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DEVICES

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Perioperative hematoma with subcutaneous ICD implantation: Impact of anticoagulation and antiplatelet therapies

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Abstract

Background: The safety of perioperative anticoagulation (AC) and antiplatelet (AP) therapy with subcutaneous implantable cardioverter-defibrillator (S-ICD) implantation is unknown. The purpose of this study was to identify the risk factors associated with hematoma complicating S-ICD implantation.

Methods: Records were retrospectively reviewed from 200 consecutive patients undergoing S-ICD implantation at two academic medical centers. A hematoma was defined as a device site blood accumulation requiring surgical evacuation, extended hospital stay, or transfusion.

Results: Among 200 patients undergoing S-ICD implantation (age 49 ± 17 years, 67% men), 10 patients (5%) had a hematoma, which required evacuation in six patients (3%). Warfarin was bridged or uninterrupted in 12 and 13 patients, respectively (6% and 6.5%). Four of 12 patients with warfarin and bridging AC (33%) and two of 13 patients with uninterrupted warfarin (15%) developed a hematoma. Neither of the two patients with uninterrupted DOAC had a hematoma. No patients on interrupted AC without bridging (n = 26, 13 with warfarin, 13 with DOAC) developed a hematoma. A hematoma was also more likely with the use of clopidogrel (n = 4/10 vs 10/190, 40% vs 5.3%, P < 0.0001) in combination with aspirin in 12/14 patients. Any bridging AC (odds ratio [OR] 10.3, 1.8–60.8, P = 0.01), clopidogrel (OR 10.0, 1.7–57.7, P = 0.01), and uninterrupted warfarin without bridging (OR 11.1, 1.7–74.3, P = 0.013) were independently associated with hematoma formation.

Conclusion: AC and/or AP therapy with clopidogrel appears to increase the risk for hematoma following S-ICD implantation. Interruption of AC without bridging should be considered when it is an acceptable risk to hold AC.

KEYWORDS

anticoagulation, antiplatelet therapy, direct oral anticoagulant, hematoma, subcutaneous implantable cardioverter-defibrillator

1 | INTRODUCTION

Transvenous cardiac implantable electronic device (CIED) procedures are frequently performed on therapeutic oral anticoagulation (AC) in patients with an AC indication. A randomized controlled trial demonstrated a decreased incidence of pocket hematoma with transvenous CIED surgery on uninterrupted therapeutic warfarin compared with bridging heparin.[1] Transvenous CIED surgery with uninterrupted or limited missed doses of direct oral anticoagulation (DOAC) may have similar bleeding risks to uninterrupted warfarin.[2] Furthermore, there was no difference in hematoma with interrupted versus uninterrupted DOAC with transvenous CIED surgery in a recent randomized study.[3] Meanwhile, multiple studies demonstrate a high risk of hematoma with perioperative antiplatelet (AP) agents during transvenous CIED surgery.[2,4]

Subcutaneous implantable cardioverter-defibrillators (S-ICDs) offer several advantages relative to transvenous CIEDs and maintain a high efficacy in treatment of ventricular arrhythmias.[5] Due to the

absence of an intravascular lead, there is a decreased risk of lead and venous complications,[6] as well as lower risk associated with removal should it be necessary. They do not currently, however, have the capability of pacing or providing painless treatment of ventricular tachycardia (antitachycardia pacing).

S-ICD implantation relative to transvenous CIED implantation requires the creation of a larger pocket and two or three incisions in areas of the chest remote from conventional transvenous CIED implantation. The generator pocket location may be prone to difficulties with hemostasis due to surgical visibility limitations ("deeper" pocket relative to incision location) and anatomical constraints that limit the ability for the surrounding tissue to exert pressure on the pocket to "tamponade" any potential bleeding. Although randomized data exists for perioperative AC management in the transvenous CIED population, the safety of perioperative AC and/or AP therapy and associated risk for perioperative hematoma complicating S-ICD implantation is uncertain. We sought to identify the risk factors associated with perioperative hematoma complicating S-ICD implantation.

