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Safety of anticoagulation with uninterrupted warfarin vs. interrupted dabigatran in patients requiring an implantable cardiac device

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Background: The optimal strategy of peri-procedural anticoagulation in patients undergoing permanent cardiac device implantation is controversial. Our objective was to compare the major bleeding and thromboembolic complications in patients managed with uninterrupted warfarin (UW) vs. interrupted dabigatran (ID) during permanent pacemaker (PPM) or implantable cardioverter defibrillators (ICD) implantation.

Methods: A retrospective cohort study of all eligible patients from July 2011 through January 2012 was performed. UW was defined as patients who had maintained a therapeutic international normalized ratio (INR) on the day of the procedure. ID was defined as stopping dabigatran ≥ 12 hours prior to the procedure and then resuming after implantation. Major bleeding events included hemothorax, hemopericardium, intracranial hemorrhage, gastrointestinal bleed, epistaxis, or pocket hematoma requiring surgical intervention. Thromboembolic complications included stroke, transient ischemic attack, deep venous thrombosis, pulmonary embolism, or arterial embolism.

Results: Of the 133 patients (73.4 \pm 11.0 years; 91 males) in the study, 86 received UW and 47 received ID. One (1.2%) patient in the UW group sustained hemopericardium perioperatively and died. In comparison, the ID patients had no complications. As compared to the ID group, the UW group had a higher median CHADS₂ score (2 vs. 3, P=0.04) and incidence of Grade 1 pocket hematoma (0% vs. 7%, P=0.09). Neither group developed any thromboembolic complications.

Conclusions: Major bleeding rates were similar among UW and ID groups. Perioperative ID appears to be a safe anticoagulation strategy for patients undergoing PPM or ICD implantation.

Keywords: Dabigatran; warfarin; pacemaker; defibrillator; perioperative anticoagulation

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Introduction

Approximately 176,000 patients receive permanent pacemakers (PPM) or implantable cardioverter defibrillators (ICD) annually in the USA (1). Of these, a significant proportion receive chronic oral anticoagulation therapy with warfarin for treatment of atrial fibrillation (2). As such, an understanding of appropriate management of anticoagulation in the context of device implantation is crucial (3,4). Unfortunately, agreement on an optimal perioperative strategy remains controversial.

In the last decade, various anticoagulation regimens have been employed and respective outcomes compared (3-8). Approaches are classified as either “interrupted” or “continued” anticoagulation. Interrupted anticoagulation places patients at higher risk for cardioembolic events, but continued therapy may increase the risk of bleeding complications such as pocket hematomas (5,6). A previously proposed method based on ACC/AHA guidelines of interrupted warfarin therapy with low molecular weight heparin (LMWH) bridging has been abandoned in many centers due to a concomitant high incidence of pocket hematomas (6-9). Instead, uninterrupted warfarin (UW) has become an accepted strategy as it has been linked to reduced rates of bleeding complications and shorter hospital stays (5,10-13).

However, the availability of newer anticoagulants such as dabigatran brings the possibility of superior outcomes for this patient population. The more predictable pharmacological profiles of these new drugs allow for short-term interruption that may potentially improve device implantation safety by reducing bleeding complications. Additionally, the ability to stop these drugs for a short period of time before clot formation can occur may lead to similar efficacy in regards to prevention of thromboembolic adverse outcomes in high risk patients. However, certain agents such as LMWH with short half-lives have been linked to increased risk of pocket hematoma development (4). This immediate post-operative risk of increased bleeding is not as well-known with newer anticoagulants such as dabigatran.

The RE-LY trial demonstrated superior efficacy of dabigatran in the prevention of stroke and systemic embolism, as well as similar rates of major bleeding when compared to warfarin (14). There are few articles regarding safety of perioperative anticoagulation with dabigatran (15-18). In this retrospective study, we compared the safety of UW to interrupted dabigatran (ID) in patients requiring

a PPM or ICD. We hypothesized that the risk of major bleeding would be similar between UW and ID therapy and the use of perioperative dabigatran in patients undergoing device implantation would be a safe strategy.

