ORIGINAL PAPERS

Adv Clin Exp Med 2016, **25**, 1, 83–91
DOI: 10.17219/acem/42317

ISSN 1899–5276

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Venous Stenosis and Occlusion in the Presence of Endocardial Leads

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A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of article

Abstract

Background. Venous stenosis and occlusion in the presence of endocardial leads constitute one of the complications of permanent cardiac pacing either by pacemaker, implantable cardioverter-defibrillator or cardiac resynchronization therapy.
Objectives. The aim of this study was to assess the incidence of stenosis and occlusions and determine the risk factors in patients with endocardial leads in a prospective single-center study.
Material and Methods. Two hundred eighty consecutive patients aged 25–95 years (male 68.8%) were included. A contrast venography examination of the ipsilateral access vein was performed. The whole study population was divided into 2 groups, based on the presence (group I) or absence (group II) of endocardial leads.
Results. Venous stenosis/occlusion was identified in 51 patients (37.5%) in group I and in 3 patients (3.6%) in group II; $p < 0.0001$. The lead presence most highly correlated with venous complications (OR = 4.172; $p < 0.001$). In patients with endocardial leads divided into I A and I B according to venous patency diabetes mellitus was proved in multivariate analysis to be the only protective factor against the development of venous stenosis/occlusion (OR = 0.473; $p = 0.010$).
Conclusions. The presence of endocardial leads is a predisposing factor for venous stenosis/occlusion and increases the risk 4-fold. The venous lesions in the presence of endocardial leads are less frequent among patients with diabetes mellitus (**Adv Clin Exp Med 2016, 25, 1, 83–91**).

Key words: complications, pacemaker, venous stenosis, venous occlusion, venography.

Stenosis and occlusion of venous vessels with indwelling transvenous leads constitute one of the complications of permanent cardiac pacing either by pacemaker (PM), implantable cardioverter-defibrillator (ICD) or cardiac resynchronization therapy (CRT). The unobstructed contact of transvenous leads with the vein endothelium plays a major role in the pathophysiology of this phenomenon, which subsequently results in permanent inflammation. A chronic inflammatory process leads to venous endothelial injury, lead endothelialisation, narrowing of the vessel and, in severe cases, complete vein occlusion [1–3]. The diagnosis of the incidence of venous stenosis and occlusion is usually challenging, because the majority of patients remain asymptomatic [3–14].

With a growing number of pacing device and defibrillator implantations [12, 15], venous stenosis and, in particular, occlusion, are becoming a significant clinical problem. Venous obstruction of ipsilateral access vein impedes, or even prevents placement of a lead in a patient's body, requiring the use of sophisticated equipment [3, 16]. The trans-venous lead extraction procedures (TLE) among patients with vein occlusions are more challenging – apart from standard tools the supplementary advanced extraction tools are often needed [9, 16].

Early occurrence of access vein stenosis/occlusion was examined in several prospective studies which differed in methodology and definition of this medical condition [4, 7, 13, 17]. Antonelli et al., Korkeila et al. and Da Costa et al. performed contrast venography and found a narrowing of veins with trans-venous leads in 23% of 40, 31% of 150 and 64% of 202 patients, respectively, in the examined cohort [4, 7, 17]. Van Roden et al. confirmed the diagnosis of venous obstruction during the first post-implantation year with Doppler ultrasound in 23% of a population consisting of 145 patients with PM or ICD [13]. In previously mentioned studies, 2% to 6% of patients exhibited clinical symptoms of venous obstruction [4, 7, 13].

According to retrospective studies, in which a total number of 727 patients prior to follow-up PM or ICD procedure were evaluated mainly by contrast venography, the incidence of venous stenosis was established between 23% and 33% [3, 5, 8–10, 16]. Furthermore, Zuber et al., utilizing Doppler ultrasound, demonstrated stenosis/occlusion of veins in 57% of patients after a mean of 41 months post PM/ICD implantation [14].

The discrepancies in reported incidence of venous obstruction may be explained by different baseline characteristics of study populations, diagnostic methods (contrast venography vs. Doppler ultrasound) and various lead dwell time in cardiovascular system.

The association between lead dwell time and the incidence of venous stenosis/occlusion assessed by Doppler US was prospectively studied by Roden et al. who demonstrated a lower incidence of venous complications in the first post-implantation year compared with Zuber et al., who retrospectively determined the incidence after a mean follow-up of 41 months after PM/ICD implantation [9, 13].

