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ORIGINAL ARTICLE

Effect of selected prothrombotic and proinflammatory factors on the incidence of venous thrombosis after pacemaker implantation

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Abstract

Background: Venous thrombosis (VT), a major cause of venous obstruction, is a rather rare but dangerous complication of pacemaker (PM) implantation.

Aim: To assess the prognostic value of selected proinflammatory and prothrombotic markers in predicting symptomatic venous obstruction after PM implantation.

Methods: The study involved 81 patients (31 females; mean age 71 ± 8 years) divided into 2 groups depending on the occurrence of venous obstruction. Group I included 71 patients (29 females; mean age 71 ± 2 years) without this complication and group II included 10 patients (2 females, mean age 71.6 ± 2) with venous obstruction. All patients were followed up for 19 months. Transthoracic echocardiography and venous ultrasonography were performed before PM implantation and at the time of incident venous obstruction. Interleukin-6 (IL-6), high-sensitivity C-reactive protein (hsCRP), D-dimer, fibrinogen, tissue factor (TF), factor VII and plasminogen activator inhibitor-1 (PAI-1) levels were measured at baseline and within 7 days after PM implantation.

Results: Patients in group II had a significantly lower left ventricular ejection fraction (LVEF), higher left ventricular end--diastolic diameter (LVEDD) and impaired left ventricular filling (Vp) compared to group I. Patients in group II developed VT on average at 13.06 (range 7–18) months following PM implantation. At baseline, IL-6, hsCRP, D-dimer, fibrinogen, TF, factor VII, and PAI-1 levels were significantly higher in group II compared to group I. In all patients, levels of prothrombotic factors were higher following PM implantation compared to baseline values, with the exception of fibrinogen level in group I. Cut-off values indicating increased thrombosis risk were determined for the examined parameters (LVEF, LVEDD, Vp, IL-6, hsCRP, D-dimer, fibrinogen, factor VII, TF, PAI-1) based on the ROC curves. Major predictors of thrombotic risk included LVEF, LVEDD, and D-dimer, fibrinogen and TF levels. Highest predictive values were noted for LVEDD > 58 mm (OR = 52.8) and D-dimer level > 498 mg/L (OR = 3003).

Conclusions: 1. Patients who developed VT after PM implantation had elevated baseline levels of IL-6, hsCRP, fibrinogen, D-dimer, TF, factor VII, and PAI-1. 2. Levels of pro-inflammatory markers increased after the implantation procedure in all patients. 3. Parameters with the highest diagnostic value for predicting incident VT included decreased LVEF, increased LVEDD and elevated D-dimer, fibrinogen and TF levels.

Key words: permanent cardiac pacing, venous thrombosis, prothrombotic and proinflammatory markers, ejection fraction

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INTRODUCTION

Despite major advances in the technique of pacemaker (PM) implantation, these procedures are still associated with many complications, occurring both early and late during follow-up. One major complication is venous thromboembolism, including pulmonary embolism [1], venous obstruction [2], intracardiac thrombi [3], superior vena cava syndrome [4, 5], cor pulmonale, recurrent thrombosis, and post-thrombotic syndrome [6]. Symptomatic thrombosis develops in about 0.5–5%, and life-threatening conditions occur in 0.6–3.5% of all patients undergoing PM implantation [6].

Interpretation of studies evaluating venous thrombosis (VT) is difficult due to various modalities used to detect thrombosis and varying duration of follow-up. Rozmus et al. [7] performed a meta-analysis of studies on incident VT, including a total of 711 patients with cardiac PM. An abnormal result of venography was found in 38% of patients, and venous obstruction in 11% of patients, while symptomatic VT was detected in only 2.6% of patients. In contrast, digital subtraction angiography showed venous obstruction of a lesser or greater degree in 32.9% of patients after PM implantation [8], often preceded by local infection [4, 9] or leaving a non-functional lead *in situ* [10].

Probable predictors of thrombosis include earlier insertion of a temporary pacing lead, previous myocardial infarction, heart failure, previous systemic infection, venous anomalies, hormonal replacement therapy, lack of anticoagulant therapy, and cigarette smoking. Another predisposing factor may be the presence of multiple leads, although some authors believe that this does not affect the obstruction rate [7, 9, 10].