2 | METHODS

2.1 | Study design

Medical records from consecutive S-ICD implantations at two academic medical centers between January 2014 and September 2017 were reviewed for inclusion in this retrospective, multicenter cohort study. S-ICD implantation was performed utilizing conventional techniques as described elsewhere.[7–10] All devices were implanted in the subcutaneous and not the intramuscular/submuscular space. All patients were monitored overnight. The operative notes were reviewed to determine details of S-ICD implantation, including any complications. The medical records were reviewed to determine baseline patient characteristics, medications, perioperative medication management, laboratory values, and complications. Subsequent international normalized ratios (INRs) were collected for the next month for patients on AC with warfarin. AC was defined as therapeutic AC anytime within 7 days prior or 30 days postprocedure. A hematoma was defined as a device site blood accumulation requiring surgical evacuation, extended hospital stay, or transfusion. An extended hospital stay was defined as a new hospitalization or the addition of at least one night of extended hospitalization to facilitate monitoring, evacuation, and/or AC management that would not have been necessary in the absence of a hematoma. The decision to perform hematoma evacuation was at the discretion of the operator and was often due to progressive pain/swelling refractory to conservative management, drainage from the incision, or compromised incision integrity due to pressure from the hematoma. A supratherapeutic INR was defined as an INR > 3.0. The Institutional Review Board of each institution approved the study.

2.2 | Statistical analysis

Descriptive statistics are presented as mean and standard deviation for normally distributed continuous variables, median and interquartile range for abnormally distributed continuous variables, or number and percentage for categorical variables. Parameters of interest were compared between groups using the Pearson's χ^2 test for categorical variables and two-sample Student's *t*-test for continuous variables. Logistic regression analysis was used to determine the independent predictors of hematoma. The final multivariate model was selected in a stepwise manner (removing one nonsignificant parameter at a time) using characteristics with univariate P-values of < 0.20 as candidate variables. JMP version 13.0 (SAS Institute, Cary, NC, USA) was used for all statistical testing and P-values of < 0.05 were considered to be statistically significant.

3 | RESULTS

3.1 | Patient characteristics

Two hundred patients were included in the study (Table 1). The mean age of patients was 49 ± 17 years (67% men). The average patient was overweight (body mass index [BMI] 29.8 ± 7.3). Fifty-one patients had an ischemic cardiomyopathy (25.5%). Surgical procoagulant was utilized in three patients (1.5%).

3.2 | Perioperative hematoma

Ten patients (5%) had a perioperative hematoma between 0 and 52 days postoperatively. All hematomas occurred at the lateral surgical site and not the parasternal incisions. Six patients (60%) underwent hematoma evacuation between 2 and 52 days postoperatively. Risk factors associated with hematoma formation are presented in Table 2 and clinical details regarding the 10 patients with hematoma in Table 3. Seven patients (70%) had a new or extended hospitalization due to the hematoma. Device infection occurred in two of 10 patients with hematoma (20%). One of these patients had delayed wound dehiscence in the setting of a hematoma and underwent device removal on postoperative day (POD) #52. The other infected patient had hematoma evacuation with subsequent wound dehiscence requiring device removal. No patients required administration of blood products or vitamin K.

3.3 | AC and AP management

AC and AP therapy was utilized in 56 (28%) and 104 (52%) of the patients, respectively. The indications for AC included: atrial fibrillation/flutter (n = 29, 52%), venous thromboembolism (n = 11, 20%), left ventricular (LV) assist device (n = 4, 7%), left ventricular thrombus (n = 3, 5%), LV noncompaction (n = 3, 5%), mechanical valve replacement (n = 2, 4%), venous hypercoagulable state (n = 2, 4%), peripartum cardiomyopathy (n = 1, 2%), and LV dysfunction with apical aneurysm (n = 1, 2%). AC was more frequently utilized in patients with versus without hematoma formation (60% vs 26%, n = 6/10 and 50/190, P = 0.021). Six of 30 patients (20%) with uninterrupted and/or bridged AC developed a hematoma (two uninterrupted warfarin, one uninterrupted warfarin with bridging postoperative unfractionated heparin

TABLE 1 Patient characteristics (n = 200)

Age (years) at implant	49 ± 17
Male sex	134 (67)
BMI (kg/m^2)	29.8 ± 7.3
Baseline Cr (mg/dL)	0.95 [0.79–1.19]
CHA2DS2-VASc	2.6 ± 1.7
Comorbidities	
Ischemic CM	51 (25.5)
Nonischemic CM	98 (49)
Hypertrophic CM	9 (4.5)
CAD	72 (36)
LVAD	4 (2)
Atrial fibrillation/flutter	50 (25)
Hypertension	110 (55)
Diabetes mellitus	54 (27)
Prior stroke or TIA	16 (8)
Chronic kidney disease	38 (19)
ESRD on dialysis	12 (6)
Valve replacement	10 (5)
Medications	
Anticoagulation	56 (28)
Warfarin	38 (19)
DOAC	16 (8)
Rivaroxaban	10 (5)
Apixaban	5 (2.5)
Dabigatran	1 (0.5)
Bridging UFH or LMWH	15 (7.5)
Antiplatelet (any)	104 (52)
Aspirin	102 (51)
Clopidogrel	14 (7)
Ticagrelor	5 (2.5)
Prasugrel	4 (2)
Medication Combinations	
AC and dual AP	5 (2.5)
AC and single AP	26 (13)
AC w/o AP	25 (12.5)
Dual AP	21 (10.5)
Echocardiographic Data	
Baseline LV end-diastolic diameter (mm)	57 [51–65]
Baseline LV EF (%)	31 [25–55]

