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Dual Antiplatelet Therapy and Heparin "Bridging" Significantly Increase the Risk of Bleeding Complications After Pacemaker or Implantable Cardioverter-Defibrillator Device Implantation

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Objectives This study was designed to assess the risk of significant bleeding complications in patients receiving antiplatelet or anticoagulation medications at the time of implantable cardioverter-defibrillator (ICD) device implantation.

Background Periprocedural management of antiplatelet or anticoagulation therapy at the time of device implantation remains controversial.

Methods We performed a retrospective chart review of bleeding complications in all patients undergoing ICD or pacemaker implantation from August 2004 to August 2007. Aspirin or clopidogrel use was defined as taken within 5 days of the procedure. A significant bleeding complication was defined as need for pocket exploration or blood transfusion; hematoma requiring pressure dressing or change in anticoagulation therapy; or prolonged hospitalization.

Results Of the 1,388 device implantations, 71 had bleeding complications (5.1%). Compared with controls not taking antiplatelet agents ($n = 255$), the combination of aspirin and clopidogrel ($n = 139$) significantly increased bleeding risk (7.2% vs. 1.6%; $p = 0.004$). In patients taking aspirin alone ($n = 536$), bleeding risk was marginally higher than it was for patients taking no antiplatelet agents (3.9% vs. 1.6%, $p = 0.078$). The use of periprocedural heparin ($n = 154$) markedly increased risk of bleeding when compared with holding warfarin until the international normalized ratio (INR) was normal ($n = 258$; 14.3% vs. 4.3%; $p < 0.001$) and compared with patients receiving no anticoagulation therapy (14.3% vs.1.6%; $p < 0.0001$). There was no statistical difference in bleeding risk between patients continued on warfarin with an INR ≥ 1.5 ($n = 46$) and patients who had warfarin withheld until the INR was normal ($n = 258$; 6.5% vs. 4.3%; $p = 0.50$).

Conclusions Dual antiplatelet therapy and periprocedural heparin significantly increase the risk of bleeding complications at the time of pacemaker or ICD implantation. (J Am Coll Cardiol 2010;55:2376–82) © 2010 by the American College of Cardiology Foundation

Normal hemostasis is dependent upon a series of complex, well-regulated steps mediated by the vascular wall, platelets, and the coagulation cascade (1). Disruption of this delicate balance with antiplatelet or anticoagulation medications can have profound consequences on periprocedural bleeding complications.

The majority of patients referred for cardiac pacemaker or implantable cardioverter-defibrillator (ICD) implantation at our center are taking some form of antiplatelet or anticoagulation medications. Common indications for warfarin include atrial fibrillation, mechanical prosthetic valves, cerebrovascular disease, reduced left ventricular systolic function, left ventricular apical thrombus, and prior deep venous thrombosis or pulmonary embolism. Patients are often taking antiplatelet agents such as aspirin and/or clopidogrel for primary or secondary prevention of coronary artery disease, particularly after percutaneous coronary interventions.

From a clinical perspective, the appropriate periprocedural management of these medications often poses a

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dilemma. Simply withholding or reversing these medications places patients at risk for subsequent thromboembolic events, whereas continuing these medications may unnecessarily increase bleeding complications.

One common practice is to hold warfarin for a period of 4 to 5 days to achieve a goal international normalized ratio (INR) <1.5 (2–5). Heparin "bridging" is then instituted in patients deemed at high risk for thromboembolic events (2–4). Such practices, however, can prolong hospital stay and lead to periods of inadequate or excessive anticoagulation, thereby increasing the risk for thromboembolic or bleeding complications. Additionally, recent studies challenge this practice, suggesting that continuation of warfarin with a therapeutic INR poses no greater risk than simply withholding warfarin during device implantation (6–8).

The purpose of this study was to investigate the influence of antiplatelet or anticoagulation therapy on the risk of bleeding complications at the time of cardiac device implantation. We hypothesized that dual antiplatelet therapy and periprocedural heparin increase the risk of significant bleeding complications at the time of cardiac device implantation.

Abbreviations and Acronyms

CI = confidence interval
ICD = implantable cardioverter-defibrillator
INR = international normalized ratio
OR = odds ratio

Methods

We performed a retrospective chart review of bleeding complications in patients undergoing primary ICD or pacemaker implantation from August 2004 to August 2007. Exclusion criteria included age <18 years, known coagulation or bleeding disorders, thrombocytopenia (defined as platelet count <50 K/mm^3), use of other antiplatelet or anticoagulation medications (e.g., cilostazol, pentoxyfylline, ticlopidine), or an unusual combination of medications not meeting predefined medication subgroups (i.e., concomitant use of clopidogrel and warfarin).

