ORIGINAL STUDY

PACE DRAP: a simple score for predicting significant bleeding complications after cardiac implantable electronic device surgery

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KEY WORDS

bleeding risk score, cardiac implantable electronic device, pocket hematoma, significant bleeding

ABSTRACT

INTRODUCTION Currently, no risk score for predicting significant bleeding complications (SBCs) after cardiac implantable electronic device (CIED) surgery is available.

OBJECTIVES We aimed to develop a new scoring system for predicting SBCs after CIED surgery.

PATIENTS AND METHODS We included 1100 consecutive patients undergoing CIED surgery. The occurrence of SBCs including significant pocket hematoma or significant bleeding was evaluated within 30 days after surgery.

RESULTS The incidence of SBCs was 4.5%. Based on multivariable analyses, the following predictors of SBCs were identified: age ≥75 years (odds ratio [OR], 8.10; 95% CI, 3.54–18.54); cardiac resynchronization therapy or implantable cardioverter-defibrillator surgery (OR, 5.96; 95% CI, 2.48–14.32); upgrade procedure (OR, 10.22; 95% CI, 4.05–25.78); uncontrolled arterial hypertension (OR, 4.82; 95% CI, 1.78–13.06); presence of valvular prosthesis (OR, 7.85; 95% CI, 3.15–19.58); current malignancy (OR, 6.11; 95% CI, 1.81–20.66); renal failure (OR, 4.28; 95% CI, 1.86–9.87); and the use of antiplatelet drugs (clopidogrel [OR, 6.69; 95% CI, 2.48–18.04] or ticagrelor [OR, 22.25; 95% CI, 4.56–108.46]). The score was created using the weighted points proportional to the β regression coefficient of each predictor rounded to the nearest integer, and the acronym PACE DRAP corresponds to the predictor's first letter. The cutoff point for the high risk of SBCs was 6 points with a sensitivity of 88.24% and a specificity of 87.23%. The PACE DRAP showed good predictive ability (area under the curve, 0.95; $P < 0.001$).

CONCLUSIONS The PACE DRAP score is useful in identifying patients at high risk for SBCs after CIED surgery.

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INTRODUCTION Expansion in the indications for cardiac implantable electronic devices (CIEDs) as well as an increase in the average life expectancy necessitate a more complex and prolonged device therapy over a patient's lifetime. It has been reported that nearly half of the patients undergoing CIED implantation receive some form of anticoagulant or antiplatelet treatment due to multimorbidity.[1,2] Perioperative management of these patients is challenging due to an increased risk of bleeding. A significant bleeding complication (SBC) is a potentially life-threatening condition. Considering the worldwide implantation rate, the medical and financial burden of postoperative SBCs also seems to be relevant.[2]

In clinical practice, simple scoring systems can serve as a useful tool to help providers estimate the risk of SBCs. However, to our knowledge, there is currently no bleeding score dedicated to patients undergoing CIED surgery. Therefore, there is a need for an accurate risk scoring system that would use readily available clinical information to predict the occurrence of SBCs after CIED procedures, especially in patients who

WHAT'S NEW?

The number of cardiac implantable electronic device (CIED) procedures in patients with various cardiac rhythm disorders or heart failure has significantly increased worldwide over the last decades and has continued to rise along with the growing indications for CIED and population aging. Significant bleeding complications (SBCs) are a potentially life-threatening condition. Currently, no scoring system dedicated to bleeding risk evaluation in patients undergoing CIED surgery is available. This paper focuses on the rate of SBCs in patients undergoing CIED surgery. We propose a new bedside PACE DRAP score for predicting SBCs after CIED surgery. The acronym PACE DRAP corresponds to the first letter of each predictor: valve prosthesis (P); arterial hypertension uncontrolled (A); cancer (C); elderly (E); device type (D); renal failure (R); antiplatelets (A); and procedure type (P). The cutoff point for the high risk of SBCs in the PACE DRAP score is 6 points.

use drugs affecting hemostasis. To address this need, we aimed to develop a new scoring system for predicting SBCs after CIED procedures.

PATIENTS AND METHODS This was a prospective study including 1100 consecutive patients who underwent CIED (pacemaker, implantable cardioverter defibrillator [ICD], cardiac resynchronization therapy [CRT]–pacemaker [CRT-P], or CRT–defibrillator [CRT-D]) primary implantation, generator replacement, or system upgrade) in our department between June 2015 and June 2018.

