Original Article

Antithrombotic Management and Device-Related Bleeding Complications in Patients Undergoing Cardiac Implantable Electronic Device Implantations: A Single-Center Study

Nithit Tianchetsada MD[1], Arisara Suwanagool MD[1]

[1] Department of Medicine, Division of Cardiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Background: Each year, 1.65 million people around the world are implanted with Cardiac Implantable Electronic Devices [CIEDs], and 14% to 35% of those patients are receiving oral anticoagulants [OACs] or antiplatelet therapy prior to the surgery. These drugs increased bleeding complications in CIED implantations. Currently, we have no data on device-related bleeding complications [DRBCs] among Thai patients receiving OACs and/or antiplatelet therapy prior to CIED implantation.

Materials and Methods: We retrospectively reviewed consecutive patients who underwent CIED implantations and continued to follow-up at the Siriraj Device Clinic in 2016. The baseline characteristics, comorbidities, types of CIED, CIED indications, types of antithrombotic and DRBCs data were collected. Siriraj protocol requires that patients follow-up at the device clinic 12 to 16 days post implantation and be evaluated for DRBCs by two device-clinic staff. If DRBCs are detected, a caliper is used to measure the size in three dimensions. Our primary outcome is the incidence of DRBCs among patients who received antithrombotic drugs and the secondary outcome is the incidence of DRBCs for each group of antithrombotic drugs. This study was approved by the Institutional Review Board [IRB].

Results: Three hundred patients underwent CIEDs implantations then continued follow-up at the device clinic between January and December 2016; their mean age was 69.7±14.5 years, and 60.3% were male. The implanted CIEDs consisted of pacemakers (59.7%), automated implantable cardioverter defibrillators (AICDs, 28.3%) and cardiac resynchronization therapy device (CRTs, 12%). Antithrombotic used, found in 73% (218) of the implanted CIED patients, was distributed into the following groups, single-antiplatelet therapy (SAPT, 31%, 93), dual antiplatelet therapy (DAPT, 13%, 39), OAC plus antiplatelet (9.7%, 29), triple therapy (DAPT plus OAC, 1.3%, 4), warfarin (14.7%, 44) and non-vitamin K antagonist OAC (NOAC, 3%, 9). The primary outcome showed a DRBC incidence of 12.8% among patients using antithrombotics. Of those patients, the DRBCs detected 9.7% (9) of patients in the SAPT group, 15.4% (6) in the DAPT group, 13.8% (4) in the OAC-plus-antiplatelet group and 20.5% (9) in the warfarin group. No DRBCs were detected in either the no-antithrombotic group (82) or the NOAC group (9). However, almost all the DRBC patients resolved spontaneously without intervention. Unfortunately, one DRBCs patient who only took aspirin (81 mg) was admitted for a hematoma evacuation. The different in size of the CIED revealed a significant correlation in the incidence of DRBCs, as shown in the analysis, the CRTD-implanted patients had more DRBCs than the pacemaker-implanted patients (OR 4.36, 95% CI 1.61 to 11.8, *p*-value 0.004). Moreover, a multivariate analysis demonstrated an increased level of DRBCs among patients in the CAD and warfarin groups (OR 3.41, 95% CI 1.01 to 11.5, *p*-value 0.048) and (OR 2.96, 95% CI 1.17 to 7.46, *p*-value 0.022) respectively. Surprisingly, the level of DRBCs was decreased among patients who had used statins in the non-CAD group (OR 0.17, 95% CI 0.04 to 0.80, *p*-value 0.024).

Conclusion: A comparison of CIED-implantation patients who had been using and had not been using antithrombotic drugs prior to surgery revealed that, although the incidence of DRBCs increased when antithrombotics were used, those DRBCs were still not clinically significant as they resolved spontaneously without the need for treatment. This finding supports the safety of continuing to use antithrombotic drugs on patients undergoing CIEDs implantations.

