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AIMS AND SCOPE

The primary aim of *World Journal of Cardiology (WJC, World J Cardiol)* is to provide scholars and readers from various fields of cardiology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJC mainly publishes articles reporting research results and findings obtained in the field of cardiology and covering a wide range of topics including acute coronary syndromes, aneurysm, angina, arrhythmias, atherosclerosis, atrial fibrillation, cardiomyopathy, congenital heart disease, coronary artery disease, heart failure, hypertension, imaging, infection, myocardial infarction, pathology, peripheral vessels, public health, Raynaud's syndrome, stroke, thrombosis, and valvular disease.

INDEXING/ABSTRACTING

The WJC is now abstracted and indexed in Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 edition of Journal Citation Reports® cites the 2021 Journal Citation Indicator (JCI) for WJC as 0.35. The WJC's CiteScore for 2021 is 0.9, and Scopus CiteScore rank 2021: Cardiology and Cardiovascular Medicine is 260/336.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Hua-Ge Yin*; Production Department Director: *Xiang Li*; Editorial Office Director: *Yun-Xiaojiao Wu*.

NAME OF JOURNAL

World Journal of Cardiology

ISSN

ISSN 1949-8462 (online)

LAUNCH DATE

December 31, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Ramdas G Pai, Dimitrios Tousoulis, Marco Matteo Ciccone, Pal Pacher

EDITORIAL BOARD MEMBERS

<https://www.wjnet.com/1949-8462/editorialboard.htm>

PUBLICATION DATE

April 26, 2023

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INSTRUCTIONS TO AUTHORS

<https://www.wjnet.com/bpg/gerinfo/204>

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PUBLICATION ETHICS

<https://www.wjnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.fcpublishing.com>

Observational Study

Perioperative coagulation activation after permanent pacemaker placement

Roman Kalinin, Igor Suchkov, Vladislav Povarov, Nina Mzhavanadze, Olga Zhurina

Specialty type: Cardiac and cardiovascular systems**Provenance and peer review:** Invited article; Externally peer reviewed.**Peer-review model:** Single blind**Peer-review report's scientific quality classification**Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0**P-Reviewer:** Abrignani MG, Italy;
Shen F, China**Received:** December 27, 2022**Peer-review started:** December 27, 2022**First decision:** February 20, 2023**Revised:** March 5, 2023**Accepted:** April 12, 2023**Article in press:** April 12, 2023**Published online:** April 26, 2023**Roman Kalinin, Igor Suchkov, Vladislav Povarov, Nina Mzhavanadze**, Department of Cardiovascular, Endovascular Surgery and Diagnostic Radiology, Ryazan State Medical University, Ryazan 390026, Russia**Vladislav Povarov**, Department of Surgical Treatment of Cardiac Arrhythmias and Cardiac Pacing, Ryazan State "Regional Clinical Cardiology Dispensary", Ryazan 390026, Russia**Olga Zhurina**, Scientific and Clinical Center for Hematology, Oncology and Immunology, Ryazan State Medical University, Ryazan 390026, Russia**Corresponding author:** Nina Mzhavanadze, MD, PhD, Professor, Department of Cardiovascular, Endovascular Surgery and Diagnostic Radiology, Ryazan State Medical University, Vysokovolt'naya 9, Ryazan 390026, Russia. nina_mzhavanadze@mail.ru**Abstract****BACKGROUND**

Bradyarrhythmias are typically treated with permanent pacemakers (PM). The elimination of bradyarrhythmia by PM implantation improves the patient's quality of life and prognosis, but it can also result in a number of sequelae. It is still unclear how PM implantation affects the hemostasis system's parameters and how such parameters relate to different consequences after PM placement.

AIM

To assess the blood coagulation factor activity in PM patients throughout the perioperative period.

METHODS

Patients treated in the Department of Surgical Therapy of Cardiac Arrhythmias and Pacing at the Ryazan State "Regional Clinical Cardiology Dispensary" from April 2020 to December 2021 were included in the study. Before surgery, 7 and 30 d after PM placement, peripheral venous blood samples were withdrawn to measure the level of blood coagulation factor I (FI) and the activity of blood coagulation factors II (FII), V (FV), VII (FVII), VIII (FVIII), IX (FIX), X (FX), XI (FXI), XII (FXII). We used an automatic coagulometer Sysmex CA 660 (Sysmex Europe, Germany) and reagents from Siemens (Siemens Healthcare Diagnostics Products GmbH, Germany).