Patients The characteristics of patients, including demographic data, indications for the CIED procedure, comorbidities, and indications for and the type of chronic antiplatelet therapy (APT) or anticoagulant therapy (ACT), as well as procedural details for postimplant wound management were collected at the time of the CIED surgery. All comorbidities were diagnosed according to the current guidelines of the relevant international societies, and the appropriate treatment recorded in the documentation confirmed the diagnosis of a specific diseases. However, it should be emphasized that uncontrolled arterial hypertension was diagnosed when systolic blood pressure was at least 160 mm Hg and/or diastolic blood pressure was at least 100 mm Hg on 2 or more independent measurements during hospitalization. Patients were divided into 4 main groups: 1) ACT group (vitamin K antagonist [VKA] in doses dependent on the international normalized ratio [INR] level, direct oral anticoagulant [DOAC], or low-molecular-weight heparin [LMWH]); 2) APT group (single antiplatelet therapy [SAPT] with aspirin or clopidogrel at a dose of 75 mg/d or double antiplatelet therapy [DAPT] with aspirin [75 mg/d] and clopidogrel [75 mg/d], or aspirin [75 mg/d] and ticagrelor [180 mg/d], or aspirin [75 mg/d] and prasugrel [10 mg/d]); 3) triple antithrombotic therapy (TAT) group (DAPT with VKA or DOAC); and 4) control group (patients not receiving ACT or APT). Moreover, the ACT group was divided into 4 subgroups according to the type of an anticoagulant: 1) VKA I (warfarin or acenocoumarol) for patients with an INR of 2 or higher on the day of the procedure; 2) VKA II for patients with an INR of less than 2 on the day of the procedure; 3) DOAC (rivaroxaban, apixaban, or dabigatran in renal dosing [edoxaban is not registered in our country]); and 4) LMWH (enoxaparin / dalteparin or nadroparin in weight-adjusted dosing) (FIGURE 1). An antiplatelet agent was administered during the procedure. Anticoagulant agents were managed according to European Heart Rhythm Association [EHRA] recommendations. In patients with an intermediate and high risk of a thromboembolic event, VKA was administered perioperatively in patients with an INR of 3 or less (or 3.5 or less in patients with mechanical valve prosthesis), but in patients with a low thromboembolic risk, it was discontinued 3 to 4 days prior to the procedure.[3] Treatment with DOAC was interrupted for 24 to 36 hours during the procedure, the duration depending on the drug type and renal function. Of note, patients in the LMWH subgroup were on chronic heparin treatment, and there were no patients on a bridging therapy with LMWH.

Written informed consent was obtained from each patient included in the study. The patients' privacy was protected by the anonymization of all data. Exclusion criteria were pregnancy, refusal to sign the informed consent form, lead and / or device extraction surgery, diagnosed thrombophilia or thrombocytopenia, and inability to attend follow-up visits for logistic reasons. The study protocol (Supplementary material) was in accordance with the Declaration of Helsinki and was approved by the bioethics committee of the Poznan University of Medical Sciences in Poznań, Poland (no. 613/15).

Significant bleeding complications All patients were evaluated for SBCs occurring during hospitalization or during a 30-day follow-up. The complications included significant pocket hematoma (SPH) or significant bleeding (SB). Significant pocket hematoma was defined as a swelling and painful mass extending the margin of the generator, requiring surgical intervention and / or prolonging hospitalization for at least 24 hours after the CIED procedure due to interruption of ACT or APT. Significant bleeding was defined according to International Society on Thrombosis and Hemostasis criteria as fatal or symptomatic bleeding in a critical area (eg, pericardial or gastrointestinal) or any bleeding causing a decrease in hemoglobin concentrations of more than 1.24 mmol/l or leading to transfusion of 2 or more units of red blood cells.[4]

Statistical analysis Patient characteristics were expressed as frequency (percentage) for categorical variables and medians (interquartile ranges) for continuous variables. None of the assessed parameters had a normal distribution as assessed using the Shapiro–Wilk test.

