Central venous obstruction and clinical predictors in patients with permanent pacemaker

Kalıcı kalp pili olan olgularda santral venöz oklüzyon ve klinik öngörücüleri

Murat Yeşil, Serdar Bayata, Erdinç Arıkan, Selim Ekinci[1], Erdal Gürsul, Nursen Postacı

From 1. Cardiology Clinic, Atatürk Teaching and Research Hospital, İzmir-*Turkey*
[1]Clinic of Cardiology, Pazar State Hospital, Rize-*Turkey*

ABSTRACT

Objective: This study investigated the proportion of silent venous obstruction in patients who underwent pacemaker or lead reimplantation for various reasons. We also investigated independent predictors or risk factor of venous obstruction in this patient population.

Methods: Seventy-three patients who underwent pacemaker pulse generator and/or lead reimplantation in our institution between 2007 and 2010 were enrolled for this retrospective case-control study. Prior to procedure, patients underwent ipsilateral venography. Patients' venographies were classified as non-significant obstruction (stenosis ≤70%, including normal venogram), significant obstruction (stenosis >70%) and complete obstruction. Continuous and categorical data were compared with Mann-Whitney U test and Chi-square statistics respectively. Logistic regression analysis was used to identify independent predictors of venous obstruction.

Results: Complete or significant silent central venous obstruction (CVO) proportion was detected as 9.5% (n=7). Basal characteristics of patients with or without CVO were comparable. Significantly increased pacemaker pocket erosion incidence (57% vs 0%, p=0.001, in groups with and without CVO respectively) and significantly higher mean pacemaker age (15.3±10.2 years vs 10.4±5.1 years, p=0.047, in groups with and without CVO respectively) were found in group with CVO. Pacemaker pocket erosion (OR 3.00; 95% CI 1.024-9.302; p=0.001), higher pacemaker age (OR 1.33; 95% CI 1.026-1.733; p=0.02) were found as independent CVO predictors in multiple logistic regression analysis. Correlation analysis also revealed a significant correlation between previous or current pacemaker pocket erosion and CVO (r=0.80, p=0.001).

Conclusion: Ipsilateral venography is a useful procedure prior to pacemaker or lead reimplantation to detect CVO. In addition to the increased pacemaker age, current or past history of erosion and infection at pacemaker pocket are probable clinical conditions related to CVO. These clinical conditions create a predisposition to CVO with unknown mechanisms, according to the results of this preliminary study.

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Key words: Central venous occlusion, clinical predictors, pacemaker, logistic regression analysis

ÖZET

Amaç: Bu çalışmanın amacı değişik nedenlerle pacemaker veya elektrot reimplantasyonuna alınan olgularda asemptomatik venöz tıkanıklık sıklığının saptanmasıdır. Ayrıca venöz tıkanmanın bağımsız öngörücüleri de araştırılmıştır.

Yöntemler: Kliniğimizde 2007-2010 yılları arasında kalıcı kalp pili ve/veya elektrot reimplantasyonuna alınan 73 olgu bu retrospektif olgu-kontrol çalışmasına dahil edildi. İşlem öncesi hastalara pil tarafındaki kübital venden venografi yapıldı. Hastaların venografileri ciddi olmayan darlık (≤%70 veya normal), anlamlı darlık (darlık >%70) ve tam tıkalı olarak sınıflandırıldı. Sürekli ve kategorik veriler sırası ile Mann-Whitney U testi ve Ki-kare testi ile karşılaştırıldı. Venöz tıkanmanın bağımsız öngörücülerini tespit etmek için çoklu lojistik regresyon analizi kullanıldı.

Bulgular: Tam tıkanma ya da anlamlı darlık tipinde sessiz santral venöz tıkanma (SVT) yüzdesi %9.5 (n=7) bulundu. Santral venöz tıkanması olan ve olmayan hasta gruplarının bazal özelliklerinin karşılaştırılması anlamlı farklılık göstermedi. Santral venöz tıkanıklıklı hasta grubunda SVT'siz hasta grubu ile karşılaştırıldığında anlamlı derecede artmış pacemaker cep erozyonu yüzdesi (%57 ve %0, p=0.001) ve anlamlı derecede daha yüksek ortalama pacemaker yaşı (15.3±10.2 yıla karşın 10.4±5.1 yıl, p=0.047) bulundu. Pacemaker cep erozyonu (OR 3.00; %95 GA 1.024-9.302; p=0.001), daha yüksek pacemaker yaşı (OR 1.33; %95 GA 1.026-1.733; p=0.02) çok değişkenli regresyon analizinde SVT'nin bağımsız öngörücüleri olarak saptandı. Korelasyon analizi önceki ya da şimdiki pacemaker cep erozyonu ve SVT arasında anlamlı bir korelasyon olduğunu gösterdi (r= 0.80, p=0.001).