Regarding the definition of venous stenosis and occlusion, it depended on the type of a diagnostic method. When Doppler ultrasound was used [13, 14], the diagnosis was based on visualizations of thrombotic masses, an abnormal compression ultrasonography result and monophasic venous flow. Additionally, Doppler ultrasound did not provide information on the presence of collateral circulation, which in turn facilitates contrast venography [13]. In venography-based studies the classification of venous stenosis degree differed substantially among authors [3–5, 7–11, 16]. Antonelli et al. stratified stenosis as partial and complete and did not perform the assessment of incomplete occlusion grade and collateral circulation [4]. Da Costa et al. evaluated the grade of venous stenosis according to the percentage of intraluminal contrast filling defect, classifying it as mild (up to 20%), moderate (21–69%), severe (70–99%) and occlusion (100%). Collateral circulation degree was classified according to the number and flow of the new vessels in mild (one vessel and lower flow), moderate (two vessels and moderate flow), and important (three or more vessels and an adequate flow) [7].

The risk factors for venous stenosis/occlusion development were presented in several studies and include multiple leads, dual-coil ICD leads, infection, left ventricle ejection fraction under 40%, history of previous venous thrombosis and female hormone use [3, 5, 7, 9, 13, 16]. Use of antiplatelet/anticoagulant drugs had preventive effect on venous lesions [3, 9, 13, 16]. The predisposing factors leading to venous abnormalities are not fully understood.

To address the issue of risk factors and determine the incidence of stenosis and occlusions in patients with endocardial leads, we designed a prospective single-center study.

Material and Methods

Two hundred eighteen consecutive patients were admitted to hospital for their cardiac implantable electronic device (CIED) implantation, device upgrade, generator replacement or transvenous lead extraction. Patients who had undergone TLE procedure in the past and patients who were referred with infectious indications for TLE were excluded from the analysis. Prior to the operation, a contrast venography examination of the ipsilateral access vein was performed. The study was approved by the Ethics Committee. The study inclusion criteria included the absence of contraindications to venography and written consent obtained from the patient.

Performance and Assessment of Venography

In the operating room, 10 to 20 mL of high quality contrast medium Iomeron 350 (350 g iodine/mL) was injected through the peripheral arm vein on the side which was to be studied. Contrast medium flow in the cephalic, axillary, subclavian and brachiocephalic veins, as well as the superior *vena cava*, was observed and recorded by cineangiography.

The narrowing of the vessel was identified and graded in the percentage of obstructed vein lumen in the presence of venous contrast filling defect, filmed in frontal (PA) projection. A positive result of venography (significant abnormality in venous patency) was defined as a total venous occlusion

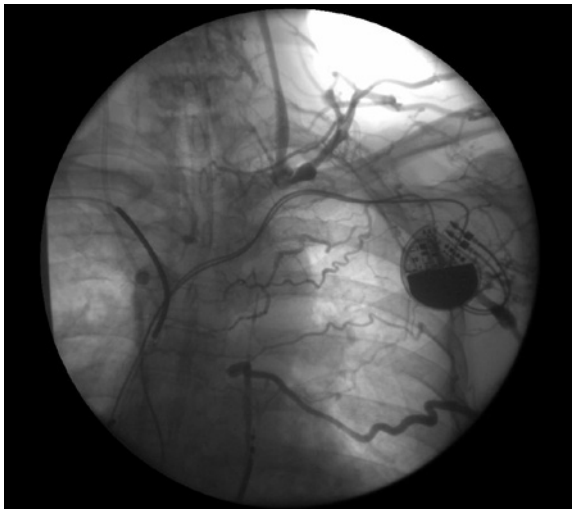

Fig. 1. Complete obstruction of the left subclavian vein. A well-developed collateral circulation bypassing the site of obstruction

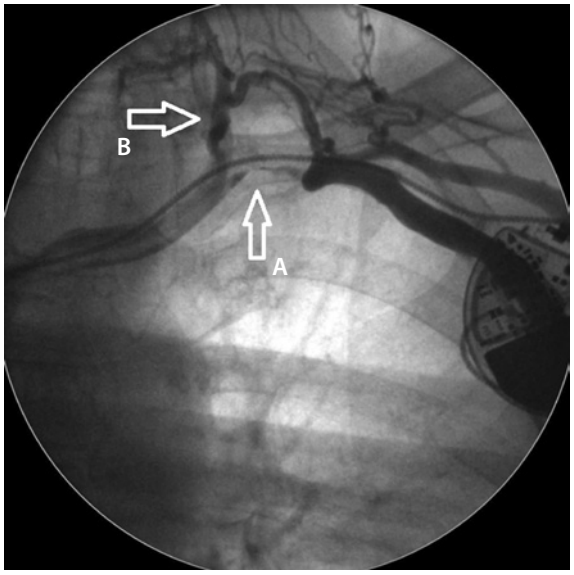

Fig. 2. A significant stenosis of left subclavian vein (A) with cervical collateral circulation (B)

