

Meta-Analysis of Bleeding Complications Associated With Cardiac Rhythm Device Implantation

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Background—Many patients receiving cardiac rhythm devices have conditions requiring antiplatelet (AP) and/or anticoagulant (AC) therapy. Current guidelines recommend a heparin-bridging strategy (HBS) for anticoagulated patients with moderate/high risk for thrombosis. Several studies reported lower bleeding risk with continued oral anticoagulation rather than HBS. The best strategy for perioperative management of patients on AP therapy is less clear. The present study was designed as a meta-analysis of device implantation-associated bleeding complications using different AC/AP therapies.

Methods and Results—PubMed and Cochrane Database searches identified articles based on design, outcomes, and available data. Device recipients were grouped as follows: no therapy, aspirin only, AC held, AC continued, dual AP, and HBS. The primary outcome was defined as a bleeding complication including hematoma, transfusion, or prolonged hospital stay. Thirteen articles were identified for analysis including 5978 patients. The combined incidence of bleeding complications was 274 of 5978 (4.6%), ranging from 2.2% (no therapy) to 14.6% (HBS). The estimated odds of bleeding were increased by 8.3 (95% CI, 5.5–12.9) times in the HBS group, 5.0 (95% CI, 3.0–8.3) for dual AP therapy, 1.7 (95% CI, 1.0–3.1) for AC held, 1.6 (95% CI, 0.9–2.6) for AC continued, and 1.5 (95% CI, 0.9–2.3) for aspirin only relative to the no therapy group. HBS significantly increased bleeding events compared with holding or continuing AC. Continuing AC did not increase bleeding events compared with no therapy.

Conclusions—Continuing AC appears safer than HBS for device implantation. Dual AP therapy but not continuing AC carries a significant risk of bleeding. (*Circ Arrhythm Electrophysiol.* 2012;5:468-474.)

Key Words: anticoagulants ■ heparin ■ implantable cardioverter-defibrillator ■ pacemakers

Implantation of pacemakers or cardiac defibrillators among patients receiving anticoagulant (AC) therapies is a common occurrence. Maintaining anticoagulation increases the risk of bleeding complications for most operative procedures, whereas discontinuing AC may increase the risk of thromboembolic complications. This led to the common practice of discontinuing warfarin and bridging with heparin to allow anticoagulation with an agent that can be more rapidly discontinued. The most current surgical guidelines on device implantation in the setting of AC therapy for patients at high risk for thromboembolism recommend a heparin-bridging strategy (HBS).¹ Less specific recommendations are made for those with low or moderate risk of thromboembolism. An alternative strategy that has emerged more recently is to continue oral anticoagulation rather than use an HBS. The issue of perioperative bleeding complications is further complicated by the more frequent use of antiplatelet therapy, particularly dual agents among patients with concomitant coronary artery or vascular disease. Dedicated analysis of perioperative management of bleeding risk for cardiac device implantation has been proposed.²

However, it is unclear if there is widespread adoption of any particular strategy.³ Give the paucity of randomized or even multicenter studies of bleeding associated with cardiac device implantation using different AC/antiplatelet strategies,⁴⁻²² the present study was designed as a meta-analysis to compare these strategies.

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Methods

The meta-analysis was conducted using standard published guidelines.^{23,24} PubMed and Cochrane Library databases were searched for publications with the following criteria: (Pacemaker) OR (ICD) OR (Implantable cardioverter defibrillator) AND (Bleeding OR anticoagulation OR antiplatelet). There were 19 of 203 articles selected for review. Criteria for inclusion were: (1) assessment of ≥ 1 cohorts falling into 1 of the following categories Group 1: no therapy, Group 2: AC held or international normalized ratio < 1.5 , Group 3: AC continued or international normalized ratio > 1.5 , Group 4: single antiplatelet therapy, Group 5: dual antiplatelet therapy, Group 6: HBS including either unfractionated heparin or low-molecular-weight heparin; (2) standard definition and assessment of bleeding complications; and (3) routine follow-up after device implantation. Exclusion criteria included: (1) incomplete or unavailable data; (2) confounding medical or surgical therapy; (3)

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lack of appropriate follow-up; and (4) inability to categorize data accurately into these groups. Thirteen articles were selected for analysis including 5978 patients. Bleeding complications were defined as any complication that met criteria for the individual articles. All reported major or minor bleeding events were categorized as a bleeding complication. There were nonuniform definitions of major and minor bleeding in a few of the referenced articles. Based on the select articles in which major and minor definitions were provided, classification of bleeding complications could be derived as follows. Major bleeding defined as any bleeding leading to transfusion, surgical intervention for pocket evacuation or revision, pericardial effusion, hemothorax, or life-threatening bleed. Minor bleeding was defined as any hematoma requiring conservative management only, blood loss not requiring transfusion, or discontinuation of medication. Thromboembolic events were classified as transient ischemic attacks, cerebrovascular accidents, or any other systemic embolism.