Note: AC = anticoagulation; AP = antiplatelet agent; BMI = body mass index; CAD = coronary artery disease; CM = cardiomyopathy; Cr = creatinine; DOAC = direct oral anticoagulant; EF = ejection fraction; ESRD = end-stage renal disease; LMWH = low-molecular-weight heparin; LV = left ventricular; LVAD = left ventricular assist device; LVEF = left ventericular ejection fraction; TIA = transient ischemic attack; UFH = unfractionated heparin.

TABLE 2 Clinical characteristics and association with pocket hematoma

	Hematoma (n = 10)	No hematoma (n = 190)	P-value
Age (years) at implant	56.1 ± 16.2	48.4 ± 17.0	0.17
Male Sex	9 (90)	125 (65.8)	0.11
BMI (kg/m^2)	27.0 ± 5.6	30.0 ± 7.3	0.20
Baseline Cr (mg/dL)	1.0 [0.8–1.3]	1.0 [0.8–1.2]	0.67
CHA2DS2-VASc	2.9 ± 1.7	2.6 ± 1.7	0.62
Comorbidities			
Ischemic CM	3 (30)	48 (25.3)	0.74
Nonischemic CM	4 (40)	94 (49.5)	0.56
Hypertrophic CM	0 (0)	9 (4.7)	0.48
CAD	5 (50)	67 (35.3)	0.34
LVAD	1 (10)	3 (1.6)	0.06
Atrial fibrillation/flutter	1 (10)	49 (26.1)	0.25
Hypertension	7 (70)	103 (54.2)	0.33
Diabetes mellitus	3 (30)	51 (26.8)	0.83
Prior stroke or TIA	1 (10)	15 (7.9)	0.81
COPD	1 (10)	12 (6.3)	0.65
Chronic kidney disease	0 (0)	38 (20)	0.12
ESRD on dialysis	0 (0)	12 (6.3)	0.41
Valve replacement	1 (10)	9 (4.7)	0.46
Medications			
Anticoagulation	6 (60)	50 (26.3)	0.021
Warfarin	6 (60)	32 (16.8)	0.0007
DOAC	0 (0)	16 (8.4)	0.34
Rivaroxaban	0 (0)	10 (5.3)	0.46
Apixaban	0 (0)	5 (2.6)	0.60
Dabigatran	0 (0)	1 (0.5)	0.82
Bridging UFH or LMWH	4 (40)	11 (5.8)	<0.0001
Anti-platelet	8 (80)	96 (50.5)	0.069
Aspirin	7 (70)	95 (50)	0.22
Clopidogrel	4 (40)	10 (5.3)	<0.0001
Ticagrelor	0 (0)	5 (2.6)	0.60
Prasugrel	0 (0)	4 (2.1)	0.64
Medication Combinations			
AC and dual AP	1 (10)	4 (2.1)	0.12
AC and single AP	3 (30)	23 (12.1)	0.10
AC and single or dual AP	4 (40)	27 (14.2)	0.028
AC w/o AP	2 (20)	23 (12.1)	0.46
Dual AP	3 (30)	18 (9.5)	0.039
AC and AP Management			
AC uninterrupted and/or bridged	6 (60)	24 (12.6)	<0.0001
AC interrupted w/o bridging	0 (0)	26 (13.7)	0.21
Warfarin uninterrupted (no bridging)	2 (20)	11 (5.8)	0.08

(Continues)

TABLE 2 (Continued)

	Hematoma (n = 10)	No hematoma (n = 190)	P-value
Warfarin bridged	4 (40)	8 (4.2)	<0.0001
Warfarin interrupted w/o bridging	0 (0)	13 (6.8)	0.39
Echocardiographic Data			
Baseline LV end-diastolic diameter (mm)	52 [48.75–62.5]	57 [51–65]	0.48
Baseline LV EF (%)	25 [25–55]	31 [25–53]	0.78