Keywords: CIED, Pacemaker, AICD, CRTD, Hematoma, Bleeding, Anticoagulant, Antiplatelet, Warfarin

J Med Assoc Thai 2018; 101 (1): 33-9
Website: http://www.jmatonline.com

Each year, 1.65 million people around the world are implanted with cardiac implantable electronic devices [CIEDs][1] and 14% to 35% of those patients are receiving oral anticoagulants [OACs] or antiplatelet therapy prior to surgery[2-5]. These drugs increase device-related bleeding complications [DRBCs] in CIED implantations[6].

Regarding the antithrombotic management of patients who are undergoing electrophysiological procedures and are already on anticoagulants, the European Heart Rhythm Association [EHRA], Heart

Correspondence to:

Suwannagool A, Division of Cardiology, Department of Medicine, Siriraj Hospital Mahidol University, Bangkok 10700, Thailand.
Phone: +66-2-4196104-5, Fax: +66-2-4127412
Email: aucardi@gmail.com

How to cite this article: Tianchetsada N, Suwanagool A. Antithrombotic management and device-related bleeding complications in patients undergoing cardiac implantable electronic device implantations: a single-center study. J Med Assoc Thai 2018;101:33-9.

Rhythm Society [HRS] and Asia Pacific Heart Rhythm Society [APHRS] published in 2015[7] recommends that heparin bridging not be necessary; instead, their OACs should be continued and proceed to the surgical procedure. However, there are some limitations. With respect to the use of non-vitamin K antagonist OACs [NOACs] during the surgical procedures, the association recommends that NOAC usage should be discontinued in the manner prescribed by the instructions for each drug. In the case of patients on antiplatelet therapy, the recommendations for antiplatelet duration vary with their bleeding risk and whether they are receiving single antiplatelet therapy [SAPT] or dual antiplatelet therapy [DAPT]. It is recommended that patients on SAPT continue with that therapy and advance to the surgical procedure. On the other hand, patients on DAPT may discontinue the P2Y12 drug five to seven days before surgery if there is no further indication for DAPT. As for patients on triple antithrombotic therapy (DAPT plus OAC), the association recommends the usage of DAPT for the shortest duration possible, based on the bleeding risk. If that risk is high, the DAPT usage should not exceed one month; conversely, if the bleeding risk is low, the DAPT use should not exceed six months. For the timing of the surgery, it depends on the urgency.

Most DRBC data has been derived from Caucasians populations. However, a study of a Chinese population by Chen et al[6] showed that DRBCs increased significantly among patients in a heparin-bridging strategy [HBS]/DAPT group, which was a similar outcome to that found among Caucasians populations. However, to date, we have no data on the incidence of DRBCs among Thai's receiving OACs and/or antiplatelet therapy prior to CIEDs implantation.

Recently, the Faculty of Medicine, Siriraj Hospital, introduced a revised protocol for antithrombotic management prior to CIEDs implantation. Essentially, the protocol requires that OACs, antiplatelet therapies and DAPTs should be continued during the surgical procedure, whereas NOAC should be discontinued in the manner prescribed by the instructions for each drug[8]. We subsequently proceeded to collect and review data to determine the incidence of DRBCs among Thai patients.

Materials and Methods

We retrospectively reviewed each consecutive patient who underwent a CIED implantation by our certified clinical cardiac electrophysiologists at Faculty of Medicine Siriraj Hospital between January and December 2016 then continued post implantation follow-up at the Siriraj Device Clinic as per Siriraj protocol. Each patient may have at least one antithrombotic prescribed by primary doctor or cardiologist or not have any.

Siriraj protocol have requirement as follow:

1. Instruction for those who have antithrombotic prior CIED implantation will divided into three groups

1.1 Patient who was on vitamin K antagonist, OAC will continue same dose of OAC with therapeutic international normalized ratio [INR] level during the implantation.

1.2 Patient who was on NOAC will require to stop medication 24 hours prior the implantation.

1.3 Patient who was on Aspirin, SAPT, DAPT, or triple antithrombotic therapy, to continue the medication as required.

2. All patients will schedule a follow-up at the device clinic 12 to 16 days' post CIED implantation.

3. DRBC define as any bleeding complication followed the CIED implantation that include ecchymosis, pocket hematoma, hemothorax, any vascular tear or post implantation anemia which required blood transfusion.

