

Recent Landmark Trials in Cardiology Newer Evidence in Atrial Fibrillation Management

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Atrial Fibrillation (AF) is associated with increased risk for stroke and reduced survival. Novel oral anticoagulants have emerged as a promising treatment modality and have appeared safer and even more efficacious than warfarin. A recent trial has challenged the practice of bridging anticoagulation in patients of AF without prosthetic valves who go for elective procedures. At the same time metaanalysis of LA appendage closure device has shown it be noninferior to warfarin and safer in patients at risk for bleed with anticoagulation. Another trial has discussed the role of surgical ablation at time of mitral valve surgery

Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation.

James D. Douketis, Alex C. Spyropoulos, Scott Kaatz, et al. N Engl J Med 2015;373:823-33.

Bridging Anticoagulation in Patients who Require Temporary Interruption of Warfarin Therapy for an Elective Invasive Procedure or Surgery (BRIDGE) trial

For patients with atrial fibrillation who are receiving warfarin and require an elective operation or other invasive procedure, the need for bridging anticoagulation during perioperative interruption of warfarin treatment has been uncertain. The authors hypothesized that forgoing bridging anticoagulation would be noninferior to bridging with low- molecular weight heparin (LMWH) for the prevention of perioperative arterial thromboembolism and would be superior to bridging with respect to major bleeding.

It was a double blind, placebo controlled trial in which 1884 patients were randomized to receive bridging

anticoagulation therapy with LMWH (100 IU of dalteparin per kilogram of body weight) or matching placebo administered subcutaneously twice daily, from 3 days before the procedure until 24 hours before the procedure and then for 5 to 10 days after the procedure. Warfarin treatment was stopped 5 days before the procedure and was resumed within 24 hours after the procedure. Follow-up of patients continued for 30 days after the procedure. The primary outcomes were arterial thromboembolism (stroke, transient ischemic attack, systemic embolism) and major bleeding.

Patients were eligible to participate in the trial if they were ≥ 18 years of age; had chronic (permanent or paroxysmal) atrial fibrillation or flutter (patients with atrial fibrillation associated with valvular disease were eligible); had received warfarin therapy for 3 months or longer, with an international normalized ratio (INR) therapeutic range of 2.0 to 3.0; and had at least one of the following CHADS2 stroke risk factors: congestive heart failure or left ventricular dysfunction, hypertension, age of 75 years or older, diabetes mellitus, or previous ischemic stroke, systemic embolism, or transient ischemic attack. Patients were not eligible if they had one or more of the following: a mechanical heart valve; stroke, systemic embolism, or transient ischemic attack within the previous 12 weeks; major bleeding within the previous 6 weeks; creatinine clearance of less than 30 ml/minute; platelet count < 100000 per cubic millimeter; or planned cardiac, intracranial, or intraspinal surgery.

About 950 patients were assigned to receive no bridging therapy and 934 assigned to receive bridging therapy. The incidence of arterial thromboembolism was 0.4% in the no-bridging group and 0.3% in the bridging group ($P = 0.01$ for noninferiority). The incidence of major bleeding was 1.3% in the no-bridging group and 3.2% in the bridging group (relative risk, 0.41; 95% CI, 0.20 to 0.78; $P = 0.005$ for superiority).

Perspective

In patients with atrial fibrillation who had interruption

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of warfarin treatment for an elective operation or other elective invasive procedure, forgoing bridging anticoagulation was noninferior to perioperative bridging with LMWH for the prevention of arterial thromboembolism and decreased the risk of major bleeding.

Left Atrial Appendage Closure as an Alternative to Warfarin for Stroke Prevention in Atrial Fibrillation: A Patient Level Meta-Analysis

David R. Holmes, Shephal K. Doshi, Saibal Kar et al. J Am Coll Cardiol 2015;65:2614–23

Left atrial appendage closure (LAAC) is an alternative to systemic oral anticoagulation in selected patients with high-risk nonvalvular atrial fibrillation (NVAF) for stroke prevention. The risk-benefit ratio of LAAC versus systemic therapy (warfarin) for prevention of stroke, systemic embolism, and cardiovascular death in NVAF requires continued evaluation. This meta-analysis included 2,406 patients with 5,931 patient-years (PY) of follow-up from the PROTECT AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation) and PREVAIL (Prospective Randomized Evaluation of the Watchman LAA Closure Device In Patients With Atrial Fibrillation Versus Long Term Warfarin Therapy) trials, and their respective registries (Continued Access to PROTECT AF registry and Continued Access to PREVAIL registry).

With mean follow-up of 2.69 years, patients receiving LAAC with the Watchman device had significantly fewer hemorrhagic strokes (0.15 vs. 0.96 events/100 patient-years [PY]; hazard ratio [HR]: 0.22; $P = 0.004$), cardiovascular/unexplained death (1.1 vs. 2.3 events/100 PY; HR: 0.48; $P = 0.006$), and nonprocedural bleeding (6.0% vs. 11.3%; HR: .51; $P = 0.006$) compared with warfarin. All-cause stroke or systemic embolism was similar between both strategies (1.75 vs. 1.87 events/100 PY; HR: 1.02; 95% CI: 0.62 to 1.7; $P = 0.94$). There were more ischemic strokes in the device group (1.6 vs. 0.9 and 0.2 vs. 1.0 events/100 PY; HR: 1.95 and 0.22, respectively; $P = 0.05$ and 0.004, respectively).

Both trials and registries identified similar event rates and consistent device effect in multiple subsets.

Perspective

In patients with NVAF at increased risk for stroke or bleeding who are candidates for chronic anticoagulation,

LAAC resulted in improved rates of hemorrhagic stroke, cardiovascular/unexplained death, and nonprocedural bleeding compared to warfarin.

Surgical Ablation of Atrial Fibrillation during Mitral-Valve Surgery

A. Marc Gillinov, Annetine C. Gelijns, Michael K. Parides et al. N Engl J Med 2015;372:1399-409.

Atrial Fibrillation is present in 30-50% of patients presenting with mitral valve surgery and is associated with decreased survival and increased risk of stroke. Surgical ablation of atrial fibrillation is being increasingly used, but evidence regarding its safety and effectiveness is limited.

260 patients with persistent or long-standing persistent atrial fibrillation who required mitral-valve surgery were randomly assigned to undergo either surgical ablation (ablation group) or no ablation (control group) during the mitral-valve operation. Patients in the ablation group underwent further randomization to pulmonary vein isolation or a biatrial maze procedure. All patients underwent closure of the left atrial appendage. The primary end point was freedom from atrial fibrillation at both 6 months and 12 months

More patients in the ablation group than in the control group were free from atrial fibrillation at both 6 and 12 months (63.2% vs. 29.4%, $P < 0.001$). There was no significant difference in the rate of freedom from atrial fibrillation between patients who underwent pulmonary-vein isolation and those who underwent the biatrial maze procedure (61.0% and 66.0%, respectively; $P = 0.60$). One-year mortality was 6.8% in the ablation group and 8.7% in the control group (hazard ratio with ablation, 0.76; 95% confidence interval, 0.32 to 1.84; $P = 0.55$). Ablation was associated with more implantations of a permanent pacemaker than was no ablation (21.5 vs. 8.1 per 100 patient-years, $P = 0.01$). There were no significant differences in major cardiac or cerebrovascular adverse events, overall serious adverse events, or hospital readmissions.

Perspective

The addition of atrial fibrillation ablation to mitral-valve surgery significantly increased the rate of freedom from atrial fibrillation at 1 year among patients with persistent or long-standing persistent atrial fibrillation, but the risk of implantation of a permanent pacemaker was also increased.