Address for Correspondence/Yazışma Adresi: Dr. Serdar Bayata, Atatürk Eğitim ve Araştırma Hastanesi, 1. Kardiyoloji Kliniği, İzmir-*Türkiye*
Phone: +90 232 464 97 97 Fax: +90 232 244 91 15 E-mail: sbayata@hotmail.com

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Sonuç: İpsilateral venografi, pacemaker veya elektrot reimplantasyonu öncesinde SVT'yi saptamada faydalı bir işlemdir. Bu çalışmanın sonuçlarına göre artmış pacemaker yaşı ve pacemaker cep erozyonu muhtemel klinikle ilişkili durumlardır ve bilinmeyen mekanizmalarla SVT'ye yatkınlık yaratmaktadırlar. *(Anadolu Kardiyol Derg 2012; 12: 401-5)*
Anahtar kelimeler: Santral venöz oklüzyon, klinik öngörücüler, pacemaker, lojistik regresyon analizi

Introduction

The number of patients with permanent pacemaker has increased exponentially recently. Complications associated with the implantation procedure are uncommon, but include bleeding, hematoma, infection, or pneumothorax. Pacemaker problems can rarely occur long after the implantation procedure. These "late" complications include generator failure, lead failure, lead dislodgment, malfunction due to other mechanical factors, pericarditis, infection, skin erosion, hematoma, and venous thrombosis (1). Device-associated central venous obstruction (CVO) is rare but generally presents as unilateral arm edema (2). Treatment includes extremity elevation and anticoagulation. Venous obstruction at the access site may be silent and may be detected during re-implantation of a new lead due to lead failure, pacemaker upgrade or infection. The incidence of central venous obstruction is well documented but predictors of CVO are not clear (2).

This study investigated the incidence of silent venous obstruction in patients who underwent pacemaker or lead reimplantation for various reasons. We also investigated independent predictors or risk factor of venous obstruction in this patient population.

Methods

Study design

This study has a retrospective case-control design.

Study population

Seventy-three consecutive patients who underwent antibradycardic pacemaker pulse generator and/or lead reimplantation in our institution between 2007 and 2010 were enrolled for this retrospective case-control study. Patient with renal dysfunction (creatinine >1.2 mg/dL) and patients who were allergic to contrast media did not underwent venography and excluded from this study.

Study protocol

All patients who were operated for antibradycardic pacemaker pulse generator and/or lead reimplantation in our institution underwent ipsilateral venography through the ipsilateral cubital vein prior to procedure. These patients' data were reviewed retrospectively to detect the incidence and predictors of CVO in this population. Data were obtained from patient charts between 2007 and 2010 in our pacemaker department.

Variables

Baseline demographic, clinical, laboratory, procedural data were obtained from patients' charts. Patient's venographies were analyzed for the presence of CVO.

Venography

Patients underwent venography through the ipsilateral cubital vein (Philips, H 3000, The Netherlands). During the ipsilateral venography procedure, 40 ml non-ionic contrast agent iopamidol (Iopamiro 300, Bracco Spa, Italy) was given from cubital vein. Venograms were obtained with conventional angiography and were analyzed with quantitative angiography by the operator. Patients' venographies were classified as non-significant obstruction (stenosis ≤70%, including normal venogram), significant obstruction (stenosis >70%) and complete obstruction. Previous pacemaker pocket intervention was defined as surgical manipulation of pacemaker pocket for any reason which includes generator and/or lead replacement, lead revision, hematoma, pocket erosion, etc.

Statistical analysis

Statistical analysis was performed with SPSS version 13.0 (Chicago, IL, USA). Continuous data were expressed as mean±standard deviation. Age, pacemaker age and ejection fraction were also expressed as median (minimum-maximum). Categorical data were expressed as number (percentage). Continuous and categorical data were compared with Mann-Whitney U test and Chi-square statistics respectively. Significantly different variables between groups in univariate analysis underwent multiple analyses. Binary multiple logistic regression analysis was used to identify independent predictors of venous obstruction. A correlation analysis was performed with Spearsman's correlation test.

Results

Baseline and procedural characteristics

Baseline characteristics of patient population were shown in Table 1. Complete or significant silent central venous obstruction (CVO) proportion was detected as 9.5% (n=7) in our study population. Obstruction was complete in 5 cases and significant (>70%) in 2 cases. Obstruction involved subclavian vein in all cases and also involved innominate vein in only one case. We did not detect any obstruction at the level of superior vena cava. Of these 7, only 2 patients required implantation of a new pacemaker lead. Ipsilateral venous puncture was thought impossible in these patients. In these cases, pacemaker system was removed and reimplantation was performed through the contralateral subclavian vein.