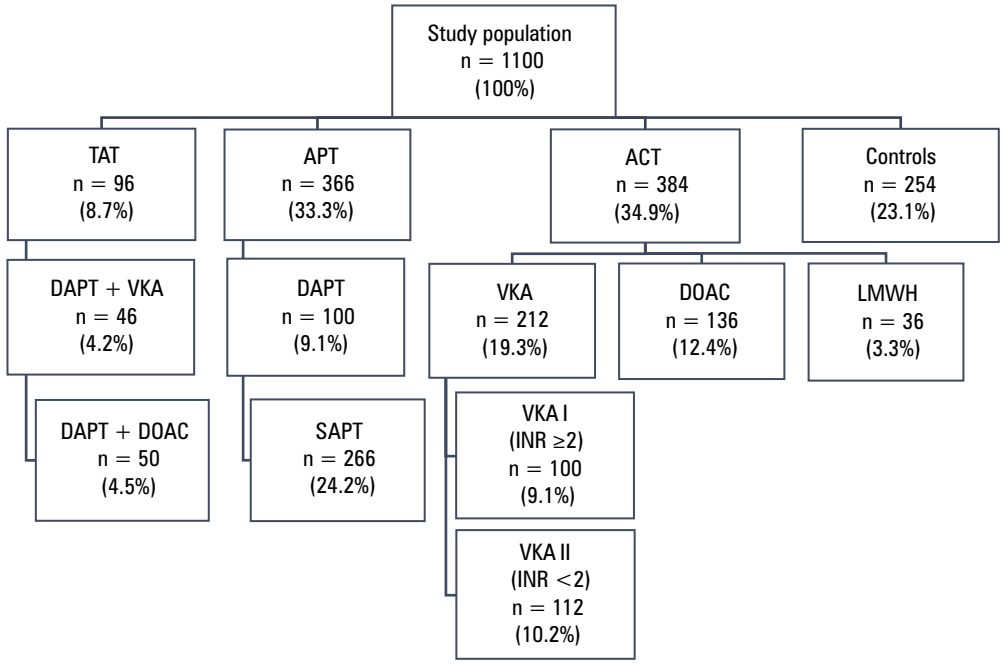

FIGURE 1 Study groups depending on the use of periprocedural therapy affecting hemostasis
Abbreviations: ACT, anticoagulant therapy; APT, antiplatelet therapy; DAPT, double antiplatelet therapy; DOAC, direct oral anticoagulant; INR, international normalized ratio; LMWH, low-molecular-weight heparin; SAPT, single antiplatelet therapy; TAT, triple antithrombotic therapy; VKA, vitamin K antagonist; VKA I, vitamin K antagonist with INR ≥2 on the day of procedure; VKA II, vitamin K antagonist with INR <2 on the day of procedure

Categorical variables were compared using the 2-tailed Fisher exact test or the χ^2 test as appropriate, and continuous variables were assessed using the Kruskal–Wallis analysis of variance test. A 2-tailed α of 0.05 was considered significant.

Univariate logistic regression was used to evaluate the magnitude of association between potential risk factors and SBCs. A multivariable analysis was performed with selected variables that were significant in the univariate analysis. A *P* value of less than 0.05 was considered significant. In each model, the odds ratio (OR) for each independent variable was determined with a confidence interval (CI) of 95%. A receiver operating characteristic curve analysis was performed to determine the cutoff values for the predictive level of SBC development and for the evaluation of the models. Independent predictors were then assigned weighted points. The β regression coefficients were rounded to the nearest integer to derive weights (weighing scheme, Beta/integer), and the points were summed up across the predictors for a total score for each patient. The performance of the score in terms of SBC prediction was evaluated by the receiver operating characteristic curve analysis, and its predictive ability was determined by using c-statistics as well as by calculation of the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, as well as positive and negative likelihood ratio for SBC development. All statistical analyses were performed using Statistica version 13.7 (StatSoft, Inc., Tulsa, Oklahoma, United States).

RESULTS The number of patients in the ACT, APT, TAT, and control groups was 384, 366, 96, and 254, respectively (FIGURE 1). The median patient age was 70 years (range, 18–97 years). Of the 1100 patients, 61.3% were male and 38.7% were female. Patient and procedural characteristics at baseline are presented in TABLE 1.

The incidence of 30-day CIED surgery–related SBCs in the entire study population was 4.5% (50 of the 1100 patients). Most frequently, SBCs occurred in the TAT group (8.3%), followed by the ACT (6.5%) and APT (3.8%) groups. In the ACT subgroup analysis, SBCs were most frequent in the LMWH subgroup (22.2%; 8 of 36 patients). Data on the frequency of SBCs are shown in TABLE 2.

Predictors of serious bleeding complications The results of the univariate and multivariable analyses for all potential predictors are presented in TABLE 3. The following characteristics were identified as independent predictors of SBCs: age ≥75 years (OR, 8.1; 95% CI, 3.54–18.54); CRT/ICD surgery (OR, 5.96; 95% CI, 2.48–14.32); upgrade procedure (OR, 10.22; 95% CI, 4.05–25.78); uncontrolled arterial hypertension (OR, 4.82; 95% CI, 1.78–13.06); presence of valvular prosthesis, either biological or mechanical (OR, 7.85; 95% CI, 3.15–19.58); current malignancy (OR, 6.11; 95% CI, 1.81–20.66); coexistence of renal failure (OR, 4.28; 95% CI, 1.86–9.87); and the use of antiplatelet drugs (clopidogrel [OR, 6.69; 95% CI, 2.48–18.04] or ticagrelor [OR, 22.25; 95% CI, 4.56–108.46]). It should be noted that the use of ticagrelor was the strongest risk factor.

TABLE 1 Baseline patient and procedural characteristics (continued on the next page)