Search continues for significant factors predisposing to VT in patients undergoing PM implantation. The purpose of the present study was to evaluate prognostic significance of selected proinflammatory and prothrombotic markers and parameters of left ventricular systolic and diastolic function evaluated before PM implantation, with the aim of selecting patients at risk of symptomatic venous obstruction, mostly due to thrombosis. In addition, we evaluated the effect of the implantation procedure itself on patient haemostatic status in the early postoperative period.

METHODS

Patients

We studied 81 patients (31 women, 50 men, mean age 71.1 ± ± 7.6 years) selected for PM implantation. Depending on the occurrence of VT in the postoperative period, patients were retrospectively divided into two groups: group I (n = 71; 29 women, 42 men, mean age 71.0 ± 7.7 years) included patients without thrombosis, and group II (n = 10; 2 women, 8 men, mean age 71.6 ± 7.0 years) included patients with thrombosis developing on average 13 (range 7–18) months after PM implantation.

Exclusion criteria

Patients were not entered into the study if: (1) they did not give consent for study participation; (2) had venous stenosis within the upper limbs, shoulder girdle region, or the neck found before PM implantation; (3) required PM replacement or pacing mode change; (4) underwent previous valvular prosthesis implantation or coronary intervention; or (5) had incomplete data and/or inconclusive or lacking imaging findings. All patients gave written informed consent for participating in the study. The study was approved by the ethics committee at the Jagiellonian University (approval No. KBET/63/B/2009).

Previous myocardial infarction was noted in 27 patients, arterial hypertension in 49 patients, heart failure in 31 patients, hypercholesterolaemia in 30 patients, paroxysmal or permanent atrial fibrillation (AF) in 32 patients, and complete heart block requiring temporary pacing in 13 patients (all in group II). In group I, permanent AF was diagnosed in 21 patients (with ventricular pacing) and paroxysmal AF in 9 patients, while in group II, paroxysmal AF was found in only 1 patient. Chronic anticoagulant therapy was used in 30 patients in group I compared to none of the patients in group II. Anticoagulant therapy was interrupted before PM implantation and reintroduced within 7 days after the procedure, preceded by biochemical testing performed for the purpose of the present study, and subsequently continued throughout the 19-month follow-up.

Echocardiography

Transthoracic echocardiography (TTE) was performed using the Aloka ProSound Alfa 10 ultrasound system. Left ventricular ejection fraction (LVEF) was determined using the Simpson method. Left ventricular diastolic function was assessed based on the propagation velocity of early mitral inflow (Vp), measured in M-mode in the apical four-chamber view. In addition, left ventricular end-diastolic diameter (LVEDD) was measured.

Venous ultrasonography

Upper limb, neck girdle region, and jugular venous ultrasonography was performed using the Vivid 7 Expert system and a 5–13 MHz linear probe. Vessel morphology and venous flow was evaluated in real-time by duplex Doppler scanning. The TTE and venous ultrasonography were performed before PM implantation, with repeated venous ultrasonography in cases of symptomatic venous obstruction.

Laboratory testing

Blood for laboratory testing was collected from the median cubital vein at 7 AM after obtaining written informed patient consent. Citrated plasma and serum was stored at –70°C until assayed. Citrated plasma was used to determine D-dimer level using the immunoturbidimetric method (D-dimer test and

ACL analyser; Instrumentation Laboratory/Comesa), fibrinogen level using the coagulation method (Sysmex CA-500), plasminogen activator inhibitor-1 (PAI-1) using the immunoenzymatic method (Biopool, Ventura, CA, USA), tissue factor (TF) using the immunoenzymatic method (Imubind Tissue Factor ELISA KIT; American Diagnostica Inc. USA), and factor VII activity as assessed by prothrombin time measured using IL Coagulation and ELECTRA analysers (Hemosil kit, I.L., MA, USA). Serum samples were used to determine high-sensitivity C-reactive protein (hsCRP) level using the nephelometric method (DADE Boehring) and interleukin (IL)-6 using the immunoenzymatic method (Quantikine High Sensitivity IL-6 ELISA KIT; R&D Systems, Inc. MN, USA). Biochemical testing was performed before PM implantation and within 7 days after the implantation procedure, without confounding by anticoagulant therapy.