4. If pocket hematoma occurred, it will be measured by two device-clinic staff using a caliper to measure the size of the hematoma in three dimensions then graded into mild (diameter 1 to 3 cm), moderate (diameter >3 to 10 cm) and severe (diameter >10 cm).

The antithrombotics used were divided into six groups: SAPT, DAPT, OAC, OAC plus SAPT, triple antithrombotic therapy, and NOAC. Data on the patients' baseline characteristics, comorbidities, types of CIED, CIED indications, types of antithrombotic, and DRBCs were collected.

Our primary outcome was to determine the incidence of DRBCs in patients who received antithrombotic drugs, while the secondary outcome was to establish the incidence of DRBCs for each of the six antithrombotic, drug groups.

In this study, the categorical variables are presented as percentages, continuous variables are presented as mean ± SD, and the comparison data between two groups will be analyzed by the Chi-squared test for both univariate and multivariate analysis. After the univariate analysis, those factors that *p*-value of 0.5 or less will be selected for further multivariate analyzed with *p*-value of 0.05 or less defined as significant. SPSS version 20 was used for all statistical calculation. This study was approved by the Institutional Review Board [IRB].

Results

The baseline characteristic of each consecutive patient who underwent CIED implantation is shown in Table 1. Three hundred patients underwent CIED implantations and continued to follow-up at the device clinic between January and December 2016; their mean age was 69.7±14.5 years, and 60.3% were male. The types of implanted CIEDs comprised of pacemakers (59.7%), AICDs (28.3%) and CRTs (12%). Antithrombotic use was found in 73% (218) of the implanted CIED patients, and it was distributed into six groups as follow: SAPT (31%, 93), DAPT (13%, 39), OAC plus SAPT (9.7%, 29), triple antithrombotic therapy group (1.3%, 4), warfarin (14.7%, 44) and NOAC (3%, 9).

By comparing those DRBC patients vs. no DRBC patients, their baseline characteristics were not clinically significant different as shown in Table 2. The primary outcome revealed an incidence of DRBCs of 12.8% among all antithrombotic-use patients as shown in Table 3, and all DRBCs that occurred were only ecchymosis and pocket hematoma. Table 3 also showed the secondary outcome of those 218 DRBC patients, 9.7% (9) of the DRBCs were detected in the SAPT group, 15.4% (6) in the DAPT group, 13.8% (4) in the OAC plus antiplatelet group and 20.5% (9) in the warfarin group. No DRBCs were detected in the no-antithrombotic group (82) the NOAC group (9) or the triple antithrombotic group (4).

However, almost all DRBCs patients resolved spontaneously without intervention. Unfortunately, one DRBCs patient, who only took aspirin (81 mg) was admitted for a hematoma evacuation due to large size hematoma with severe pain.

From the study, we found that difference in size of CIEDs did reveal significant correlation in DRBCs as patients in CRTD implanted group had significantly more DRBCs incidence than those receiving a pacemaker implantation (OR 4.36, 95% CI 1.61 to 11.8, $p = 0.004$). Moreover, multivariate analysis demonstrated an increased level of DRBCs among patients in the CAD and warfarin groups (OR 3.41, 95% CI 1.01 to 11.5, $p = 0.048$ and OR 2.96, 95% CI 1.17 to 7.46, $p = 0.022$, respectively). Surprisingly, the incidence of DRBCs was lower among patients who had used statins in the non-CAD group (OR 0.17, 95% CI 0.04 to 0.80, $p = 0.024$) (Table 4).

Discussion

Nowadays, the use of antithrombotic drugs is climbing, commensurate with an increase in the related indications. This has also resulted in a growth

Table 1. Baseline characteristic of each consecutive patient who underwent CIED implantation between January and December 2016 (n = 300)