Table 1. Baseline characteristics

Patients, n	73
Mean age, years	68.8±13.5
Women, n (%)	41 (56)
Hypertension, n (%)	27 (37)
Diabetes mellitus, n (%)	12 (16)
Hyperlipidemia, n (%)	15 (21)
Smoking, n (%)	10 (13)
Antiplatelet therapy, n (%)	25 (34)
Anticoagulant therapy, n (%)	4 (5)
Mean pacemaker age, year	10.8±5.7
Previous PM replacement, n (%)	24 (33)
Previous PM pocket intervention, n (%)	27(37)
Patients with one PM lead, n (%)	40 (55)
Patients with more than one PM leads, n (%)	33(45)
Previous or current PM pocket erosion, n (%)	4(5)
Ejection fraction, %	57.6±6.7

Continuous data are expressed as Mean±SD, categorical data are expressed as n (%)
PM - pacemaker

Comparative analysis of patients with and without CVO

Comparison of basal characteristics of patients with or without CVO revealed nonsignificant difference. There was no significant difference between patients with or without CVO according to age, gender, number of previous replacements, number of leads, systolic function. Concomitant antiplatelet and anticoagulant medications were also found comparable in both groups. Significantly increased pacemaker pocket erosion proportion (57% vs 0%, p=0.001, in patient groups with and without CVO respectively) and also significantly higher mean pacemaker age (15.3±10.2 years vs 10.4±5.1 years, p=0.047, in patient groups with and without CVO respectively) were found in patient group with CVO (Table 2).

Predictors of CVO

Significantly different variables between groups in univariate analysis underwent multiple analyses. Pacemaker pocket erosion (OR 3.00; 95% CI 1.024-9.302; p=0.001), higher pacemaker age (OR 1.33; 95% CI 1.026-1.733; p=0.02) were found as independent CVO predictors in binary multiple logistic regression analysis (Table 3). However, absence of anticoagulant and antiplatelet therapy were not independent CVO predictors. Correlation analysis also revealed a significant correlation between previous or current pacemaker pocket erosion and CVO (r=0.80, p=0.001).

Discussion

The results of this preliminary study demonstrate that previous or current pacemaker pocket erosion and increased pacemaker age create predisposition to ipsilateral venous obstruction.

Table 2. Baseline characteristics of patients with and without central venous obstruction

Variables	Patients with CVO (n=7)	Patients w/o CVO (n=66)	*p
Age, years	68.5 7.1 69 (59-77)	68.8±14.0 73 (26-88)	0.37
Women, n (%)	3 (43)	38 (58)	0.75
Hypertension, n (%)	2 (28)	25 (38)	0.84
Diabetes, n (%)	2 (28)	10 (15)	0.24
Hyperlipidemia, n (%)	2 (28)	13 (20)	0.41
Smoking, n (%)	1 (14)	9 (14)	0.33
Antiplatelet therapy, n (%)	2 (28)	23 (35)	0.96
Anticoagulant therapy, n (%)	1 (14)	3 (5)	0.59
PM age, years	15.3±10.2 16.5 (1-26)	10.4±5.1 10.0 (1-27)	0.047
Previous PM replacement, n (%)	4 (57)	20 (30)	0.55
Previous PM pocket intervention, n (%)	4 (57)	23 (35)	0.61
Patients with one PM lead, n (%)	4 (57)	36 (55)	0.80
Patients with more than one PM leads, n (%)	3 (43)	30 (46)	0.78
Previous or current PM pocket erosion, n (%)	4 (57)	0	0.001
Ejection fraction, %	58.3±6.8 60 (45-64)	57.6±7.1 60 (20-65)	0.55

Data are expressed as Mean±SD, median (range), and number (percentage) values
*Chi-square and Mann-Whitney U tests
CVO - central venous obstruction, NS - not significant, PM - pacemaker

Table 3. Independent predictors of central venous obstruction

Parameters	OR	95% CI	p
Pacemaker age	1.33	1.026-1.733	0.02
Previous or current PM pocket erosion	3.00	1.024-9.303	0.001

Binary multiple logistic regression analysis, R^2=0.33 p<0.05
CI - confidence interval, NS - not significant, OR - odds ratio, PM - pacemaker

Central venous occlusion may develop at any time after the implantation of transvenous permanent pacemaker, but usually occurs after several years (1). An early obstruction after pacemaker implantation mainly results from thrombosis or rarely vasospasm, in the absence of stenosis, but a delayed obstruction may be the result of fibrotic stenosis (2, 3). Pacemaker-induced venous obstruction is mainly caused by the pacemaker leads, which can result in thrombosis and stenosis. The pacemaker lead tension can irritate the endothelial side of venous wall, especially at the site of multiple leads intersection. Local endothelial trauma and irritation due to the endothelial lead can lead to fibrosis and thrombosis, which may also occur by puncturing the vein or merely by manipulating the guide wire. Other supposed causes include severed leads left behind within the

circulation, and a history of recent or remote infection (4). The most common area of lead related fibrotic stenosis is the junction between the superior vena cava and innominate vein. Thrombosis or stenotic lesions may also occur in the axillary, subclavian and innominate veins, or in the superior vena cava, and silent lesions have been reported to be relatively common. Significant venous thrombosis of the innominate or subclavian vein has been documented in up to 30-40% of patients, and with complete occlusion in up to 20% at 2 years after implantation. However, symptomatic venous thrombosis occurs in less than 5% of patients after pacemaker implantation (5). Most patients with pacemaker related chronic obstruction of the central veins remain asymptomatic, and may be found during pacemaker lead revision.