Statistical analysis

Descriptive statistics for the analysed haemodynamic and biochemical parameters included the arithmetic mean, standard deviation, median, minimum, maximum, and the number of observations. Significance of the differences between groups was evaluated using the Student t-test or the Mann-Whitney test. Student t-test for paired samples or the Wilcoxon test was used to evaluate significance of serial measurement changes. Diagnostic performance of various haemodynamic and biochemical parameters in predicting the risk of VT was assessed using receiver operating characteristic (ROC) curves. Significance of the differences between the areas under ROC curves was evaluated using the Z test. In addition, cut-off values were determined for the evaluated variables using the Youden index.

Odds ratios (OR) and 95% confidence intervals (CI) were determined after dichotomous recalculation of each parameter using the established cut-off values and the study group assignment. An alpha level of 0.05 was used to determine statistical significance. Calculations were performed using the STATISTICA 9.0 (StatSoft Polska 2010) and MedCalc software.

RESULTS

Distribution of pacing modes did not differ between the groups (Table 1). In group II, significantly lower LVEF, higher LVEDD and left atrial (LA) dimension, and abnormal mitral inflow were found before PM implantation as compared to group II (Table 2).

Table 1. Cardiac pacing modes

Pacing mode	Group I	Group II
DDDR	35 (49.3%)	5 (50%)
DDD	7 (9.9%)	
AAIR	5 (7.0%)	
AAI	1 (1.4%)	
VDD	2 (2.8%)	
VVIR	19 (26.8%)	5 (50%)
VVI	2 (2.8%)	
With AVS	50 (70.4%)	5 (50%)
Without AVS	21 (29.6%)	5 (50%)

P = NS for all comparisons; AVS — atrio-ventricular synchronisation

Symptomatic VT developed in all 10 patients in group II (12.3% of the overall study population) on average at 13.06 (range 7–18) months after the PM implantation, with venous obstruction involving the ipsilateral subclavian and axillary veins.

In group II, significantly higher levels of proinflammatory (IL-6, hsCRP) and prothrombotic (D-dimer, fibrinogen, TF, factor VII, PAI-1) markers were found before PM implantation as compared to group I (Table 3). In all patients, proinflammatory and prothrombotic marker levels were higher within 7 days after the implantation procedure compared to baseline values, with the exception of fibrinogen level in group I (Table 4). Based on ROC curves, cut-off values of the evaluated haemodynamic (LVEF, LVEDD, LA dimension, Vp) and biochemical (hsCRP, D-dimer, fibrinogen, TF, and PAI-1) parameters were determined that indicated a significantly increased risk of VT (Table 5, Figs. 1, 2).

Based on the differences between the areas under ROC curves for the evaluated haemodynamic and biochemical parameters, variables with the highest prognostic value for incident VT were selected. These included LVEF and LVEDD among the haemodynamic parameters, and D-dimer, fibrinogen, and TF levels among the biochemical parameters

Table 2. Comparison of baseline haemodynamic parameters between patients without (group I) and with venous thrombosis (group II)

Haemodynamic parameters	Group I (n = 71)			Group II (n = 10)			P
	$\bar{x} \pm s$	Me	Min–max	$\bar{x} \pm s$	Me	Min–max	
LVEF [%]	53.7 ± 15.3	55.0	20.0–78.0	33.3 ± 5.2	33.50	25.0–45.0	0.000
LVEDD [mm]	52.7 ± 9.9	48.0	42.0–72.0	66.4 ± 4.0	68.00	59.0–72.0	0.000
LA dimension [mm]	45.1 ± 10.5	40.0	32.0–67.0	54.3 ± 4.7	55.50	46.0–60.0	0.008
Vp [m/s]	43.1 ± 4.3	45.0	34.0–48.0	39.7 ± 4.4	39.00	33.0–47.0	0.023

LVEF — left ventricular ejection fraction; LVEDD — left ventricular end-diastolic dimension; LA — left atrial; Vp — propagation velocity of early mitral inflow

Table 3. Comparison of biochemical parameters at baseline and at 7 days after pacemaker implantation between patients without (Group I) and with venous thrombosis (Group II)