RESULTS

The study included 146 patients. The activity of factors FV [147.7 (102.1-247.55)% *vs* 103.85 (60-161.6)% *vs* 81.8 (67.15-130.65)%, $P = 0.002$], FVIII [80.4 (60.15-106.25)% *vs* 70.3 (48.5-89.1)% *vs* 63.7 (41.6-88.25)%, $P = 0.039$], FIX [86.2 (70.75-102.95)% *vs* 75.4 (59.2-88.3)% *vs* 73.9 (56.45-93.05)%, $P = 0.014$], FX [188.9 (99.3-308.18)% *vs* 158.9 (83.3-230)% *vs* 127.2 (95.25-209.35)%, $P = 0.022$], FXI [82.6 (63.9-103.6)% *vs* 69.75 (53.8-97.6)% *vs* 67.3 (54.25-98.05)%, $P = 0.002$], FXII [87.6 (67.15-102.3)% *vs* 78.9 (63.4-97.05)% *vs* 81.2 (62.15-97.4)%, $P < 0.001$] decreased at 7 and 30 d after surgery; FII activity [157.9 (109.7-245.25)% *vs* 130 (86.8-192.5)% *vs* 144.8 (103.31-185.6)%, $P = 0.021$] decreased at 7 d and increased at 30 d postoperatively. There were no statistically significant changes in the FVII activity within 30 d after PM placement [182.2 (85.1-344.8)% *vs* 157.2 (99.1-259)% *vs* 108.9 (74.9-219.8)%, $P = 0.128$]. Subgroup analysis revealed similar changes only in patients on anticoagulant therapy. FXII activity decreased in patients on antiplatelet therapy [82 (65.8-101.9)% *vs* 79.9 (63.3-97.1)% *vs* 89.7 (75.7-102.5)%, $P = 0.01$] 7 d after surgery, returning to baseline values at 30 d postoperatively.

CONCLUSION

PM placement and anticoagulant therapy were associated with decreased activity of clotting factors FV, FVIII, FIX, FX, FXI, FXII in the postoperative period. FVII activity did not decrease within 30 d after PM placement, which may indicate endothelial injury caused by lead placement.

Key Words: Hemostasis; Blood coagulation; Cardiac pacemaker; Anticoagulants; Postoperative complications

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Core Tip: Permanent pacemaker placement and anticoagulant therapy are associated with decreased activity of factors V (FV), FVIII, FIX, FX, FXI, FXII in the postoperative period. FVII activity does not decrease within 30 d after PM placement, which may be suggestive of ongoing endothelial injury.

Citation: Kalinin R, Suchkov I, Povarov V, Mzhavanadze N, Zhurina O. Perioperative coagulation activation after permanent pacemaker placement. *World J Cardiol* 2023; 15(4): 174-183

URL: <https://www.wjgnet.com/1949-8462/full/v15/i4/174.htm>

DOI: <https://dx.doi.org/10.4330/wjc.v15.i4.174>

INTRODUCTION

Cardiac implantable electronic devices (CIED), which include pacemakers (PM), are widely used to treat patients with arrhythmias and chronic heart failure[1,2]. Bradyarrhythmias are typically treated with permanent PM. The elimination of bradyarrhythmia by PM implantation improves the patient's quality of life and prognosis, but it can also result in a number of sequelae[1,3,4]. It is still unclear how PM implantation affects the hemostasis system's parameters and how those parameters relate to different problems and other consequences. The aim of our study was to assess the blood coagulation factor activity in PM patients throughout the perioperative period.

MATERIALS AND METHODS

Study population and data collection

The study included patients treated in the Department of Surgical Treatment of Cardiac Arrhythmias and Cardiac Pacing at the Ryazan State "Regional Clinical Cardiology Dispensary" from April 2020 to December 2021. Inclusion criteria for the study were indications for pacemaker implantation and age over 40 years; non-inclusion criteria were presence of a previously implanted pacemaker, contraindications to antithrombotic therapy, pregnancy or breastfeeding, and active cancer or remission for less than 5 years. After the patient consented to participate in the study and signed the informed consent form, the following data were collected: Age, sex, height, weight, underlying disease, comorbidities, history of surgical interventions, the type of antithrombotic therapy used. Peripheral venous blood samples were taken to analyze the activity of the studied blood coagulation factors on the day of surgery.