	Mean ± SD or n (%)
Age (years)	69.7±14.5
Sex: male	181 (60.3)
Diabetic mellitus	81 (27.0)
Hypertension	179 (59.7)
Dyslipidemia	131 (43.7)
Chronic kidney disease	45 (15.0)
Coronary artery disease	107 (35.7)
Percutaneous intervention	64 (63.4)
Coronary artery bypass graft	37 (36.6)
Heart failure	119 (39.7)
NYHA class I	30 (25.2)
NYHA class II	46 (38.7)
NYHA class III	31 (26.1)
NYHA class IV	12 (10.1)
Atrial fibrillation	107 (35.7)
Paroxysmal	65 (60.7)
Permanent/persistent	42 (39.3)
Valvular heart disease	41 (13.7)
Thyroid disease	16 (5.3)
Type of implantation	
1st implantation	202 (67.3)
Pulse generator replacement	79 (26.3)
Device upgrade	15 (5.0)
Device relocation	1 (0.3)
Lead adjustment	3 (1.0)
Type of device	
Pacemaker	179 (59.7)
AICD	85 (28.3)
CRTD	36 (12.0)
Antithrombotic	218 (73.0)
Aspirin	150 (69.0)
Clopidogrel	52 (24.0)
Ticagrelor	4 (2.0)
Prasugrel	2 (1.0)
Warfarin	72 (33.0)
Dabigatran	4 (2.0)
Apixaban	6 (2.8)
Rivaroxaban	4 (2.0)
Antithrombotic used group	
SAPT	93 (31.0)
DAPT	39 (13.0)
Warfarin	44 (14.7)
NOAC	9 (3.0)
OAC plus antiplatelet	29 (9.7)
Triple therapy (OAC plus DAPT)	4 (1.3)
Miscellaneous drug	
Amiodarone	33 (11.0)
Statin	198 (66.0)
Complication	
DRBCs	28 (12.8)
- Mild (1 to 3 cm)	1 (3.6)
- Moderate (>3 to 10 cm)	25 (89.3)
- Severe (>10 cm)	0 (0.0)
- Ecchymosis	2 (7.1)
Wound dehiscence	1 (0.3)
Pericardial effusion	1 (0.3)
Perforation	1 (0.3)

AICD = automated implantable cardioverter defibrillator; CIED = cardiac implantable electronic device; CRTD = cardiac resynchronization therapy defibrillator; DAPT = dual antiplatelet therapy; DRBCs = device-related bleeding complications; NOAC = non-vitamin K antagonist oral anticoagulant; NYHA = New York Heart Association; OAC = oral anticoagulant; SAPT = single antiplatelet therapy

Table 2. Comparisons of each consecutive patient's baseline characteristics who underwent CIED implantation at Faculty of Medicine Siriraj Hospital between January and December 2016 and continued post implantation follow-up at the Siriraj Device Clinic as per Siriraj protocol (n = 300)

Factor	DRBCs (n = 28)	No DRBCs (n = 272)	*p*-value
Age (years)	72.1±10.6	69.1±14.6	0.289
Sex			0.096
Male	21 (75.0)	160 (58.8)	
Female	7 (25.0)	112 (41.2)	
Type of implantation			0.190
First implantation	16 (57.1)	186 (68.4)	
Replacement pulse generator	8 (28.6)	71 (26.1)	
Device upgrade	4 (14.3)	11 (4.0)	
Device relocation	0 (0.0)	1 (0.3)	
Lead adjustment	0 (0.0)	3 (1.1)	
Type of device			0.009
Pacemaker	11 (39.3)	168 (61.8)	
AICD	9 (32.1)	76 (27.9)	
CRTD	8 (28.6)	28 (10.3)	
Hypertension	15 (53.6)	164 (60.3)	0.490
Diabetes	5 (17.9)	76 (27.9)	0.252
Dyslipidemia	10 (35.7)	121 (44.5)	0.373
Chronic kidney disease	12 (42.9)	33 (12.1)	0.680
Coronary artery disease	16 (57.1)	91 (33.5)	0.013
Heart failure	18 (64.3)	101 (37.1)	0.493
NYHA class I	7 (25.0)	23 (8.5)	
NYHA class II	6 (21.4)	40 (14.7)	
NYHA class III	3 (10.7)	28 (10.3)	
NYHA class IV	2 (7.1)	10 (3.7)	
Atrial fibrillation	13 (46.4)	94 (34.6)	0.079
Valvular heart disease	7 (25.0)	34 (12.5)	0.155
Thyroid disease	3 (10.7)	13 (4.8)	1.000
Antithrombotic drug			
Aspirin	19 (67.9)	131 (48.2)	0.072
Clopidogrel	5 (17.9)	47 (17.3)	1.000
Ticagrelor	1 (3.6)	3 (1.1)	0.326
Prasugrel	0 (0.0)	2 (0.7)	1.000
Warfarin	13 (46.4)	59 (21.7)	0.004
Dabigatran	0 (0.0)	4 (1.5)	1.000
Apixaban	0 (0.0)	6 (2.2)	1.000
Rivaroxaban	0 (0.0)	4 (1.5)	1.000
Amiodarone	4 (14.3)	29 (10.7)	0.582
Statin	15 (53.6)	183 (67.3)	0.145
INR before implantation	2.1±0.5	1.8±0.6	0.070
CHA_2DS_2VASc	3.2±1.4	3.1±1.7	0.865

