ORIGINAL ARTICLE

Pacemaker or Defibrillator Surgery without Interruption of Anticoagulation

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ABSTRACT

BACKGROUND

Many patients requiring pacemaker or implantable cardioverter–defibrillator (ICD) surgery are taking warfarin. For patients at high risk for thromboembolic events, guidelines recommend bridging therapy with heparin; however, case series suggest that it may be safe to perform surgery without interrupting warfarin treatment. There have been few results from clinical trials to support the safety and efficacy of this approach.

METHODS

We randomly assigned patients with an annual risk of thromboembolic events of 5% or more to continued warfarin treatment or to bridging therapy with heparin. The primary outcome was clinically significant device-pocket hematoma, which was defined as device-pocket hematoma that necessitated prolonged hospitalization, interruption of anticoagulation therapy, or further surgery (e.g., hematoma evacuation).

RESULTS

The data and safety monitoring board recommended termination of the trial after the second prespecified interim analysis. Clinically significant device-pocket hematoma occurred in 12 of 343 patients (3.5%) in the continued-warfarin group, as compared with 54 of 338 (16.0%) in the heparin-bridging group (relative risk, 0.19; 95% confidence interval, 0.10 to 0.36; P<0.001). Major surgical and thromboembolic complications were rare and did not differ significantly between the study groups. They included one episode of cardiac tamponade and one myocardial infarction in the heparin-bridging group and one stroke and one transient ischemic attack in the continued-warfarin group.

CONCLUSIONS

As compared with bridging therapy with heparin, a strategy of continued warfarin treatment at the time of pacemaker or ICD surgery markedly reduced the incidence of clinically significant device-pocket hematoma. (Funded by the Canadian Institutes of Health Research and the Ministry of Health and Long-Term Care of Ontario; BRUISE CONTROL ClinicalTrials.gov number, NCT00800137.)

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Each year, an estimated 1.25 million pacemakers and 410,000 implantable cardioverter–defibrillators (ICDs) are implanted worldwide.[1] Between 14 and 35% of patients receiving these devices require long-term oral anticoagulation therapy,[2-5] and their periprocedural treatment presents a dilemma to physicians. This is particularly true for the subset of patients at moderate-to-high risk (≥5% per year) for thromboembolic events.[6] Current guidelines recommend interruption of oral anticoagulation therapy and the use of bridging therapy with intravenous unfractionated heparin or subcutaneous low-molecular-weight heparin around the time of surgery.[6]

However, there are a number of potential drawbacks to bridging with heparin in the perioperative period. This approach consumes considerable health care resources.[7] Bridging with heparin also involves a short period of normal coagulability (perhaps even hypercoagulability related to the prothrombotic state of surgery) with an associated risk of thromboembolism. Finally, among patients undergoing pacemaker or ICD surgery, there is a substantial risk of device-pocket hematoma (17 to 31%) when bridging with heparin is used.[8-11] Device-pocket hematomas can have serious consequences for patients, such as the need for prolonged cessation of all oral anticoagulation therapy with the attendant risk of thromboembolism,[9,12] prolongation of hospitalization,[13] the need for further surgery (e.g., hematoma evacuation), and an increased risk of infection.[14,15]

In response to these issues, some centers have started performing pacemaker and ICD surgery without interruption of anticoagulation therapy with warfarin.[16,17] However, there have been limited data from clinical trials to support the safety and efficacy of this approach. Two small, randomized trials have been inconclusive.[18,19] In the first of these trials, device-pocket hematoma developed in 4 of 51 patients (7.8%) in the heparin-bridging group and in 4 of 50 (8.0%) in the continued-warfarin group after implantation.[19] In the second trial, only 7 patients received bridging therapy with heparin.[18] We sought to resolve this dilemma with an adequately powered, randomized clinical trial.