Biochemical parameters	Group I (n = 71)			Group II (n = 10)			P
	$\bar{x} \pm s$	Me	Min–max	$\bar{x} \pm s$	Me	Min–max	
Baseline values							
D-dimer [μg/L]	299.5 ± 99.0	290.0	121–498	570.2 ± 55.9	550.00	500–665	< 0.001
Fibrinogen [g/L]	3.6 ± 0.8	3.5	1.8–5.6	6.1 ± 1.0	5.65	4.9–7.7	< 0.001
TF [ng/mL]	213.7 ± 54.7	190.0	160–440	390.8 ± 43.1	389.00	320–460	< 0.001
Factor VII [%]	90.7 ± 16.6	90.0	60.0–129.0	116.2 ± 8.4	120.00	100–126	< 0.001
PAI-1 [ng/mL]	11.7 ± 4.7	11.0	5.0–23.0	21.1 ± 1.9	22.00	18.0–23.0	< 0.001
IL-6 [pg/mL]	2.8 ± 1.7	2.2	0.7–8.3	4.7 ± 2.0	4.40	2.1–8.6	0.001
hsCRP [mg/L]	2.1 ± 1.2	2.0	0.5–5.0	4.9 ± 0.7	5.00	4.0–6.0	< 0.001
Repeated testing at 7 days							
D-dimer(7) [μg/L]	312.2 ± 106.3	324.0	126–525	592.4 ± 65.8	575.00	510–700	< 0.001
Fibrinogen(7) [g/L]	3.6 ± 0.8	3.5	1.8–5.6	6.6 ± 0.8	6.74	5.6–7.9	<0.001
TF(7) [ng/mL]	226.1 ± 70.9	200.0	160–459	425.8 ± 37.5	430.00	360–470	< 0.001
Factor VII(7) [%]	91.4 ± 17.0	90.0	60.0–130.0	132.8 ± 8.7	132.00	120–145	< 0.001
PAI-1(7) [ng/mL]	13.1 ± 5.3	12.0	6.0–26.0	25.3 ± 1.9	25.50	22.0–28.0	< 0.001
IL-6(7) [pg/mL]	3.6 ± 1.9	3.3	0.8–8.8	5.5 ± 2.0	5.11	2.3–9.3	0.004
hsCRP(7) [mg/L]	3.2 ± 1.8	3.0	1.0–8.0	9.9 ± 2.1	9.50	8.0–14.0	< 0.001

TF — tissue factor; PAI-1 — plasminogen activator inhibitor-1; IL-6 —interleukin-6; hsCRP — high-sensitivity C-reactive protein

Table 4. Comparison of biochemical parameters at baseline and at 7 days after pacemaker implantation in Groups I and II

	Group I: 0 *vs* 7 days (p)	Group II: 0 *vs* 7 days (p)
hsCRP	< 0.0001	< 0.0001
IL-6	< 0.0001	< 0.0001
D-dimer	< 0.0001	< 0.005
Fibrinogen	NS	< 0.05
TF	< 0.01	< 0.001
Factor VII	< 0.025	< 0.0001
PAI-1	< 0.0001	< 0.0001

Abbreviations as in Table 3

(Tables 6, 7). For all parameters with a determined cut-off value, OR and 95% CI were then calculated for the risk of incident thrombosis (Table 7). For example, in a patient with D-dimer level of > 498 μg/L, there is a 95% probability that the risk of incident VT is increased at least 56-fold compared to a patient with D-dimer level of < 498 μg/L (Table 8).

DISCUSSION

In our study, we evaluated factors predisposing to venous obstruction which is mostly causes by VT. Venous stasis resulting from vein ligation, increased blood viscosity, and endothelial damage (Virchow's triad) due to the presence of intracardiac lead may result in local inflammatory response in

Table 5. Areas under ROC curves and optimal cutoff values for haemodynamic and biochemical parameters

Variable	AUC	95% CI for AUC	P	Cut-off	Sensitivity	Specificity
LVEF	0.865	0.772–0.931	< 0.0001	≤ 35	90.0	83.1
LVEDD	0.853	0.757–0.922	< 0.0001	> 58	100.0	71.8
LA dimension	0.749	0.640–0.838	< 0.0001	> 45	100.0	57.8
Vp	0.708	0.597–0.804	0.0122	≤ 40	70.0	69.0
D-dimer	1.000	0.955–1.000	< 0.0001	> 498	100.0	100.0
Fibrinogen	0.987	0.933–1.000	< 0.0001	> 4.7	100.0	88.7
TF	0.976	0.915–0.997	< 0.0001	> 300	100.0	94.4
Factor VII	0.901	0.815–0.957	< 0.0001	> 99	100.0	67.6
PAI-1	0.942	0.866–0.982	< 0.0001	> 17	100.0	85.9
IL-6	0.778	0.672–0.863	0.0001	> 2.45	90.0	60.6
hsCRP	0.967	0.901–0.994	< 0.0001	> 3	100.0	81.7