Material and methods

Study design

This was a single center retrospective study comparing major bleeding and thromboembolic events in patients who underwent PPM or ICD placement with either UW or ID therapy during a six-month period, July 2011 to January 2012, at Spectrum Health—Butterworth Hospital, a 989-bed teaching hospital in West Michigan. Five experienced cardiac electrophysiologists, who implant approximately 1,250 devices each year, performed all procedures. Patient charts were reviewed systematically to obtain demographic, clinical, and laboratory characteristics pre- and post-procedure. The study was approved by the hospital institutional review board.

Inclusion/exclusion criteria

All patients who required a new device implantation or had an existing device replaced and met the inclusion criteria were included. Inclusion criteria included documented diagnosis of atrial fibrillation and currently on chronic anticoagulation with either warfarin or dabigatran. The exclusion criteria included age <18 years, pregnancy, history of mechanical heart valves, international normalized ratio (INR) >4 and patients who switched therapy from dabigatran to warfarin or vice versa in the perioperative time period.

Clinical procedures

Perioperative anticoagulation protocols were based on the clinical judgment of the attending cardiac electrophysiologist. If a patient was in the UW cohort, INR was checked the morning of the procedure to confirm that the INR was <4. All patients in the ID group had non-valvular atrial fibrillation, as well as a creatinine clearance greater than 30 mL/min and had dabigatran held at least 12 hours prior to the procedure. Patients received a dose of dabigatran at a mean time of 23.3 hours (range, 12-91 hours) prior to the start of procedure and resumed dosing at a mean time of 21.0 hours (range, 9-54 hours)

after the procedure. PPM and ICD leads were placed under fluoroscopic guidance. Leads were implanted through the subclavian or axillary vein after administration of prophylactic antibiotic and local anesthesia. Both active and passive fixation leads were used for atrial and ventricular leads.

Outcome variables and definitions

The primary outcome of the study was major bleeding within one-month post procedure. Major bleeding was defined as hemothorax, hemopericardium, intracranial hemorrhage, gastrointestinal bleed, epistaxis, or pocket hematoma requiring surgical intervention. Pocket hematoma was defined as a palpable and visible soft mass in the pacemaker pocket with or without the need for evacuation. Pocket hematomas were graded 0 to 3 based on severity. A pocket hematoma score of 0 described either skin ecchymosis or minimal hematoma, whereas a score of 3 described a hematoma that required surgical evacuation. Scores of 1 and 2 correlated to a hematoma size smaller than or greater than the size of the generator, respectively. All patients were followed up within 1-2 weeks post-procedure for surgical site assessment in the electrophysiology outpatient clinic or in the hospital. Thromboembolic complications included stroke, transient ischemic attack, deep venous thrombosis, pulmonary embolism, or arterial embolism. All-cause mortality within 1-month post-procedure was obtained from patient charts and verified using the social security death index.

Statistical analysis

Summary statistics were calculated. Continuous variables are expressed as the mean \pm SD, categorical data as percentages, and the CHADS₂ data as the median (range). Differences among quantitative variables for the two groups were determined using the *t*-test. Categorical variables were analyzed using the Fisher's Exact test. CHADS₂ data were compared using the Mann-Whitney test. Significance was assessed at $P < 0.05$. Statistical analyses were performed using IBM SPSS Statistics version 20 (Armonk, NY, USA).

Results

A total of 133 patients met the inclusion criteria resulting in 86 (64.7%) in the UW cohort and 47 (35.3%) in the ID cohort. Baseline characteristics are shown in *Table 1*.

The mean age of the sample was 73 years and the majority of patients were males. Patients in the UW group had significantly higher median CHADS₂ scores than the ID group. Notably, the prevalence of prior stroke or TIA was over two-fold higher in the UW group than in the ID cohort, although this was not a significant difference. With regards to the other comorbidities, there were no significant differences between the groups. Of note, mean INR on the day of procedure in the UW group was 2.3 ± 0.7 (*Table 1*).