Operative techniques

PM placement was carried out in accordance with the “European Heart Rhythm Association expert consensus statement and practical guide on optimal implantation technique for conventional PM and implantable cardioverter-defibrillators” [1]. Endocardial leads were implanted *via* cephalic vein; subclavian vein was used as vascular access only when the cephalic vein was not suitable. All patients had the same PM models, single- and dual-chamber, and leads. Atrial leads with active-fixation systems were implanted in the right atrial appendage, whereas all ventricular leads with passive-fixation systems were placed in the right ventricle's apex. The PM was placed either in the pectoralis major muscle or in the subcutaneous tissues above the fascia of the muscle.

Postoperative follow-up period

After the PM placement, the patients were allowed to stay in bed for 12 h. Moreover, an ice load was administered to the surgical site for 2 h in order to prevent PM pocket hematoma. The patients spent an average of 6 d at the hospital. Venous blood sampling was repeated on the 7th and 30th days after PM placement.

Coagulation factors assessment

Venous blood samples were centrifuged; the resulting plasma was used to assess the studied parameters: The level of blood coagulation factor I (FI) and the activity of blood coagulation factors II (FII), V (FV), VII (FVII), VIII (FVIII), IX (FIX), X (FX), XI (FXI), XII (FXII). We used an automatic coagulometer Sysmex CA 660 (Sysmex Europe, Germany) and reagents from Siemens (Siemens Healthcare Diagnostics Products GmbH, Germany).

Biostatistics

Statistical analysis was performed using IBM SPSS Statistics 26.0 for Windows (SPSS Inc. Chicago, IL, United States). Numbers and percentages were used to express categorical data. The χ^2 test and Fisher exact test were used to analyze categorical data. Shapiro-Wilk test was used to assess normality. Most data were expressed as medians since they were not normally distributed. Wilcoxon test, Mann-Whitney test, Friedman test, Kruskal-Wallis test, and post-hoc tests were used as non-parametric tests for data comparison between two groups. Several cases with normal distribution were analyzed using parametric statistical analysis techniques. *P* values less than 0.05 were considered to indicate statistical significance.

RESULTS

Patients' characteristics

A total of 213 patients were screened to participate in the study. At the screening stage, 57 (26.7%) patients were withdrawn from the study: 38 (17.8%) refused to participate in the study, 19 (8.9%) had indications for placement of the other types CIED rather than a PM. As a result, 156 patients were included in the study, and 146 patients successfully completed the trial. Among 10 patients who dropped out of the study, 6 died and 4 withdrew their consent (Figure 1).

All patients signed an informed consent. This study was approved by the Local Ethics Committee of the Ryazan State Medical University. The clinical characteristics of the patients are shown in Table 1.

Antithrombotic therapy

All patients in the study received antithrombotic therapy (Table 1). All patients with atrial fibrillation received anticoagulants in accordance with clinical guidelines. Dabigatran etexilate was provided at a dose of 150 (110) mg twice day, apixaban at a dose of 5 (2.5) mg twice daily, and rivaroxaban at a dose of 20 (15) mg once daily. Warfarin was provided once daily; warfarin dosage was adjusted to achieve international normalized ratio of 2 to 3. The rest of the patients received acetylsalicylic acid at a dose of 100 mg once daily due to ischemic heart disease. None of the patients received anticoagulants and antiplatelets simultaneously. Antithrombotic therapy was not canceled or changed during the perioperative period.

Perioperative assessment of coagulation parameters

There was a decrease in the activity of factors FV, FVIII, FIX, FX, FXI, and FXII at 7 and 30 d after the procedure, while the activity of FII decreased after 7 d and increased after 30 d. During the observation period, changes in FI levels and FVII activity were not statistically significant (Table 2).

Subgroup analysis

A subgroup analysis was conducted in order to identify the variables impacting the investigated parameters. The type of antithrombotic medication the patient received had the greatest impact on the variables in this study (Table 3).