Abbreviations as in Table 2 and 3

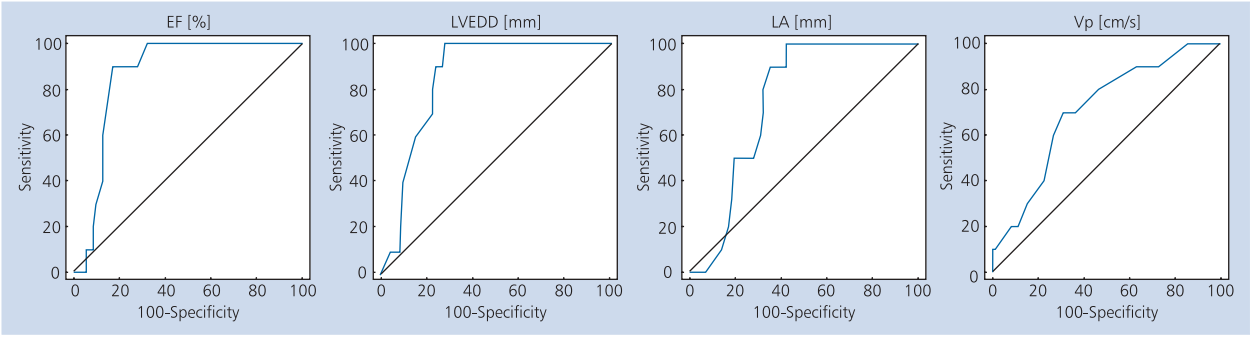

Figure 1. Receiver operating characteristic (ROC) curves for haemodynamic parameters; abbreviations as in Table 2