Methods

Study Design

We conducted the Bridge or Continue Coumadin for Device Surgery Randomized Controlled Trial (BRUISE CONTROL) as a multicenter, single-blind, randomized, controlled trial. The trial was designed to determine whether a strategy of continued warfarin treatment at the time of pacemaker or ICD surgery, in patients at moderate-to-high risk for thromboembolic events, reduces the incidence of clinically significant device-pocket hematoma, as compared with the current standard of practice of bridging with heparin. Full details of the trial design have been published previously.[20]

The trial was designed by the steering committee (see the Supplementary Appendix, available with the full text of this article at NEJM.org). The protocol (available at NEJM.org) was approved by the research ethics board at each of the participating centers. The University of Ottawa Heart Institute Cardiovascular Research Methods Centre coordinated the study, collected the data, maintained the database, and performed all the data analyses. All the authors attest to the accuracy and completeness of the reported data, as well as the fidelity of this report to the study protocol. There was no commercial support or involvement in this trial.

Patients

We enrolled patients at 17 centers in Canada and at 1 center in Brazil.[20] In brief, patients were eligible if they had an annual predicted risk of thromboembolism of 5% or more (see the Supplementary Appendix),[21] were taking warfarin, and required nonemergency device (pacemaker or ICD) surgery. Device surgery included implantation of a new device, pulse-generator change, lead replacement, or pocket revision. All patients provided written informed consent.

Study Procedures

Eligible patients were randomly assigned in a 1:1 ratio to continued warfarin treatment or bridging therapy with heparin. Randomization was performed with the use of sealed, opaque, serially numbered envelopes and randomly selected block sizes of four to six and was stratified according to clinical center.

In the continued-warfarin group, the international normalized ratio (INR) on the day of surgery was targeted to be 3.0 or lower, except for patients with one or more mechanical valves, for whom an INR of 3.5 or less was permitted. Patients in the heparin-bridging group discontinued warfarin 5 days before the procedure and

started receiving full therapeutic doses of low-molecular-weight heparin or intravenous heparin 3 days before the procedure.

For patients receiving bridging therapy with low-molecular-weight heparin, the final dose was given the morning of the day before the procedure (i.e., >24 hours before the procedure). For patients receiving bridging therapy with intravenous heparin, the infusion was discontinued at least 4 hours before surgery. The administration of heparin was reinitiated 24 hours after the procedure and was continued until a therapeutic INR was achieved. Full details of the heparin-bridging protocol are provided in the Supplementary Appendix.

Clopidogrel was stopped for 5 days before surgery in patients who had undergone implantation of a bare-metal stent more than 1 year previously. Clopidogrel was continued in patients with more recently implanted bare-metal stents and in patients with drug-eluting stents. The timing of reinitiation of clopidogrel therapy after device surgery was at the physician's discretion. Aspirin was continued in all patients.

Patients were aware of the assigned study treatment; blinding was not possible because of the very different nature of the two treatments. To ensure that the investigators were unaware of the study assignments, each center was required to identify two patient-care teams. Each team consisted of one or more research coordinators and one or more physicians. One team had knowledge of the treatment assignments and was responsible for device implantation and follow-up of programming and function but was not allowed any involvement in the evaluation for or management of a device-pocket hematoma. The second team, which had no knowledge of treatment assignments, was responsible for monitoring the surgical wound during the initial hospitalization, at 1 to 2 weeks of follow-up, and during any hospital visits or subsequent admissions and for diagnosing and making all decisions about the management of device-pocket hematomas. Patients in whom a clinically significant hematoma developed were followed until it resolved. Follow-up included monitoring for any additional complications related to the hematoma (e.g., infection).

OUTCOME MEASURES

The primary outcome was clinically significant device-pocket hematoma, defined as a hematoma requiring further surgery, resulting in prolongation of hospitalization, or requiring interruption of oral anticoagulation therapy. Prolongation of hospitalization was defined as extended hospitalization or rehospitalization for at least 24 hours after the index surgical procedure, primarily due to the hematoma. Interruption of anticoagulation therapy was defined as reversal or intentional withholding of oral anticoagulation treatment because of a device-pocket hematoma, resulting in subtherapeutic anticoagulation for at least 24 hours.