This meta-analysis assessed the risk of periprocedural bleeding complications in 13 studies that consider ≥ 1 of 6 anticoagulant or antithrombotic strategies before device implantation. For each study, the outcome considered was a count of patients who experienced a bleeding complication. Each study considered at least 2 anticoagulant or antithrombotic treatments and as many as 6.

To screen for publication bias and study heterogeneity (ie, whether study-specific factors affect the rate of bleeding complications), marginal estimates for the log odds of bleeding were plotted against the corresponding standard error for each study (ie, a “funnel” plot) stratified by treatment. When no publication bias or study heterogeneity exists, the plotted points are expected to lie within a funnel shape and to be symmetrical about the funnel axis. Asymmetry is indicative of publication bias. Study heterogeneity is evident when many points fall outside the expected funnel shape.

For 9 of the studies, mean age and sex distribution were reported within treatment groups. Because age and sex distribution were reported in aggregate, their effect on bleeding complication is confounded with the study effect. Because bleeding complication counts arising from the same study may further correlate due to unspecified factors, a Bayesian mixed effects logistic regression model was evaluated in these data.²⁵ Treatment effects were evaluated as fixed, and study effects were evaluated as random. Bayesian analysis formalizes the notion of prior evidence about quantities under study, that is, the evidence at hand before an experiment is carried out. In this meta-analysis, the quantities under study are log odds of perioperative bleeding. Prior evidence may be updated in light of experimental data to yield the posterior evidence. The Bayesian method encodes evidence as a probability distribution. Hence, a prior distribution is specified to reflect prior evidence, and the posterior evidence is summarized using a posterior distribution. The log odds were each assigned a normal γ prior distribution with mean 0 and small (0.1) shape and rate parameters. The resulting prior distribution was heavy-tailed and symmetrical about 0. This choice of prior distribution reflected conservative (0 mean) but weak (heavy-tailed) prior evidence regarding the effects of treatment and study on the log odds of bleeding. To further illustrate, suppose that an antiplatelet/anticoagulant therapy is considered “safe” with regard to bleeding complications when the estimated log odds is 0 and there is strong evidence that the estimate is accurate to within 5 events per 100 patients (ie, that the log odds is confined within the interval -0.2 to 0.2 with high probability). Although the prior estimate is 0, there is weak prior evidence (prior probability <0.08) that the log odds is accurate to within 5 events per 100 patients. Hence, there is no basis for a clinical conclusion a priori. This weak prior ensures that evidence brought by experimental data will dominate the posterior evidence.

Statistical inference about the treatment and study effects was conducted using the posterior distribution over the log odds of bleeding complications. Samples were drawn from the posterior distribution using conventional Gibbs sampling methods and diagnostics. These samples were used to construct 95% credible intervals, fixed intervals that contain the log odds with 0.95 posterior probability. Hence, a credible interval summarizes the posterior evidence in terms of posterior probability. This contrasts with a 95% CI; roughly, a random

interval that contains the log odds with frequency of 0.95 in repeated hypothetical experiments. Although quite different in construction, credible intervals and CIs both measure the evidence about a quantity of interest and often take similar values. In the following text, “95% CI” refers to a 95% credible interval.

Treatment effects on the risk of bleeding complications are presented as partial log odds ratios relative to the no therapy (NT) group. A partial log OR was considered statistically significant when its credible interval did not include 0. This indicated that the odds of bleeding complication in the corresponding treatment group were significantly greater than in the NT group. Other partial log ORs were constructed for special comparisons. Study effects are presented as partial log odds. Study effects were considered statistically significant when their 95% credible interval did not include 0. This indicates that the odds of bleeding complication in the corresponding study were significantly greater or less than the overall odds. Statistical analyses were carried out using JAGS²⁶ and R²⁷ software packages.