Patients were grouped according to medications taken at the time of device implantation, as shown in Figure 1. Hospital records, including medication administration records, were reviewed to determine medications taken immediately before and after device implantation. "On treatment" was defined as medication use within 5 days of the procedure for aspirin and clopidogrel. The 5-day period was chosen on the basis of reports of increased bleeding complications in patients undergoing cardiac and noncardiac procedures (9,10). Patients taking warfarin were grouped on the basis of INR values regardless of the duration warfarin was withheld. An INR cutoff of 1.5 was used to differentiate patients with evidence of an anticoagulant effect (i.e., INR ≥1.5) from those without (i.e., INR <1.5) at the time of device implantation (2,11). For purpose of analysis, patients taking aspirin with warfarin or heparin were grouped together with those taking warfarin or heparin alone. Patients receiving either unfractionated heparin or low molecular weight heparin were grouped together. Records from the index hospitalization and clinic notes within 6 weeks of the procedure were reviewed for documentation of procedure-related complications.

All devices were placed by 1 of 12 board-certified or board-eligible electrophysiologists at Johns Hopkins Hospital and Johns Hopkins Bayview Medical Center. Leads were placed using an axillary approach (12). Rarely, a

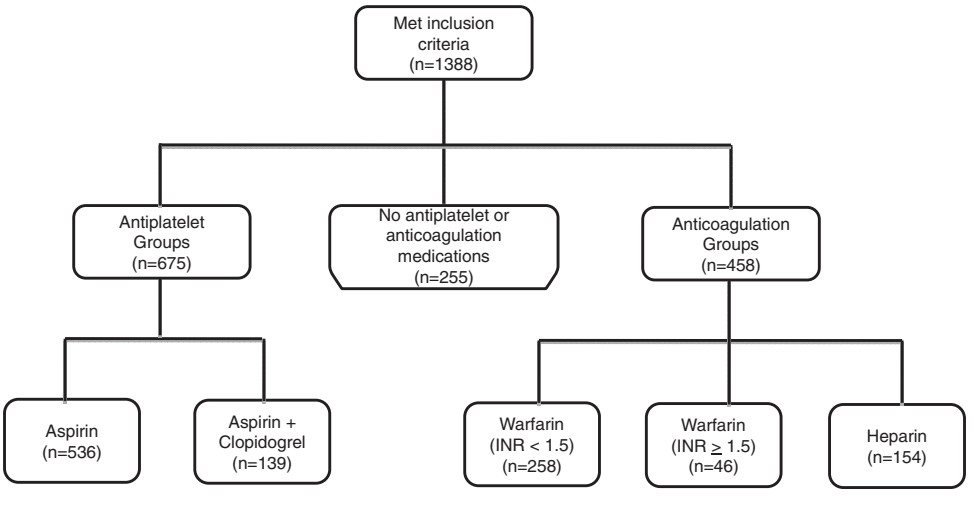

Figure 1 Antiplatelet/Anticoagulant Medication Subgroups

The assignment of patients to medication subgroups on the basis of medications taken during the periprocedural period is displayed. INR = international normalized ratio.

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Table 1 Baseline Characteristics

