Cardiovascular Therapeutics

Association of Uninterrupted Oral Anticoagulation During Cardiac Device Implantation with Pocket Hematoma

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Abstract

Purpose: Implantation of permanent pacemakers (PPMs) or implantable cardiac defibrillators (ICDs) may be complicated by the development of pocket hematomas. Current practice guidelines provide little guidance to clinicians about the preferred strategy for chronic oral anticoagulation (OAC). The purpose of this study was to examine the frequency and clinical significance of pocket hematoma among patients receiving uninterrupted OAC during cardiac device implantation.

Methods: This was a retrospective cohort study of adult patients undergoing cardiac device implantation between January 1, 2011, and December 31, 2012, at an academic teaching hospital. Medical records were reviewed for demographics, comorbidities, and medications. The primary outcome was development of pocket hematomas within 30 days of device implantation. Clinical significance was based on the need for additional intervention. Data were assessed using descriptive statistics, logistic regression, and chi-square tests.

Results: The final cohort included 380 patients. The median age was 68.4 years, and 56.6% were male. Cardiovascular comorbidities were common. Among 80 patients receiving uninterrupted OAC, 71.3% were taking warfarin, 11.2% rivaroxaban, and 17.5% dabigatran. The incidence of pocket hematomas for the entire cohort was 9.7%, of which 1.3% were clinically significant. Pocket hematoma occurred in 21.4% of patients continued on OAC versus 7.7% of those not anticoagulated ($P = .001$). Pocket hematoma was more common among those receiving ICDs than PPMs (18.5% vs 5.7%, respectively; $P < .001$).

Conclusions: Continuing chronic OAC increased pocket hematoma formation but most were clinically insignificant. Pocket hematoma occurred irrespective of the oral anticoagulant drug used, but additional study is needed to determine comparative risks among the drugs.

Key Words—anticoagulation, cardiac device, implantation, pocket hematoma

Hosp Pharm—2015;50:761–766

BACKGROUND

Pocket hematoma, a localized swelling and collection of blood underneath the skin, is a recognized early postoperative complication of cardiac device implantation. Pocket hematoma may result in numerous complications including increased hospitalization, pocket infection, or need for reopera-

tion.¹ Many patients who require a cardiac device for rhythm management have comorbidities that necessitate the use of chronic oral anticoagulation (OAC). Although warfarin is still the most commonly prescribed oral anticoagulant, newer target-specific agents such as rivaroxaban, apixaban, or dabigatran may also be used.

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Specific guidelines for the periprocedural management of anticoagulation during cardiac device implantation are lacking due to the paucity of trial evidence in this population. Instead the standard of care has been based on general guidelines for patients undergoing various operative procedures.² For patients considered moderate to high risk for thromboembolism, warfarin is typically stopped 5 days before the procedure and the patient is bridged with therapeutic doses of either unfractionated heparin or low-molecular-weight heparin (LMWH). After the procedure, the patient is restarted on warfarin; once therapeutic levels are reached, bridging therapy is stopped. Studies suggest that the incidence of pocket hematoma with heparin bridging is 12% to 23% compared to only 2% to 4% for nonanticoagulated patients.^{3,4} Pooled analyses from multiple studies suggest fewer bleeding complications and similar risks of thromboembolism with an alternative strategy of uninterrupted warfarin as compared to heparin bridging.^{5,6} The majority of studies, however, did not examine the clinical significance of the pocket hematomas. No studies evaluated the risks for the target-specific oral anticoagulants (TSOACs). We conducted an observational study to determine the frequency of pocket hematoma of clinical significance and association with uninterrupted use of warfarin or a TSOAC in patients undergoing permanent pacemaker (PPM) or implantable cardiac defibrillator (ICD) implantation.