AICD = automated implantable cardioverter defibrillator; CIED = cardiac implantable electronic device; CRTD = cardiac resynchronization therapy defibrillator; DRBCs = device-related bleeding complications; NYHA = New York Heart Association

Data presented as mean ± SD or n (%)

Table 3. Incidence of DRBCs in each consecutive patient who underwent CIED implantation at Faculty of Medicine Siriraj Hospital between January and December 2016 and continued post implantation follow-up at the Siriraj Device Clinic as per Siriraj protocol

	n (%)
Primary outcome	
Incidence of DRBCs in all antithrombotic drugs	28/218 (12.8)
Secondary outcomes	
Incidence of DRBCs in SAPT	9/93 (9.7)
Incidence of DRBCs in DAPT	6/39 (15.4)
Incidence of DRBCs in OAC plus antiplatelet	4/29 (13.8)
Incidence of DRBCs in warfarin	9/44 (20.5)
Incidence of DRBCs in triple therapy	0 (0.0)
Incidence of DRBCs in NOAC	0 (0.0)

CIED = cardiac implantable electronic device; DAPT = dual antiplatelet therapy; DRBCs = device-related bleeding complications; NOAC = non-vitamin K antagonist oral anticoagulant; OAC = oral anticoagulant; SAPT = single antiplatelet therapy

in the incidence of DRBCs. DRBCs following CIED implantations are complications that lead to many consequences, such as local discomfort, prolonged hospital stays, CIED infections, and/or the needed for device/pocket revisions.

Most of the results of the present study tended to be similar to those of studies by Kutinsky et al[9] and Bernard et al[10], except for the DRBC incidences for the warfarin-use groups (the present study: 20.5%, Kutinsky et al[9]: 6.9% and Bernard et al[10]: 2.8%).

In detail, the incidences of DRBCs found by Kutinsky et al[9] were, overall 9.5%, SAPT 5.2%, DAPT 24.2%, warfarin 6.9%, warfarin plus aspirin 10.3% and triple antithrombotic therapy 9.5%. By comparison, the study by Bernard et al[10] had the following incidences, overall 4.6%, SAPT 3.9%, DAPT 9.4% and warfarin 2.8%. The present study revealed these figures, overall 12.8%, SAPT 9.7%, DAPT 15.4%, OAC plus SAPT 13.8% and warfarin 20.5%. The INR level in the warfarin group before CIED implantation was 2.13±0.47 vs. 1.82±0.55 in patients without DRBCs.

A study by Chao et al of the stroke and bleeding risks among Asians with atrial fibrillation[11] showed a higher incidence of bleeding complications among those Asian patients taking warfarin. This may support the present study's finding of a higher incidence of DRBCs in the warfarin group than found in the other studies[9,10], whose populations were non-Asian.

