Continuation of warfarin during pacemaker or implantable cardioverter-defibrillator implantation: A randomized clinical trial

Alan Cheng, MD, Saman Nazarian, MD, Jeffrey A. Brinker, MD, Christine Tompkins, MD, MS, David D. Spragg, MD, Charles T. Leng, MD, Henry Halperin, MD, MA, Harikrishna Tandri, MD, Sunil K. Sinha, MD, Joseph E. Marine, MD, FHRS, Hugh Calkins, MD, FHRS, Gordon F. Tomaselli, MD, FHRS, Ronald D. Berger, MD, PhD, FHRS, Charles A. Henrikson, MD, MPH

From the Section of Cardiac Electrophysiology, Division of Cardiology, Johns Hopkins Medical Institutes, Baltimore, Maryland.

BACKGROUND Management of oral anticoagulation in patients undergoing pacemaker (PPM) or implantable cardioverter-defibrillator (ICD) implantation remains controversial. Prior studies demonstrate that continuation of warfarin may be safer when compared with strategies requiring interruption and/or heparin bridging. Limited data from randomized trials exist.

OBJECTIVE We conducted a randomized trial to determine whether warfarin continuation is superior to warfarin interruption during PPM or ICD implantation.

METHODS Patients on oral anticoagulation referred for PPM or ICD implantation were randomized to warfarin continuation versus interruption. Patients randomized to warfarin interruption were further stratified into two groups based on their risk for thromboembolic events in the absence of warfarin. Moderate-risk patients were randomized to warfarin continuation versus warfarin interruption. High-risk patients were randomized to warfarin continuation versus warfarin interruption with heparin bridging. The primary combined outcome included thromboembolic events, anticoagulant-related complications, or any significant bleeding necessitating additional intervention or discontinuation of anticoagulation.

RESULTS We studied 100 patients (average age 70.8 years, 21% female, mean body mass index 28.4) who underwent 64 ICD and 36 PPM implantations. Fifty patients were assigned to continue warfarin. The randomized groups were well matched. Among patients randomized to warfarin interruption, there were two pocket hematomas, one pericardial effusion, one transient ischemic attack, and one patient who developed heparin-induced thrombocytopenia. No events were noted among patients continuing warfarin ($P = .056$).

CONCLUSIONS While the results were not statistically significant, there was a trend toward reduced complications in patients randomized to warfarin continuation. This strategy should be considered in patients undergoing PPM or ICD implantation.

KEYWORDS ICD; Pacemaker; Anticoagulation; Heparin; Warfarin; Bleeding; Stroke

ABBREVIATIONS **ICD** = implantable cardioverter-defibrillator; **INR** = international normalized ratio; **PPM** = permanent pacemaker; **TIA** = transient ischemic attack

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Introduction

Among patients undergoing pacemaker (PPM) or implantable cardioverter-defibrillator (ICD) implantation, approximately 12.4%–45% are on anticoagulation therapy.[1,2] Given the low risk of thromboembolism with short-term warfarin interruption[3] and the concern for increased bleeding while anticoagulated, current guidelines suggest discontinuation of warfarin with and without heparin bridging in the periprocedural period.[4] While this strategy may be appropriate in cases involving major surgery, this may not be applicable in device-based procedures where implantations typically occur above the pectoral fascia. In fact, significant hematomas have been shown to occur in approximately 30% of patients managed with heparin bridging in these settings.[1,5]

Previous studies have demonstrated that continuation of warfarin in the periprocedural period may be safe.[6–8] While the management of warfarin before device implantation varies widely, especially in individuals at high risk for embolic events,[9,10] more recent reports have shown that warfarin discontinuation with heparin bridging is associated with more significant bleeding events.[11,12] These data, coupled with prior systematic reviews,[13] suggest that warfarin continuation may be superior to warfarin interruption. Unfortunately, no randomized data demonstrating that warfarin continuation is superior to warfarin discontinuation exist.[14]