METHODS

This retrospective observational study was conducted at a large academic teaching hospital and was approved by the institutional review board. Potential patients were identified using the Healthcare Enterprise Repository for Ontological Narration (HERON), which is an aggregate database of de-identified patient information from electronic medical records. HERON allows for the identification of possible patient cohorts who meet specific requirements without individual patient records being reviewed. All patients who received either a PPM or an ICD between January 1, 2011, and December 31, 2012, were identified and extracted from HERON. Patient charts were then reviewed to extract patient demographics, comorbid conditions that could impact pocket hematoma development, use of anticoagulants, and concomitant medications such as antiplatelet drugs that increase bleeding risk. Patients were considered to be anticoagulated if the periprocedural international normalized ratios (INRs) for warfarin were within the therapeutic range (INR 2-3) or doses of the TSOACs

were continued throughout the procedure. Patients were excluded if the chart review indicated that they died during the procedure, had not received a device implantation, or had received bridging therapy with either unfractionated heparin or LMWH. The primary outcome was pocket hematoma within 30 days of device implantation, which was identified by searching the patient's medical record during hospitalization and clinic follow-up for the term "pocket hematoma." Pocket hematomas were further classified as clinically significant if the patient required additional intervention such as rehospitalization, antibiotic therapy, surgical intervention, or discontinuation of OAC. Non-clinically significant pocket hematomas were defined as those that required only monitoring and resolved without further intervention.

Demographics were analyzed using frequencies and means. The incidence of both pocket hematomas and clinically significant pocket hematomas was calculated by counting the number of each during the study period. All patient demographics, comorbidities, and concurrent medications were assessed as possible risk factors for the development of pocket hematomas through a forward stepwise logistic regression. Time to pocket hematoma between anticoagulated and non-anticoagulated patients was evaluated with a *t* test. Differences in pocket hematoma formation between anticoagulated and non-anticoagulated patients and those receiving ICD or PPM were assessed using the chi-square test. An a priori significance was set at 0.05. Statistical analysis was completed using IBM SPSS version 20 (IBM, Armonk, NY).

RESULTS

Of the 467 patients identified in HERON, 87 were excluded based on our criteria, which left a final study cohort of 380 patients. Patient demographics for the study cohort are presented in **Table 1**. Among the 80 patients with therapeutic OAC, 71.3% (109) were receiving warfarin, 17.5% (14) dabigatran, and 11.2% (9) rivaroxaban. During the 2-year study period, 37 patients (9.7%) developed a pocket hematoma, of which 5 (1.3%) were classified as clinically significant. The incidence of pocket hematoma was 7.7% in those patients who were not receiving an OAC versus 21.4% (*n* = 17) in the 80 patients who were receiving therapeutic levels of OAC at the time of implant (9 on warfarin, 3 on dabigatran, and 5 on rivaroxaban) (*P* = .001). The average time to pocket hematoma was 5.7 days after the procedure, with no significant differences between patients who were or were not therapeutically anticoagulated (4.9 days vs 6.4 days, respectively; *P* = .268).

Table 1. Patient baseline demographics (*N* = 380)

Demographics	Full cohort	PPM	ICD	<i>P</i>
No. of patients	380	261	119	
Mean age, years	68.4	71.3	61.9	<.001*
Mean weight, kg	85	83.2	88.9	.028*
Mean height, cm	170.3	168.7	174	<.001*
Mean BMI	29.4	29.3	29.5	.851
Mean SCr	1.4	1.4	1.3	.415
Male gender	215 (56.6)	130 (49.8)	85 (71.4)	<.001*
<i>Comorbid conditions</i>				
Hypertension	274 (72.1)	192 (73.6)	82 (68.9)	.348
Coronary artery disease	196 (51.6)	128 (49)	68 (57.1)	.143
Atrial fibrillation	149 (39.2)	117 (44.8)	32 (26.9)	.001*
Diabetes	115 (30.3)	80 (30.7)	35 (29.4)	.807
Heart failure	81 (21.3)	46 (17.6)	35 (29.4)	.009*
Chronic kidney disease	81 (21.3)	56 (21.5)	25 (21)	.921
Valvular heart disease	78 (20.5)	62 (23.8)	16 (13.4)	.021*
Stroke	43 (11.3)	33 (12.6)	10 (8.4)	.226
DVT/PE	28 (7.4)	23 (8.8)	5 (4.2)	.111
Peripheral vascular disease	21 (5.5)	16 (6.1)	5 (4.2)	.445
Mechanical heart valve	13 (3.4)	11 (4.2)	2 (1.7)	.208
<i>Concomitant medications</i>				
Aspirin	259 (68.2)	169 (64.8)	90 (75.6)	.035*
Clopidogrel	48 (12.6)	29 (11.1)	19 (16)	.186
NSAIDs	22 (5.8)	16 (6.1)	6 (5)	.674
Prasugrel	3 (0.8)	2 (0.8)	1 (0.8)	.940
<i>Anticoagulant</i>				
Warfarin	109 (28.7)	80 (30.7)	29 (24.4)	.209
Dabigatran	14 (3.7)	11 (4.2)	3 (2.5)	.416
Rivaroxaban	9 (2.4)	8 (3.1)	1 (0.8)	.186
None	248 (65.3)	162 (62.1)	86 (72.3)	.053