Note: Clinical associations with hematoma are presented above, including utilization of anticoagulation and anti-platelet therapy. Uninterrupted and/or bridged anticoagulation use was higher in patients with than without hematoma. AC = anticoagulation; AP = antiplatelet agent; BMI = body mass index; CAD = coronary artery disease; CM = cardiomyopathy; COPD = chronic obstructive pulmonary disease; Cr = creatinine; DOAC = direct oral anticoagulant; EF = ejection fraction; ESRD = end-stage renal disease; LMWH = low-molecular-weight heparin; LV = left ventricular; LVAD = left ventricular assist device; Preop = preoperative; Postop = postoperative; TIA = transient ischemic attack; UFH = unfractionated heparin.

[UFH], one uninterrupted warfarin with bridging postoperative low-molecular-weight heparin [LMWH], and two with interrupted warfarin and pre- and postoperative bridging UFH). No patients on interrupted AC without bridging experienced hematoma (n = 26, 0%, 13 with warfarin, 13 with DOAC).

3.4 | Warfarin

Warfarin use was higher in patients with versus without hematoma (n = 6/10 vs 32/190, 60% vs 16.8%, P = 0.0007). Warfarin was uninterrupted in 13 of 38 patients (34%), bridged with LMWH or UFH in 12 patients (32%), and interrupted without bridging in 13 patients (34%). There was a trend toward higher use of uninterrupted warfarin (without bridging) in patients with versus without hematoma (n = 2/10 vs 11/190, 20% vs 5.8%, P = 0.08). There was a higher use of warfarin with bridging among patients with versus without hematoma (n = 4/10 vs 8/190, 40% vs 4.2%, P < 0.0001). No patients with interrupted warfarin without bridging developed a hematoma (n = 13). The median INR among those with uninterrupted and interrupted (w/o bridging) AC was 2.4 [2.1–2.7] and 1.4 [1.2–1.6]. A supratherapeutic INR was present in 14 patients within 30 days postoperatively, including three of 10 (30%) patients with perioperative hematoma (INRs of 4.1 on POD #1, 4.5 on POD #6, and 7.3 on POD #3).

3.5 | Direct oral anticoagulants

Sixteen patients (8.4%) were on a DOAC perioperatively (10 on rivaroxaban, five on apixaban, and one on dabigatran). No patients on a DOAC had a hematoma. The DOAC was interrupted in 14 of 16 (87.5%) patients: 24–48 hours preoperatively in 11 patients and > 48 hours in three patients. Only one patient on a DOAC received additional bridging AC. The DOAC was resumed in < 24 hours in one patient, 24–48 hours in 12 patients, and > 48 hours in one patient.

3.6 | Bridging AC

Bridging AC with UFH or LMWH (11 patients with UFH, six patients with LMWH, two patients received both UFH and LMWH) was more common in those with versus without hematoma (n = 4/10 vs n = 11/190, 40% vs 5.8%, P < 0.0001). Among the 15 patients with bridging AC, bridging was more frequent preoperative (n = 13/15, 87%) than postoperative (n = 7/15, 47%). UFH was held for 6–12 hours preimplant and restarted in four patients 6 hours–6 days postimplant. LMWH was held for one dose and resumed in three patients 24 hours–7 days postimplant. A hematoma occurred in two of 13 patients with preoperative bridging (15.4%, both with UFH, both also received postoperative bridging) and four of seven patients with postoperative bridging (57%, three with UFH and one with LMWH). No hematoma occurred in patients receiving preoperative bridging AC without postoperative bridging. Hematoma occurred in three patients on UFH (n = 3/11, 27%) and one patient with LMWH (n = 1/6, 17%).

3.7 | Prophylactic AC

Twenty-five patients (12.5%) received prophylactic dose UFH or LMWH within 72 hours preoperatively and was held in all patients preoperatively. It was resumed in only two patients (1%) postoperatively. Only one patient with prophylactic UFH or LMWH had a hematoma.

3.8 | AP use

AP medications were utilized in 104 patients (52%). There was a nonsignificant trend toward higher use of AP therapy in those with hematoma versus no hematoma (80% vs 50.5%, P = 0.069). Doses of AP agents were infrequently held perioperatively (three of 102 with aspirin, one of five with ticagrelor, and none with prasugrel). Clopidogrel usage was higher in patients with versus without hematoma (40% vs 5.3%, P < 0.0001). The majority of patients on clopidogrel were on dual AP therapy with aspirin (n = 12/14, 86%), including three of four (75%) patients with hematoma associated with clopidogrel. Dual AP therapy was utilized in 21 patients (10.5%), including 30% of those with a hematoma versus 9.5% of those without hematoma (P = 0.039). One of five patients (20%) on oral AC and dual AP therapy developed a hematoma.