Secondary outcomes included each component of the primary outcome, the composite of all other major perioperative bleeding events (hemothorax, cardiac tamponade, or clinically significant pericardial effusion), thromboembolic events (transient ischemic attack, stroke, deep-vein thrombosis, pulmonary embolism, systemic embolism, or valve thrombosis), death from any cause, quality of life, perioperative pain, and patient satisfaction. Details of the assessments of quality of life, pain, and patient satisfaction are provided in the Supplementary Appendix.

STATISTICAL ANALYSIS

We calculated that a sample size of 984 patients would provide 80% power to detect a 30% reduction in the relative risk of the primary outcome in the continued-warfarin group, with the use of a two-sided alpha level of 0.05. We did not expect substantial rates of noncompliance or loss to follow-up. Two interim analyses were planned, when 33% and 66% of the patients had completed follow-up, with review by an independent data and safety monitoring board. We used a group-sequential method with an O'Brien–Fleming boundary, with P values of 0.0002 and 0.0119 for the first and second interim analyses, respectively.

Descriptive statistics were used for all baseline variables, with means and standard deviations for normally distributed variables, medians and interquartile ranges for nonnormally distributed variables, and rates and proportions for discrete outcomes in each treatment group. Primary and secondary outcomes were compared between treatment groups with the use of the chi-square test. Prespecified subgroup analyses included comparisons of outcomes according to whether patients were taking clopidogrel, whether patients were taking any antiplatelet agent, and whether the planned surgery was for implantation of a new device, a pulse-generator change

alone, or a pulse-generator change plus an additional procedure. Analyses were conducted with the use of SAS software, version 9.2 (SAS Institute).

RESULTS

STUDY PATIENTS

Data on 668 patients were reviewed by the data and safety monitoring board at the second prespecified interim analysis, on February 27, 2013, at which time the board recommended termination of the study. All patients who had undergone both randomization and device surgery before this date were followed until study completion. We therefore report data on 681 patients enrolled between October 2009 and February 2013. Details of trial enrollment and follow-up are shown in Figure 1. The baseline clinical and demographic characteristics of the patients were similar in the two groups (Table 1).

DEVICE SURGERY AND PERIOPERATIVE ANTICOAGULATION

Preoperative bridging therapy was performed with the use of low-molecular-weight heparin (in 89.0% of patients), intravenous heparin (in 10.7%), or both (in 0.3%). Postoperative bridging therapy was performed with the use of low-molecular-weight heparin (in 82.2% of patients), intravenous heparin (in 15.9%), or both (in 1.9%). The median INR on the day of surgery was 1.2 (interquartile range, 1.1 to 1.3) in the heparin-bridging group and 2.3 (interquartile range, 2.0 to 2.6) in the continued-warfarin group ($P<0.001$). There were no significant between-group differences in any other perioperative variables (Table 2).

Surgery was postponed in eight patients in the continued-warfarin group because of a supratherapeutic INR on the day of surgery (mean [±SD] INR, 3.9±0.4). In the heparin-bridging group, surgery was postponed in three patients ($P=0.27$);