Results

Primary Analysis

There were 5978 patients from 13 studies included in the analysis. Event rates for all studies are shown in Table 1. The combined rate of bleeding complications was 3.7% (95% CI, 1.4–12.3). Unadjusted, pooled rates of bleeding complications using different anticoagulant and antiplatelet therapies are shown in Figure 1. The lowest rate of bleeding complications was observed among patients with no anticoagulation or antiplatelet therapy. In contrast, the highest rate of bleeding was noted in the subgroup with heparin-bridging therapy. Intermediate rates were noted with antiplatelet or oral anticoagulation. Adjusting for study heterogeneity, the estimated rate of bleeding complications for patients on NT was 1.0% (95% CI, 0.2–3.7). Using the NT group as a reference, ORs for the remaining AC or antiplatelet therapies are summarized in Figure 2. Adjusting for study heterogeneity, the estimated odds of bleeding were increased by 8.3- (95% CI, 5.5–12.9) fold in the HBS group, 5.0 (95% CI, 3.0–8.3) for dual antiplatelet therapy, 1.7 (95% CI, 1.0–3.1) for AC held, 1.6 (95% CI, 0.9–2.6) for AC continued, and 1.5 (95% CI, 0.9–2.3) for aspirin only relative to the NT group. Dual antiplatelet therapy (DAPT) and HBS were associated with significant increases in bleeding risk, whereas AC continuation, AC interruption, and aspirin therapy trended toward higher rates but had no significant difference compared with NT. The OR of bleeding risk for HBS compared with AC continued was 5.3 (95% CI, 3.4–8.5).

Data were presented in 11 of 13 articles allowing differentiation between minor and major bleeding (Table 2). There were no reported severe or life-threatening bleeding events. Major bleeding events occurred in 0.1% (1 of 961) NT, 0.2% (2 of 1044) AC held, 0.5% (5 of 1079) AC continued, 2.0% (11 of 551) HBS, 0.2% (1 of 618) single antiplatelet therapy, and 1.9% (5 of 263) DAPT groups. Major events were higher in HBS and DAPT groups in proportions similar to that observed in the overall analysis. Minor bleeding events occurred in 1.5% (15 of 961) NT, 2.1% (22 of 1044) AC held, 2.2% (24 of 1079) AC continued, 9.1% (50 of 551) HBS, 1.6% (15 of 618) single antiplatelet therapy, and 3.0% (8 of 263) DAPT groups. HBS was clearly associated with increased minor events, whereas DAPT only had a small

Table 1. Results of Bleeding Complications Using Different Perioperative Anticoagulant/Antiplatelet Strategies

Article	No.	No Therapy	AC Held	AC Continued	SAPT	DAPT	HBS
Goldstein, 1998	150	2/113 (1.8%)		2/37 (5.4%)			
Michaud, 2000	192	2/115 (1.7%)		1/28 (3.6%)			10/49 (20.4%)
Guidici, 2004	1025		9/555 (1.62%)	9/470 (1.91%)			
Tischendo, 2009	272	5/117 (4.3%)		9/117 (7.7%)			9/38 (23.7%)
Tolosana, 2009	101			4/50 (8%)			4/51 (7.8%)
Ahmed, 2010	459		2/114 (1.75%)	1/222 (0.5%)	7/123 (5.7%)		
Dreger, 2010	427	3/318 (0.9%)				1/109 (0.9%)	
Ghanbari, 2010	123	3/74 (4.0%)	1/20 (5.0%)	6/29 (20.7%)			
Klutinsky, 2010	713	9/164 (5.5%)		8/121 (6.6%)	17/327 (5.2%)	16/66 (24.2%)	9/35 (25.7%)
Thal, 2010	179	0/43 (0%)		1/39 (2.6%)	1/82 (1.2%)	3/15 (20%)	
Tompkins, 2010	1388	3/255 (1.2%)	10/258 (3.9%)	2/46 (4.4%)	20/536 (3.7%)	9/139 (6.5%)	23/154 (14.9%)
Cano, 2011	849	9/375 (2.4%)			7/220 (3.2%)	8/63 (12.7%)	29/191 (15.2%)
Cheng, 2011	100		1/43 (2.3%)	0/50 (0%)			2/7 (28.6%)

AC indicates anticoagulant; SAPT, single antiplatelet therapy; DAPT, dual antiplatelet therapy; HBS, heparin-bridging strategy.

increase in minor events. Although major events are less frequent than minor events, there is no evidence to suggest that they are distributed differently among the treatment groups. Therefore, the pooled analysis of both major and minor events is consistent with the findings of the primary meta-analysis.