3.9 | Multivariate analysis

Any bridging AC (odds ratio [OR] 10.3, 1.8–60.8, P = 0.010), clopidogrel (OR 10.0, 1.7–57.7, P = 0.010), and uninterrupted warfarin without bridging AC (OR 11.1, 1.7–74.3, P = 0.013) were independently associated with hematoma formation (Figure 1, Table 4). BMI, sex, and age were not independently associated with hematoma formation.

3.10 | Nonhematoma complications

Seven patients (3.5%) had device infection requiring removal, two of which were preceded by hematoma. One patient underwent subsequent S-ICD reimplantation and the remainder underwent either transvenous ICD implantation or no reimplantation. Six patients (3%)

TABLE 3 Details on patients with hematoma following subcutaneous ICD implantation

Pt #	Age/Sex	Hematoma evacuation	Evacuation POD	AC & Indication	AC Details	AP	AP Details	INR– POD#1/ Highest for month	Cr (mg/dL)
1	55 M	Yes (also infected)	52	N/A	N/A	ASA 81	No interruption	N/A	0.6
2	54 M	Yes	7	Warfarin Noncompaction	No interruption	None	N/A	1.9/2.6 (POD 7)	1.3
3	35 M	Yes	14	Warfarin/LMWH LVAD	No interruption, Received LMWH starting POD #7	ASA 81	No interruption	1.7/2.5 (POD 2)	1.1
4	55 M	Yes	7	PRx only	Held pre-op (6 hours)	DAPT (ASA 81 and Clopidogrel	No interruption	N/A	0.9
5	57 M	No	N/A	N/A	N/A	ASA 81	No interruption	N/A	1.0
6	57 M	No	N/A	Warfarin/UFH DVT/PE	No interruption, received UFH POD#6	Clopidogrel	No interruption	2.0/7.3 (POD 3)	0.9
7	77 M	No	N/A	N/A	N/A	DAPT (ASA 81 and Clopidogrel)	No interruption	N/A	1.3
8	28 F	Yes	2	Warfarin AF	No interruption	N/A	N/A	3.3 / 4.1 (POD 1)	0.5
9	82 M	Yes	2	Warfarin/UFH DVT/PE	No interruption, received UFH POD 2	DAPT (ASA 81 and Clopidogrel)	No interruption	1.4 / 2.6 (POD 30)	3.1
10	59 M	No	N/A	Warfarin/UFH Mechanical valve	Held preop/UFH until 12 hours before and resumed 6 hours later	ASA 81	Held pre-op	1.5 / 4.5 (POD 6)	1.1

Note: Details of the 10 patients with hematoma complicating S-ICD implantation are presented above. AC = anticoagulation; AF = atrial fibrillation; AP = anti-platelet; ASA = aspirin; Cr = creatinine; DAPT = dual anti-platelet therapy; DVT = deep vein thrombosis; F = female; ICD = implantable cardioverter-defibrillator; INR = international normalized ratio; LMWH = low-molecular-weight heparin; LVAD = left ventricular assist device; M = male; N/A = not applicable; PE = pulmonary embolism; POD = postoperative day; PRx = prophylaxis; Pt = patient; S-ICD = subcutaneous ICD; SubQ = subcutaneous; UFH = unfractionated heparin.

TABLE 4 Multivariate associations with hematoma after subcutaneous ICD implantation

Variable	OR (95% CI)	P-value
Any bridging AC (UFH or LMWH)	10.3 (1.8–60.8)	0.010
Clopidogrel	10.0 (1.7–57.7)	0.010
Uninterrupted warfarin (no bridging)	11.1 (1.7–74.3)	0.013
BMI	1.1 (0.94–1.28)	0.20

Note: Any bridging anticoagulation, clopidogrel, and uninterrupted warfarin are independently associated with hematoma complicating S-ICD implantation. Additional univariate factors included in the initial iterations of the multivariate analysis included age and sex. BMI is per unit change. AC = anticoagulation; BMI = body mass index; CI = confidence interval; ICD = implantable cardioverter-defibrillator; LMWH = low-molecular-weight heparin; OR = odds ratio; S-ICD = subcutaneous ICD; UFH = unfractionated heparin.

had S-ICD removal for noninfectious causes: pain (n = 1), oversensing/inappropriate therapies (n = 3), allergy (n = 1), and desire for transvenous ICD to facilitate antitachycardia pacing (n = 1). One patient underwent lead revision (POD #12) due to skin irritation and discomfort from an electrode implanted too superficially. No patient had perioperative stroke/transient ischemic attack, myocardial infarction, arterial embolism, or died from perioperative complications.