(Fig. 1) or visible stenosis with collateral circulation on venogram (Fig. 2).

Furthermore, all the patients filled out the questionnaire regarding the clinical symptoms of obstruction in upper body venous flow, such as superficial venous collaterals on the chest, skin color changes, paresthesia and swelling of ipsilateral upper extremity, neck and face and anus hemorrhoids.

We determined the incidence of venography-based significant venous obstructions, the clinical symptoms and predictive factors.

The following clinical and demographic parameters were evaluated as potential risk factors for vein-related complications: age, sex, antiplatelet/anticoagulant drugs, statins, comorbidities and selected blood tests:

– white blood cells count (WBC) [×1000/μL]),
– diabetes mellitus,
– chronic obstructive pulmonary disease (COPD),
– nicotinism,
– history of venous thrombosis,
– paroxysmal or permanent supraventricular tachyarrhythmia: atrial flutter/fibrillation (AT/AF)
– heart failure defined as left ventricle ejection fraction ≤ 40%,
– chronic kidney disease defined as an increase in serum creatinine over 1.2 mg/dL or estimated glomerular filtration rate (eGFR) by CKD-EPI formula less than 60 mL/min/1.73 m^2,
– the presence of cardiac implants other than endocardial leads,
– history of surgical procedures and injuries in the area of neck and chest (strumectomy, sternotomy),
– only in patients qualified for elective transvenous lead extraction and in patients with heart failure: C-reactive protein (CRP), N-terminal prohormone of brain natriuretic peptide (NT-proBNP) and D-dimer tests,
– additional type of PM/ICD lead insulation.

The whole study population was divided into two groups, based on the presence or absence of endocardial leads in the cardiovascular system. Group I consisted of 136 patients with implanted endocardial leads (68.8% men), average age 68.0 ± 12.1 years, qualified for following procedures: 1) generator change (33 pts – 24.3%), 25 pts first reimplantation, 8 pts second and consecutive reimplantation; 2) device upgrade (22 pts – 16.1%), 17 pts upgrade of single lead device (PM – 4, ICD – 6) and 5 patients upgrade of dual-chamber devices (PM – 4, ICD – 1); 3) transvenous lead extraction (81 – 59.6%).

Group II (control) consisted of 82 patients (56 male), average age 73.1 years and before first implantations: PM – 63 pts, ICD 16 pts, CRT 3 pts.

The prevalence of potential risk factors mentioned above was compared in both groups.

The group with implanted leads was then divided into subgroup I A – with substantial abnormalities in venous blood flow, and I B – with correct blood flow. In these two subgroups (I A and I B) we performed an analysis of demographic factors, comorbidities and risk factors for venous stenosis/occlusion with regard to the lead number and type, lead insulation type, lead dwell time in cardiovascular system, presence of abandoned/non-functional and/or fractured, dropped-in leads forming loops in the heart and blood vessels.

Statistical Analysis

The data was evaluated using STATISTICA 10 by StatSoft. Quantitative variables are presented as a mean with standard deviations. Categorical variables are presented as an exact number and percentage of the whole analyzed group. Normality of continuous variables was evaluated using Shapiro-Wilk test. Differences between two groups were tested by Mann-Whitney *U*-test. The comparisons of categorical variables (frequency tables) were analyzed using χ^2 independence test. Two-way tables were assessed with the χ^2 test with Yates correction or Fisher exact test. Univariate and multiple logistic regression analyses were used to determine factors that were associated with risk of venous occlusion. A p-value < 0.05 was considered significant.

Results

None of the 218 patients aged 25 to 95 years (average 70.2 years) exhibited any adverse reaction to contrast dye. Group I (patients with already implanted leads) was larger than group II (before first implantation) – 62.4% of the study cohort. The risk factors and venogram results for the whole population are listed in Table 1.