Characteristics		All patients (n = 1100)	ACT (n = 384)	APT (n = 366)	TAT (n = 96)	Controls (n = 254)	*P* value
Demographic data							
Age, y, median (IQR)		70 (60–79)	74 (64–81)	69 (62–78)	70 (61–78)	63 (43–77)	<0.001
Sex	Male	674 (61.3)	224 (58.9)	256 (70.3)	71 (74.2)	121 (47.6)	<0.001
	Female	426 (38.7)	160 (41.1)	108 (29.7)	25 (26)	133 (52.1)	
BMI, kg/m^2, median (IQR)		27 (24.2–30.5)	27 (24.5–31)	27.1 (24.3–30.5)	26.2 (23–29.4)	26.4 (23.3–30)	0.01
LVEF, %, median (IQR)		50 (32–57)	50 (35–55)	45 (30–55)	35 (30–55)	55 (50–60)	<0.001
Indication for antiplatelet or anticoagulant therapy							
Coronary artery disease		485 (44.6)	111 (28.9)	273 (74.8)	96 (100)	–	<0.001
Previous myocardial infarction		365 (33.2)	76 (19.8)	215 (58.7)	72 (75)	–	<0.001
Percutaneous coronary intervention		386 (35.1)	77 (20.1)	216 (59.1)	89 (92.7)	–	<0.001
Coronary artery bypass grafting		103 (9.4)	30 (7.8)	53 (14.5)	20 (20.8)	–	<0.001
Previous ischemic stroke		74 (6.7)	36 (9.4)	24 (6.6)	13 (13.5)	–	<0.001
Transient ischemic attack		42 (3.8)	30 (7.8)	8 (2.2)	4 (4.2)	–	<0.001
Presence of valve prosthesis	Total	79 (7.1)	46 (12)	8 (2.2)	17 (17.7)	–	<0.001
	Mechanical	61 (5.5)	40 (10.4)	–	13 (13.5)	–	<0.001
	Biological (TAVI)	18 (1.6)	6 (1.6)	8 (2.2)	4 (4.2)	–	0.05
Atrial fibrillation/atrial flutter		409 (37.2)	318 (82.8)	15 (4.1)	76 (79.2)	–	<0.001
Previous pulmonary embolism/venous thrombosis		28 (2.5)	17 (4.4)	–	11 (11.5)	–	<0.001
Antiphospholipid syndrome		6 (0.5)	6 (1.6)	–	–	–	<0.001
Other medical history parameters							
Congestive HF		603 (54.8)	296 (77.1)	223 (60.9)	57 (59.4)	27 (10.6)	<0.001
HF NYHA class I–II		460 (41.8)	249 (64.9)	160 (43.7)	29 (30.2)	22 (8.7)	<0.001
HF NYHA class III–IV		143 (13)	47 (12.2)	63 (17.2)	28 (29.2)	5 (2)	<0.001
Arterial hypertension		785 (71.4)	291 (75.8)	289 (80)	71 (74)	134 (52.8)	<0.001
Renal failure (GFR <60 ml/min/m^2)		267 (24.3)	115 (30)	89 (24.3)	30 (31.3)	33 (13)	<0.001
Type 2 diabetes mellitus		254 (23.1)	102 (26.6)	100 (27.3)	19 (19.8)	33 (13)	<0.001
Anemia		25 (2.3)	8 (2.1)	6 (1.6)	4 (4.2)	7 (2.8)	0.30
Malignancy		69 (6.3)	26 (6.8)	26 (7.1)	2 (2.1)	15 (5.9)	0.15
Previous hemorrhagic stroke		6 (0.5)	4 (1)	1 (0.3)	1 (1)	–	0.41
Medications							
β-Blockers		713 (64.8)	253 (66)	256 (70)	86 (89.6)	118 (46.5)	<0.01
Calcium channel blockers		279 (25.4)	65 (16.9)	58 (15.8)	64 (66.6)	92 (36.2)	<0.01
Sartans		71 (6.5)	30 (7.8)	19 (5.2)	9 (9.4)	13 (5.1)	0.05
ACEIs		625 (56.8)	250 (65.1)	230 (62.8)	90 (93.8)	55 (21.6)	<0.001
Diuretics		669 (60.8)	261 (67.9)	242 (66.1)	48 (50)	118 (46.5)	0.11
Statins		607 (55.2)	200 (52.1)	300 (81.9)	96 (100)	11 (4.3)	<0.001
Antiarrhythmic drugs		238 (21.6)	157 (40.9)	3 (0.8)	76 (79.2)	2 (0.8)	<0.001
Others		467 (42.5)	170 (44.3)	172 (47)	40 (41.7)	85 (33.4)	0.09
Type of device							
Pacemaker		607 (55.2)	246 (64.1)	162 (44.3)	38 (39.6)	161 (63.4)	<0.001
DDD		477 (43.3)	154 (40.1)	125 (34.1)	28 (29.2)	170 (67.2)	<0.001
VVI		108 (9.8)	88 (29.2)	10 (2.7)	10 (10.4)	–	<0.001
AAI		22 (2)	4 (1)	9 (2.5)	–	9 (3.6)	0.08
CRT		214 (19.5)	75 (19.5)	94 (25.6)	27 (28.1)	18 (7.1)	0.06
CRT-D		196 (17.8)	65 (16.9)	88 (24)	25 (26)	18 (7.1)	<0.01
CRT-P		18 (1.6)	10 (2.6)	6 (1.6)	2 (2.1)	–	0.3
ICD		279 (25.4)	63 (16.4)	129 (35.6)	31 (32.3)	56 (22)	<0.001
DDD		95 (8.6)	19 (4.9)	36 (9.8)	9 (9.4)	31 (12.2)	0.01
VVI		184 (16.8)	44 (11.5)	93 (25.4)	22 (22.9)	25 (9.9)	<0.01

TABLE 1 Baseline patient and procedural characteristics (continued from the previous page)