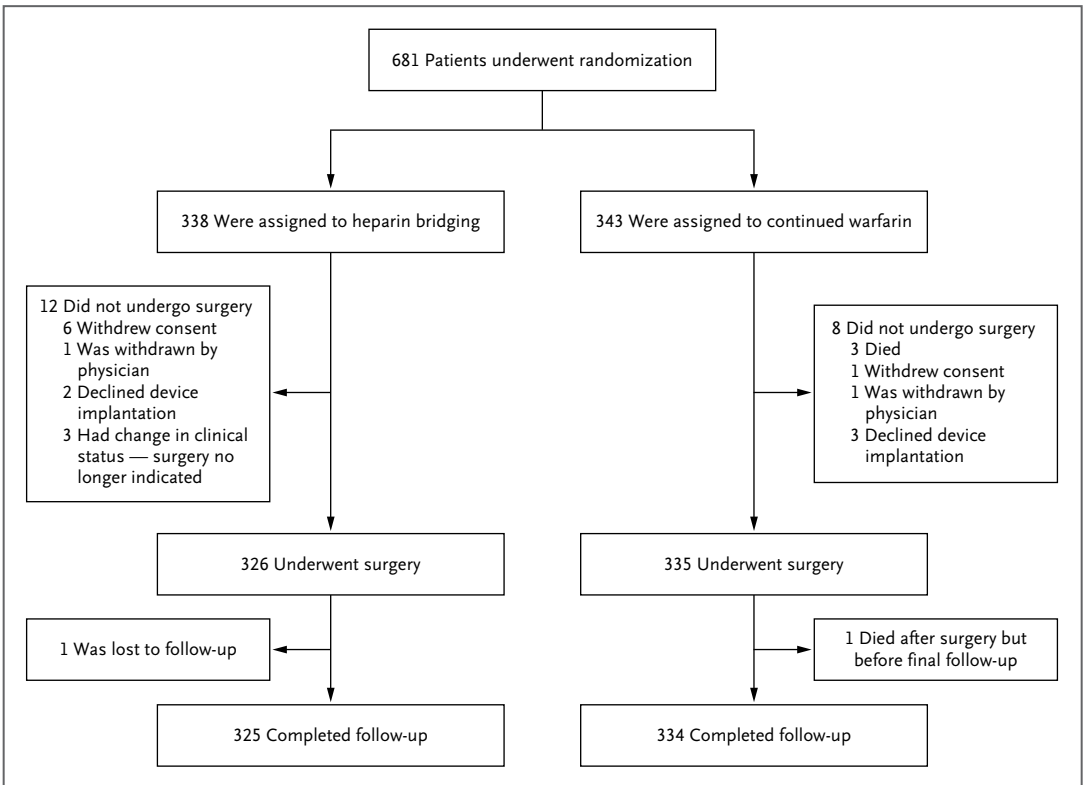

Figure 1. Trial Enrollment and Follow-up.

A total of 681 patients were enrolled between October 2009 and February 2013. The data and safety monitoring board recommended termination of the study at the second prespecified interim analysis, on February 27, 2013. All patients who had undergone both randomization and device surgery before this date were followed until study completion.

two patients had supratherapeutic INRs of 1.9 and 2.8, and bridging therapy in one patient had not been discontinued according to protocol.

PRIMARY OUTCOME

The primary outcome occurred in 12 of 343 patients (3.5%) in the continued-warfarin group as compared with 54 of 338 (16.0%) in the heparin-bridging group (relative risk, 0.19; 95% confidence interval (CI), 0.10 to 0.36; P<0.001). There were significant differences in each of the three components of the primary outcome (Table 3). Treatment effects were consistent in each of seven subgroups (Fig. 2).

SECONDARY OUTCOMES

Secondary outcomes are shown in Table 3. There were no embolic events in the heparin-bridging group. Two patients in the continued-warfarin group had embolic events; both patients had nonvalvular atrial fibrillation and a high risk of stroke as determined at enrollment according to the $CHADS_2$ score (an index of the risk of stroke among patients with atrial fibrillation, with scores ranging from 0 to 6 and higher scores indicating a greater risk of stroke). A stroke in the right occipital lobe occurred 2 days after surgery in an 89-year-old woman with a $CHADS_2$ score of 5 and an INR of 1.2 on the day of surgery. A transient ischemic attack occurred 2 days after surgery in an 88-year-old woman with a $CHADS_2$ score of 4 and an INR of 1.0 on the day of surgery. In both patients, the subtherapeutic INR was not intentional.

There was one episode of cardiac tamponade requiring pericardiocentesis in the heparin-bridging group. Six patients in the heparin-bridging group (1.8%) and two in the continued-warfarin group (0.6%) had infections related to the device system (P=0.17). In all eight patients, the infection necessitated complete system extraction. As compared with patients in the heparin-bridging group, those in the continued-warfarin group reported greater satisfaction with the management of their perioperative anticoagulation therapy, but there were no significant differences in quality of life or perioperative pain scores (Table S1 in the Supplementary Appendix).