Female patients were in the minority (31.2%). Among the underlying disease conditions the most common were supraventricular arrhythmias (43.1%) and heart failure (34.4%). A large percentage of patients used statins (46.8%) and antiplatelet/anticoagulation drugs (40.4%). Abnormal venograms were detected after the examination of 54 patients (24.8%). The patients with endocardial leads (group I) were compared with the patients from the control-group (group II), regarding the incidence of venous complications and the risk factors. The results are presented in Table 2.

The narrowing was identified in 51 patients (37.5%) in group I and in 3 patients (3.6%) in group II; p < 0.0001. One patient with a total occlusion of the left brachiovephalic vein after cardiac sugery, 2 patients with anatomical variability. These two groups did differ significantly in terms of demographic factors and the presence of comorbidities. The patients in group II were significantly older and presented worse kidney function. On the other hand, patients with heart failure and left ventricular ejection fraction ≤ 40% were significantly more prevalent in group I, which is somehow reflected by a higher portion of ICD/CRT patients in group I – 26.9% vs. 22% in group II. In univariate analysis conducted for the whole study cohort, the only statistically significant factor which predisposed to substantial venous stenosis was the presence of endocardial leads (OR = 3.975; p < 0.001). Multivariate analysis confirmed the predisposing role of endocardial leads (OR = 4.172; p < 0.001). The lead presence most highly correlated with venous complications and was associated with approximately four-fold (OR = 4.2) increased risk (Table 3).

We compared patients with endocardial leads divided into I A and I B according to venous patency. The findings are presented in Table 4. Diabetes

Table 1. The risk factors and venograms results for study population

Number of pts	218
Female gender	68 (31.2)
Use of statins	102 (46.8)
AT/AF	94 (43.1)
Anticoagulation treatment	88 (40.4)
Heart failure (left ventricle ejection fraction ≤ 40%)	75 (34.4)
Diabetes	41 (18.8)
Injuries/operations of the neck and chest	36/200* (16.5)
Tabacco	35 (16.1)
COPD	17 (7.8)
Chronic kidney disease (eGFR less than 60 mL/min/1.73 m^2)	12 (5.5)
The presence of cardiovascular implant (excluding PM/ICD leads)	7/200* (3.5)
History of thrombosis	7 (3.2)
Use of hormone replacement therapy (among women)	1/68* (1.5)
WBC (×1000/μL)	215* 6.7 ± 1.9
Creatinine (mmol/L)	214* 93.8 ± 47.8
eGFR – CKD-EPI formula (mL/min/1.73 m^2)	214* 69.1 ± 17.3
CRP (mg/L)	93* 12.5 ± 41.6
NT-pro BNP (pg/mL)	87* 1844 ± 4880
D-dimer (μg/L)	81* 769 ± 1073
Presence of stenosis/occlusion	54 (24.8)

* number of patients countable in the analysis.
Data are presented as mean ± standard deviation or number (percentage). AF – atrial fibrillation, AT – atrial tachycardia, COPD – chronic obstructive pulmonary disease, CRP – C reactive protein, eGFR – estimated glomerular filtration rate, NT-pro BNP – N-terminal prohormone of brain natriuretic peptide, WBC – white blood cells count.

Table 2. Comparison of the risk factors and venous complications incidence between group I and group II

Parameter	Presence of PM/ICD leads [Group I]	Initial PM/ICD implantation [Group II]	p-value
No. of patients	136	82	–
Age (years)	68.0 ± 12.1	73.8 ± 9.6	< 0.001
Female gender	42 (30.2)	26/82 (31.7)	0.8986
Chronic kidney disease (eGFR< 60 mL/min/1.73 m^2)	5/132* (3.8)	7/82 (8.5)	0.2234
Diabetes	27 (19.8)	14/82 (17.1)	0.6109
History of sternotomy	20 (14.7)	13/82 (15.8)	0.8188
History of strumectomy	1 (0.7)	2/82 (2.4)	0.5580
Tabacco	19 (14.0)	16/82 (19.5)	0.2803
COPD	13 (9.6)	4/82 (4.9)	0.3232
AT/AF	55 (40.4)	39/82 (47.6)	0.3038
History of thrombosis	3 (2.2)	4/82 (4.9)	0.2419
LVEF ≤ 40%	54 (39.7)	21/82 (25.6)	0.0338
Use of statins	62 (45.6)	40/82 (48.8)	0.6473
Anticoagulation treatment	56 (41.2)	32/82 (39.0)	0.7537
Use of hormone replacement therapy (among women)	1/42* (0.7)	0/26* (0.0)	1.0000
WBC (×1000/μL)	133* 6.6 ± 1.9	6.8 ± 1.8	0.2654
Creatinine (mmol/L)	132* 93.5 ± 58.1	94.4 ± 23.2	0.0883
eGFR – CKD-EPI formula (mL/min/1.73 m^2)	132* 71.8 ± 18.1	64.9 ± 15.1	0.0026
Presence of stenosis/occlusion	51/136 (37.5)	3/82 (3.7)	< 0.0001