	Cohort (n = 1,388)	None (n = 255) A	Aspirin (n = 536) B	Aspirin + Clopidogrel (n = 139) C	Warfarin (INR <1.5) (n = 258) D	Warfarin (INR ≥1.5) (n = 46) E	Heparin (n = 154) F	p Value
Age, yrs	64.7 ± 15.5	56.4 ± 18.8	67.3 ± 14.4	66.4 ± 11.3	66.5 ± 12.8	68.5 ± 13.3	63.6 ± 16.5	<0.05*
Sex, %	Male 65.2	53.7	66.6	73.4	63.6	69.6	72.1	<0.05*
Race, %	White 73.7;	70.2	74.2	71	79.1	80.4	70.8	NS
	black 23.1	23.9	23.4	26	19.4	15.2	27.3	
Weight, kg	82.6 ± 20.4	79.8 ± 18.5	82.1 ± 20.8	83.6 ± 19.4	85.1 ± 21.7	88.5 ± 24	82.3 ± 19.2	<0.05†
Hb	12.8 ± 2.0	13.1 ± 2	12.8 ± 1.9	12.4 ± 2.1	12.9 ± 1.8	12.9 ± 2.3	12.1 ± 2.2	<0.05‡
Plt	217.6 ± 79.2	226 ± 69	216 ± 75	216 ± 80	210 ± 85	209 ± 76	228 ± 95	NS
INR	1.10 ± 0.3	1.04 ± 0.1	1.06 ± 0.1	1.07 ± 0.1	1.07 ± 0.3	1.81 ± 0.4	1.16 ± 0.4	<0.05§
Cr	1.44 ± 4.6	1.54 ± 6.6	1.58 ± 5.8	1.28 ± 0.9	1.23 ± 1.0	1.33 ± 0.6	1.36 ± 1.0	NS
PM, %	40.1	43.9	42.2	26.6	34.5	47.8	45.5	<0.05‖
ICD, %	59.9	44.3	44.0	63.3	41.1	41.3	39.6	<0.05¶
BiV ICD, %	15.1	11.8	13.8	10.1	24.4	10.9	14.9	<0.05#
LVEF**	23.7 ± 9.3	22.7 ± 9.7	24.8 ± 9.7	25.1 ± 9.3	22.1 ± 7.8	23.8 ± 11.2	21.9 ± 9	NS

*A versus B, C, D, E, F. †A versus D. ‡F versus A, B, D. §F versus A, B, C, D, E; E versus B, C, D. ‖A versus B, C, D; B versus C, D; C versus E, F; D versus F. ¶C versus A, B, D, E, F. #D versus A, B, C, E, F. **Includes ICD patients only.

BiV = biventricular; Cr = creatinine; Hb = hemoglobin; ICD = implantable cardioverter-defibrillator; INR = international normalized ratio; LVEF = left ventricular ejection fraction; NS = not significant; Plt = platelet count; PM = pacemaker.

cutdown procedure was performed to access the cephalic vein, on the basis of physician preference.

The composite primary end point used to define significant bleeding complications consisted of need for pocket exploration or blood transfusion, hematoma requiring pressure dressing or change in medical therapy, or prolonged hospitalization. Secondary end points consisting of other procedure-related complications were also recorded. These were divided into 2 groups: "thrombosis-related" and "other." Thrombosis-related complications included stroke/transient ischemic attack, myocardial infarction, and deep venous thrombosis. Other complications included cardiac tamponade, pneumothorax, lead dislodgement, and pericarditis.

Statistical analysis. Standard statistical methods were used to evaluate the data. Proportional variables were assessed using chi-square statistics and continuous variables with 1-way analysis of variance, expressed as mean ± SD. A p value of <0.05 considered statistically significant. The post-hoc Bonferroni's correction was used to adjust the type I error for multiple comparisons. Logistic regression analysis was used to estimate the magnitude of association (i.e., odds ratios [ORs]) between the use of anticoagulation or antiplatelet medications and the risk of developing the primary composite end point. The study was approved by the internal review board committee at the Johns Hopkins Hospital.

Results

A total of 1,512 charts were reviewed. Of these, 1,388 were included in the study. Table 1 outlines the baseline characteristics for the entire cohort. The mean patient age was 65 years; 905 (65.2%) were male. A total of 556 patients (40%) underwent placement of a pacemaker, and 832 patients (60%) received an ICD. Of patients who received an ICD, 209 (15%) received a biventricular ICD. Patients receiving ICDs had an average left ventricular ejection fraction of 23.7%.

In all, there were 71 bleeding complications (5.1%) among the 1,388 patients included in the study. The contribution of each component to the primary end point is shown in Table 2. The composite end point was primarily driven by hematoma formation and discontinuation of antiplatelet or anticoagulation medications.

As shown in Figure 2, the difference in the incidence of bleeding complications was statistically significant among patients receiving aspirin and clopidogrel versus neither (7.2% vs. 1.6%; p = 0.004). The difference in the incidence

Table 2 Breakdown of the Primary Composite End Point

	Pocket Exploration	Blood Transfusion	Medication Discontinued	Prolonged Hospitalization	Hematoma
Entire cohort (n = 1,388)	5	4	17	4	41
None (n = 255)	0	0	0	1	3
Aspirin only (n = 536)	1	0	2	1	17
Aspirin + clopidogrel (n = 139)	1	1	2	1	5
Warfarin INR <1.5 (n = 258)	1	1	2	1	6
Warfarin INR ≥1.5 (n = 45)	0	1	1	0	0
Heparin (n = 155)	2	1	10	0	10

INR = international normalized ratio.