Three patient groups in the current study did not experience DRBCs, the no- antithrombotic drug group (n = 82), the NOAC group (n = 4) and the triple-antithrombotic-therapy group (n = 9). With regard to the zero-DRBC-incidence finding for the triple-antithrombotic-therapy group, the study by Kutinsky et al[9] reported an incidence of 9.5%. The discrepancy in the two studies' findings is probably due to the very small number of triple-therapy and NOAC group

Table 4. Univariate and Multivariate analyses of possible factors determining DRBCs in each consecutive patient who underwent CIED implantation at Faculty of Medicine Siriraj Hospital between January and December 2016 and continued post implantation follow-up at the Siriraj Device Clinic as per Siriraj protocol

Factor	Univariate analysis, OR (95% CI)	*p*-value	Multivariate analysis, OR (95% CI)	*p*-value
Sex: female	0.48 (0.20 to 1.16)	0.102	0.77 (0.28 to 2.13)	0.613
CAD	2.65 (0.17 to 0.83)	0.015	3.41 (1.01 to 11.50)	0.048
Valvular heart disease	2.09 (0.82 to 5.32)	0.122	1.59 (0.55 to 4.63)	0.394
Aspirin	2.27 (0.99 to 5.20)	0.052	2.63 (0.82 to 8.45)	0.105
Warfarin	3.13 (1.41 to 6.94)	0.005	2.96 (1.17 to 7.46)	0.022
Statin	0.56 (0.26 to 1.23)	0.149	0.25 (0.08 to 0.76)	0.014

CAD = coronary artery disease; CIED = cardiac implantable electronic device; DRBCs = device-related bleeding complications

patients in the present study. This is an area that can be explained in a future study.

A multivariate analysis identified the following factors influence DRBCs, an underlying CAD (OR 3.41, 95% CI 1.01 to 11.50, $p = 0.048$), warfarin use (OR 2.96, 95% CI 1.17 to 7.46, $p = 0.022$) and statin use (OR 0.25, 95% CI 0.08 to 0.76, $p = 0.014$). Surprisingly, a subgroup-analysis discovered that statin use by patients in the non-CAD group reduced the incidence of DRBCs (OR 0.17, 95% CI 0.04 to 0.08, $p = 0.024$), and as expected, the incidence of DRBCs in the CRTD group was higher than in the pacemaker group (OR 4.36, 95% CI 1.61 to 11.8, $p = 0.004$).

DRBCs were graded into mild (1 to 3 cm), moderate (>3 to 10 cm) and severe (>10 cm). Most DRBCS patients were graded with a moderate severity (89.3%). Only one patient (in the aspirin group) had to have hematoma evacuation. This data confirms the safety of continuing to use antithrombotic drugs during surgical procedures related to CIED implantation.

Conclusion

A comparison of the data related to CIED-implantation patients who had been receiving and had not been receiving antithrombotic drugs prior to surgery revealed that the incidence of DRBCs increased slightly when antithrombotics were used. Nevertheless, the DRBCs were still not clinically significant as they resolved spontaneously without any treatment being needed. This data supports the safety of continuing antithrombotic drugs usage in patients undergoing CIED implantations.

What is already known on this topic?

The incidence of DRBCs in Caucasian populations is highest among patients on DAPT.

What this study adds?

This study adds to the information about the incidence of DRBCs in the Thai population. The overall incidence of DRBCs among Thai patients using antithrombotics was 12.8%, with most occurring in the warfarin group (20.5% of the DRBCs) and DAPT group (15.4% of the DRBCs). However, the DRBCs in both groups had no clinical significance as they resolved spontaneously.

This data supports the safety of uninterrupted antithrombotic and anticoagulant drugs usage in patients undergoing CIEDs implantations.

Potential conflicts of interest

None.

References

1. Mond HG, Proclemer A. The 11th world survey of cardiac pacing and implantable cardioverter-defibrillators: calendar year 2009--a World Society of Arrhythmia's project. Pacing Clin Electrophysiol 2011;34:1013-27.
2. Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med 2005;352:225-37.
3. Greenspon AJ, Hart RG, Dawson D, Hellkamp AS, Silver M, Flaker GC, et al. Predictors of stroke in patients paced for sick sinus syndrome. J Am Coll Cardiol 2004;43:1617-22.
4. Nielsen JC, Thomsen PE, Hojberg S, Moller M, Vesterlund T, Dalsgaard D, et al. A comparison of single-lead atrial pacing with dual-chamber pacing in sick sinus syndrome. Eur Heart J 2011; 32:686-96.
5. Tang AS, Wells GA, Talajic M, Arnold MO, Sheldon R, Connolly S, et al. Cardiac-resynchronization therapy for mild-to-moderate heart failure. N Engl J Med 2010;363:2385-95.
6. Chen HC, Chen YL, Guo BF, Tsai TH, Chang JP, Pan KL, et al. Thrombocytopenia, dual antiplatelet