Data are expressed as mean ± standard deviation or number (percentage); p-value < 0.05 was considered significant.
* number of patients countable in the analysis. AF – atrial fibrillation, AT – atrial tachycardia, COPD – chronic obstructive pulmonary disease, eGFR – estimated glomerular filtration rate, LVEF – left ventricular ejection fraction, WBC – white blood cells count.

mellitus was significantly more frequent in patients without venous complications – group I B; p = 0.01. Furthermore, univariate analysis revealed that the diabetes mellitus was the only protective factor against the development of venous lesions in patients with CIED (PM, ICD, CRT) (OR = 0.479; p = 0.01). In multivariate analysis diabetes mellitus was proved to be independently associated with lower risk of venous stenosis (OR = 0.473; p = 0.01) (Table 5).

Regarding the clinical symptoms of venous obstruction in group I, 6 patients (4.4%) had visible superficial cutaneous collateral veins on chest, 3 patients exhibited the skin color changes, paresthesia and/or swelling of the upper extremity. None of the patients experienced swelling of the head.

Discussion

Considering the occurrence of venous stenosis/occlusion in the presence of endocardial leads we must take into consideration the utilized venous visualization method, the definition of venous stenosis/occlusion and the lead dwelling time.

The assessment of vein patency among patients with endocardial lead and controls was performed by contrast venography, which is considered the gold standard [6]; however, there exist other methods such as venous Doppler ultrasound [13, 14] and isotope studies [18].

In the present study venous occlusion and stenosis was detected in 37.5% of patients with indwelling endocardial leads. The previous studies reported lower incidence of the complication except for two authors who identified venous occlusion and stenosis in higher percentage of patients

Table 3. Univariate and multivariate analysis of risk factors of venous complications in the whole study population

Parameter	Univariate analysis			Multivariate analysis		
	OR	95% CI	p-value	OR	95% CI	p-value
Age (years)	0.982	0.957–1.008	0.182			
Female gender	1.129	0.815–1.563	0.466			
Presence of PM/ICD	3.975	2.177–7.257	< 0.001	4.172	2.276–7.648	< 0.001
History of sternotomy	1.017	0.660–1.566	0.939			
History of strumectomy	0.809	0.241–2.713	0.731			
Tabaco	1.176	0.753–1.837	0.477			
COPD	1.260	0.662–2.397	0.482			
AT/AF	0.846	0.617–1.160	0.299			
LVEF ≤ 40%	1.139	0.828–1.565	0.424			
Use of statins	1.177	0.862–1.607	0.305			
Anticoagulation treatment	0.865	0.628–1.190	0.372			
History of neoplasm	0.952	0.490–1.849	0.884			
WBC (× 1000/μL)	0.972	0.823–1.147	0.737			
Creatinine (mmol/L)	0.997	0.988–1.007	0.575			
eGFR – CKD-EPI formula (mL/min/1.73 m^2)	1.007	0.989–1.025	0.475			
NYHA class III, IV	0.801	0.491–1.307	0.375			

Univariate and multiple logistic regression analyses. P-value < 0.05 was considered significant; OR – odds ratio, CI – confidence interval; AF – atrial fibrillation, AT – atrial tachycardia, COPD – chronic obstructive pulmonary disease, eGFR – estimated glomerular filtration rate, ICD – implantable cardioverter defibrillator, LVEF – left ventricular ejection fraction, PM – pacemaker, WBC – white blood cells count.

– 57% and 64% [7, 14]. The substantial differences among authors depend more on the criteria which were used to define venous stenosis/occlusion in the presence of endocardial leads rather than the lead dwell time or method of venous visualisation.