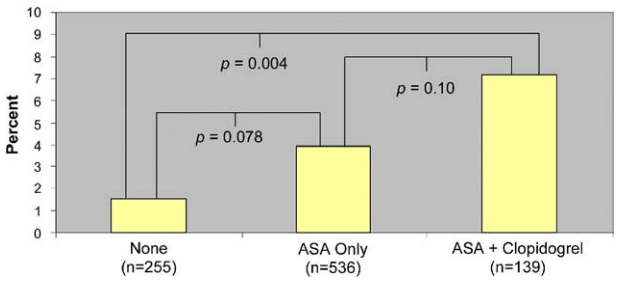

Figure 2 **Effect of Antiplatelet Agents on Composite Primary End Point**

The percentage of patients taking antiplatelet medications who experienced the composite primary end point is displayed. Significant bleeding complications occurred with greater frequency among patients taking aspirin (acetylsalicylic acid [ASA]) and clopidogrel compared with patients taking ASA or with controls, who were taking neither antiplatelet nor anticoagulation medications.

of bleeding complications between aspirin and controls was of borderline significance (3.9% vs. 1.6%; p = 0.078). There was no statistical difference between patients receiving aspirin and clopidogrel versus patients receiving aspirin therapy alone (7.2% vs. 3.9%; p = 0.10).

Warfarin itself was associated with a trend toward increased bleeding complications when compared with controls, even when held to allow the INR to decrease below 1.5, as shown in Figure 3. There was no statistical difference in bleeding risk between patients continued on warfarin with an INR ≥1.5 (n = 46) and patients who had warfarin withheld until the INR was normal (n = 258; 6.5% vs. 4.3%; p = 0.50).

Heparin was held an average of 9.4 ± 8.8 h preprocedure and restarted 22.2 ± 15.6 h after device implantation. The use of periprocedural heparin (enoxaparin or unfractionated heparin; n = 154) markedly increased the risk of bleeding when compared with holding warfarin until the INR was normal (n = 258; 14.3% vs. 4.3%; p < 0.001)

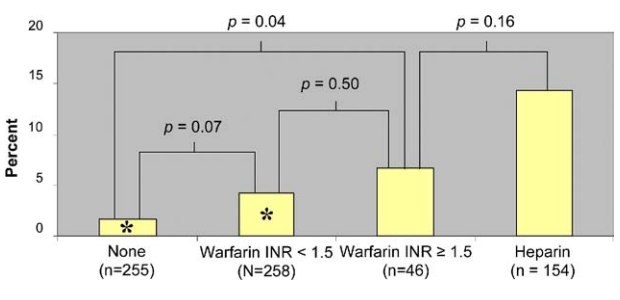

Figure 3 **Effect of Anticoagulation Agents on Composite Primary End Point**

The percentage of patients taking anticoagulation medications who experienced the composite primary end point is displayed. Significant bleeding complications occurred with greater frequency among patients receiving heparin compared with patients who held warfarin (international normalized ratio [INR] <1.5) and patients who continued on warfarin (INR ≥1.5). *p < 0.001 versus heparin.

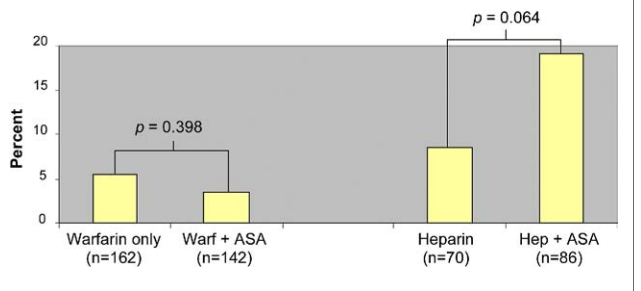

Figure 4 **Effect of ASA Combined With Anticoagulation Agents on Primary End Point**

The effect of adding aspirin (acetylsalicylic acid [ASA]) to either warfarin (Warf) or heparin (Hep) is compared. The addition of ASA to heparin markedly increased the risk of composite primary end point occurrence. A similar association was not seen with warfarin.

and to patients on no anticoagulation therapy (14.3% vs.1.6%; p < 0.0001). There was a trend toward increased bleeding complications with heparin when compared with warfarin with an INR ≥1.5, but this did not reach statistical significance.