4 | DISCUSSION

We report the collective experience of S-ICD implantation in a population at two tertiary academic centers. The key findings of this study include: (1) uninterrupted AC and/or bridging is independently associated with hematoma complicating S-ICD implantation; (2) clopidogrel (generally as part of dual anti-platelet therapy with aspirin) is independently associated with hematoma; and (3) interruption of AC (warfarin or DOAC) without bridging is associated with a low risk of hematoma following S-ICD implantation.

A perioperative hematoma can have disastrous consequences. The reported 1-year risk for infection in patients with transvenous CIED postoperative hematoma was 11%.[11] Evacuation may be required in some patients, further increasing the risk of infection. It can also result in prolonged hospitalizations and readmissions with associated risks. The reported incidence of hematoma complicating S-ICD implantation is 0.2–5.8% (Table 5).[5,10,12–14] This study reports a high rate of hematoma which may be due to increased AC and AP usage, comorbidities, less surgical procoagulant usage, differences in the threshold for hematoma evacuation, and the possibility of underreporting of hematoma in prior studies. Of note, a similarly elevated risk for hematoma (5.8%) was reported during a recent single-center S-ICD cohort that included many patients on uninterrupted warfarin.[12]

Perioperative AC and AP management strategies utilized with transvenous CIED surgery may not be suitable for S-ICD implantation. S-ICD implantation has two or three incisions, a larger surface area, limited surgical visibility ("deeper" pocket relative to incision location), and anatomical constraints that limit the ability for the surrounding tissue to exert pressure on the pocket to "tamponade" any potential bleeding. Furthermore, patients receiving S-ICD may have a higher incidence of chronic kidney disease and other comorbidities, increasing the bleeding risk relative to transvenous CIED patients. Bridging AC during transvenous CIED surgery with UFH or LMWH has been reported to have a much higher risk of hematoma than uninterrupted warfarin (16.0% vs 3.5%).[1] Similarly, we report a particularly high risk of hematoma with S-ICD implantation and postoperative bridging. While transvenous CIED implantation with oral warfarin and/or AP therapy has been associated with a higher risk of hematoma,[15] a recent randomized study found no difference in hematoma with interrupted versus continued DOAC at the time of transvenous CIED implantation.[3] As our study only included two patients on uninterrupted DOAC, the safety of S-ICD implantation with this AC management strategy is uncertain.

A recent single-center retrospective study in 137 patients undergoing S-ICD implantation reported a higher incidence of pocket hematoma with uninterrupted warfarin versus no warfarin (25% vs 1.5%, P = 0.001). Similarly, we report an elevated risk of hematoma in patients with uninterrupted and/or bridged AC with S-ICD implantation. The risk was particularly high with postoperative bridging. This study expands on the findings of Azfal et al. in a larger two-center population while addressing the risk of pocket hematoma with perioperative bridging AC, DOACs, and AP therapy.[12]

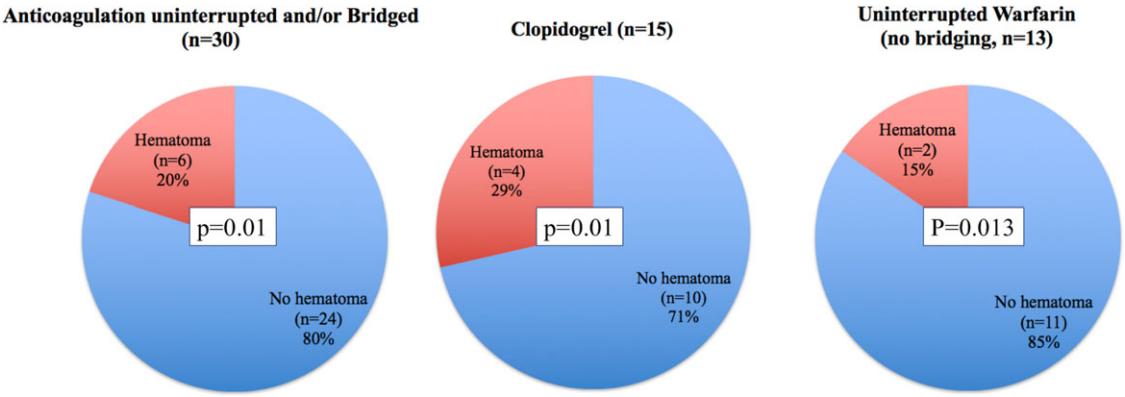

FIGURE 1 Three factors independently associated with hematoma complicating S-ICD implantation. Anticoagulation uninterrupted and/or bridged, clopidogrel, and uninterrupted warfarin are each independently associated with hematoma complicating S-ICD implantation. S-ICD = subcutaneous implantable cardioverter-defibrillator [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 5 Reported hematoma rate with subcutaneous ICD implantation