therapy, and heparin bridging strategy increase pocket hematoma complications in patients undergoing cardiac rhythm device implantation. Can J Cardiol 2013;29:1110-7.
7. Sticherling C, Marin F, Birnie D, Boriani G, Calkins H, Dan GA, et al. Antithrombotic management in patients undergoing electrophysiological procedures: a European Heart Rhythm Association (EHRA) position document endorsed by the ESC Working Group Thrombosis, Heart Rhythm Society (HRS), and Asia Pacific Heart Rhythm Society (APHRS). Europace 2015; 17:1197-214.
8. Heidbuchel H, Verhamme P, Alings M, Antz M, Diener HC, Hacke W, et al. Updated European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation. Europace 2015;17:1467-507.
9. Kutinsky IB, Jarandilla R, Jewett M, Haines DE. Risk of hematoma complications after device implant in the clopidogrel era. Circ Arrhythm Electrophysiol 2010;3:312-8.
10. Bernard ML, Shotwell M, Nietert PJ, Gold MR. Meta-analysis of bleeding complications associated with cardiac rhythm device implantation. Circ Arrhythm Electrophysiol 2012;5:468-74.
11. Chao TF, Chen SA. Stroke and bleeding risk in Asians with atrial fibrillation. Washington, DC: American College of Cardiology; 2016.

ภาวะแทรกซ้อนที่มีเลือดออกในผู้ป่วยที่ได้รับยาต้านลิ่มเลือดก่อนใส่เครื่องอิเล็กทรอนิกส์ชนิดฝังในร่างกาย

นิธิศ เทียนเจษฎา, อริศรา สุวรรณกูล

ภูมิหลัง: ในแต่ละปีทั่วโลกมีการใส่เครื่องกระตุ้นหัวใจ (pacemaker) และเครื่องกระตุกหัวใจอัตโนมัติ (implantable cardioverter defibrillator, ICD) 1.65 ล้านคน 14-35% ของผู้ป่วยกลุ่มนี้จำเป็นต้องได้รับยาต้านการแข็งตัวของเลือด (oral anticoagulant, OAC) และยาต้านเกล็ดเลือด (antiplatelet) การได้ยาทั้ง 2 กลุ่มนี้ก่อนใส่เครื่องอิเล็กทรอนิกส์ชนิดฝังในร่างกาย(cardiovascular implantable electronic devices, CIEDs) จะเพิ่มภาวะแทรกซ้อนที่มีเลือดออก (device-related bleeding complications, DRBCs) เนื่องจากในประเทศไทยยังไม่มีการรายงานข้อมูลการเกิด DRBCs ในผู้ป่วยที่ได้รับยา antithrombotic ก่อนใส่ CIEDs จึงเป็นที่มาของการศึกษานี้

วัสดุและวิธีการ: เป็นการศึกษาแบบ retrospective study ในผู้ป่วยที่ใส่ CIEDs ที่ติดตามการรักษาที่ โรงพยาบาลศิริราช และได้รับยา antithrombotic ภายในปี พ.ศ. 2559 โดยเก็บข้อมูลพื้นฐานของผู้ป่วย (baseline characteristic) โรคร่วม(comorbidities) ชนิดของ CIEDs (types of CIEDs) ข้อบ่งชี้ในการใส่ CIEDs (CIEDs indication) ชนิดของยาต้านลิ่มเลือด (types of antithrombotic) และภาวะ DRBCs ผู้ป่วยทุกคนได้รับการติดตามรักษา (follow-up) ภายหลังใส่ CIEDs 12-16 วัน ที่ device clinic เพื่อประเมินภาวะ DRBCs โดยพยาบาลและเจ้าหน้าที่ ใช้ caliper วัดความกว้างและความสูงของก้อนเลือด (hematoma) ที่อยู่เหนือต่อเครื่อง CIEDs โดยเจ้าหน้าที่ทั้ง 2 คน เห็นตรงกันว่าเกิด hematoma จริง Primary outcome คืออุบัติการณ์การเกิดภาวะ DRBCs ในผู้ป่วยที่ใส่ CIEDs และได้รับยา antithrombotic, Secondary outcome คือ อัตราการเกิดภาวะ DRBCs ในผู้ป่วยที่ได้รับยา antithrombotic แต่ละกลุ่ม การศึกษานี้ได้รับการรับรองจากคณะกรรมการจริยธรรมการวิจัยในคน (IRB)