Overall, 71 patients (53.4%) received a PPM while 62 (46.6%) had ICD placed. Among the UW cohort, 45 (52.3%) received a PPM and 41 (47.7%) received an ICD. Of those patients who received an ICD in UW group, 23 (26.7%) had biventricular ICD. In the ID group, 26 (55.3%) received a PPM and 21 (44.7%) received an ICD. Fourteen patients (29.8%) in the ID cohort received biventricular ICDs. Indications for implantation of the device are shown in *Table 2*.

Among the 133 patients included in the study, there was one major bleeding event, which occurred in the UW group (*Table 3*). This was also the only patient who died within one month of the procedure. The incidence of pocket hematomas was higher in the UW group (7%) than in the ID group (0%), but this was not statistically significant ($P = 0.09$). All pocket hematomas were identified as grade 1 and none required surgical evacuation or anticoagulation cessation. Overall, there was no statistically significant difference in thromboembolism and bleeding between the UW and ID cohorts.

Discussion

This study suggests that dabigatran use perioperatively in patients requiring a PPM or ICD when compared to continued anticoagulation with warfarin may lead to less bleeding complications. Previous studies have demonstrated a higher incidence of hemorrhagic events associated with heparin bridging without warfarin reversal (19,20). A higher incidence of hemorrhage associated with post-operative use of heparin has also been described in the literature (6,7,21). Cheng *et al.* showed that LMWH used post-operatively causes an increased incidence of pocket hematoma (4). Continued anticoagulation with UW has been shown to be safer than heparin bridging in prior studies (5,10-13).

To date, few studies have investigated the safety and efficacy of dabigatran in the perioperative period. Rowley *et al.* performed a prospective observational study of patients receiving dabigatran but only included 25 patients

Table 1 Patient baseline characteristics

Characteristic	All patients [n=133]	Uninterrupted warfarin [n=86]	ICD [n=47]	P value
Age (years)*	73.4±11.0	73.0±11.6	74.0±9.7	0.63
Gender—male	68.4% [91]	67.4% [58]	70.2% [33]	0.85
Race—caucasians	97% [129]	95.3% [82]	100% [47]	0.30
BMI (kg/m ²)*	29.2±6.2	28.9±6.1	29.8±6.5	0.46
CHADS ₂ score [^]	3 [0-6]	3 [1-6]	2 [0-5]	0.004
Stroke/TIA	21.1% [28]	25.6% [22]	12.8% [6]	0.12
Hypertension	80.5% [107]	82.6% [71]	76.6% [36]	0.49
CAD	51.9% [69]	55.8% [48]	44.7% [21]	0.28
DM	30.8% [41]	30.2% [26]	31.9% [15]	0.85
PE	3% [4]	4.7% [4]	0% [0]	0.30
DVT	6.8% [9]	9.3% [8]	2.1% [1]	0.16
Epistaxis	0% [0]	0% [0]	0% [0]	>0.999
Aspirin use	51.1% [68]	52.3% [45]	48.9% [23]	0.72
Clopidogrel use	4.5% [6]	3.5% [3]	6.4% [3]	0.67
Previous PPM/ICD	31.6% [42]	34.9% [30]	25.5% [12]	0.33
Ejection fraction (%)*	40.7±16.7	39.3±17.0	44.1±15.7	0.11
Hemoglobin*	13.2±1.8	13.0±1.8	13.6±5.4	0.33
Creatinine*	1.2±0.6	1.3±0.8	1.1±0.3	0.14
GFR*	48.5±13.6	47.3±14.0	51.0±12.9	0.13
INR*				
@ Procedure		2.3±0.7		
@ 1 Week		2.5±0.7		
@ Complication		2.8±0.8		

*, Data are shown as means±SD; ^, data are shown as median (range). The CHADS₂ score is a measure of the risk of stroke in which congestive heart failure, hypertension, an age of 75 years or older, and diabetes mellitus are each assigned 1 point and previous stroke or transient ischemic attack is assigned 2 points; the score is calculated by summing all points for a given patient. CAD, coronary artery disease; DM, diabetes mellitus; PE, pulmonary embolism; DVT, deep vein thrombosis; PPM, permanent pacemaker; ICD, implantable cardioverter defibrillators; BUN, blood urea nitrogen; GFR, glomerular filtration rate; TIA, transient ischemic attack.