DEATHS

There were four deaths, all occurring in the continued-warfarin group (P=0.12). Three patients died before surgery: one patient died suddenly from

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Heparin Bridging (N=338)	Continued Warfarin (N=343)
Age — yr	71.4±10.6	71.8±9.9
Male sex — no. (%)	247 (73.1)	248 (72.3)
Body-mass index†	28.4±6.4	28.3±5.4
Medical history — no. (%)		
Rheumatic heart disease	28 (8.3)	30 (8.7)
Embolic transient ischemic attack	63 (18.6)	62 (18.1)
Embolic stroke	60 (17.8)	65 (19.0)
Non-CNS embolism	13 (3.8)	8 (2.3)
Hypertension	237 (70.1)	247 (72.0)
Diabetes mellitus	133 (39.3)	133 (38.8)
Cardiomyopathy	217 (64.2)	233 (67.9)
Coronary-artery bypass surgery	87 (25.7)	96 (28.0)
Indication for anticoagulation therapy — no. (%)		
Mechanical heart-valve replacement‡	108 (32.0)	95 (27.7)
Mechanical mitral-valve replacement	56 (16.6)	48 (14.0)
Caged-ball or tilting-disk aortic valve	13 (3.8)	9 (2.6)
Bileaflet aortic-valve prosthesis	56 (16.6)	51 (14.9)
Atrial fibrillation or atrial flutter	298 (88.2)	305 (88.9)
Deep-vein thrombosis or pulmonary embolus	16 (4.7)	21 (6.1)
Protein C or S deficiency or antiphospholipid antibodies§	3 (0.9)	7 (2.0)
$CHADS_2$ score¶	3.4±1.0	3.4±0.9
Medications — no. (%)		
Aspirin	129 (38.2)	139 (40.5)
Clopidogrel	21 (6.2)	21 (6.1)
Clopidogrel continued perioperatively	16 (4.7)	17 (5.0)
Statin	234 (69.2)	256 (74.6)
Angiotensin-converting–enzyme inhibitor	191 (56.5)	202 (58.9)
Angiotensin-receptor blocker	77 (22.8)	80 (23.3)
Amiodarone	49 (14.5)	51 (14.9)
Beta-blocker	258 (76.3)	259 (75.5)
Loop diuretic	224 (66.3)	231 (67.3)

* Plus–minus values are means ±SD. There were no significant between-group differences in any variable at a P value of less than 0.05. CNS denotes central nervous system.
† The body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ A patient could have more than one valve.
§ Data are for the 30 patients (15 patients in each treatment group) who underwent testing for protein C or S deficiency or antiphospholipid antibodies.
¶ The $CHADS_2$ score is an index of the risk of stroke in patients with atrial fibrillation. Scores range from 0 to 6, with higher scores indicating a greater risk of stroke.

Table 2. Operative Details.*

Variable	Heparin Bridging (N=326)	Continued Warfarin (N=335)
Surgical procedure — no. (%)		
New implant		
Pacemaker		
Single-chamber or dual-chamber	56 (17.2)	56 (16.7)
Cardiac-resynchronization therapy	1 (0.3)	2 (0.6)
Implantable cardioverter–defibrillator		
Single-chamber or dual-chamber	55 (16.9)	54 (16.1)
Cardiac-resynchronization therapy	40 (12.3)	44 (13.1)
Device replacement or revision		
Pulse-generator change only	105 (32.2)	106 (31.6)
Pulse-generator change with additional procedure†	69 (21.2)	73 (21.8)
Preoperative INR		
Median	1.2	2.3
Interquartile range	1.1–1.3	2.0–2.6
Duration of procedure — min		
Median	53	51
Interquartile range	30–83	31–85
Venous-access guidance — no. (%)		
Peripheral venography	72 (22.1)	91 (27.2)
Ultrasonography	4 (1.2)	2 (0.6)
Intrapocket administration of prohemostatic agent — no. (%)	7 (2.1)	9 (2.7)
Pressure dressing applied postoperatively — no. (%)	176 (54.0)	201 (60.0)
Sandbag applied postoperatively — no. (%)	24 (7.4)	23 (6.9)
Defibrillation-threshold testing — no. (%)	61 (18.7)	60 (17.9)
Specialty of physician performing surgery — no. (%)		
Electrophysiologist	305 (93.6)	313 (93.4)
Surgeon	15 (4.6)	17 (5.1)
Cardiologist	6 (1.8)	5 (1.5)
Fellow or resident participation in the procedure — no. (%)	153 (46.9)	166 (49.6)
Venous access for leads — no./total no. (%)		
Cephalic	52/223 (23.3)	60/229 (26.2)
Subclavian	86/223 (38.6)	96/229 (41.9)
Axillary	85/223 (38.1)	73/229 (31.9)