Note: Values are given as *n* (%), unless otherwise indicated. BMI = body mass index; DVT/PE = deep vein thrombosis or pulmonary embolism; ICD = implantable cardiac defibrillator; NSAIDs = nonsteroidal anti-inflammatory drugs; PPM = permanent pacemaker; SCr = serum creatinine.

* Statistically significant at *P* < .05.

Overall, baseline patient demographics were similar between those patients who developed a clinically significant pocket hematoma and those who developed a nonsignificant pocket hematoma. However, those with a clinically significant pocket hematoma were more likely to be using warfarin (80% vs 18.75%; *P* = .014) and have a higher INR (2.7 vs 1.85; *P* = .049).

Several predictors of pocket hematoma formation were identified through logistic regression. The full patient cohort produced 4 predictors: the device type, either ICD or PPM (*P* < .001); rivaroxaban use (*P* = .006); aspirin use (*P* = .035); and therapeutic OAC (*P* = .001). Variations were seen in these predictors when patients were analyzed by device type. For patients receiving a PPM, use of rivaroxaban

($P = .007$) or therapeutic OAC ($P = .058$) remained predictive of pocket hematoma. In contrast, ICD patients were at higher risk of pocket hematoma with therapeutic OAC ($P = .01$), concomitant bleeding-risk medications (eg, antiplatelets such as aspirin, clopidogrel) ($P = .017$), or history of valvular heart disease ($P = .028$).

DISCUSSION

Each year more than 1.5 million people receive an implantable cardiac device.⁷ Pocket hematoma is a recognized early complication following device implantation; however, not all pocket hematomas are clinically significant. Some pocket hematomas resolve on their own without further intervention while others may result in rehospitalization, surgical intervention, device removal, prolonged discontinuation of OAC, or pocket infection.⁸⁻¹⁰

Due to the high prevalence of comorbidities such as atrial fibrillation that increase thromboembolic risk in this population, many patients are receiving chronic OAC. Balancing the risks of thromboembolism from interrupted therapy versus bleeding from continued therapy presents additional challenges for those involved in the management of these patients.

Based on general practice guidelines for periprocedural management, it has been common to interrupt warfarin therapy and provide bridging with either unfractionated heparin or LMWH.² However, this strategy has been shown to be less than optimal. In addition to the potential for brief periods of increased thromboembolic risk during drug transitions, bridging has been associated with relatively high rates of bleeding complications including pocket hematoma.^{11,12} Additionally, length of hospitalization may be increased due to the time required to reestablish therapeutic levels of warfarin. In response to these concerns, several retrospective studies have suggested that an alternative approach of maintaining uninterrupted warfarin therapy during procedures such as cardiac device implantation may be a safer strategy.¹²⁻¹⁵