Table 1 Baseline characteristics of patients included in the study, *n* (%)

| Variable (<i>n</i> = 146) | Data |
|---|--------------|
| Age, years | 73 (67-81) |
| Body mass index, kg/m ² | 27.5 (25-31) |
| Gender | |
| Male | 77 (52.7) |
| Female | 69 (47.3) |
| Pacemaker placement indication | |
| Atrioventricular block | 49 (33.6) |
| Sick sinus syndrome | 47 (32.2) |
| Atrial fibrillation with impaired atrioventricular conduction | 50 (34.2) |
| Comorbidity | |
| Ischemic heart disease | 146 (100) |
| Exertional angina | 44 (30.1) |
| Arterial hypertension | 143 (97.9) |
| Atrial fibrillation | 96 (65.8) |
| Congestive heart failure | 146 (100) |
| NYHA Class I | 7 (4.8) |
| NYHA Class II | 60 (41.1) |
| NYHA Class III | 79 (54.1) |
| NYHA Class IV | 0 (0) |
| History of myocardial infarction | 28 (19.2) |
| History of stroke | 12 (8.2) |
| Atherosclerotic peripheral arterial disease | 4 (2.7) |
| Varicose veins | 31 (21.2) |
| History of venous thromboembolism | 8 (5.5) |
| Type 2 diabetes mellitus | 39 (21.2) |
| History of coronavirus disease | 4 (2.7) |
| Antithrombotic therapy | |
| Antiplatelet therapy (aspirin) | 55 (37.7) |
| Oral anticoagulants | 91 (62.3) |
| Rivaroxaban | 57 (39) |
| Apixaban | 20 (13.7) |
| Dabigatran etexilate | 7 (4.8) |
| Warfarin | 7 (4.8) |
| Surgery features | |
| Pacemaker | |
| Single-chamber | 50 (34.2) |
| Dual-chamber | 96 (65.8) |
| Pacemaker placement side | |
| Left side | 142 (97.3) |
| Right side | 4 (2.7) |
| Vascular access | |

| | |
|------------------------------------|------------|
| Cephalic vein (section) | 132 (90.4) |
| Subclavian vein (puncture) | 14 (9.6) |
| Pacemaker pocket localization | |
| Above the pectoral fascia | 133 (91.1) |
| Inside the pectoralis major muscle | 13 (8.9) |
| Mean surgery time, min | 54 (41-60) |

NYHA: New York Heart Association.

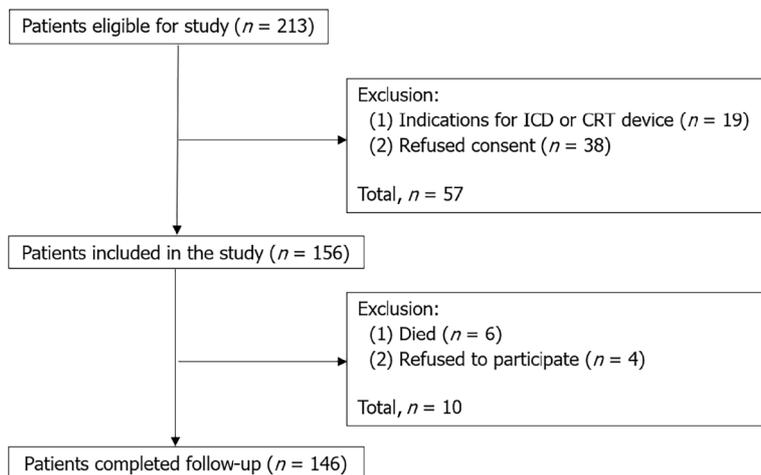
Table 2 Perioperative coagulation parameters (n = 146)

| Variable | Before implantation | 7 d after implantation | 30 d after implantation | P value |
|----------|-------------------------------------|------------------------|-------------------------|---------|
| FI | 2.61 (2.05-3.11) | 2.76 (2.08-3.42) | 2.54 (2.16-2.91) | 0.669 |
| FII | 157.9 (109.7-245.25) ^a | 130 (86.8-192.5) | 144.8 (103.31-185.6) | 0.021 |
| FV | 147.7 (102.1-247.55) ^{a,b} | 103.85 (60-161.6) | 81.8 (67.15-130.65) | 0.002 |
| FVII | 182.2 (85.1-344.8) | 157.2 (99.1-259) | 108.9 (74.9-219.8) | 0.128 |
| FVIII | 80.4 (60.15-106.25) ^{a,b} | 70.3 (48.5-89.1) | 63.7 (41.6-88.25) | 0.039 |
| FIX | 86.2 (70.75-102.95) ^{a,b} | 75.4 (59.2-88.3) | 73.9 (56.45-93.05) | 0.014 |
| FX | 188.9 (99.3-308.18) ^{a,b} | 158.9 (83.3-230) | 127.2 (95.25-209.35) | 0.022 |
| FXI | 82.6 (63.9-103.6) ^{a,b} | 69.75 (53.8-97.6) | 67.3 (54.25-98.05) | 0.002 |
| FXII | 87.6 (67.15-102.3) ^{a,b} | 78.9 (63.4-97.05) | 81.2 (62.15-97.4) | < 0.001 |

^a*P* < 0.05 vs 7 d after pacemaker implantation.