Interestingly, when combined with warfarin, regardless of INR, the addition of aspirin did not increase bleeding complications (Fig. 4). The same was not true for the combination of aspirin and heparin, which was associated with a trend toward markedly elevated bleeding complications.

The use of dual antiplatelet therapy (OR: 5.4; 95% confidence interval [CI]: 1.7 to 17.3; p = 0.005) or heparin (OR: 11.0; 95% CI: 3.73 to 32.5; p < 0.001) were major predictors of significant bleeding complications by univariate analysis, as shown in Table 3. In addition, procedure time, defined as per 10 min of procedure time, (OR: 1.004; 95% CI: 1.00 to 1.01; p = 0.004) and use of aldosterone antagonists (OR: 1.79; 95% CI: 1.03 to 3.12; p = 0.038) were also significant predictors of the primary end point by univariate analyses. Increased body weight (OR: 0.98; 95% CI: 0.97 to 0.99; p = 0.007) was protective against developing significant bleeding complications. African Americans tended to be less likely than Caucasians to have bleeding complications (OR: 0.6; 95% CI: 0.35 to 1.00; p = 0.051).

Table 3 **Univariate Analysis of Predictors of Primary Composite End Point**

Variable	Odds Ratio	p Value	95% CI
Aspirin	2.43	0.108	1.82–7.19
Aspirin + clopidogrel	5.39	0.005	1.68–17.27
Heparin	11.02	0.000	3.73–32.53
Warfarin INR <1.5	3.06	0.056	0.97–9.62
Warfarin INR ≥1.5	4.38	0.059	0.95–20.25
Procedure time, per 10 min	1.004	0.004	1.00–1.01
Aldosterone antagonist	1.79	0.038	1.03–3.12
African American	0.6	0.051	0.35–1.0
Weight	0.98	0.007	0.97–0.99

CI = confidence interval; INR = international normalized ratio.

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Table 4 Multivariate Analysis of Predictors of Primary Composite End Point

Variable	Odds Ratio	p Value	95% CI
Aspirin	2.27	0.157	0.73–7.08
Aspirin + clopidogrel	3.84	0.040	1.07–13.79
Heparin	9.88	<0.0001	3.16–30.91
Warfarin INR <1.5	3.20	0.060	0.95–10.75
Warfarin INR ≥1.5	5.64	0.034	1.14–28.06
Male	2.51	0.005	1.33–4.74
African American	0.51	0.025	0.25–0.92
Weight	0.97	0.001	0.96–0.99
Procedure time, per 10 min	1.04	0.006	1.01–1.06

Abbreviations as in Table 3.

The use of dual antiplatelet therapy (OR: 3.84; 95% CI: 1.07 to 13.79; p = 0.040) or heparin (OR: 9.88; 95% CI: 3.16 to 30.9; p < 0.001) remained significant independent predictors of the primary end point developing by multivariate analysis (Table 4). Multivariate analysis also identified male sex (OR: 2.51; 95% CI: 1.33 to 4.74; p = 0.005) and longer procedure time, grouped by 10-min intervals (OR: 1.04; 95% CI: 1.01 to 1.06; p = 0.006) as predictors of significant bleeding complications. This finding may reflect additional time spent obtaining hemostasis.

Overweight patients (OR: 0.97; 95% CI: 0.96 to 0.99; p = 0.001) and African Americans (OR: 0.5; 95% CI: 0.25 to 0.92; p = 0.025) were less likely to have significant bleeding complications by multivariate analysis.

The type of device implanted did not appear to significantly influence the risk of bleeding complications (Fig. 5). Patients who received single-chamber pacemakers were more likely to have a bleeding complication when compared with patients receiving a dual-chamber pacemaker (7.7% vs. 2.6%, respectively; p = 0.019). However, this difference can be attributed to the increased use of heparin among patients receiving single-chamber pacemakers (29.5% vs. 9.6%, respectively; p < 0.001). Patients receiving dual-chamber ICDs were also more likely to have bleeding complications when compared with patients receiving dual-chamber pacemakers (6.5% vs. 2.6%, respectively; p = 0.012). Increased heparin exposure likely contributed to this finding as well (12.6% vs. 9.6%, respectively; p = NS).