ผลการศึกษา: ในการศึกษานี้มีผู้ป่วย 300 ราย ที่ได้รับการใส่ CIEDs และติดตามการรักษาที่ device clinic ตั้งแต่เดือนมกราคม พ.ศ. 2559 ถึง ธันวาคม พ.ศ. 2559 อายุเฉลี่ย 69.7±14.5 ปีเป็นชาย 60.3% ประเภทของ CIEDs ประกอบด้วย pacemaker 59.7%, AICD 28.3% และ CRTD 12% ผู้ป่วยที่ได้รับยา antithrombotic ในการศึกษานี้คิดเป็น 73% (218 ราย) โดยแบ่งเป็น กลุ่มที่ได้รับ SAPT 31% (93), DAPT 13% (39), OAC plus SAPT 9.7% (29), triple therapy (OAC plus DAPT) 1.3% (4), warfarin 14.7% (44) และ NOAC 3% (9) Primary outcome พบอุบัติการณ์ DRBCs ในผู้ป่วยที่ได้รับยา antithrombotic 12.8%, Secondary outcome พบอุบัติการณ์ DRBCs ในกลุ่ม SAPT 9.7% (9), DAPT 15.4% (6), OAC plus antiplatelet13.8% (4) และ warfarin 20.5% (9) ไม่พบ DRBCs ในกลุ่มที่ไม่ได้รับยา antithrombotic, NOAC และ triple therapy อย่างไรก็ตามผู้ป่วยที่เกิดภาวะ DRBCs เกือบทั้งหมดสามารถหายได้เอง มีเพียง 1 ราย (aspirin group) เท่านั้นที่ต้องได้รับการรักษาโดยการทำ hematoma evacuation ในการทำ univariated analysis พบว่าขนาดของเครื่อง CIEDs มีความสัมพันธ์กับภาวะ DRBCs โดยพบว่าการใส่เครื่อง CRTD จะเพิ่มอุบัติการณ์ DRBCs เมื่อเปรียบเทียบกับผู้ป่วยที่ใส่ pacemaker (OR 4.36, 95% CI 1.61-11.8, p = 0.004) ในการทำ multivariated analysis พบปัจจัยที่เพิ่มอุบัติการณ์ DRBCs ได้แก่ กลุ่มผู้ป่วย CAD (OR 3.41, 95% CI 1.01-11.5, p = 0.048) และ กลุ่มผู้ป่วยที่ได้รับยา warfarin (OR 2.96, 95% CI 1.17-7.46, p = 0.022) ส่วนปัจจัยที่ลดอุบัติการณ์ DRBCs ได้แก่ กลุ่ม statin used in non-CAD (OR 0.17, 95% CI 0.04-0.80, p = 0.024)

สรุป: การเปรียบเทียบข้อมูลระหว่างผู้ป่วยที่ได้รับและไม่ได้รับยา antithrombotic ก่อนใส่เครื่อง CIEDs พบอุบัติการณ์ของ DRBCs เพิ่มขึ้นในกลุ่มที่ได้รับยา antithrombotic แต่ไม่มีความสำคัญทางคลินิก เนื่องจากภาวะ DRBCs สามารถหายได้เองโดยไม่ต้องได้รับการรักษาใดๆ ข้อมูลนี้สนับสนุนความปลอดภัยของการใช้ยา antithrombotic ระหว่างใส่เครื่อง CIEDs