Table 2 Indications for device implantation

Characteristic	All patients [%] [n=133]	Uninterrupted warfarin [%] [n=86]	Interrupted dabigatran [%] [n=47]
Indication			
Bradycardia	18 [24]	12.8 [11]	27.7 [13]
Slow atrial fibrillation	6 [8]	7 [6]	4.3 [2]
RFA/permanent pacing	19.5 [26]	20.9 [18]	17 [8]
VT/VF	9 [12]	10.5 [9]	6.4 [3]
CHF req. biventricular device	40.6 [54]	41.9 [36]	38.3 [18]
Mobitz type 2 AV block	3.0 [4]	3.5 [3]	2.1 [1]
Type 3 AV block	3.8 [5]	3.5 [3]	4.3 [2]

AV, atrioventricular; CHF, congestive heart failure; RFA, radiofrequency ablation with permanent pacing; VF, ventricular fibrillation; VT, ventricular tachycardia.

Table 3 Perioperative bleeding and thromboembolic complications*

Characteristic	All patients [n=133]	Uninterrupted warfarin [n=86]	Interrupted dabigatran [n=47]	P value
Major complication	0.8 [1]	1,2 [1]	0 [0]	P>0.999
Major bleeding				
Hemothorax	0 [0]	0 [0]	0 [0]	P>0.999
Hemopericardium	0.8 [1]	1.2 [1]	0 [0]	P>0.999
ICH	0 [0]	0 [0]	0 [0]	P>0.999
GI Bleed	0 [0]	0 [0]	0 [0]	P>0.999
Epistaxis req. packing	0 [0]	0 [0]	0 [0]	P>0.999
Thromboembolic				
Stroke/TIA	0 [0]	0 [0]	0 [0]	P>0.999
DVT	0 [0]	0 [0]	0 [0]	P>0.999
PE	0 [0]	0 [0]	0 [0]	P>0.999
Arterial embolism	0 [0]	0 [0]	0 [0]	P>0.999
Minor complication [#]	4.5 [6]	7.0 [6]	0 [0]	0.09
Mortality				
1 month mortality	0.8 [1]	1.2 [1]	0 [0]	P>0.999

*, Perioperative time window was defined as 30 days post-implant; [#], all pocket hematomas, all less than the size of the generator. DVT, deep venous thrombosis; GI, gastrointestinal; ICH, intracranial hemorrhage; PE, pulmonary embolism; TIA, transient ischemic attack.

in their investigation (15). In concordance with results from this study, there was no significant increase of thrombosis or major bleeding complications. Healey *et al.* performed a retrospective analysis of 4,591 patients from the RE-LY study undergoing various invasive procedures who were receiving anticoagulation therapy with either warfarin or dabigatran (22). There was no significant difference in rates of periprocedural major bleeding in various dabigatran cohorts compared to warfarin. However, there was a large range in dosing time of dabigatran pre- and post-procedure.

Similarly, we found no significant differences in major bleeding events between the ID and UW groups in our study. Patients in the UW group were associated with a statistically non-significant trend towards increased pocket hematoma formation compared to the ID cohort. This is an interesting finding since an increased risk of pocket hematoma development has been linked to the use of agents with short half-lives in prior studies when compared to an UW strategy. Incidence of pocket hematoma while on an UW strategy in this study was consistent with a previous well-constructed small randomized trial (23). The increased bleeding trends in pocket hematomas in the UW may be due to the fact that patients are no longer fully anticoagulated at the time of implant in the ID group but

remain therapeutically anticoagulated in the UW group. A similar study performed by Kosiuk *et al.* confirmed our findings and showed a statistically non-significant trend toward reduced number of pocket hematomas with ID use compared to UW in patients receiving implantable devices (17). This study adds to the current body of literature suggesting this latter finding of reduced bleeding trends in ID group versus UW groups.