Secondary end points. Of the original 1,512 charts reviewed, a total of 13 patients had clopidogrel held for 5 or more days despite having drug-eluting stents previously placed. These patients were excluded from the primary end point analysis because they failed to meet entry criteria. Interestingly, however, there were no ischemic cardiac events among these patients. Additionally, there were no cardiac ischemic events among 154 patients who received dual antiplatelet therapy within 5 days of device implantation. There was a trend toward increased risk of upper extremity deep venous thrombosis in the absence of antiplatelet or anticoagulation agents, but this was not statistically significant (Table 5).

A total of 3 cerebrovascular events were identified in the cohort. Two of the 3 cerebrovascular events were classified as transient ischemic attacks after thorough neurologic assessment, with complete reversal of symptoms and no visible infarction on neuroimaging. One patient with a history of atrial fibrillation had warfarin held before ICD implantation. Defibrillation threshold testing resulted in cardioversion of atrial fibrillation. Two days later, the patient had acute neurologic deficits treated emergently with tissue plasminogen activator. This patient subsequently had a large hematoma, which was managed conservatively with a pressure dressing.

The prevalence of other complications was quite low in all groups and was not affected by the use of antiplatelet or anticoagulation agents. There was a total of 6 cases of pericardial tamponade, 12 cases of pneumothorax, 29 lead dislodgements, and 5 cases of pericarditis. One patient with a pre-procedure INR of 1.6 had pericardial tamponade after dual-chamber pacemaker implantation that was treated with emergent pericardiocentesis and reversal with fresh frozen plasma.

Discussion

The results of this observational study support our initial hypothesis that heparin and the combination of aspirin and clopidogrel significantly increase the bleeding risk at the time of cardiac device implantation. Although marginally higher, the bleeding risk associated with cardiac device implantation while continuing warfarin (INR ≥1.5) is not significantly different from withholding warfarin to allow the INR to decrease to <1.5.

Normal hemostasis involves a series of complex, well-regulated interactions between the vascular wall, platelets, and coagulation cascade intended to reduce bleeding and promote vascular repair after injury (1,13). Primary hemostasis involves interactions between the vascular wall and platelets, leading to formation of platelet plug. Aspirin, clopidogrel, and to some extent, heparin affect the develop-

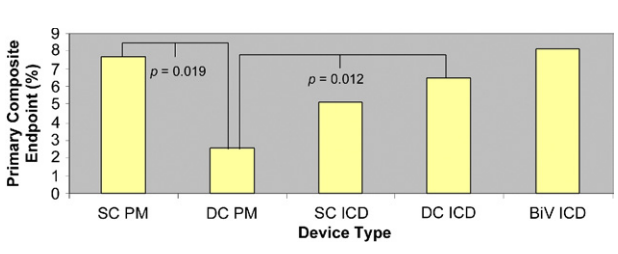

Figure 5 Primary Composite End Point by Device Type

The percentage of patients who experienced the composite primary end point on the basis of the type of device implanted is displayed. Neither the device type nor the number of leads implanted contributed significantly to the development of the composite end point. BiVICD = biventricular internal cardioverter-defibrillator; DC = dual chamber; ICD = implantable cardioverter-defibrillator; PM = pacemaker; SC = single chamber.

Table 5 Summary of Secondary End Points

	None (n = 255)	Aspirin (n = 536)	Aspirin + Clopidogrel (n = 139)	Warfarin INR <1.5 (n = 258)	Warfarin INR ≥1.5 (n = 46)	Heparin (Warfarin Held) (n = 154)
Stroke/TIA	0	0	1 (0.72%)	1 (0.39%)	0	1 (0.65%)
MI	0	0	0	0	0	0
DVT, UE	4 (1.57%)	5 (0.93%)	1 (0.72%)	1 (0.39%)	0	0

DVT = deep venous thrombosis; MI = myocardial infarction; TIA = transient ischemic attack; UE = upper extremity; other abbreviations as in Table 3.

ment of the primary hemostatic plug by disrupting platelet adhesion and aggregation (14–16). In contrast to heparin, warfarin does not specifically inhibit platelet function (17). Secondary hemostasis involves reinforcement of the platelet plug by fibrin cross-linking. Both warfarin and heparin exhibit their anticoagulation effect by disrupting the formation of fibrin and, thus, platelet plug reinforcement (16,17).