Characteristics	All patients (n = 1100)	ACT (n = 384)	APT (n = 366)	TAT (n = 96)	Controls (n = 254)	*P* value
Type of procedure						
Primary implantation	516 (46.9)	150 (39.1)	184 (50.3)	66 (68.7)	114 (44.9)	<0.001
Generator replacement	472 (42.9)	184 (47.9)	152 (41.5)	21 (21.9)	115 (45.3)	<0.001
System upgrade	112 (10.2)	50 (13)	29 (7.9)	9 (9.4)	24 (9.5)	0.001
Type of wound suturing						
Continuous intradermal absorbable	662 (69.3)	288 (75)	283 (77.1)	70 (76.9)	121 (47.6)	<0.001
Nonabsorbable single	338 (30.7)	95 (25)	84 (22.9)	26 (27.1)	133 (52.4)	<0.001
Procedure duration, min, median (IQR)						
Primary implantation	38 (16–63)	38 (16–63)	35 (18–45)	39 (25–58)	39 (22–53)	0.15
Generator replacement	16 (10–21)	16 (10–21)	17 (10–21)	16 (14–21)	15 (10–21)	0.12
System upgrade	35 (18–60)	37 (18–60)	38 (16–59)	30 (20–54)	32 (23–55)	0.1

Data are presented as number (percentage) unless otherwise indicated.

Abbreviations: AAI, atrial demand pacing; ACEI, angiotensin-converting enzyme inhibitor; BMI, body mass index; CHF, congestive heart failure; CRT, cardiac resynchronization therapy; CRT-D, cardiac resynchronization therapy with defibrillator; CRT-P, cardiac resynchronization therapy with pacing; DDD, atrial and/or ventricular demand pacing; GFR, glomerular filtration rate; HF, heart failure; ICD, implantable cardioverter defibrillator; IQR, interquartile range; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; TAVI, transcatheter aortic valve implantation; VVI, ventricular demand pacing; others, see FIGURE 1

TABLE 2 Frequency of significant bleeding complications at 30 days after cardiac implantable electroinic device surgery in study groups

Bleeding complications	All patients (n = 1100)	ACT subgroups					APT (n = 366)	TAT (n = 96)	Controls (n = 254)
		All ACT (n = 384)	VKA I (n = 100)	VKA II (n = 112)	DOAC (n = 136)	LMWH (n = 36)			
All SBCs	50 (4.5)	25 (6.5)	4 (4)	7 (6.3)	6 (4.4)	8 (22.2)	14 (3.8)	8 (8.3)	3 (1.2)
SPH requiring evacuation	6 (0.4)	4 (1)	1 (1)	2 (1.8)	1 (0.7)	–	1 (0.3)	1 (1)	–
SPH prolonging hospitalization	41 (3.6)	20 (5.2)	3 (4)	5 (6.8)	4 (2.9)	8 (22.2)	13 (3.7)	6 (6.2)	2 (1)
SB	3 (0.3)	1 (0.3)	–	–	1 (0.7)	–	–	1 (1)	1 (0.4)
No SBCs	1050 (95.5)	359 (93.5)	96 (96)	105 (93.8)	128 (94.1)	28 (77.8)	352 (96.2)	90 (93.7)	251 (98.8)

Data are presented as number (percentage).

Abbreviations: SB, significant bleeding; SBC, significant bleeding complication; SPH, significant pocket hematoma; others, see FIGURE 1

The new PACE DRAP scoring system Based on the SBC risk factors identified in the multivariable analysis, we propose a new simple score termed PACE DRAP. PACE DRAP is an acronym corresponding to each predictor: presence of valvular prosthesis (P), uncontrolled arterial hypertension (A); cancer (C); elderly (E); device type (D); renal failure (R); antiplatelets (A); and procedure type (P). The score was created using the weighted points proportional to the β regression coefficient rounded to the nearest integer in the multivariable analysis. The maximal score is 16 points. A detailed description of the factors that are included in the PACE DRAP acronym and the appropriate scoring are presented in TABLE 4. The PACE DRAP score significantly predicted the occurrence of SBCs (area under the curve [AUC], 0.95; P <0.001), and a score of 6 was identified as the cutoff point for high risk of SBCs with a sensitivity of 88.24% and a specificity of 87.23% (FIGURE 2).

Prognostic performance of the PACE DRAP score Our analyses showed that the final PACE DRAP model had a discriminatory ability with an accuracy of 87.26%. Among the entire studied population, 178 patients were classified as having a high risk of SBCs, 44 of whom actually developed SBCs within 30 days after CIED surgery (PPV, 24.7%; NPV, 99.3%). The detailed predictive performance of the PACE DRAP score is presented in TABLE 5.

DISCUSSION

Bleeding complications and periprocedural management of patients taking drugs that affect hemostasis constitute an increasingly significant challenge in modern cardiology, especially in the face of the growing number of CIED procedures.[5,6]

Significant bleeding complications In this study, the frequency of SBCs in the entire population was quite low (4.5%). The reported incidence of SBCs varies widely, from 0.7% to 5.7%, with an increasing trend in recent years, which is probably associated with the high number of CIED procedures and an increasing percentage of more

TABLE 3 Univariate and multivariable analyses of predictors of significant bleeding complications after cardiac implantable electronic device surgery