* There were no significant between-group differences in any variables, except for the preoperative international normalized ratio (INR) (P<0.001).
† Additional procedures included the repositioning or addition of one or more leads, device-pocket revision, and upgrade from pacemaker to implantable cardioverter–defibrillator.

a cardiac cause while awaiting elective surgery for a pulse-generator change, one patient died after metastatic pancreatic cancer was diagnosed and the device implantation was canceled, and one patient died from intraperitoneal hemorrhage after paracentesis (INR, 1.3). The fourth patient died from end-stage heart failure 10 days after surgery.

CLINICALLY SIGNIFICANT HEMATOMA

Three risk factors had independent predictive value for the development of clinically significant device-pocket hematoma: randomized assignment to continued warfarin (relative risk, 0.16; 95% CI, 0.08 to 0.32; P<0.001), diabetes mellitus (relative risk, 0.48; 95% CI, 0.26 to 0.86; P=0.01), and use of aspirin (relative risk, 2.04; 95% CI, 1.19 to 3.48;

Table 3. Primary and Secondary Outcomes.*

Outcome	Heparin Bridging (N=338)	Continued Warfarin (N=343)	Relative Risk (95% CI)	P Value
Primary outcome				
Clinically significant hematoma — no. (%)	54 (16.0)	12 (3.5)	0.19 (0.10–0.36)	<0.001
Components of primary outcome				
Hematoma prolonging hospitalization — no. (%)	16 (4.7)	4 (1.2)	0.24 (0.08–0.72)	0.006
Hematoma requiring interruption of anticoagulation — no. (%)	48 (14.2)	11 (3.2)	0.20 (0.10–0.39)	<0.001
Hematoma requiring evacuation — no. (%)	9 (2.7)	2 (0.6)	0.21 (0.05–1.00)	0.03
Secondary outcomes				
Death from any cause — no. (%)	0	4 (1.2)		0.12
Pneumothorax — no. (%)	1 (0.3)	1 (0.3)		1.00
Hemothorax — no. (%)	0	0		—
Cardiac tamponade — no. (%)	1 (0.3)	0		0.50
Transient ischemic attack — no. (%)	0	1 (0.3)		1.00
Stroke — no. (%)	0	1 (0.3)		0.50
Non-CNS embolism — no. (%)	0	0		—
Deep-vein thrombosis — no. (%)	0	0		—
Pulmonary embolism — no. (%)	0	0		—
Valve thrombosis — no. (%)	0	0		—
Lead dislodgement — no. (%)	4 (1.2)	1 (0.3)		0.21
Superficial wound infection — no. (%)	3 (0.9)	1 (0.3)		0.37
Infection related to device system — no. (%)	6 (1.8)	2 (0.6)		0.17
Myocardial infarction — no. (%)	1 (0.3)	0		0.50
Patient-satisfaction score†	5.9±1.8	6.4±1.5		<0.001

* Plus–minus values are means ±SD.
† Scores for patient satisfaction were obtained with the use of a 7-point Likert scale, with values ranging from 1 ("very dissatisfied") to 7 ("very satisfied").