^b*P* < 0.05 vs 30 d after pacemaker implantation.

FI: Factor I; FII: Factor II; FV: Factor V; FVII: Factor VII; FVIII: Factor VIII; FIX: Factor IX; FX: Factor X; FXI: Factor XI; FXII: Factor XII.



DOI: 10.4330/wjc.v15.i4.174 Copyright ©The Author(s) 2023.

Figure 1 Flowchart diagram providing patients included in the study. ICD: Implanted cardioverter-defibrillator; CRT: Cardiac resynchronization therapy.

Patients with dual-chamber PMs on anticoagulant therapy 7 d after surgery had lower values of FI (*P* = 0.033), and lower activity of FV (*P* = 0.045), FVIII (*P* < 0.001), FIX (*P* < 0.001), FXI (*P* = 0.004); lower activity of FVIII (*P* = 0.049), FIX (*P* < 0.001), FXI (*P* = 0.003) was seen at 30 d after surgery as compared with patients on antiplatelet therapy. There were no differences in the studied parameters between patients receiving anticoagulant therapy with single-chamber and dual-chamber PM as well as different indications for PM placement (*P* > 0.05).

Table 3 Perioperative coagulation parameters in patients on antiplatelet ($n = 55$) and anticoagulant ($n = 91$) therapy

| Variable | Antithrombotic therapy | Before implantation | 7 d after implantation | 30 d after implantation | P value |
|----------|------------------------|-----------------------------------|------------------------|-------------------------|---------|
| FI | Antiplatelet | 2.66 (2.13-2.99) | 2.85 (2.47-3.3) | 2.56 (2.19-3.16) | 0.513 |
| | Anticoagulant | 2.55 (1.9-3.19) | 2.58 (1.93-3.44) | 2.49 (2.16-2.85) | 0.957 |
| | P value | 0.675 | 0.092 | 0.599 | - |
| FII | Antiplatelet | 156.9 (94.5-237.3) | 139 (86.8-192.5) | 163.5 (112.4-203) | 0.289 |
| | Anticoagulant | 186.2 (113.8-256.8) | 118.5 (86.8-173) | 128.4 (99.6-170.5) | 0.067 |
| | P value | 0.458 | 0.609 | 0.263 | - |
| FV | Antiplatelet | 164.9 (103.4-267.5) | 115.5 (92.8-198.9) | 98.6 (82.6-155.3) | 0.245 |
| | Anticoagulant | 133.3 (96.6-187.9) ^{a,b} | 80.1 (45.9-152.8) | 73.4 (55.4-84.3) | 0.005 |
| | P value | 0.196 | 0.033 | 0.004 | - |
| FVII | Antiplatelet | 203.4 (113-352.1) | 200 (116.4-438.3) | 223 (107.9-376.6) | 0.683 |
| | Anticoagulant | 182.1 (87.3-384.6) | 122.3 (80.3-209.9) | 83.7 (64.6-154.8) | 0.153 |
| | P value | 0.691 | 0.024 | 0.002 | - |
| FVIII | Antiplatelet | 82.1 (62.5-114.3) | 81.6 (63.8-97.5) | 75.5 (59.1-100.5) | 0.104 |
| | Anticoagulant | 78.5 (58.7-99.7) ^{a,b} | 59.6 (41.7-82) | 55.1 (40.8-84.4) | 0.001 |
| | P value | 0.21 | 0.001 | 0.033 | - |
| FIX | Antiplatelet | 85.4 (74.8-106.9) | 84.2 (78-105.8) | 96.7 (87.2-104) | 0.438 |
| | Anticoagulant | 87 (68.4-99.6) ^{a,b} | 69.6 (55.6-81.8) | 63.2 (45.5-76.8) | 0.004 |
| | P value | 0.331 | <0.001 | <0.001 | - |
| FX | Antiplatelet | 200 (105.8-308.2) | 163.8 (81.7-228.4) | 171.6 (120.2-240) | 0.708 |
| | Anticoagulant | 187.8 (98.6-286.1) ^{a,b} | 152.6 (89-248.2) | 109.8 (82-163.5) | 0.007 |
| | P value | 0.837 | 0.983 | 0.03 | - |
| FXI | Antiplatelet | 87.2 (69.8-100.8) | 93.8 (63.1-108.2) | 96.7 (84.2-108) | 0.957 |
| | Anticoagulant | 74.8 (62.5-106.9) ^{a,b} | 61 (49.9-82.6) | 59.5 (47.5-86.5) | < 0.001 |
| | P value | 0.377 | 0.001 | < 0.001 | - |
| FXII | Antiplatelet | 82 (65.8-101.9) ^a | 79.9 (63.3-97.1) | 89.7 (75.7-102.5) | 0.01 |
| | Anticoagulant | 80.7 (69.4-110.2) ^{a,b} | 78.9 (63.4-97) | 73.8 (69.8-90.3) | 0.001 |
| | P value | 0.989 | 0.629 | 0.027 | - |