Predictor	Univariate analysis			Multivariable analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Age ≥75 y	8.23	3.8–13.77	<0.001	8.1	3.54–18.54	<0.001
CRT/ICD surgery	5.37	3.37–8.02	<0.001	5.96	2.48–14.32	<0.001
System upgrade	5.74	3.16–10.43	<0.001	10.22	4.05–25.78	<0.001
Congestive heart failure	4.18	2.35–7.43	<0.001	–		
Uncontrolled hypertension (BP ≥160/100 mm Hg)	8.62	3.65–20.38	<0.001	4.82	1.78–13.06	0.002
Prosthesis (biological/mechanical valvular)	17.2	9.3–31.94	<0.001	7.85	3.15–19.58	<0.001
Stroke	3.05	1.62–5.72	<0.001	–		
Atrial fibrillation/flutter	2.02	1.15–3.57	0.014	–		
Cancer	2.96	1.33–6.56	0.007	6.11	1.81–20.66	0.004
Anemia	2.68	1.89–5.9	<0.001	–		
Renal failure (GFR <60 ml/min/m^2)	9.9	5.51–17.81	<0.001	4.28	1.86–9.87	<0.001
Clopidogrel	4.5	2.44–8.34	<0.001	6.69	2.48–18.04	<0.001
Ticagrelor	9.3	3.16–27.57	<0.001	22.25	4.56–108.46	<0.001
DAPT	2.82	1.59–5.01	<0.001	–		
Acenocoumarol	0.96	0.68–1.34	0.8	–		
Warfarin	1.39	0.54–3.62	0.49	–		
Rivaroxaban	0.89	0.94–2.4	0.88	–		
Dabigatran	1.79	0.53–6.03	0.35	–		
Apixaban	2.62	0.32–21.36	0.37	–		
LMWH	2.82	1.59–5.01	<0.001	–		

Abbreviations: BP, blood pressure; CRT, cardiac resynchronization therapy; ICD, implantable cardioverter defibrillator; OR, odds ratio; others, see **FIGURE 1** and **TABLE 1**

TABLE 4 New simple bedside PACE DRAP score for predicting significant bleeding complications after cardiac implantable electronic device surgery

Letter designation	Risk factor	Definition	OR	β regression coefficient	Points
P	Prosthesis	Biological/mechanical valvular prosthesis	7.85	2.09	+2
A	Arterial hypertension uncontrolled	Blood pressure ≥160/100 mm Hg	4.82	1.57	+2
C	Cancer	Any malignancy diagnosed or treated within the last 5 years	6.11	1.81	+2
E	Elderly	Age ≥75 y	8.10	2.09	+2
D	Device type	CRT/ICD surgery	5.96	1.78	+2
R	Renal failure	GFR <60 ml/min/m^2	4.28	1.45	+1
A	Antiplatelets	Clopidogrel	6.69	1.9	+2
		Ticagrelor	22.25	3.1	+3
P	Procedure type	System upgrade	10.22	2.32	+2

Abbreviations: see **TABLES 1** and **3**

complex systems.[1,7,8] Another important reason may be patients' longevity, which results in more frequent interventions in the elderly population, who are burdened with severe comorbidities, which may increase the risk of complications.

In this study, SBCs were most frequent in the TAT group. Patients in this group underwent CIED implantation within 2 months after an acute coronary incident or drug-eluting stent implantation. Data on bleeding complications in patients receiving TAT are limited. However, other studies have shown an increased risk of bleeding, with no difference in the risk of a thromboembolic or cardiovascular event in patients receiving TAT compared with those receiving warfarin and clopidogrel.[9,10]

Previous studies showed that periprocedural bridging therapy significantly increases the risk of pocket hematoma.[8] One of the reasons for the increased incidence of SPHs in patients on LMWH