The primary goal in choosing an appropriate perioperative anticoagulation regimen is to prevent embolic events and reduce bleeding complications. Our results revealed no thromboembolic events in either group although this study was not powered to show differences in this outcome. One would expect that an uninterrupted anticoagulation strategy would reduce thromboembolic events better than an interrupted strategy, therefore favoring UW over ID. In our ID group, the mean time off dabigatran was 23.3 hours and the mean time to resume the dose was 21.0 hours post-procedure. One would expect most cardioembolic events would occur if anticoagulation were to be held for more than 48 hours. Since the half-life of dabigatran is 12-17 hours in patients with preserved renal function, one could postulate that withholding one or two doses of dabigatran would mean that a patient would remain not

anticoagulated for less than the 48 hours window where the risk of clot formation is low and thus represent a reasonable perioperative bridging strategy.

It is still unknown whether uninterrupted dabigatran would be a viable option for patients undergoing implantable cardiac devices. The lack of a reversal agent makes this option less attractive and difficult to study. Perhaps in the future, once reversal agents become available, this strategy could be employed and formally studied in a large cohort study.

Our data support the use of ID as a reasonable strategy of treating patients undergoing cardiac device implantation. The results suggest that ID is at least as safe as continued warfarin in regards to bleeding. Though thromboembolic events were not different between the two groups, a large randomized trial powered to show those differences is needed. Survey data collected by Nascimento *et al.* has been useful in describing utilization and prescribing patterns of perioperative dabigatran use alongside other new oral anticoagulants among multiple centers in a large population (18). However, inter-center variability in anticoagulation stop and restart times limits accurate assessment of safety and efficacy outcomes. This highlights the need for a large randomized control trial to guide further therapy in this cohort of patients.

This study adds to the current literature regarding anticoagulation with dabigatran and can be utilized for future large-scale investigations.

Limitations

This study was not a randomized trial and therefore patients may have been prone to a selection bias, which likely accounted for the baseline CHADS₂ score differences. Further, a relatively small sample size such as used in our study would be expected to show no difference in cardioembolic events due to lack of power. However, it is one of the largest studies available to date on this matter. It does support the fact that hematomas are not increased with the use of ID and may even be reduced compared to UW, which is consistent with findings from other studies (17).

Conclusions

This study suggests that ID and UW strategies are both reasonable approaches to managing patients requiring an ICD or a PPM. There was a trend towards lower pocket hematoma development in the ID group though

this difference was not statistically significant. A large multicenter randomized trial is needed in order to definitively investigate any differences in thromboembolic events between these two strategies.

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None.

Footnote

Conflicts of Interest: DA Elmouchi and AJ Gauri are members of the Speakers Bureau for Boehringer Ingelheim. DA Elmouchi and NT Chalfoun are also members of the Speakers bureau for Pfizer and Bristol Myers Squibb. NT Chalfoun is a member of the Speakers Bureau for Janssen Pharmaceuticals.

References

1. Rosamond W, Flegal K, Furie K, et al. Heart disease and stroke statistics--2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2008;117:e25-146.
2. McComb JM, Gribbin GM. Chronic atrial fibrillation in patients with paroxysmal atrial fibrillation, atrioventricular node ablation and pacemakers: determinants and treatment. *Europace* 1999;1:30-4.
3. Dunn AS, Turpie AG. Perioperative management of patients receiving oral anticoagulants: a systematic review. *Arch Intern Med* 2003;163:901-8.
4. Cheng M, Hua W, Chen K, et al. Perioperative anticoagulation for patients with mechanic heart valve(s) undertaking pacemaker implantation. *Europace* 2009;11:1183-7.
5. Ahmed I, Gertner E, Nelson WB, et al. Continuing warfarin therapy is superior to interrupting warfarin with or without bridging anticoagulation therapy in patients undergoing pacemaker and defibrillator implantation. *Heart Rhythm* 2010;7:745-9.
6. Wiegand UK, LeJeune D, Boguschewski F, et al. Pocket hematoma after pacemaker or implantable cardioverter defibrillator surgery: influence of patient morbidity, operation strategy, and perioperative antiplatelet/ anticoagulation therapy. *Chest* 2004;126:1177-86.
7. Jamula E, Douketis JD, Schulman S. Perioperative anticoagulation in patients having implantation of a cardiac pacemaker or defibrillator: a systematic review