^a $P < 0.05$ vs 7 d after pacemaker implantation.

^b $P < 0.05$ vs 30 d after pacemaker implantation.

FI: Factor I; FII: Factor II; FV: Factor V; FVII: Factor VII; FVIII: Factor VIII; FIX: Factor IX; FX: Factor X; FXI: Factor XI; FXII: Factor XII.

When evaluating the effect of each individual anticoagulant on the studied parameters, we found that patients who took apixaban had lower FIX ($P = 0.049$) activity at 7 d after surgery, and lower activity of FV ($P = 0.046$), FIX ($P = 0.015$), and FXI ($P = 0.014$) at 30 d after surgery as compared with patients who received acetylsalicylic acid. Patients who took rivaroxaban had lower activity of FIX ($P = 0.004$), FXI ($P = 0.02$) at 7 d after surgery, and lower activity of FIX ($P = 0.006$), FXI ($P = 0.004$) at 30 d after surgery as compared with patients who took acetylsalicylic acid. Patients who took dabigatran etexilate had lower FIX activity at 7 d ($P = 0.023$) and 30 d ($P = 0.024$) after surgery as compared with patients who took acetylsalicylic acid. Patients who took warfarin had lower FIX activity at 7 d ($P = 0.023$) and 30 d ($P = 0.001$) after surgery as compared to patients who received acetylsalicylic acid.

Female patients had higher baseline FVII ($P = 0.001$) and FIX ($P = 0.003$) activity, regardless of antithrombotic therapy type as compared with males.

DISCUSSION

Our aim was to study coagulation in patients with PM in the perioperative period. As a result, we discovered that at 7 and 30 d following surgery, the activity of coagulation factors V, VIII, IX, X, XI, and XII diminished. A more extensive statistical analysis revealed that patients on anticoagulant therapy experienced such changes more frequently. FXII activity in individuals who received acetylsalicylic acid decreased at 7 d after surgery before returning to baseline levels at 30 d after surgery. Patients undergoing antiplatelet and anticoagulant therapy did not show statistically significant changes in FVII activity or FI levels within 30 d of PM implantation.

Coagulation is one of the components of the human hemostasis system. Blood coagulation factors such as transglutaminases, glycoproteins, and serine proteases are part of the coagulation system[5]. The cascade model was once regarded as the primary coagulation model. This paradigm distinguishes between intrinsic and extrinsic coagulation pathways, which include the successive activation of blood coagulation components. Both pathways merge into a common coagulation pathway, which results in the formation of fibrin, which strengthens the thrombus[6,7].

The modern concept of coagulation is a cell-based model that describes the close relationship between the blood coagulation factors, platelets and endothelial cells. The coagulation process is broken down into three parts by the cell model: initiation, amplification, and propagation. When the vascular endothelium is injured during the initiation phase, cells that express tissue factor (such as smooth muscle cells) interact with FVII (initiation phase). This complex triggers the activation of FII, FIX, and FX. In the amplification phase, FII interfaces with the platelet membrane, where FXI, FVIII, and FV activation start. The propagation phase starts when activated FVIII and FIX combine to generate a complex capable of activating a significant amount of FX. Afterwards, FII and FI are activated, much like in the cascade model. Other interactions of blood coagulation factors in the cell-based model of hemostasis are also described, in addition to those described above. Coagulation is controlled by the anticoagulant system of blood. A cell-based model of hemostasis shifts our understanding of the blood clotting process to a different level, not excluding the cascade model[5,6,8].