P=0.01) (Table S4 and S5 in the Supplementary Appendix). Patients with hematomas had significant increases in perioperative pain and significant decreases in quality of life. Details of follow-up data for patients with hematomas are provided in the Supplementary Appendix.

DISCUSSION

In this large, randomized trial, we evaluated the safety of performing pacemaker or ICD surgery without interruption of warfarin therapy in patients requiring oral anticoagulation therapy. We found that this strategy is associated with a significantly lower rate of device-pocket hematoma, as compared with bridging therapy with heparin (3.5% vs. 16.0%). We also found that continued warfarin therapy, with a median INR of 2.3 (interquartile range, 2.0 to 2.6), was not associated with any major perioperative bleeding events and was associated with greater patient satisfaction. These results suggest that continuation of warfarin during pacemaker or ICD surgery may be preferable to bridging therapy with heparin, at least for patients like those enrolled in our trial.

The significantly lower rate of device-pocket hematoma that we observed with continued warfarin may seem counterintuitive. One explanation that has been proposed is the concept of an "anticoagulant stress test."[9] That is, if patients undergo surgery while receiving full-dose anticoagulation therapy, any excessive bleeding will be detectable and appropriately managed while the wound is still open. In contrast, if bridging

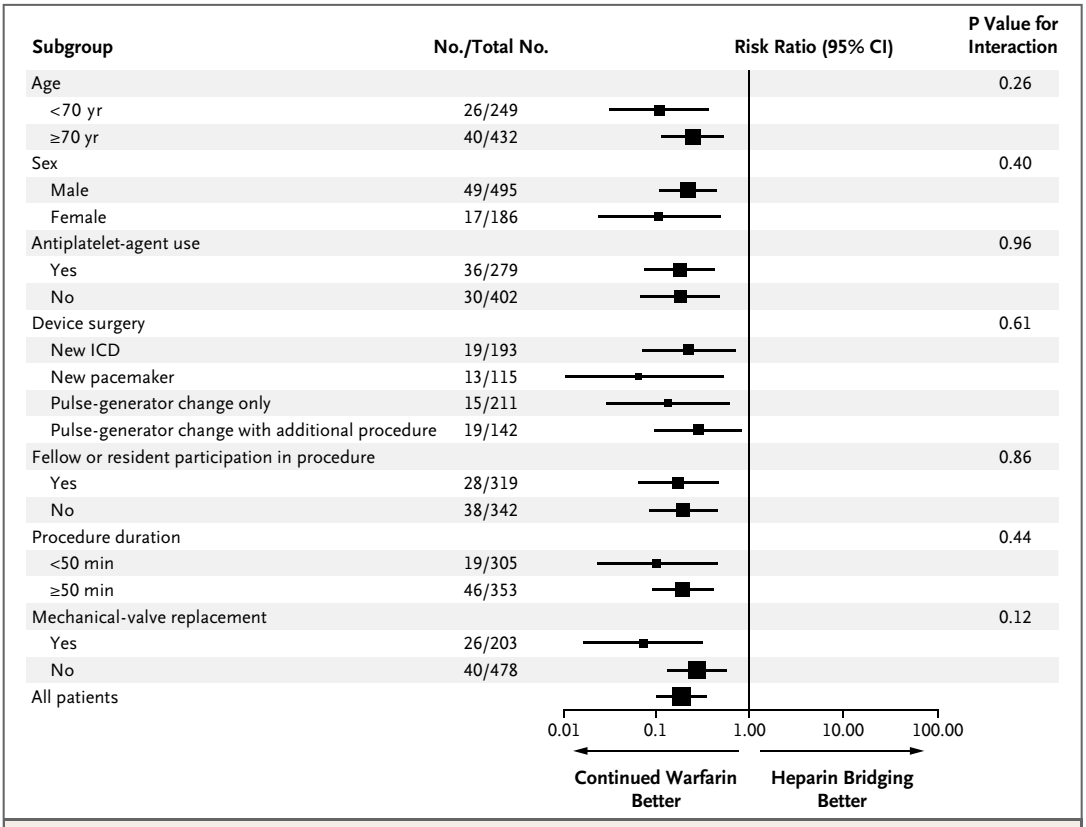

Figure 2. Subgroup Analyses of Clinically Significant Device-Pocket Hematoma.