We defined a simple criterion of venous complication, which is complete occlusion or an obvious narrowing with collateral vein development. Da Costa et al. [7] considered any change in the contour of venous vessel with endocardial leads as a venous stenosis and revealed the high rate of venous stenosis/occlusion (64%) after much shorter mean lead dwell time (6 months). In other venography-based studies the changes in veins with or without the presence of collateral circulation were detected in 23–33% of patients regardless the length of lead dwell time [3–5, 8, 10, 13, 16, 17]. Only three discussed studies presented comparably long lead dwell time of 72 months and the rate of abnormal contrast flow reached 25%, 23% and 26% respectively [5, 8, 9]. In study by Bracke et al. and Goto et al. the detailed criteria of VSO were not specified. Li et al. found the total venous occlusion in 26% of patients in a population which was comparable to our patient population with respect to mean lead dwell time and sample size. According to Li et al., total venous occlusion was observed in 11% of patients without device related infections and in 32% of patients referred to TLE due to infectious indications [9].

In our study clinical manifestation of signs or symptoms of venous obstruction were present in 6 patients (4.4%), which correlates with data from the literature (2–6%) [4, 7, 13, 14]. It is reasonable to assume that the symptoms related to venous stenosis/occlusion correlate negatively with collateral circulation degree [7].

The analysis of the control group revealed the rates of venous stenosis/occlusion (3.6% vs. 37.5% in group I). The venous anomalies in the control-group were infrequent and related to intersubject variations of the anatomy. Due to the determination of venous stenosis/occlusion in the control cohort we demonstrated that indwelling leads facilitate the development of venous obstruction. It is noteworthy that there have been no randomized

Table 4. Comparison of patients with endocardial leads divided into group IA and IB according to venous patency

No. of patients	**51**	**85**	–
Age (years)	68.9 ± 14.0	67.5 ± 10.9	0.3993
Female gender	19 (37.2)	23 (27.1)	0.2918
Number of leads (1)	1.63 ± 0.56	1.59 ± 0.66	0.5112
Lead dwell time (months)	98.0 ± 68.5	108.4 ± 76.0	0.4902
Diabetes	4 (7.8)	23 (27.1)	**0.0125**
Chronic kidney disease (eGFR less than 60 mL/min/1.73 m^2)	2 (3.9)	3 (3.5)	1.0000
History of sternotomy	6 (11.8)	14 (16.5)	0.6170
History of strumectomy	1 (2.0)	0 (0.0)	0.3750
Tabacco	7 (13.7)	12 (14.1)	0.8481
COPD	3 (5.9)	10 (11.8)	0.4075
AT/AF	20 (39.2)	35 (41.2)	0.8215
History of thrombosis	0 (0)	3 (3.5)	0.2917
LVEF ≤ 40%	18 (35.3)	36 (42.3)	0.4154
Use of statins	20 (39.2)	42 (49.4)	0.2478
Anticoagulation treatment	19 (37.2)	37 (43.5)	0.4717
Use of hormone replacement therapy (among women)	0/19* (0)	1/23* (4.3)	1.0000
WBC (×1000/μL)	50* 6.7 ± 1.7	83* 6.6 ± 2.0	0.7136
Creatinine (mmol/L)	50* 91.3 ± 24.1	82* 94.8 ± 71.5	0.4786
eGFR – CKD-EPI formula (mL/min/1.73 m^2)	50* 69.6 ± 16.6	82* 73.2 ± 18.9	0.2279
CRP (mg/L)	32* 15.6 ± 67.3	49* 7.9 ± 13.8	0.1531
D-dimer (μg/L)	30* 667 ± 759	48* 740 ± 1152	0.9713
NT-pro BNP (pg/mL)	32* 1161 ± 1147	48* 2379 ± 6469	0.5264
Lead insulation:			
silicone insulation	39 (76.5)	59 (69.4)	0.3744
polyurethane insulation	6 (11.7)	12 (14.1)	0.6951
silicone and polyurethane insulation	4 (7.8)	10 (11.8)	0.6620
silicone and Optim insulation	0 (0)	1 (1.2)	0.9999
polyurethane and optim insulation	1 (2.0)	0 (0)	0.3750
optim insulation	1 (2.0)	3 (3.5)	0.9999

Data are presented as mean ± standard deviation or number (percentage); p-value < 0.05 was considered significant; * number of patients countable in the analysis; AF – atrial fibrillation;AT – atrial tachycardia; COPD – chronic obstructive pulmonary disease; eGFR – estimated glomerular filtration rate; HDL – high-density lipoprotein; ICD – implantable cardioverter defibrillator; LDL – low-density lipoprotein; LVEF – left ventricular ejection fraction; NT-pro BNP – N-terminal prohormone of brain natriuretic peptide; PM – pacemaker; TCH – total cholesterol; TG – total glyceride; WBC – white blood cells count.

controlled trials assessing the venous complications in CIED recipients.