The majority of PM patients are elderly people who frequently have a variety of comorbidities and illnesses linked to a hypercoagulable state of the hemostasis system. Atrial fibrillation, arterial hypertension, coronary heart disease, chronic heart failure, obesity, and other disorders fall under this category. Prior to PM implantation, bradyarrhythmia significantly influences the development of chronic heart failure and hypercoagulability in such patients[9,10]. Participants in the study who received anticoagulants displayed a decrease in the activity of intrinsic pathway factors such as FV, FVIII, FIX, FX, FXI, or amplification and propagation phases factors (according to the cell-based model). The baseline values of the examined parameters in these patients would likewise be lower than in patients receiving antiplatelet medications, but this was not the case in our study. In this instance, the use of anticoagulants and the elimination of bradyarrhythmia by PM implantation both likely contributed to the decline in the activity of the examined parameters. Elimination of bradyarrhythmia in patients receiving antiplatelets only temporarily reduced FXII activity.

Vascular access to the right ventricle of the heart is necessary for PM implantation operation. The lead is passed through the venous system after the subclavian vein is punctured or the cephalic vein is sectioned during surgery. Conditions are produced at the damaged area to enable the hemostasis system to function. A rise in tissue factor and von Willebrand factor in patients following pacemaker implantation supports this idea[3,9,11]. The second place of activation of the hemostasis system is the area of contact of the lead with endocardium. Gjesdal *et al*[12] showed high platelet activity *in vitro* when stimulated with PM bipolar leads. Palatianos *et al*[13] in an experiment on pigs noted that the largest accumulation of platelets was detected at the distal end of the PM lead. Although it is thought that lead has a low thrombogenicity, blood clots could still form for a variety of reasons, including a disruption of the laminar blood flow through the vein[13,14]. In our work, FVII activity does not decline in patients throughout the course of the 30-d observation period. This might be because tissue factor continues to activate FVII at the locations where the electrode caused endothelium damage. The persistence of FII activity shows that this coagulation route (extrinsic pathway of the cascade model, initiation phase of the cell-based model) is active during the entire observation time.

Our study did not aim to assess each individual anticoagulant medication's effect on the coagulation hemostasis measures. Amplification phase factors FV, FIX, and FXI's activity was shown to be decreased by apixaban and rivaroxaban when compared to acetylsalicylic acid due to FX's inhibition. Patients taking dabigatran etexilate had lower FIX activity because FII was inhibited as compared to patients receiving acetylsalicylic acid[4,5,15].

Many studies on the topic of coagulation in PM patients have been published in the international literature. The majority of these studies focus on how these patients' coagulation patterns relate to deep vein thrombosis (DVT) of the upper extremities and venous thromboembolism in general[3,11,14,16,17]. Zhang *et al*[3] noted an increase in FVIII activity 7 d after surgery. Lelakowski *et al*[11] observed an increase in FVII activity at the same period. The findings of our previous studies have demonstrated the predictive value of D-dimer levels in relation to the occurrence of DVT in the upper extremities following the initial implantation of the PM and the association between a high level of D-dimer and impaired patency of the veins in the upper extremities in patients with already implanted PM[16,18].

One of the limitations of our study was inability to assess the changes of the studied parameters in patients with single-chamber PM who require antiplatelet therapy. Currently, single-chamber PMs in the vast majority of cases are implanted in patients with permanent atrial fibrillation who require anticoagulant therapy. Placement of a single-chamber PM in the atrial position in patients with sick sinus syndrome, who could potentially receive antiplatelet agents and be investigated in this regard, is not common these days[1,19]. The study was also characterized by a limited number of postoperative visits and a certain choice of antiplatelet therapy (acetylsalicylic acid), non-inclusion of certain categories of patients such as younger patients, children, patients with leadless PM, *etc.*

CONCLUSION

PM placement and anticoagulant therapy were associated with decreased activity of clotting factors FV, FVIII, FIX, FX, FXI, FXII in the postoperative period. FVII activity did not decrease within 30 d after PM placement, which may indicate endothelial injury caused by lead placement. We think that further investigation of hemostasis system will contribute to the creation of newer approaches to the detection, prognosis, management, and prevention of numerous hemorrhagic and thromboembolic complications in patients requiring PM implantation.