Details of the indications for anticoagulation were provided in 6 studies. For the 917 patients included in these studies, the indications were atrial fibrillation in 658 of 917 (71.8%), mechanical heart valves in 173 of 917 (18.9%), venothromboembolic disease in 51 of 917 (5.6%), and all other indications in 35 of 917 (3.9%). There was no uniform consensus among articles with regard to assigning risk. In general, patients at high risk for thromboembolism include those with a history of prosthetic mechanical heart valves, chronic atrial fibrillation, cerebrovascular accident/transient ischemic attack, intracardiac thrombus, or hypercoagulable disorders. Those at low risk include those patients without any condition requiring systemic anticoagulation and patients with paroxysmal atrial fibrillation with CHADS score ≤ 1 . Moderate-risk patients are those with risk factors for cerebrovascular accident who do not meet criteria for either high or low risk (ie, persistent atrial fibrillation with CHADS score ≥ 2). By the criteria noted, of the 938 patients from 6 articles categorized into risk, there were 50.5%, 17.2%, and 32.2% or high-, moderate-, and low-risk patients, respectively.

Secondary Analysis

Of the 7 studies that reported thromboembolic events,^{5,7,11–13,17,19} cumulative rates were low, 9 of 2375 (0.4%). Pooled rates of thromboembolic events were 0.5%, 0.2% and 0.5% in AC held, AC continued, and HBS groups, respectively (Table 3). In only 1 study were the rates of thromboembolic events significantly different with 3 of 114 (2.6%) patients in AC held versus 0 of 222 (0%) in AC continued experiencing transient ischemic attacks.¹¹ In no study did a HBS protect against thromboembolic events.

The partial log odds of bleeding complications associated with each study are presented in Figure 3. These effects are independent of treatment and represent the contribution of all unspecified factors that may have been heterogeneous among studies, including patient sample and study protocol. Only 1 study exhibited significantly greater partial log odds of bleeding complications relative to the overall odds. Partial log odds for the 2 randomized controlled trials were not significant from 0. Funnel plot analysis was performed to assess for publication bias (Figure 4). No conspicuous asymmetry was identified about the funnel axes. The greatest imbalance occurred among studies of continued AC therapy. For this treatment, 7 of the marginal estimates were greater than the average log odds and 4 were below. Hence, there is little evidence of publication bias in these data. There is evidence of study heterogeneity, as indicated by points that lie outside

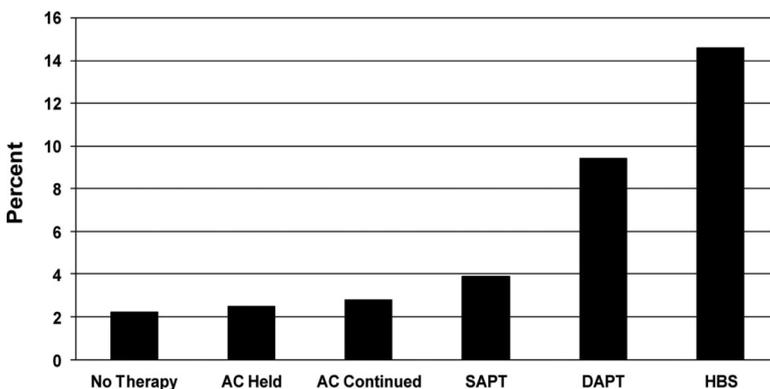


Figure 1. Unadjusted, pooled rates of bleeding complications. Bleeding event rates were 33 of 1500 (2.2%) for no therapy, 26 of 1044 (2.5%) for AC held, 34 of 1200 (2.8%) for AC continued, 45 of 1165 (3.9%) for SAPT, 37 of 392 (9.4%) for DAPT, and 99 of 677 (14.6%) for HBS. AC indicates anticoagulant; SAPT, single antiplatelet therapy; DAPT, dual antiplatelet therapy; HBS, heparin-bridging strategy.