	Number of implants	Hematoma incidence	Age (years)	ESRD on dialysis	AC use	AP use
Weiss *et al*. 2013[10] (IDE study)	321	Not reported	51.9 ± 15.5	Excluded – 0 (0%)	Not reported	Not reported
Burke *et al*. 2015[5] (EFFORTLESS Registry)	882	4 (0.4%)	50.3 ± 16.9	Not reported	Not reported	Not reported
Friedman *et al*. 2016[13] (NCDR ICD Registry)	3717	11 (0.3%)	53.5 ± 15.6	744 (20.1%)	Warfarin 690 (18.6%, held in 74% of these)	Not reported
Gold *et al*. 2017[14] (Post-Approval Study/Registry)	1637	7 (0.4%)	53.2 ± 15.0	219 (13.4%)	Not reported	Not reported
Afzal *et al*. 2017[12] (Single-center cohort)	137	8 (5.8%)	49.1	Not reported	Warfarin 35 (25.5%, held in 31% of these)	Aspirin: 50 (36.5%) DAPT: 34 (24.8%)
Sheldon *et al*. 2018 (Two-center cohort)	200	10 (5%)	49 ± 17	12 (6%)	Warfarin: 38 (19%) DOAC: 16 (5.3%) Bridging UFH/LMWH: 15 (7.5%)	Aspirin: 102 (51%) Other antiplatelet: 23 (11.5%) DAPT: 21 (10.5%)

Note: Comparison of hematoma rates with subcutaneous ICD implantation in various studies. Anticoagulation and antiplatelet management were reported in only a portion of these studies. AC = anticoagulation; AP = antiplatelet; DAPT = dual antiplatelet therapy; DOAC = direct oral anticoagulants; ESRD = end-stage renal disease; ICD = implantable cardioverter-defibrillator; LMWH = low-molecular-weight heparin; UFH = unfractionated heparin.

Clopidogrel is associated with increased hematoma formation during transvenous CIED surgery.[4] We found that clopidogrel use at the time of S-ICD implantation, generally as part of dual AP therapy, is also associated with hematoma independent of AC use and other clinical factors. The utilization of other AP agents was too infrequent to draw reliable conclusions.

An important finding of this study was that no patients on interrupted AC with either warfarin or a DOAC without bridging AC developed a hematoma. A recent randomized controlled trial found a lower risk of perioperative bleeding without an increase in arterial thromboembolism when atrial fibrillation patients were not bridged with LMWH, although patients with recent stroke or mechanical valves were excluded.[16] Accordingly, it is prudent to consider interruption of AC if the risk of doing so is acceptable.[17] If the risk of interruption is not acceptable, it may be preferable to continue oral AC without interruption rather than bridging with UFH/LMWH.[1,3] Although many patients undergoing S-ICD implantation have chronic kidney disease,[14] we did not find an association between chronic kidney disease and hematoma formation.

4.1 | Limitations

This is a retrospective study and is subject to associated bias. Data were collected from two tertiary centers and thus there is the potential of referral bias (sicker patients compared with community populations). Perioperative AC and AP management was not standardized and was at the discretion of the operating electrophysiologists. Furthermore, the management of hematoma was at the discretion of the operating electrophysiologist and differences in the threshold for hematoma evacuation may have been present. The documentation of a pressure dressing was incomplete and thus not included in data analysis. The presence of uninterrupted AC was pooled with bridging AC due to a small number of patients with uninterrupted AC and no bridging. There were insufficient patients to definitively comment on the risk with an uninterrupted AC without bridging. There were also too few patients to comment on relative bleeding risk with bridging UFH versus LMWH. There was limited utilization of AP agents other than aspirin and clopidogrel. Few patients were on clopidogrel without aspirin. As only two patients were on uninterrupted DOAC, this study was underpowered to assess the safety of this strategy.

4.2 | Future directions

A randomized study is necessary in the S-ICD population to determine the optimal perioperative management of AC and AP agents.