In the group of patients with endocardial leads, diabetes mellitus was proved to be a protective factor against the development of venous stenosis (OR = 0.47). Such an observation has not been reported in the literature yet. Implantation of devices or biomaterials triggers a series of host reactions at the injury site that include interactions material/tissue, provisional matrix formation, acute and chronic inflammation, granulation tissue development, foreign body reaction, and fibrosis and fibrous capsule development. Much of the knowledge on this adverse healing following foreign body material implantation has come from normoglycemic individuals. An adverse foreign body reaction that invariably occurs adjacent to implant devices is poorly characterized in the

Table 5. Univariate and multivariate analysis of risk factor of significant vein occlusion in group I – patients with presence of PM/ICD leads

Parameter	Univariate analysis			Multivariate analysis		
	OR	95% CI	p-value	OR	95% CI	p-value
Age (years)	1.010	0.980–1.039	0.263			
Female gender	1.265	0.873–1.834	0.214			
Diabetes	0.479	0.273–0.842	0.010	0.473	0.268–0.835	0.010
Number of leads (1)	1.106	0.634–1.930	0.722			
Lead dwell time (months)	0.998	0.993–1.003	0.427			
No. of PM/ICD/CRT replacement (1)	1.207	0.732–1.992	0.461			
AT/AF	1.042	0.731–1.485	0.395			
LVEF ≤ 40%	1.161	0.811–1.661	0.416			
WBC (×1000/μL)	1.012	0.843–1.214	0.900			
Creatinine (mmol/L)	0.999	0.992–1.006	0.741			
GFR – CKD-EPI formula (mL/min/1.73 m^2)	0.989	0.970–1.009	0.272			
Anticoagulation treatment	1.139	0.798–1.626	0.486			
NYHA class III, IV	0.599	0.348–1.032	0.065	0.586	0.334–1.026	0.061

Univariate and multiple logistic regression analyses. P-value < 0.05 was considered significant.
OR – odds ratio; CI – confidence interval; AF – atrial fibrillation; AT – atrial tachycardia; ICD – implantable cardioverter defibrillator; LVEF – left ventricular ejection fraction; PM – pacemaker.

diabetic environment. There is evidence that hyperglycemia compromises all major components of the innate immune system, including phagocytosis, opsonization, glycosylation, and inactivation of circulating immunoglobulins. In consequence, diabetes affects the cellular response to tissue injury and delays wound healing. In a study conducted on rats it was observed that fibrous formation and presence of foreign body giant cells, the typical features of the foreign body reaction, were attenuated in the hyperglycemic environment [19]. We assume that these effects may contribute to a decreased risk of venous stenosis in patients with indwelling endocardial leads. Undoubtedly, this phenomenon requires further investigation [20].

We did not confirm previously reported risk factors, such as the number and type of leads, lead insulation usage of temporary pacing lead, heart failure with left ventricle ejection fraction below 40%, female hormone use, history of previous venous thrombosis [3, 7, 13, 16]. Our experience has shown no effect of antiplatelet/anticoagulation drugs on venous stenosis/occlusion in presence of endocardial leads in opposition to Van Roden et al. and Haghjoo et al. [13, 16].

Study Limitations

The presented study is single-center and non-randomized. Its limitation is the narrow size of the assessed population. Nevertheless, previous studies on venous occlusion/stenosis in the presence of endocardial leads were conducted in a comparable number of patients and without control group. A considerable percentage of patients were referred to TLE procedures. This fact results from the specialization of our center, which is the treatment of electrotherapy complications. Patients who underwent TLE procedure in the past or were referred for TLE due to infectious reasons were excluded from the study because still little is known about the influence of TLE procedures and infections on the late venous stenosis/occlusion formation.

The authors have concluded that the presence of indwelling endocardial leads is a predisposing factor for venous stenosis/occlusion and increases the risk 4-fold. Among patients with endocardial leads, diabetic patients develop venous stenoses significantly less frequently.

References

[1] **Candinas R, Duru F, Schneider J:** Postmortem analysis of encapsulation around long-term ventricular endocardial pacing leads. Mayo Clin Proc 1999, 74, 120–125.