Risk ratios and 95% confidence intervals are shown for the primary outcome of clinically significant device-pocket hematoma in each subgroup. ICD denotes implantable cardioverter–defibrillator.

therapy with heparin is used, such bleeding may be apparent only when full-dose anticoagulation therapy is resumed postoperatively.[9]

Our results are consistent with observations on bridging therapy in other situations. Siegal et al.[22] recently conducted a meta-analysis of the safety and efficacy of periprocedural bridging therapy, which included more than 12,000 patients in 34 studies, with only one randomized trial. The comparison groups in these studies included mostly patients in whom oral anticoagulation therapy was discontinued without bridging, with smaller numbers of patients in whom oral anticoagulation therapy was continued during surgery. The authors concluded that bridging with heparin leads to a risk of overall bleeding that is 5 times as high, and a risk of major bleeding that is 3.6 times as high, as the respective risks associated with no bridging therapy. The risk of thromboembolic events did not differ significantly between the two treatment strategies.[22]

We specifically included patients with an annual risk of thromboembolic events of more than 5%, for whom complete discontinuation of anticoagulation therapy at the time of surgery might have been too risky. The findings of our trial are not directly relevant to patients with a lower risk of thromboembolic events (<5%), and it is possible that such patients may not require any anticoagulation or bridging therapy during the periprocedural period. Additional data from large, randomized trials are needed to better define the role of periprocedural bridging therapy with heparin.

Guidelines suggest that the continuation of warfarin at the time of minor dental, dermatologic, or ophthalmologic procedures is associated with an acceptable risk of bleeding.[6,21] Although not directly relevant, the results of our study are consistent with this recommendation, particularly since the bleeding risk is low with these other procedures, whereas the risk is increased with pacemaker or ICD surgery.[6]

Physicians have begun to explore performing other procedures and operations without interruption of warfarin therapy. Case series have shown low rates of bleeding complications with coronary angiography and stenting,[23,24] minor head and neck surgery,[25] urologic procedures,[26] colonoscopic polypectomy,[27] hand surgery,[28] vascular surgery,[29] joint injections and aspirations,[30] and hip and knee replacements.[29] However, additional randomized, controlled trials are needed in these areas. It should also be recognized that a strategy of continued warfarin is unlikely to be considered in major abdominal, cardiothoracic, or neurologic surgery.

Three oral anticoagulant agents — dabigatran, rivaroxaban, and apixaban — have been approved within the past few years for the prevention of stroke in patients with atrial fibrillation.[31-33] These agents have short half-lives, with maximal anticoagulant effects observed soon after oral intake and reduction of the effects soon after discontinuation. Whether it is better for patients to undergo surgery without interruption of these agents or with temporary cessation is currently unclear. The results of our study cannot be applied to patients receiving these agents.

One limitation of our trial is the subjectivity of the primary end point and the possibility that on occasion the team that was initially unaware of the treatment assignment became aware of the assignment and allowed biases to affect the assessment of primary end-point events. The most obvious potential situation for unblinding was among patients who were prescribed postoperative intravenous heparin. However, this treatment was used in only 17.8% of the patients, and the incidence of hematoma was similar among patients treated with postoperative intravenous heparin (16.1%) and those treated with postoperative low-molecular-weight heparin (16.6%). There is additional reassurance about the veracity of the blinding from the objective data showing that patients with hematomas had significant increases in perioperative pain and significant decreases in quality of life.

In conclusion, we investigated two approaches to performing pacemaker or ICD surgery in patients requiring long-term oral anticoagulation therapy. Patients were randomly assigned to undergo the planned operation with bridging anticoagulation therapy with heparin or to undergo the surgery without interruption of warfarin therapy. Patients who underwent surgery without interruption of warfarin therapy had a markedly reduced incidence of clinically significant device-pocket hematoma, as compared with those who received bridging therapy with heparin.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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