ARTICLE HIGHLIGHTS

Research background

Bradyarrhythmias are typically treated with permanent pacemakers (PM). The elimination of bradyarrhythmia by PM implantation improves the patient's quality of life and prognosis, but it can also result in a number of sequelae.

Research motivation

It is still unclear how PM implantation affects the hemostasis system's parameters and how such parameters relate to different complications after PM placement.

Research objectives

To assess the blood coagulation factor activity in PM patients throughout the perioperative period.

Research methods

Patients treated in the Department of Surgical Therapy of Cardiac Arrhythmias and Pacing at the Ryazan State "Regional Clinical Cardiology Dispensary" from April 2020 to December 2021 were included in the study. Before surgery, 7 and 30 d after PM placement, peripheral venous blood samples were withdrawn to measure the level of blood coagulation factor I (FI) and the activity of blood coagulation factors II (FII), V (FV), VII (FVII), VIII (FVIII), IX (FIX), X (FX), XI (FXI), XII (FXII). We used an automatic coagulometer Sysmex CA 660 (Sysmex Europe, Germany) and reagents from Siemens (Siemens Healthcare Diagnostics Products GmbH, Germany).

Research results

The study included 146 patients. The activity of factors FV [147.7 (102.1-247.55)% *vs* 103.85 (60-161.6)% *vs* 81.8 (67.15-130.65)%, $P = 0.002$], FVIII [80.4 (60.15-106.25)% *vs* 70.3 (48.5-89.1)% *vs* 63.7 (41.6-88.25)%, $P = 0.039$], FIX [86.2 (70.75-102.95)% *vs* 75.4 (59.2-88.3)% *vs* 73.9 (56.45-93.05)%, $P = 0.014$], FX [188.9 (99.3-308.18)% *vs* 158.9 (83.3-230)% *vs* 127.2 (95.25-209.35)%, $P = 0.022$], FXI [82.6 (63.9-103.6)% *vs* 69.75 (53.8-97.6)% *vs* 67.3 (54.25-98.05)%, $P = 0.002$], FXII [87.6 (67.15-102.3)% *vs* 78.9 (63.4-97.05)% *vs* 81.2 (62.15-97.4)%, $P < 0.001$] decreased at 7 and 30 d after surgery; FII activity [157.9 (109.7-245.25)% *vs* 130 (86.8-192.5)% *vs* 144.8 (103.31-185.6)%, $P = 0.021$] decreased at 7 d and increased at 30 d postoperatively. There were no statistically significant changes in the FVII activity within 30 d after PM placement [182.2 (85.1-344.8)% *vs* 157.2 (99.1-259)% *vs* 108.9 (74.9-219.8)%, $P = 0.128$]. Subgroup analysis revealed similar changes only in patients on anticoagulant therapy. FXII activity decreased in patients on antiplatelet therapy [82 (65.8-101.9)% *vs* 79.9 (63.3-97.1)% *vs* 89.7 (75.7-102.5)%, $P = 0.01$] 7 d after surgery, returning to baseline values at 30 d postoperatively.

Research conclusions

PM placement and anticoagulant therapy were associated with decreased activity of clotting factors FV, FVIII, FIX, FX, FXI, FXII in the postoperative period. FVII activity did not decrease within 30 d after PM placement, which may indicate endothelial injury caused by lead placement.

Research perspectives

We think that further investigation of hemostasis system will contribute to the creation of newer approaches to the detection, prognosis, management, and prevention of numerous hemorrhagic and thromboembolic complications in patients requiring PM implantation.

ACKNOWLEDGEMENTS

The authors would like to thank the members of the Scientific and Clinical Center of Hematology, Oncology and Immunology, Ryazan State Medical University for their technical support.

FOOTNOTES

Author contributions: Kalinin R and Suchkov I were the guarantors and designed the study; Povarov V, Mzhavanadze N and Zhurina O participated in the acquisition, analysis, and interpretation of the data, and drafted the initial manuscript.

Institutional review board statement: This study was approved by the Local Ethics Committee of the Ryazan State Medical University.

Informed consent statement: All patients signed an informed consent.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Data sharing statement: No additional data are available.

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S-Editor: Liu XF

L-Editor: A

P-Editor: Yu HG

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