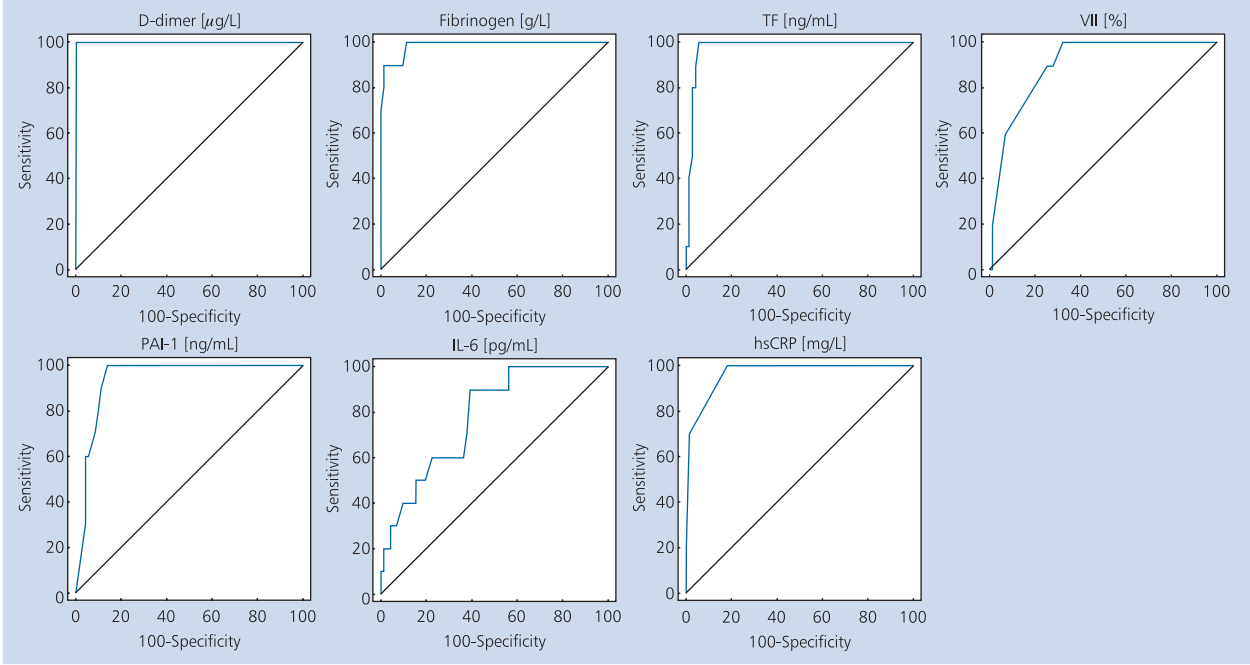

Figure 2. Receiver operating characteristic (ROC) curves for biochemical parameters; abbreviations as in Table 3

Table 6. Differences between areas under ROC curves for haemodynamic parameters

Variable	P		
	LVEF [%]	LA dimension [mm]	Vp [cm/s]
LVEDD [mm]	0.650	0.064	0.097
LVEF [%]	–	0.024	0.060
LA dimension [mm]	–	–	0.641

Abbreviations as in Table 2

the vessel wall and activation of the coagulation cascade. This is associated with the release of proinflammatory factors including IL-6 and CRP, as well as proteins of the coagulation and fibrinolytic systems such as fibrinogen and PAI-1, and is of particular importance in patients with left ventricular failure who show increased levels of these markers already before PM implantation, as was also the case in our patients.

In response to cytokines and inflammatory mediators (IL-6, hsCRP), endothelial cells express and show an increased activity of TF or tissue thromboplastin. The latter is the cellular receptor of circulating factor VII, and their interaction initiates the coagulation cascade. At the site of vascular damage, a mural thrombus develops which obstructs or occludes the vessel lumen. In less than 20% of cases, endogenous fibrinolysis results in complete thrombus resolution [11–16]. Much more commonly (in about 50–70% of patients) the thrombus undergoes uncontrolled growth, does not resolve completely and results in venous obstruction of various degree [10, 17]. The PAI-1 is another factor that plays an active role in this process.

These mechanisms constituted the rationale for the study of these phenomena in our patients. In a previous pilot

Table 7. Differences between areas under ROC curves for biochemical parameters

Variable	P					
	Fibrinogen [g/L]	IL-6 [pg/mL]	TF [ng/mL]	Factor VII [%]	hsCRP [mg/L]	PAI-1 [ng/mL]
D-dimer [μg/L]	0.269	0.001	0.126	0.010	0.058	0.020
Fibrinogen [g/L]	–	0.001	0.537	0.019	0.217	0.105
IL-6 [pg/mL]	–	–	0.003	0.067	0.003	0.025
TF [ng/mL]	–	–	–	0.025	0.683	0.153
Factor VII [%]	–	–	–	–	0.080	0.312
hsCRP [mg/L]	–	–	–	–	–	0.312

Abbreviations as in Table 3

Table 8. Odds ratios (OR) for incident venous thrombosis with 95% confidence intervals (CI) calculated for the evaluated haemodynamic and biochemical parameters

Parameter and cut-off value	OR	95% CI	P
LVEDD > 58 mm	52.8	2.95–942	0.007
LVEF > 35%	0.023	0.003–0.195	0.0006
LA dimension > 45 mm	28.6	1.61–506	0.022
Vp > 40 cm/s	0.19	0.045–0.815	0.025
D-dimer > 498 μg/L	3003	56–15916	0.0001
Fibrinogen > 4.7 g/L	156	8.4–2926	0.0007
IL-6 > 2.45 pg/mL	13.8	1.66–115	0.015
TF > 300 ng/mL	315	15–6284	0.0002
Factor VII > 99%	43.3	2.4–771	0.010
hsCRP > 3 mg/L	91.0	5.0–1650	0.002
PAI-1 > 17 ng/mL	123	6.7–2261	0.001

Abbreviations as in Tables 2 and 3

study undertaken in a separate, much smaller group of patients with implanted PM, some on anticoagulant therapy and with established risk factors for VT, we found that patients with these risk factors were characterised by increased blood levels of selected markers of endothelial damage, reduced LVEF, and increased LVEDD along with the propensity to develop VT. In addition, we found negative correlations between these parameters [18].

