2%	15%	<0.001	13% (9%, 18%)	8
Secondary Outcomes					
AF ≥2.5 minutes	2%	10%	<0.001	8% (4%, 12%)	13
Any AF	4%	20%	<0.001	16% (10%, 21%)	6

AF=atrial fibrillation; NNS=number needed to screen.

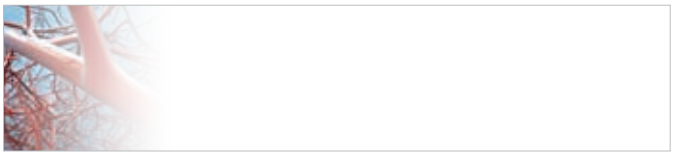
The absolute difference in AF detection between the 30-day and the repeat Holter groups was 13%, which translates into a number needed to screen of 8 patients (to identify one additional patient with AF). The prevalence of AF detected was similar whether the index event was an ischemic stroke or TIA; the yield was highest among patients aged >75 years.

Table 2. Anticoagulant Use

	Repeat Holter (n=285)	30-Day Monitor (n=287)	p Value	Absolute Treatment Difference (95% CI)
At index event	1%	1%		
At randomization	6%	5%		
At 90 days	10%	18%	0.01	8% (2%, 13%)
Switched from AP to AC	5%	13%	0.001	8% (3%, 13%)
Switched from AC to AP	1%	1%	0.997	0 (–2%, 2%)

AC=anticoagulant; AP=antiplatelet.

Dr. Gladstone noted that this study indicates that a substantial proportion of cryptogenic stroke or TIA patients have undiagnosed paroxysmal AF (1 in 6 patients aged ≥55 years; 1 in 5 patients aged >75 years), and it provides the strongest evidence to-date in support of prolonged cardiac monitoring in such patients. The findings of this trial have immediate implications for secondary stroke prevention.



DP-b99 Does Not Improve Recovery Following Acute Ischemic Stroke

Written by Phil Vinall

Despite encouraging preclinical and Phase 2 trial results [Angel I et al. *Drug Dev Res* 2002; Striem S et al. *Neural Plast* 2003; Rosenberg G et al. *Stroke* 2004; Diener HC et al. *Stroke* 2008; Barkalifa R et al. *Eur J Pharmacol* 2009], data presented by Kennedy R. Lees, MD, University of Glasgow, Glasgow, United Kingdom, showed that DP-b99, a lipophilic moderate-affinity chelator of zinc, did not improve outcome in patients with acute hemispheric ischemic stroke [Lees KR et al. *Stroke* 2013].

DP-b99 is a membrane-activated metal ion chelator that chelates ions such as zinc, a mineral that has been associated with cell signaling as well as some deleterious processes in ischemia. The rationale for the use of DP-b99 in ischemic stroke is that by chelating the zinc in the region of the membrane, there will be an improvement in ischemic damage. Although a small-scale Phase 2b study comparing DP-b99 with placebo in patients with acute ischemic stroke failed to reach its primary endpoint, its results suggested that patients with National Institutes of Health Stroke Scale (NIHSS) scores of 10 to 16 might realize some benefit from treatment with DP-b99 [Diener HC et al. *Stroke* 2008].

The Efficacy and Safety Study of DP-b99 in Treating Acute Ischemic Stroke trial [MACSI] was a Phase 3 study conducted to determine if intravenous administration of DP-b99 up to 9 hours following stroke onset and then for 3 additional days is effective in improving long-term outcomes. Patients with ischemic stroke untreated by tissue plasminogen activator (tPA), with a baseline NIHSS score of 10 to 16 and evidence of language dysfunction, visual field defect, and/or neglect were eligible. The primary study outcome was functional status measured by modified Rankin Scale (mRS) score at 90 days in the intention-to-treat population of patients with any post-treatment outcome, adjusted for initial severity. Functional and neurological recovery were secondary measures. Home time was an exploratory endpoint [Lees KR et al. *Stroke* 2013]. Planned follow-up was 3 months.

Enrollment was terminated at 446 patients after the planned interim analysis determined futility, but follow-up continued. On the primary endpoint, the mRS distributions were similar between the DP-b99 and placebo groups (p=0.10). Fewer patients in the DP-b99-treated group achieved mRS ≤1 (20.6%) compared with placebo (28.8%; p=0.05). Fewer patients in the DP-b99 group also attained NIHSS ≤1 (19.3% vs 25.6% with placebo; p=0.10; adjusted p=0.26). Mortality was similar between the DP-b99 and placebo groups (16.5% vs 15.1%, respectively; p=0.68). Home time was unchanged by treatment [Lees KR et al. *Stroke* 2013]. The outcomes were the same for all subgroups analyzed.