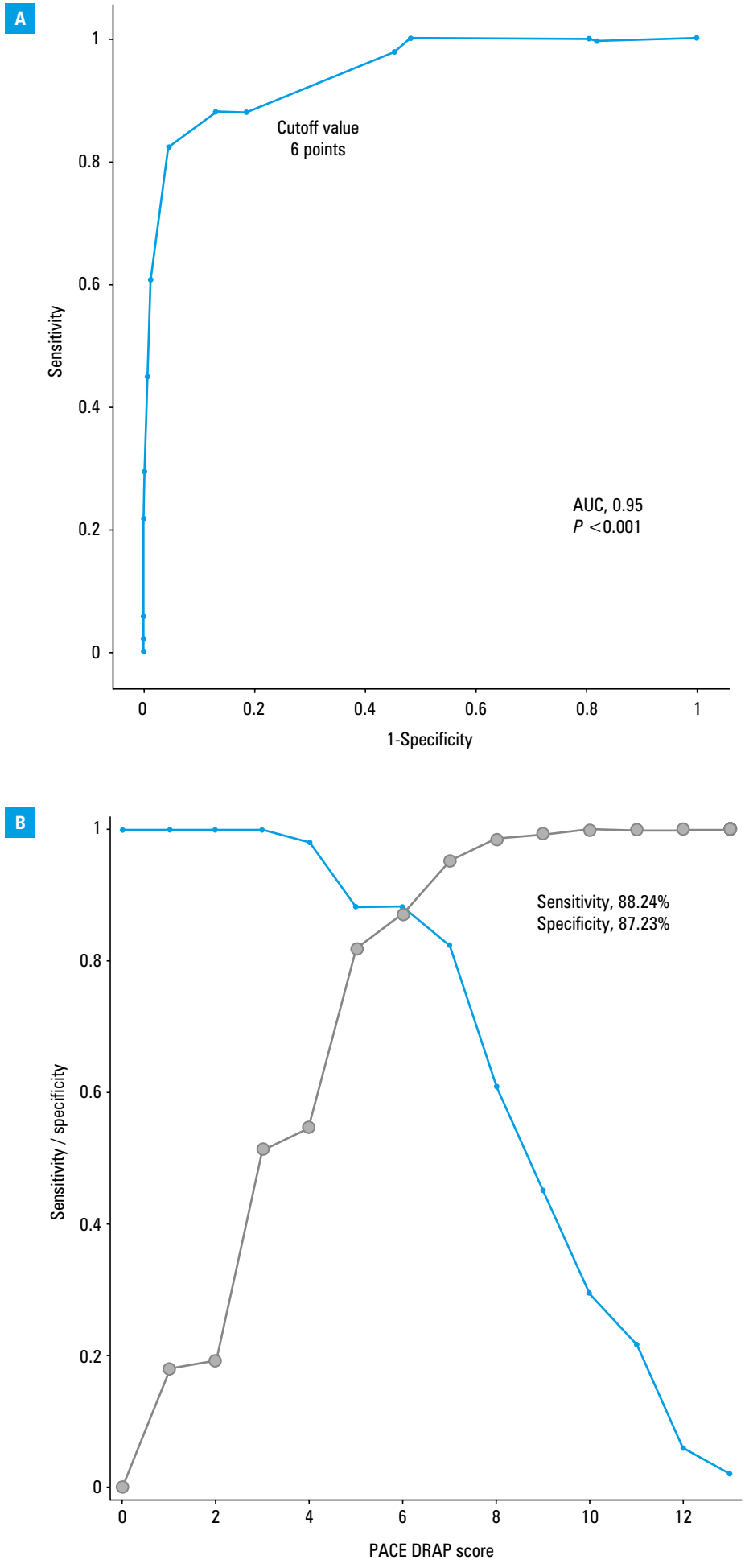

FIGURE 2 Receiver operating characteristic curve analysis of the PACE DRAP score for the prediction of significant bleeding complications within 30 days after cardiac implantable electronic device surgery: **A** – a high value of area under curve for the PACE DRAP score; **B** – high sensitivity and specificity for the cutoff point for the PACE DRAP score
Abbreviations: AUC, area under the curve

TABLE 5 Test characteristics for predicting device surgery–related significant bleeding complications depending on risk assessment using the PACE DRAP score

Parameter	High risk (≥6 points) of SBCs
Patients, n	178
Serious bleeding complications, n	44
Relative risk	37.94 (95% CI, 15.92–90.38)
Positive predictive value, %	24.7
Negative predictive value, %	99.3
Sensitivity, %	88
Specificity, %	87.22
Accuracy, %	87.26
Positive likelihood ratio	6.89
Negative likelihood ratio	0.14
Youden index	0.75

Abbreviations: see **TABLE 2**

seems to be postoperative use of heparin.[11] Although we demonstrated quite a high incidence of SPHs in the LMWH group (22%; 8 of 36 patients), the administration of heparin was not a significant risk factor in the multivariable analysis, probably due to a small number of patients receiving this form of ACT. According to current EHRA guidelines, the use of LMWH in the periprocedural period should be avoided in patients undergoing CIED surgery.[3]

The PACE DRAP score for risk assessment of significant bleeding complications

Presence of valvular prosthesis (P) The prosthetic valve is an important risk factor of SBCs. In this study, we included patients with mechanical prosthesis as well as those with biological prosthesis. Previously, Ishibashi et al[12] found an over 7-fold increase in the risk of SPH in patients with valvular disease compared with those undergoing electrotherapy procedures. Similar results were reported in the ROCKET AF study, where patients with severe valvular disease had a significantly higher bleeding rate regardless of the type of an anticoagulant used and other factors.[13] In the present study, no CIEDs had been implanted in patients with severe valvular disease prior to surgical treatment. A possible cause of an increased bleeding rate in patients with severe valvular disease or valvular prosthesis may be turbulent blood flow through the prosthesis or the affected valve, which affects the morphotic components of blood, especially platelets.

Arterial hypertension uncontrolled (A) In this study, the presence of uncontrolled arterial hypertension was associated with a nearly 5-fold increase in the risk of SBCs. Previous studies did not show a relationship between arterial hypertension and the incidence of bleeding complications after CIED surgery.[8,12] However, it was documented that arterial hypertension increases the risk of bleeding in patients using VKA independently of the INR level.[14]

Arterial hypertension represents a group of factors that may be modified by adequate pharmacotherapy and patient's education.