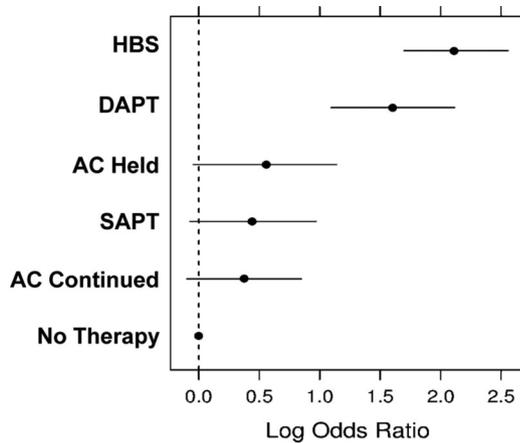


Figure 2. Forest plot of partial log odds ratios of bleeding complications for 6 anticoagulant and antiplatelet strategies. **Horizontal edges** represent 95% credible intervals. AC indicates anticoagulant; SAPT, single antiplatelet therapy; DAPT, dual antiplatelet therapy; HBS, heparin-bridging strategy.

the expected funnel shape. However, the mixed-effects modeling strategy used in this meta-analysis deliberately accounts for this unexplained study heterogeneity. The 2 randomized controlled trials, denoted “Tolo09” and “Chen11” in Figure 4, demonstrate good agreement in the estimate for continued AC therapy but less agreement for HBS.

Robustness of this analysis is supported by results from 3 studies excluded from analysis because of lack of comparable control data. Unfractionated heparin or LWMH was associated with increased bleeding complications in 1 excluded study.^{16,19,21} Wiegand used perioperative low-dose subcutaneous unfractionated heparin as a reference group for their analysis, which could diminish the effect of other anticoagulants and antiplatelet agents on hematoma formation. However, excess bleeding complications in both DAPT and HBS groups were observed.¹⁶ DAPT was linked to increased rates of bleeding complications in the same study.^{16,21} Another excluded study performed without a control group found that implantations on warfarin therapy resulted in no bleeding complications.¹⁸ Finally, a retrospective observational study reported excess bleeding complications in a HBS group compared with warfarin therapy or no therapy.²²

Table 2. Events From 11 Studies Stratified as Minor and Major Bleeding Complications

	Minor	Major
No therapy	15/961 (1.5%)	1/961 (0.2%)
AC held	22/1044 (2.1%)	2/1044 (0.2%)
AC continued	24/1079 (2.2%)	5/1079 (0.5%)
HBS	50/551 (9.1%)	11/551 (2.0%)
SAPT	15/618 (1.6%)	1/618 (0.2%)
DAPT	8/263 (3.0%)	5/263 (1.9%)

Definitions of major and minor bleeding complications are listed in the “Methods” section.

AC indicates anticoagulant; HBS, heparin-bridging strategy; SAPT, single antiplatelet therapy; DAPT, dual antiplatelet therapy.

Table 3. Pooled Analysis of Thromboembolic Complications During Device Implantation Using Different Anticoagulant Strategies

Article	AC Held	AC Continued	HBS
Michaud, 2000		1/28	0/49
Guidici, 2004	1/555	0/470	
Tischendo, 2009		0/117	0/38
Tolosana, 2009		0/50	0/51
Ahmed, 2010	3/114	0/222	1/123
Tompkins, 2010	1/258	0/46	1/154
Cheng, 2011	0/50	1/50	
Totals	5/977 (0.5%)	2/983 (0.2%)	2/415 (0.5%)

Complications included transient ischemic attack, cerebrovascular accident, or other systemic thromboembolization.

AC indicates anticoagulant; HBS, heparin-bridging strategy.

Discussion

The primary results of the present meta-analysis show that a HBS strategy and DAPT are associated with significant perioperative bleeding risks with cardiac rhythm device implantation. Specifically, HBS carries a >8-fold increase of perioperative bleeding complications compared with NT. Compared with continuing AC, the odds of bleeding are 5.3-fold with HBS (95% CI, 3.4–8.5). We also noted a 5-fold increased bleeding complications with DAPT.

These findings are consistent with several other observations on perioperative bleeding. Robinson et al¹⁴ found postoperative low-molecular-weight heparin was more predictive of adverse bleeding outcomes compared with pre-procedure heparin. The use of any low-molecular-weight heparin conferred a 23% risk of hematoma in that study. There are little data on the effects of subcutaneous unfractionated heparin; however, Wiegand et al¹⁶ used perioperative subcutaneous heparin use as a reference cohort with a 2.5%