Similarly, numerous epidemiological and clinical studies showed that biochemical markers of endothelial damage and platelet activation are associated with the risk of VT [13–16]. Pathological clotting activation and reduced fibrinolytic activity lead to thrombotic venous obstruction and may result in pulmonary embolism. Clinical research data available in the literature support increased levels of clotting factors and enhanced thrombin generation in patients with heart failure [16]. It was shown that in some patients, early thrombotic manifestations may progress due to a local hypercoagulability state present in the early phase following lead implantation. In these circumstances, a diagnostic value of venous ultrasonography was also established [19].

In our study, we used ROC curves to determine cut-off values of the examined haemodynamic parameters and proinflammatory and prothrombotic markers (IL-6, hsCRP, D-dimer, fibrinogen, TF, PAI-1) that indicate an increased risk of incident VT. The best diagnostic performance in this regard was found for decreased LVEF, increased LVEDD and elevated D-dimer, fibrinogen and TF levels.

Evaluation of genetic polymorphisms affecting proteins of the clotting system (Leiden G1691A and prothrombin G20210A mutations) is an important addition to conventional clinical research on thrombosis [17]. Research in this area continues, as are studies to evaluate venous blood flow using Doppler ultrasonography combined with simultaneous biochemical testing repeated at various time points during a longer follow-up of a larger control group of asymptomatic subjects (upon exclusion of patients on chronic anticoagulant therapy).

Management of thromboembolic complications in patients with implanted PM includes intravenous or subcutaneous heparin administration [20]. In all our patients in group II who were previously not receiving anticoagulant therapy, institution of such treatment resulted in restoration of blood

flow through the occluded veins. Some authors believe, however, that prophylactic chronic anticoagulation therapy is of limited effectiveness [21].

In summary, in patients with low LVEF and increased LVEDD who are scheduled for PM implantation, determination of D-dimer, fibrinogen, and TF levels would help identify patients at risk of VT. In addition, positive results of these screening tests might justify prophylactic postprocedural chronic anticoagulation therapy, warranting further research on this issue.

Limitations of the study

Due to a low number of patients and a relatively short duration of follow-up, we were unable to perform multivariate analysis to evaluate interactions between the examined markers of thrombotic risk.

CONCLUSIONS

1. Patients who developed VT after PM implantation had elevated baseline levels of proinflammatory and prothrombotic markers including IL-6, hsCRP, fibrinogen, D-dimer, TF, factor VII, and PAI-1.
2. Pacemaker implantation was associated with a increased prothrombotic and proinflammatory state within 7 days after the procedure.
3. Parameters with the highest predictive value for incident VT included decreased LVEF, increased LVEDD and elevated D-dimer, fibrinogen and TF levels.

Conflict of interest: *none declared*

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Wpływ wybranych markerów prozakrzepowych i prozapalnych na wystąpienie zakrzepicy żylnej po wszczepieniu rozrusznika serca

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Streszczenie

Wstęp: Zakrzepica żylna (VT) stanowi największą grupę niedrożności żylnych. Jest dość rzadkim, ale niebezpiecznym powikłaniem implantacji układu stymulującego serce (PM). Czynnikami predysponującymi są: uszkodzenie i zapalenie śródbłonka naczyń żylnych oraz niewydolność serca.

Cel: Celem pracy była ocena znaczenia prognostycznego wybranych markerów prozakrzepowych i prozapalnych przed wszczepieniem PM, aby zidentyfikować chorych zagrożonych objawową niedrożnością żylną. Ponadto starano się określić wpływ samego zabiegu implantacji PM na stan hemostatyczny organizmu we wczesnym okresie pooperacyjnym.

Metody: Badaniem objęto 81 pacjentów (31 kobiet, 50 mężczyzn, średni wiek 71,1 ± 7,6 roku) z implantowanym PM. Uwzględniając rozwinięcie się VT po zabiegu, po zakończeniu obserwacji, podzielono badanych na 2 grupy: grupę I (n = 71; 29 kobiet, 42 mężczyzn, średni wiek 71,0 ± 7,7 roku) stanowili chorzy, u których nie stwierdzono VT, oraz grupę II (n = 10; 2 kobiety, 8 mężczyzn, średni wiek 71,6 ± 7,0 roku), obejmującą chorych, u których doszło do VT średnio 13,7–18 miesięcy po zabiegu implantacji PM. Okres obserwacji badanych wynosił 19 miesięcy. Wykonywano przezklatkowe badanie echokardiograficzne, badanie ultrasonograficzne naczyń żylnych kończyn górnych oraz obręczy barkowej i szyi przed zabiegiem wszczepienia PM oraz w momencie wystąpienia powikłania. Oznaczano stężenia interleukiny 6 (IL-6), wysokoczułego białka C-reaktywnego (hsCRP) w surowicy, natomiast stężenia fibrynogenu, D-dimerów, czynnika tkankowego (TF), inhibitora aktywatora plazminogenu 1 (PAI-1) i aktywność czynnika VII w osoczu cytrynianowym. Oznaczenia wykonywano w próbkach pobranych przed zabiegiem i do 7 dni po zabiegu.