Cancer (C) The presence of a malignancy was associated with a 6-fold higher risk of SBCs. The most common types of cancer were breast (2.1%) and colorectal cancer (2%). No previously published studies included patients with malignancies. Although it is widely believed that cancer increases the risk of thromboembolic events due to hypercoagulability, previous studies have demonstrated that malignancy also increases the bleeding risk in patients on anticoagulation, even 2.5- to 6-fold as compared with patients without cancer, and is correlected with the cancer stage.[15] Potential causes include prior radiotherapy, chemotherapy, or immunotherapy, and the use of nonsteroidal anti-inflammatory drugs in pain therapy. Patients may also be predisposed to bleeding because of targeted treatment–induced platelet dysfunction. However, chemotherapy-induced thrombocytopenia was not found to affect the occurrence of bleeding.[16]

Elderly (age ≥75 years) In this study, the risk of SBCs was significantly higher in patients aged 75 years or older. One of the potential reasons may be venous anatomy, especially vessel tortuosity, which significantly hinders venous access and may increase the number of attempts to puncture the vessel.[17] Additionally, Armaganijan et al[18] showed that older people are at increased risk of pneumothorax and intracardiac electrode dislocation. Implanting the electrodes by puncture of the axillary or elbow vein using ultrasound or angiographic control may reduce the frequency of SBCs in this group.[18]

Device type (D) We showed that implantation of a CRT-P or ICD increased the risk of SBCs almost 6-fold. This is in line with a study by Yang et al,[19] who found that ICD or CRT-P implantation increased the risk of bleeding by 36% as compared with pacemaker implantation. This can be explained by the more complex structure, larger size, and increased stiffness of the ICD and CRT electrodes.

Renal failure (R) In our study, renal failure (estimated glomerular filtration rate [eGFR] <60 ml/min/1.73 m^2) increased the risk of SBCs more than 4-fold. Similar results have been reported in the literature.[20] Tompkins et al[7] showed that an eGFR of 15 to 29 ml/min/1.73 m^2 increases the risk of CIED-related SBCs more than 3-fold, and end-stage renal disease (eGFR <15 ml/min/1.73 m^2), even 7-fold. Buiten et al[21] proved that an eGFR of less than 30 ml/min/1.73 m^2 almost triples the risk of SPH. Platelet dysfunction and altered interactions, vascular endothelium, reduced nitric oxide synthesis, together with anticoagulation and fibrinolysis abnormalities, as well as malnutrition, appear to be responsible for the increased bleeding rate.[22]

Antiplatelets (A) Antiplatelet strategy is a strong predictor of bleeding after CIED surgery. In this study, DAPT with clopidogrel increased the risk of SBCs almost 7-fold, while the use of ticagrelor increased it more than 21 times. Aspirin monotherapy did not significantly affect bleeding. Similar results have been published before.[19,23] In our work, the use of ticagrelor was the strongest risk factor for SBCs, which is why it is assigned 3 points on the PACE DRAP scale. It seems that the differences in the bleeding rate between clopidogrel and ticagrelor are due to the difference in the effectiveness in inhibiting platelet activity between these two $P2Y_{12}$ receptor inhibitors and their metabolism. As ticagrelor is an active drug, which means that it does not need to be converted to an active form, it acts faster than clopidogrel. Moreover, the resistance to ticagrelor is nonsignificant. To our knowledge, this is the first study to assess the effect of ticagrelor on SBCs in patients undergoing any type of a CIED procedure, including CRT.

Procedure type (P) We demonstrated that system upgrades increase the risk of SBCs 10-fold. These results are consistent with previous literature data.[24] This can be explained by the additional dissection of fibrous tissue around the device during subsequent procedures, and greater manipulation of surrounding structures may cause damage of local blood vessels.[22] Furthermore, implanting a new electrode may contribute to direct injury and disruption of the vein or heart wall, resulting in local bleeding or, in the event of major injury, tamponade. Our results, in combination with previous data, confirm that all types of reintervention are associated with a greater risk of complications compared with first-time CIED surgery.

The simple PACE DRAP scoring system could be used as a quick and practical tool for SBCs risk estimation but requires external validation. Our internal validation showed that PACE DRAP was able to discriminate patients at high risk of SBCs with high accuracy, sensitivity, and specificity. However, other risk factors, such as the use of nonprescription drugs, should also be considered. It should be emphasized that several of the identified risk factors, such as hypertension, renal failure stage, or the use of antiplatelets, are potentially modifiable.

Study limitations This study has several limitations, the main being its observational design, which prevented an equitable division of the analyzed group in terms of the type of APT and ACT used. The study included a small number of patients from a single center. Another important limitation is the heterogeneity of the analyzed group in terms of demographic and clinical characteristics, which could potentially affect the results. Although all the prescription drugs that affect the hemostatic system were included in our data set, the use of nonprescription drugs would have gone undetected. Bleeding episodes or other significant comorbidities only revealed in the primary care setting might not have been visible in our data set and may thus be underrepresented. Another limitation is that we could not validate the accuracy of the PACE DRAP scoring system using other cohorts.

Conclusions We identified strong predictors of SBCs, several of which are potentially modifiable. We devised PACE DRAP, a simple bedside scoring system that may enable the identification of patients at high risk of SBCs related to CIED surgery without the need for laboratory testing.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/paim.

ARTICLE INFORMATION

CONTRIBUTION STATEMENT SS and AA conceived the concept of the study, contributed to the study design, analyzed the data, interpreted the results, and wrote the paper. MG, KS, WS, MW, TS, LC-M, ML, and PM contributed to data acquisition, analysis, and interpretation. All authors discussed the results and contributed to the final manuscript.

CONFLICT OF INTEREST None declared.

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