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Clinically Significant Pocket Hematoma Increases Long-Term Risk of Device Infection

BRUISE CONTROL INFECTION Study

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ABSTRACT

BACKGROUND The BRUISE CONTROL trial (Bridge or Continue Coumadin for Device Surgery Randomized Controlled Trial) demonstrated that a strategy of continued warfarin during cardiac implantable electronic device surgery was safe and reduced the incidence of clinically significant pocket hematoma (CSH). CSH was defined as a post-procedure hematoma requiring further surgery and/or resulting in prolongation of hospitalization of at least 24 h, and/or requiring interruption of anticoagulation. Previous studies have inconsistently associated hematoma with the subsequent development of device infection; reasons include the retrospective nature of many studies, lack of endpoint adjudication, and differing subjective definitions of hematoma.

OBJECTIVES The BRUISE CONTROL INFECTION (Bridge or Continue Coumadin for Device Surgery Randomized Controlled Trial Extended Follow-Up for Infection) prospectively examined the association between CSH and subsequent device infection.

METHODS The study included 659 patients with a primary outcome of device-related infection requiring hospitalization, defined as 1 or more of the following: pocket infection; endocarditis; and bloodstream infection. Outcomes were verified by a blinded adjudication committee. Multivariable analysis was performed to identify predictors of infection.

RESULTS The overall 1-year device-related infection rate was 2.4% (16 of 659). Infection occurred in 11% of patients (7 of 66) with previous CSH and in 1.5% (9 of 593) without CSH. CSH was the only independent predictor and was associated with a >7-fold increased risk of infection (hazard ratio: 7.7; 95% confidence interval: 2.9 to 20.5; $p < 0.0001$). Empiric antibiotics upon development of hematoma did not reduce long-term infection risk.

CONCLUSIONS CSH is associated with a significantly increased risk of infection requiring hospitalization within 1 year following cardiac implantable electronic device surgery. Strategies aimed at reducing hematomas may decrease the long-term risk of infection. (Bridge or Continue Coumadin for Device Surgery Randomized Controlled Trial [BRUISE CONTROL]; NCT00800137) (J Am Coll Cardiol 2016;67:1300–8) © 2016 by the American College of Cardiology Foundation.

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Device pocket hematomas are a common complication of cardiac implantable electronic device (CIED) surgery, particularly in patients receiving perioperative anticoagulation. The risk of device pocket hematoma with heparin bridging has been reported to range from 17% to 31% (1–3). The BRUISE CONTROL (Bridge or Continue Coumadin for Device Surgery Randomized Controlled Trial) demonstrated that a strategy of continued warfarin at the time of device surgery is safe and reduced the incidence of clinically significant pocket hematoma (CSH) from 16% to 3.5% (4–7).

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Reported rates of device system infections have varied between 0.68% and 2.2% of implants (8–13). Device infections occur within days to years following surgery; require complete system removal for cure; and are associated with significant morbidity, mortality, and cost to the health care system (14). There is therefore much effort to reduce infection.

Previous studies have inconsistently correlated hematoma with the subsequent development of device infection. These inconsistent results may in part relate to the largely retrospective nature of studies, lack of endpoint adjudication, and differing subjective definitions of hematoma (8,11,12,15–17). In this study, we prospectively examined the association between objectively defined CSH and subsequent device infection.

METHODS

STUDY DESIGN. The BRUISE CONTROL trial was a multicenter single-blind randomized controlled trial designed to determine whether a strategy of continued warfarin (compared with bridging with heparin) at the time of pacemaker or defibrillator surgery reduced the incidence of CSH in patients with moderate to high risk of thromboembolic events (4,18). CSH was objectively defined as a post-procedure hematoma requiring further surgery and/or resulting in prolongation of hospitalization for least 24 h, and/or requiring interruption of anticoagulation. All potential CSH were adjudicated by a blinded team of evaluators.

The current BRUISE CONTROL INFECTION (Bridge or Continue Coumadin for Device Surgery Randomized Controlled Trial Extended Follow-Up for Infection) extends the follow-up to 1 year with a primary outcome of infection requiring hospitalization.

The trial was supported by a peer-reviewed grant from the Canadian Institutes of Health Research. The protocol was approved by the research ethics board at each of the participating centers. The University of Ottawa Heart Institute Cardiovascular Research Methods Center coordinated the study, collected the data, maintained the database, and performed all data analyses. The steering committee decided to publish the data. All coauthors critically reviewed the manuscript and approved the final version.

PATIENTS. Patients were enrolled at 17 centers in Canada and 1 in Brazil. Procedures and results of the BRUISE CONTROL trial have been previously published (4). The study included patients with a >5% annual predicted risk of thromboembolism taking warfarin, and undergoing nonemergency CIED surgery. All patients provided written informed consent. Subjects that completed BRUISE CONTROL follow-up were included in the BRUISE CONTROL INFECTION study.

STUDY PROCEDURES. Patients enrolled in BRUISE CONTROL were randomized in a 1:1 ratio to continued warfarin or heparin bridging as previously described (4). A blinded team was responsible for diagnosing, following, and making all decisions about management of CSH. Patients developing CSH were followed until resolution of their hematoma for the primary analysis of BRUISE CONTROL (4).

In BRUISE CONTROL INFECTION, data collection included vital status, empiric use of antibiotics for CSH, other procedures on the device pocket, hospitalization information for device infection, evidence for the infection, culture and microorganism details, management of the infection, and complications from the infection or its management. All patients were followed up at 1 year by chart review and/or telephone contact.

OUTCOME MEASURES. The primary outcome of the present BRUISE CONTROL INFECTION study was device-related infection requiring hospitalization occurring within 12 months after CIED surgery. Infection was defined as follows: 1) pocket infection; 2) endocarditis (either valve or lead); or 3) bloodstream infection (19,20). Pocket infections were defined according to the 2008 National Healthcare Safety Network and U.S. Center for Disease Control definitions for surgical site infections (21). Endocarditis was defined according to the Modified Dukes' criteria (22), adapted as suggested to help diagnose endocarditis in patients with implantable cardiac devices (23). Secondary outcomes included repeat procedures on the pocket, whether the repeat procedure was due to hematoma, complications of infection or procedures required to manage infection, and death.

A blinded adjudication committee evaluated all potential primary endpoints (CIED-related infections requiring hospitalization). The committee consisted of an adjudication coordinator, 2 experts in cardiac

ABBREVIATIONS AND ACRONYMS

CI = confidence interval

CIED = cardiac implantable electronic device

CSH = clinically significant pocket hematoma

HR = hazard ratio

IQR = interquartile range