There are several published studies assessing different anticoagulation strategies at the time of cardiac device implantation that demonstrate similar complication rates between patients continued on warfarin therapy and patients with a normal INR while warfarin was held (6–8). Goldstein et al. (6) were among the first to report their experience implanting devices in 37 patients continued on warfarin at the time of device implantation. They found no difference in wound-related or wound-unrelated complications between patients receiving warfarin and patients not receiving anticoagulation medications. Al-Khadra et al. (7) reported similar findings in 47 patients with a mean INR 2.3 (range 1.5 to 3.1) at device implantation. Only 1 patient in their study had a small (4 × 3 cm) hematoma, which resolved spontaneously.

The largest observational study was provided by Giudici et al. (8), who assessed the risk of major bleeding complications in 1,025 patients referred for pacemaker or ICD implantation, 470 of whom were continued on warfarin therapy (mean INR 2.5, range 1.5 to 7.5). They found similar complication rates between patients continued on warfarin therapy and patients who had a normal INR while warfarin was held.

Despite these results, patients receiving continuous anticoagulation are often instructed to discontinue warfarin therapy several days before their procedure and begin heparin either intravenously or subcutaneously (2–4). That can prolong hospital stay and lead to periods of inadequate or excessive anticoagulation, increasing the risk for complications, including thromboembolism or bleeding.

A study by Michaud et al. (18) affirmed these findings, noting a 20% risk of pocket hematoma formation and prolonged hospitalizations among patients treated with intravenous heparin after cardiac device implantation. Patients receiving heparin after cardiac device implantation had a 5- or 10-fold greater risk of pocket hematoma formation when compared with patients treated with warfarin alone or no anticoagulation, respectively.

Our study demonstrates a complication rate of 14.3% for patients on heparin and 4.3% for patients who had warfarin held (INR <1.5), which translates to 3-fold increased risk of significant bleeding when compared with heparin. Patients who are not taking any medications had a complication rate of 1.6%, giving a 9-fold increased risk when compared with heparin. Similarly, patients receiving heparin were at 2-fold greater risk of significant bleeding complications when compared with patients who had an INR ≥1.5 (14.3% vs. 6.5%, respectively). Warfarin, regardless of INR, was associated with increased risk of bleeding when compared with controls. However, the risk was significantly less when compared with heparin, even for patients having an INR ≥1.5.

Our findings suggest that patients at greatest risk for thromboembolic events off anticoagulation therapy can be safely continued on warfarin rather than transitioning to heparin, whereas patients at low risk should have warfarin held without instituting heparin "bridging."

Little information has been previously published assessing the risk of bleeding complications in patients continued on dual antiplatelet therapy at the time of device implantation (5,19). In the present study, patients receiving dual antiplatelet therapy at the time of device implantation are at a 2-fold increased risk of reaching the primary end point as compared with patients taking aspirin only (7.2% vs. 3.9%, respectively), and 5-fold greater risk when compared with patients taking no medications (7.2% vs. 1.6%, respectively). There were no cardiac ischemic events among the small subset of patients who had aspirin and clopidogrel held for 5 days or more. Despite these findings, we are hesitant to suggest withholding these medications after placement of drug-eluting stents, particularly in light of our enhanced awareness of both early and late in-stent thrombosis (20). Importantly, however, patients and physicians need to understand the increased risk of bleeding complications associated with these medications.

The results of this study confirm and extend the results of prior studies. In this study, we found that both dual antiplatelet therapy and intravenous heparin significantly increase bleeding risk after cardiac device implantation. Appropriate periprocedural management requires a thorough understanding of indications for antiplatelet or anticoagulation medications and assessing the risks of thromboembolic versus bleeding complications. Holding antiplatelet or anticoagulation medications for a period of 3 to 5 days before device implantation seems an amenable approach to patients at low risk for thromboembolic events. Patients at high risk for thromboembolic events should continue war-

farin throughout the periprocedural phase, avoiding the need for heparin bridging. The use of heparin around the time of device implantation is clearly the strongest risk factor for the development of bleeding complications.

Study limitations. This was a retrospective observational study and thus subject to the limitations of this study design, notably bias and the inability to control for confounders (21). The small sample size within each medication subgroup may have been underpowered to examine certain associations, particularly using multivariate models adjusting for multiple confounders. We did not have a uniform protocol for antiplatelet and anticoagulant management during the study period, and different operators may have had preference for different strategies. However, this study highlights the importance of understanding the indication for antiplatelet or anticoagulation therapy to reduce the risk of thromboembolic events or significant bleeding complications at the time of device implantation.

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