Wyniki: U chorych z grupy II stwierdzono znamiennie mniejsze wartości frakcji wyrzutowej (EF), większe rozkurczowe wymiary lewej komory (LVEDD) i upośledzenie napełniania lewej komory (Vp) w porównaniu z pacjentami z grupy I (odpowiednio: 33,3 v. 53,7%; 66,4 v. 52,7 mm; 39,7 v. 43,2 cm/s). Wyjściowo u chorych z grupy II stwierdzono znamiennie większe średnie stężenia markerów prozapalnych (IL-6, hsCRP; odpowiednio: 4,7 *v.* 2,8 pg/ml, 4,9 *v.* 2,1 mg/l) i prozakrzepowych (fibrynogenu, D-dimerów, TF, czynnika VII, PAI-1; odpowiednio: 6,1 *v.* 3,6 g/l, 570,2 *v.* 299,5 μg/l, 390,8 *v.* 213,7 ng/ml, 116,2 *v.* 90,7%, 21,1 *v.* 11,7 ng/ml) w porównaniu z wartościami stwierdzanymi u chorych z grupy I. U wszystkich badanych wykazano większe wartości markerów osoczowych w próbkach krwi pobranych w okresie do 7. doby po zabiegu w porównaniu z wartościami wyjściowymi, z wyjątkiem stężenia fibrynogenu w grupie I. Wyznaczono wartości graniczne badanych parametrów hemodynamicznych (EF, LVEDD, LA, Vp; odpowiednio: 35%, 58 mm, 45 mm, 40 cm/s) i biochemicznych (IL-6, hsCRP, D-dimery, fibrynogen, TF i PAI-1; odpowiednio: 2,45 pg/ml, 3 mg/l, 498 μg/l, 4,7 g/l, 300 ng/ml, 17 ng/ml) wg sporządzonych krzywych ROC, powyżej (poniżej dla EF i Vp) których zwiększało się istotnie ryzyko wystąpienia VT. Na podstawie oceny różnic między polami powierzchni (AUC) pod krzywymi ROC danych hemodynamicznych i biochemicznych określono parametry o największej wartości prognostycznej wystąpienia VT. W tym zakresie największą moc diagnostyczną w przewidywaniu ryzyka powstania zakrzepu miały EF i LVEDD oraz D-dimery, fibrynogen i TF. Następnie dla każdego parametru z daną wartością punktu odcięcia obliczano ilorazy szans (OR) wystąpienia powikłania i 95% przedział ufności. Największe prawdopodobieństwo ryzyka wystąpienia VT zanotowano dla LVEDD > 58 mm (OR = 52,8) oraz dla D-dimerów > 498 μg/l (OR = 3003).

Wnioski: 1. U chorych, u których stwierdzono VT po wszczepieniu PM, obserwuje się przed zabiegiem podwyższone stężenia laboratoryjnych markerów prozapalnych i prozakrzepowych: IL-6, hsCRP, fibrynogenu, D-dimerów, TF, czynnika VII, PAI-1. 2. U wszystkich chorych poddanych zabiegowi wszczepienia PM pogorszył się stan prozakrzepowy i prozapalny do 7. doby po zabiegu. 3. Największą moc diagnostyczną w przewidywaniu wystąpienia VT po wszczepieniu PM miały obniżona EF, zwiększony LVEDD oraz podwyższone stężenia D-dimerów, TF i fibrynogenu.

Słowa kluczowe: układ stymulujący serce, zakrzepica żylna, czynniki prozakrzepowe i prozapalne, frakcja wyrzutowa

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