5 | CONCLUSION

Perioperative AC and/or AP therapy with clopidogrel appears to increase the risk for hematoma following S-ICD implantation. A randomized perioperative AC study is necessary in patients undergoing S-ICD implantation. In the meantime, interruption of AC without bridging should be considered perioperatively when it is an acceptable risk to hold AC.

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REFERENCES

1. Birnie DH, Healey JS, Wells GA, et al. Pacemaker or defibrillator surgery without interruption of anticoagulation. *N Engl J Med*. 2013;368:2084–2093.
2. Jennings JM, Robichaux R, McElderry HT, et al. Cardiovascular implantable electronic device implantation with uninterrupted dabigatran: comparison to uninterrupted warfarin. *J Cardiovasc Electrophysiol*. 2013;24:1125–1129.
3. Birnie DH, Healey J, Wells GA, et al. A randomized controlled trial of continued versus interrupted novel oral anti-coagulant at the time of device surgery (BRUISE CONTROL-2). Late-breaking science abstracts from the American Heart Association's Scientific Sessions 2017 and late-breaking abstracts in resuscitation science from the Resuscitation Science Symposium. *Circulation*. 2017;136:e448–e467.
4. Kutinsky IB, Jarandilla R, Jewett M, Haines DE. Risk of hematoma complications after device implant in the clopidogrel era. *Circ Arrhythm Electrophysiol*. 2010;3:312–318.
5. Burke MC, Gold MR, Knight BP, et al. Safety and efficacy of the totally subcutaneous implantable defibrillator: 2-year results from a pooled analysis of the IDE Study and EFFORTLESS Registry. *J Am Coll Cardiol*. 2015;65:1605–1615.
6. Brouwer TF, Yilmaz D, Lindeboom R, et al. Long-term clinical outcomes of subcutaneous versus transvenous implantable defibrillator therapy. *J Am Coll Cardiol*. 2016;68:2047–2055.
7. Bardy GH, Smith WM, Hood MA, et al. An entirely subcutaneous implantable cardioverter-defibrillator. *N Engl J Med*. 2010;363:36–44.
8. Knops RE, Olde Nordkamp LR, de Groot JR, Wilde AA. Two-incision technique for implantation of the subcutaneous implantable cardioverter-defibrillator. *Heart Rhythm*. 2013;10:1240–1243.
9. Lambiase PD, Barr C, Theuns DA, et al. Worldwide experience with a totally subcutaneous implantable defibrillator: early results from the EFFORTLESS S-ICD Registry. *Eur Heart J*. 2014;35:1657–1665.
10. Weiss R, Knight BP, Gold MR, et al. Safety and efficacy of a totally subcutaneous implantable-cardioverter defibrillator. *Circulation*. 2013;128:944–953.
11. Essebag V, Verma A, Healey JS, et al. Clinically significant pocket hematoma increases long-term risk of device infection: BRUISE CONTROL INFECTION Study. *J Am Coll Cardiol*. 2016;67:1300–1308.
12. Afzal MR, Mehta D, Evenson C, et al. Perioperative management of oral anticoagulation in patients undergoing implantation of subcutaneous implantable defibrillator. *Heart Rhythm*. 2018;15:520–523.
13. Friedman DJ, Parzynski CS, Varosy PD, et al. Trends and in-hospital outcomes associated with adoption of the subcutaneous implantable cardioverter defibrillator in the United States. *JAMA Cardiol*. 2016;1:900–911.
14. Gold MR, Aasbo JD, El-Chami MF, et al. Subcutaneous implantable cardioverter-defibrillator post-approval study: Clinical characteristics and perioperative results. *Heart Rhythm*. 2017;14:1456–1463.
15. Ghanbari H, Nallamothu BK, Wang Y, Curtis JP. Antithrombotic therapy and outcomes after ICD implantation in patients with atrial fibrillation and coronary artery disease: an analysis from the National Cardiovascular Data Registry (NCDR)(R). *J Am Heart Assoc*. 2015;4:e001331.
16. Douketis JD, Spyropoulos AC, Kaatz S, et al. Perioperative bridging anticoagulation in patients with atrial fibrillation. *N Engl J Med*. 2015;373:823–833.
17. Doherty JU, Gluckman TJ, Hucker WJ, et al. 2017 ACC expert consensus decision pathway for periprocedural management of anticoagulation in patients with nonvalvular atrial fibrillation: a report of the American College of Cardiology Clinical Expert Consensus Document Task Force. *J Am Coll Cardiol*. 2017;69:871–898.

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