Venous thrombosis and stenosis associated with pacemakers and defibrillators was thoroughly reviewed by Rozmuz, et al. (6). Symptomatic venous occlusion is rare and generally presents as unilateral arm edema or superior vena cava syndrome (2, 7). One large prospective series over ten years following 6256 patients with permanent pacemakers identified symptomatic venous hypertension in only 25 patients (0.4%) (8). Da Costa et al. (9), reported the incidence of central vein stenosis by venography as 64% in 229 patients after transvenous pacemaker implantation. However, only a small fraction of these patients (2.6%) had clinical signs and symptoms. Haghjoo et al. (10) reported a series of 100 patients with transvenous cardiac rhythm devices that underwent venography at the time of subsequent reimplantation. Seventeen percent of patients had significant venous stenosis (>70%), and 9% had complete venous occlusion. No patient had clinical signs or symptoms of venous obstruction. Another study delineated central venous anatomy prior to pacemaker implantation in 150 patients (11). Baseline venous obstruction or anomalies were found in 7% of patients. At 6 months, venography demonstrated new stenosis in 19 patients (14%), none symptomatic. A similar study utilized contrast venography to evaluate central vein stenosis in 105 consecutive patients presenting for implantable cardioverter- defibrillator generator change (12). Venous obstruction was found in 25% of cases. Previous pacemaker insertion resulted in a higher incidence of venous stenosis in this study. Another study utilized digital subtraction angiography to evaluate central veins before and after pacemaker insertion in 131 consecutive patients (13). Venous obstruction (narrowing >60%) was identified in 13.7% of patients prior to implantation. Follow up venography was performed in 79 patients. Venous obstruction was found in 26/79 patients (32.9%). No patients demonstrated clinical symptoms or physical findings of venous obstruction.

In patients with ipsilateral arteriovenous hemodialysis access, high blood flow may overwhelm the capacity of the compromised central veins resulting in symptomatic and clinically significant venous hypertension more frequently due to pacemaker-related CVO. One retrospective review demonstrated symptomatic venous hypertension in 71% of hemodialysis patients due to subclavian vein occlusion or stenosis with transvenous pacemakers and ipsilateral arteriovenous access (14).

Clinically symptomatic lead-associated venous obstruction usually treated with the elevation of effected extremity and antiplatelet-anticoagulant therapy. Percutaneous transluminal balloon angioplasty and thrombolytic therapy has also been employed to manage this complication (15). Successful pacing lead implantation has been reported after angioplasty and stent dilation of superior vena cava and innominate vein obstructions (16).

Central venous obstruction proportion was detected as 9.5% in our study population. Obstruction was complete in 5 cases and partial (>70%) in 2 cases. Obstruction involved subclavian vein in all cases and also extended into innominate vein in only one case. We did not detect any obstruction at the level of superior vena cava. All patients were asymptomatic at the time of diagnosis. It is thought, ipsilateral venography is a useful procedure prior to pacemaker or lead reimplantation to detect CVO. In addition to the increased pacemaker age, current or past history of erosion and infection at pacemaker pocket creates a predisposition to CVO with unknown mechanisms, according to the results of this study. Future studies may delineate responsible mechanisms between pocket erosion and CVO.

Study limitations

Main limitation of this study is limited sample size. This small study population also decreases power of the current study. Future studies with multicenter participation may more clearly delineate predisposing factors for venous obstruction after pacemaker implantation. The present study is also limited by the fact that the incidence of venous obstruction prior to first pacemaker implantation has not been investigated. Some previous studies have reported that the incidence of stenotic or occlusive venous lesions is not rare (10). However, successful prior pacemaker implantation may be used as a surrogate for the absence of severe CVO before lead implantation in this study population.

Conclusion

Ipsilateral venography is a useful procedure prior to pacemaker or lead reimplantation to detect silent CVO. In addition to the increased pacemaker age, current or past history of erosion and infection at pacemaker pocket are probable clinical conditions related to CVO. These clinical conditions create a predisposition to CVO with unknown mechanisms, according to the results of this preliminary study.

Conflict of interest: None declared.

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