- and practical management guide. *J Thromb Haemost* 2008;6:1615-21.
8. Chow V, Ranasinghe I, Lau J, et al. Peri-procedural anticoagulation and the incidence of haematoma formation after permanent pacemaker implantation in the elderly. *Heart Lung Circ* 2010;19:706-12.
 9. Fuster V, Rydén LE, Cannom DS, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation-executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients with Atrial Fibrillation). *Eur Heart J* 2006;27:1979-2030.
 10. Ghanbari H, Phard WS, Al-Ameri H, et al. Meta-analysis of safety and efficacy of uninterrupted warfarin compared to heparin-based bridging therapy during implantation of cardiac rhythm devices. *Am J Cardiol* 2012;110:1482-8.
 11. Bernard ML, Shotwell M, Nietert PJ, et al. Meta-analysis of bleeding complications associated with cardiac rhythm device implantation. *Circ Arrhythm Electrophysiol* 2012;5:468-74.
 12. Feng L, Li Y, Li J, et al. Oral anticoagulation continuation compared with heparin bridging therapy among high risk patients undergoing implantation of cardiac rhythm devices: a meta-analysis. *Thromb Haemost* 2012;108:1124-31.
 13. Birnie DH, Healey JS, Wells GA, et al. Pacemaker or defibrillator surgery without interruption of anticoagulation. *N Engl J Med* 2013;368:2084-93.
 14. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2009;361:1139-51.
 15. Rowley CP, Bernard ML, Brabham WW, et al. Safety of continuous anticoagulation with dabigatran during implantation of cardiac rhythm devices. *Am J Cardiol* 2013;111:1165-8.
 16. Bloom BJ, Filion KB, Atallah R, et al. Meta-analysis of randomized controlled trials on the risk of bleeding with dabigatran. *Am J Cardiol* 2014;113:1066-74.
 17. Kosiuk J, Koutalas E, Doering M, et al. Comparison of Dabigatran and Uninterrupted Warfarin in Patients With Atrial Fibrillation Undergoing Cardiac Rhythm Device Implantations. *Circ J* 2014. [Epub ahead of print].
 18. Nascimento T, Birnie DH, Healey JS, et al. Managing novel oral anticoagulants in patients with atrial fibrillation undergoing device surgery: Canadian survey. *Can J Cardiol* 2014;30:231-6.
 19. Giudici MC, Paul DL, Bontu P, et al. Pacemaker and implantable cardioverter defibrillator implantation without reversal of warfarin therapy. *Pacing Clin Electrophysiol* 2004;27:358-60.
 20. Goldstein DJ, Losquadro W, Spotnitz HM. Outpatient pacemaker procedures in orally anticoagulated patients. *Pacing Clin Electrophysiol* 1998;21:1730-4.
 21. Marquie C, De Geeter G, Klug D, et al. Post-operative use of heparin increases morbidity of pacemaker implantation. *Europace* 2006;8:283-7.
 22. Healey JS, Eikelboom J, Douketis J, et al. Peri-procedural bleeding and thromboembolic events with dabigatran compared with warfarin: results from the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) randomized trial. *Circulation* 2012;126:343-8.
 23. Tolosana JM, Berne P, Mont L, et al. Preparation for pacemaker or implantable cardiac defibrillator implants in patients with high risk of thrombo-embolic events: oral anticoagulation or bridging with intravenous heparin? A prospective randomized trial. *Eur Heart J* 2009;30:1880-4.

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