[2] **Jones GK, Swerdlow C, Reichenbach DD:** Anatomical findings in patients having had a chronically indwelling coronary sinus defibrillation lead. Pacing Clin Electrophysiol 1995, 18, 2062–2067.

[3] **Lickfett L, Bitzen A, Arepally A:** Incidence of venous obstruction following insertion of an implantable cardioverter defibrillator. A study of systematic contrast venography in patient presenting for their first elective ICD generator replacement. Europace 2004, 6, 25–31.

[4] **Antonelli D, Turgeman Y, Kaveh Z:** Short-term thrombosis after transvenous permanent pacemaker insertion. Pacing Clin Electrophysiol 1989, 12, 280–282.

[5] **Bracke F, Meijer A, Van Gelder B:** Venous occlusion of the access vein in patients referred for lead extraction: Influence of patient and lead characteristics. Pacing Clin Electrophysiol 2003, 26, 1649–1652.

[6] **Crook BR, Gishen P, Robinson CR, Oram S:** Occlusion of the subclavian vein associated with cephalic vein pacemaker electrodes. Br J Surg 1977, 64, 329–331.

[7] **Da Costa SS, Scalabrini NA, Costa R:** Incidence and risk factors of upper extremity deep vein lesions after permanent transvenous pacemaker implant: A 6-month follow-up prospective study. Pacing Clin Electrophysiol 2002, 25, 1301–1306.

[8] **Goto Y, Abe T, Sekine S, Sakurada T:** Long-term thrombosis after transvenous permanent pacemaker implantation. Pacing Clin Electrophysiol 1998, 21, 1192–1195.

[9] **Li X, Ze F, Wang L:** Prevalence of venous occlusion in patients referred for lead extraction: implications for tool selection. Europace 2014, Jun 19. pii: euu124. [Epub ahead of print].

[10] **Oginosawa Y, Abe H, Nakashima Y:** The incidence and risk factors for venous obstruction after implantation of transvenous pacing leads. Pacing Clin Electrophysiol 2002, 25, 1605–1611.

[11] **Rozmus G, Daubert J, Huang D:** Venous Thrombosis and Stenosis After Implantation of Pacemakers and Defibrillators. J Interv Card Electrophysiol 2005, 13, 9–19.

[12] **Stoney WS, Addlestone RB, Alford WC Jr:** The incidence of venous thrombosis following long-term transvenous pacing. Ann Thorac Surg 1976, 22, 166–170.

[13] **van Rooden CJ, Molhoek SG, Rosendaal F:** Incidence and risk factors of early venous thrombosis associated with permanent pacemaker leads. J Cardiovasc Electrophysiol 2004, 15, 1258–1262.

[14] **Zuber M, Huber P, Fricker U:** Assessment of the subclavian vein in patients with transvenous pacemaker leads. Pacing Clin Electrophysiol 1998, 21, 2621–2630.

[15] **Brugada J, Vardas P, Volpert C:** The EHRA White Book 2008. The Current Status of Cardiac Electrophysiology in ESC Member Countries http://www.escardio.org/communities/EHRA/publications/Documents/ehra-white-book-2008.pdf. Accessed 01.12.2014.

[16] **Haghjoo M, Nikoo MH, Fazelifar AF:** Predictors of venous obstruction following pacemaker or implantable cardioverter-defibrillator implantation: a contrast venographic study on 100 patients admitted for generator change, lead revision, or device upgrade. Europace 2007, 9, 328–332.

[17] **Korkeila P, Mustonen P, Koistinen J, Nyman K, Ylitalo A, Karjalainen P, Lund J, Airaksinen J:** Clinical and laboratory risk factors of thrombotic complications after pacemaker implantation: a prospective study. Europace 2010, 12, 817–824.

[18] **Pauletti M, Di Ricco G, Solfanelli S:** Venous obstruction in permanent pacemaker patients: an isotopic study. Pacing Clin Electrophysiol 1981, 4, 36–42.

[19] **Socarrás TO, Vasconcelos AC, Campos PP:** Foreign body response to subcutaneous implants in diabetic rats. PLoS One 2014 Nov 5, 9, e110945.

[20] **Rosenberg CS:** Wound healing in the patient with diabetes mellitus. Nurs Clin North Am 1990, 25, 247–261.

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Conflict of interest: None declared

Received: 24.02.2015
Revised: 9.04.2015
Accepted: 24.04.2015