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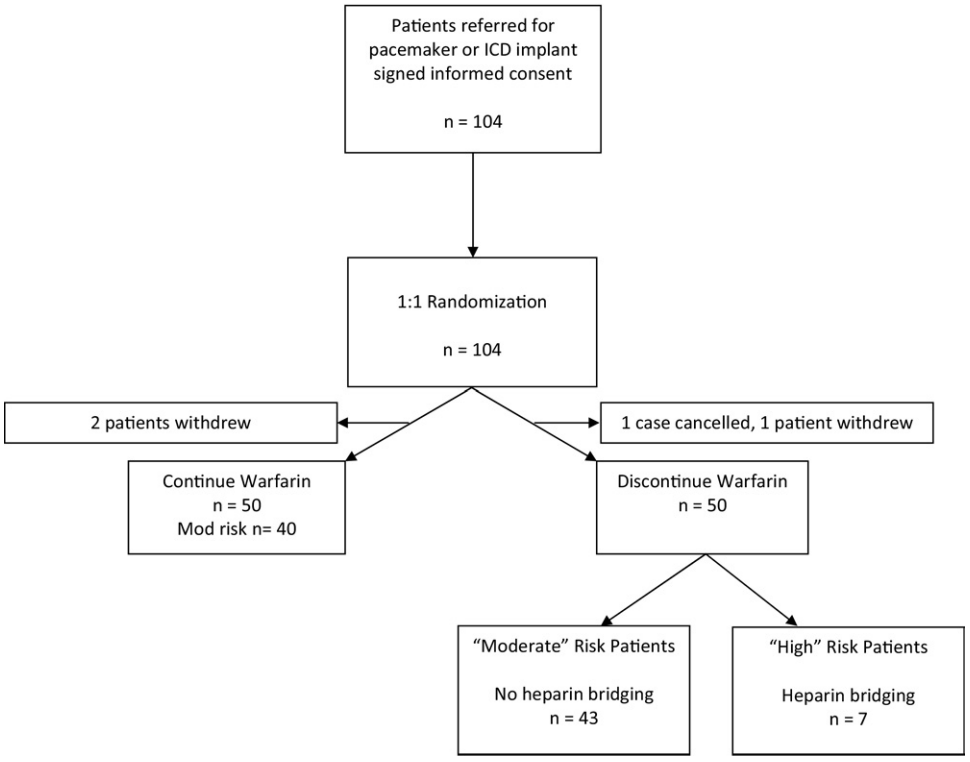

Figure 1 Patients on warfarin randomized 1:1 to warfarin continuation versus warfarin interruption. Those randomized to warfarin interruption were further stratified based on risk for thromboembolic events. Moderate-risk patients had warfarin discontinued, while high-risk patients had warfarin discontinued with heparin bridging. See text for details on risk stratification.

Methods

Patient selection and randomization schema

This was a randomized prospective study aimed to determine whether warfarin continuation in the periprocedural period is superior to warfarin interruption with or without heparin bridging (Figure 1). The study was approved by the Johns Hopkins Investigational Review Committee and was registered in the clinicaltrials.gov database (NCT00721136). All patients on oral anticoagulation who were referred for PPM or ICD implantation (including generator exchanges) were approached.

Since patients had differing risks for thromboembolic events in the absence of anticoagulation, patients were stratified into two groups based on current clinical management strategies along with available data indicating relative risks of embolic events with various conditions.[15–17] Individuals with a "moderate" risk for thromboembolism included those with a history of atrial fibrillation without a history of stroke/transient ischemic attack (TIA) and individuals with mechanical valves in the aortic position. These patients were randomized to either warfarin continuation or warfarin discontinuation without heparin bridging. Individuals with a "high" risk for thromboembolism included those with a history of atrial fibrillation and a history of stroke/TIA, those with inherited or acquired prothrombotic conditions, those with mechanical valves in the tricuspid or mitral position, and those currently being treated for a thromboembolic event (e.g., pulmonary embolus, deep venous thrombosis, left ventricular/atrial clot). This group was randomized to either warfarin continuation or warfarin discontinuation with heparin bridging. Use of unfractionated or fractioned heparin was left to the discretion of the implanting physician. Randomization was performed in a 1:1 fashion using Minim software (http://www-users.york.ac.uk/~mb55/guide/minim.htm).

Device implantation and postprocedural management

Patients underwent an upper extremity venogram before the procedure to visualize venous patency and location. All patients received either cefazolin or clindamycin periprocedurally. After adequate local anesthesia with lidocaine and bupivicaine, an incision was made and dissected down to the pectoral fascia floor. The pocket was expanded using blunt dissection. Monopolar electrocautery was used in all cases to ensure hemostasis. In cases of generator exchanges, the preexisting pocket was incised to expose the leads and expanded in situations where the generator was larger than the preexisting pocket (as was the case for Boston Scientific defibrillators). Vascular access was subsequently obtained[18] by using a modified Seldinger technique with a 21-gauge micropuncture needle (Cook Medical Inc., Bloomington, IN). None of the cases were performed with a cephalic vein cut-down. All devices were implanted above the pectoral fascia. The incision was closed with two to three layers of absorbable suture, and the skin apposed with Steri-Strips