Since our study was completed, these observational findings have been confirmed in randomized trials. A large multicenter randomized trial, FINPAC, demonstrated the safety of uninterrupted versus interrupted warfarin therapy with no bridging.¹⁶ Warfarin was discontinued in the interrupted group 2 days before surgery and restarted on the first postoperative day. A total of 213 patients were included. Any hematoma occurred in 33% of the uninterrupted group versus 40% of the interrupted group (hazard

ratio [HR], 0.86; 95% CI, 0.66-1.12; $P = .001$, for noninferiority). Large hematomas ($>100 \text{ cm}^2$) were considered clinically significant and occurred in 6% of patients in both groups. One patient required surgical revision while 2 required blood products. A significant limitation of this trial was the failure to report mean INR values for the 2 groups. Post hoc analysis of patients with clinically significant hematomas found 2 predictors: OAC and aspirin.¹⁶

The Bridge or Continue Coumadin for Device Surgery Randomized Controlled Trial (BRUISE CONTROL) demonstrated a reduction in clinically significant pocket hematomas with continued warfarin therapy versus heparin bridging (3.5% vs 16%; relative risk [RR], 0.19; 95% CI, 0.10 to 0.36; $P < .001$).¹⁷ The study was terminated early after enrolling 668 patients. For the bridged group, the median INR at the time of surgery was 1.2, and the vast majority of patients were given LMWH. For patients continued on warfarin, the median INR at the time of surgery was 2.3. Three factors were predictive of pocket hematoma: continued warfarin, diabetes, and aspirin use. Thromboembolic events were not significantly different between groups although the number of events was small.

The largest and most recent meta-analyses pooled data from 14 studies involving 3,744 patients undergoing cardiac device implantation. Compared with uninterrupted vitamin K antagonist therapy, bridging with heparin or LMWH resulted in a higher risk of bleeding events (RR, 3.10; 95% CI, 2.02-4.76; $P < .00001$) and pocket hematoma (RR, 3.58; 95% CI, 2.17-5.91; $P < .00001$), with no difference in thromboembolic risk (RR, 1.16; 95% CI, 0.36-3.67; $P = .81$).¹⁸

The findings of our study in a real-world setting are consistent with those of the randomized trials demonstrating the safety of uninterrupted warfarin therapy during device implantation. More importantly, the majority of the pocket hematomas were small and soft and resolved over time without further intervention. For the approximately 10% of pocket hematomas that were clinically significant, additional interventions were required including readmission, device removal, discontinuation of OAC, and antibiotic therapy. For patients with clinically significant pocket hematomas, it is noteworthy that INR values were in the higher end of the target range, generally above 2.5, suggesting that maintaining anticoagulation in the lower therapeutic range (eg, 2.0 to 2.5) might be preferable and should be further studied.

For the entire cohort, several predictors of pocket hematoma formation were identified that are consistent

with previous studies.^{17,19} However we also observed differences in these predictors based on device type with concomitant antiplatelet therapy and valvular heart disease being more predictive in persons receiving ICDs. Our data also raise a cautionary flag of increased pocket hematoma risk in PPM patients receiving rivaroxaban. Unfortunately, the small number of patients on this drug precludes any definitive conclusions and indicates the need for further investigation.

Like all retrospective studies, there are several limitations that must be noted. This was a single-center study. The number of patients receiving the TSOAC (dabigatran and rivaroxaban) was smaller than expected, and none were receiving apixaban. Thus, we were unable to analyze the data for relative risks among the individual drugs. Findings relied on accurate medical record documentation that could not be verified. Differences in surgical techniques among providers were not assessed. The small number of pocket hematomas limited the number of variables that could be included in the regression analysis. We did not independently verify the patients' thromboembolic or bleeding risk at baseline.

CONCLUSION

To achieve optimal outcomes with cardiac device implantation, the risk of pocket hematoma must be minimized. For patients requiring chronic OAC due to a moderate to high risk of thromboembolism, the risks and benefits of continuing therapy must be considered. Our findings are consistent with a growing body of evidence indicating that the uninterrupted use of OAC does increase the risk of pocket hematoma, however, the majority of risks are not clinically significant. A larger study is needed to examine the risks of pocket hematoma with the uninterrupted use of the TSOAC compared to warfarin.

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