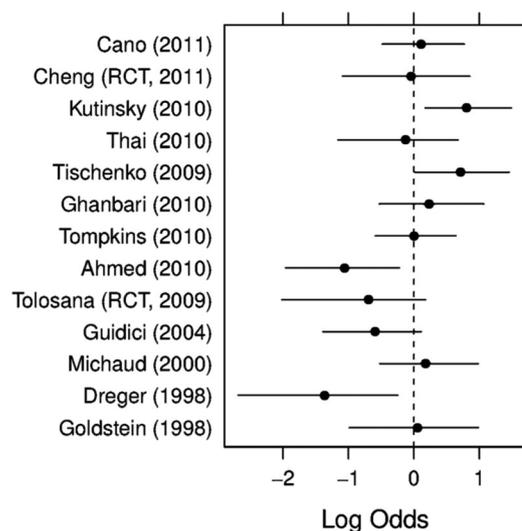


Figure 3. Forest plot of partial log odds for bleeding complications. **Horizontal edges** represent 95% credible intervals. Negative log odds represent less likelihood of bleeding complications in the given study, whereas positive log odds represent increased likelihood of reporting bleeding complications. The 2 randomized controlled trials are denoted “RCT.”

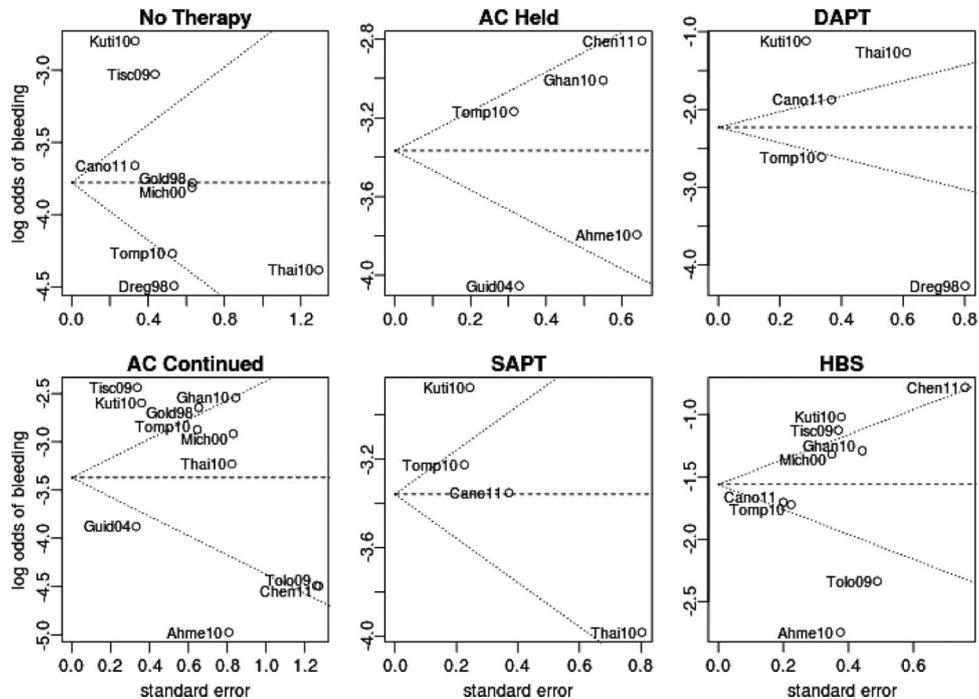


Figure 4. Funnel plots for each treatment using marginal estimates for the log odds of bleeding complications. Each point represents a single study. Points were labeled by concatenating the first 4 letters of the author's last name with the last 2 digits of the year published. The 2 randomized controlled trials are labeled "Tolo09" and "Chen11." The number of points within each plot may differ because studies investigated different subsets of the available treatments. **Dashed lines** represent the mean log odds. **Dotted lines** form approximate 95% credible "funnels" for log odds given that no publication bias or study heterogeneity is present. These funnel plots are indicative of study heterogeneity but not publication bias.

bleeding rate. The same study reported a 16.1% and 11.6% rate of hematoma formation in patients receiving low-molecular-weight heparin and unfractionated heparin, respectively. In all 4 observational studies comparing HBS versus AC continuation, there was increased risk of bleeding complications in HBS groups.^{7,9,11,13} For high-risk patients, AC continuation compared with a HBS seems to offer lower bleeding risk without resulting in excess thromboembolic risk.

