Continued Warfarin Better Than Heparin Bridging During Device Implantation

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David Birnie, MD, University of Ottawa Heart Institute, Ottawa, Ontario, Canada, presented data from the Bridge or Continue Coumadin for Device Surgery Randomized Controlled Trial [BRUISE CONTROL; Birnie D et al. *N Engl J Med* 2013].

Importantly, up to 35% of patients that undergo arrhythmic device implantation also require chronic anticoagulant treatment. Current clinical practice guidelines recommend discontinuing warfarin treatment prior to surgery and treating patients with low-molecular-weight heparin (LMWH) [Douketis JD et al. *Chest* 2012]. The BRUISE CONTROL trial tested the hypothesis that continued treatment with warfarin would reduce the number of device-pocket hematomas without increasing the risk of major perioperative bleeding events, as compared with bridging with LMWH [Birnie D et al. *N Engl J Med* 2013].

In the international Phase 4, multicenter, single-blind, randomized controlled BRUISE CONTROL trial, 681 patients were randomized to continue warfarin or discontinue warfarin and receive LMWH or intravenous heparin [Birnie D et al. *N Engl J Med* 2013]. Patients were eligible if they had a ≥5% annual risk of thromboembolism or were treated with warfarin, and required device implantation. In patients continuing warfarin, the target international normalized ratio (INR) was ≤3.0, or ≤3.5 in patients with mechanical valves. In patients receiving LMWH or heparin, warfarin was discontinued 5 days prior to surgery and LMWH or heparin was administered 3 days prior to surgery; LMWH or heparin was readministered 24 hours after surgery until therapeutic INR was reached.

At the second interim analysis, the data and safety monitoring board recommended halting the BRUISE CONTROL trial early [Birnie D et al. *N Engl J Med* 2013]. Therefore, data from 681 patients were analyzed for the primary outcome of the presence of a clinically significant hematoma within the device pocket that resulted in repeated surgery, prolonged hospitalization, and/or interruption of all anticoagulation for longer than 24 hours. Embolic events and patients' satisfaction were key secondary endpoints.

In the continued warfarin arm, 3.5% of patients experienced a clinically significant hematoma, as compared with 16% of the heparin-bridging arm ($p<0.001$), resulting in a relative risk ratio of 0.19 (95% CI, 0.10 to 0.36) [Birnie D et al. *N Engl J Med* 2013]. Embolic events were reported in two patients in the continued warfarin arm, as compared with no patients in the heparin-bridging arm. In addition, patients that continued warfarin reported greater satisfaction with their anticoagulation management than patients receiving LMWH or heparin ($p<0.001$).

In patients that continued warfarin during surgery, 0.6% developed device system infections, as compared with 1.8% of patients receiving LMWH or heparin ($p=0.17$) [Birnie D et al. *N Engl J Med* 2013]. In all cases, complete system extraction was required. In addition, one patient in the heparin-bridging arm experienced cardiac tamponade that required pericardiocentesis.

In Dr. Birnie's opinion, based on the data from the BRUISE CONTROL trial, continuing patients with warfarin therapy is preferable over bridging with heparin for device implantation. In addition, he also noted that other factors such as pressure dressings and sandbags did not appear to contribute to a reduction in device-pocket hematoma.

"To many, the substantial reduction in pocket hematoma that we observed with continued warfarin may be counterintuitive," said Dr. Birnie. "One explanation that has been proposed is the concept of an 'anticoagulant stress test.' That is, if patients undergo surgery while fully anticoagulated, any excessive bleeding will be detectable and appropriately managed while the wound is still open. In contrast, when surgery is performed with heparin bridging, such bleeding may remain latent, and appear only when full anticoagulation is resumed postoperatively," he concluded.

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