Continuation of AC did not significantly increase bleeding complications compared with NT or with those for whom AC was interrupted. However, the aggressiveness of AC varied among studies, as evidenced by the range of acceptable international normalized ratios for implantation between 1.5 and 3.5. Other studies not included in the meta-analysis support the relative safety of AC continuation. Al-Khadra¹⁸ found no bleeding complications in 47 consecutive patients undergoing device implantation on continued AC therapy. These findings are consistent with reports from other cardiovascular procedures in which AC continuation did not increase bleeding risks compared with AC cessation and were less prone to result in bleeding events compared with HBS.²⁸⁻³⁴ The concomitant use of AC and DAPT is less studied but has been associated with increased bleeding risk.^{8,21}

When assessing the increased risk of bleeding complications with DAPT compared with continuing AC, the differential thrombotic risk of interrupting AC and DAPT must be considered. Although the rates of late in-stent thrombosis are low (1%–2%), the mortality is excessive. The thromboembolic

events in >2300 patients on interrupted AC, continued AC, and HBS therapy were <1%. For the 392 patients on DAPT included in this analysis, there were no reports of acute ischemic events or in-stent thrombosis. For patients within the indicated timeframe of DAPT postdrug-eluting stent placement who require urgent device implantation, a glycoprotein IIb/IIIa bridge can be considered. For patients on DAPT remote (>1 year) from drug-eluting stent placement, switching to single antiplatelet therapy in the form of aspirin monotherapy is an option. Although excess bleeding events with DAPT were observed compared with AC therapy, the routine discontinuation of DAPT before device implantation is not supported by this study.

The results of this meta-analysis support maintaining oral warfarin perioperatively at the time of device implantation. At this time, there are no published data on the safety of device implantation on newer oral anticoagulants such as dabigatran, apixaban, and rivaroxaban. Comparison of these agents to warfarin will undoubtedly be assessed as these agents become more widely prescribed. This will be particularly important for dabigatran given the absence of a reversal agent for this direct thrombin inhibitor.

Limitations

This study should be interpreted in light of several methodologic limitations. There is no standardized definition of bleeding complications. In some studies, surgical intervention or prolonged hospitalization was required to define a bleeding complication, whereas in others, the presence of a hematoma was sufficient to be classified as a complication. Furthermore,

<20% of patients included in the meta-analysis had risk assessment and/or anticoagulation indication provided. In only a select number of these patients could the thrombotic risk and anticoagulation indication be linked to the primary outcome. There were also variations in HBSs as well as non-standardized follow-up. Aspirin doses were not reported in any of the studies; therefore, a dose-response effect of single antiplatelet therapy could not be assessed. Most of the studies are single-center observational studies with only 2 relatively small randomized trials included.^{5,12} Due to the largely observational data, the results are possibly influenced by sampling bias with more high-risk patients included in the HBS group than in moderate- and low-risk patients. However, the few randomized studies showed similar results suggesting that bias was unlikely to be contributing to the results. Finally, pulse generator size, the number of leads, and operative time may affect bleeding complications but were not controlled for in this meta-analysis.

Conclusions

Implantation of cardiac devices in patients on antiplatelet and/or AC therapy is an increasingly common occurrence. Our findings suggest that contrary to current guidelines, a strategy of continued AC is superior to HBS with regard to bleeding complications. Furthermore, there appears to be no increased risk of thromboembolic events for high-risk patients who are maintained on AC therapy compared with discontinuing anticoagulation. Finally, DAPT carries a high risk of bleeding at the time of implantation.

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Disclosures

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CLINICAL PERSPECTIVE

Most patients who undergo cardiac implantable electronic device procedures have indications for anticoagulant and/or antiplatelet therapy. The risks associated with these agents have been described in single-center studies. The present study is a meta-analysis assessing the effects of anticoagulant and antiplatelet therapy on periprocedural bleeding complications. Excess bleeding risk was observed among patients for whom a heparin-bridging strategy was used or for those on dual antiplatelet agents. In contrast, uninterrupted warfarin use was not associated with increased bleeding risk at the time of implantation. Furthermore, heparin bridging did not protect from thromboembolic events compared with interrupted or continued warfarin. Current guidelines recommend a heparin bridge for patients at high risk for thromboembolic disease at the time of cardiac implantable electronic device implantation. Our findings support an alternative strategy of continuation of warfarin for high-risk patients who undergo cardiac implantable electronic device procedures. Dual antiplatelet therapy should also be avoided if clinically appropriate.

Meta-Analysis of Bleeding Complications Associated With Cardiac Rhythm Device Implantation

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