An observational study of the effect of coronary artery disease severity on acute pacing threshold and lead impedance in patients with permanent pacemaker

Kalıcı pacemaker'lı olgularda koroner arter hastalığı ciddiyetinin akut uyarı eşiği ve lead empedansı üzerine etkisini araştıran gözlemsel bir çalışma

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ABSTRACT

Objective: This study investigated the effect of coronary artery disease (CAD) severity, distribution and left ventricular ejection fraction (LVEF) on acute ventricular pacing threshold and lead impedance at the time of pacemaker implantation.

Methods: One hundred and thirty-two patients who received a ventricular pacemaker or internal cardioverter-defibrilator (ICD) lead in our institution between 2007-2010 were included in this observational study. Patients were divided into ICD and anti-bradycardic pacemaker (PM) groups. Groups were compared for ventricular stimulation threshold, lead impedance and LVEF. Later, groups were sub-grouped according to the severity and distribution of CAD and subgroups were compared in both groups for ventricular stimulation threshold, lead impedance. Quantitative data of groups were compared by means of independent samples t-test.

Results: Ventricular pacing thresholds were found significantly higher ICD group compared with PM group (p<0.05). Impedance and LVEF values were significantly lower in ICD group (p<0.05). Impedance and ventricular pacing thresholds were comparable in subgroups of ICD and PM groups. Our study does not confirm any relationship between pacing parameters and severity-distribution of CAD and LVEF.

Conclusion: Patients with ventricular ICD lead had higher pacing thresholds but lower pacing impedance values comparing with PM group. This study did not find any significant relationship between pacing parameters at implantation and LVEF, severity and distribution of CAD.
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Key words: Coronary artery disease, pacemaker, pacing impedance, pacing threshold

ÖZET

Amaç: Bu çalışmada kliniğimizde kalıcı endokardiyal kalp pili implantasyonu yapılan hastalarda, implantasyon sırasındaki ventriküler uyarı eşiği ve empedansı ile koroner arter hastalığı (KAH) ciddiyeti, lokalizasyonu ve sol ventrikül (LV) ejeksiyon fraksiyonu (EF) arasındaki ilişki araştırılmıştır.

Yöntemler: Bu gözlemsel çalışmaya 2007-2010 tarihleri arasında kliniğimizde ventriküler lead'i bulunan kalıcı pacemaker veya internal defibrillatör-kardiyoverter (ICD) takılan 132 hasta alındı. Hastalar ICD ve antibradikardik pacemaker (PM) hastaları olarak iki gruba ayrıldı. Bu iki grup ventriküler uyarı eşiği, lead empedansı ve LVEF açısından karşılaştırıldı. Daha sonra her iki grup hasta incelenen KAH parametreleri yönünden iki alt gruba ayrılmış ve alt grupların ortalama uyarı eşiği ve empedans değerleri karşılaştırılmıştır. Gruplar arasında verilerin karşılaştırılmasında bağımsız örneklem t-testi kullanıldı.

Bulgular: İnternal defibrillator-kardiyoverter grubunda ventriküler uyarı eşiği değerleri PM grubuna göre istatistiksel olarak anlamlı yüksek bulundu. Ventriküler empedans ve LVEF değerleri ise ICD grubunda anlamlı derecede düşük bulundu (p<0.05). Altgruplar kendi aralarında karşılaştırıldığında, LVEF, KAH ciddiyeti ve lokalizasyonu ile ventriküler lead empedansı ve uyarı eşiği arasında anlamlı ilişki saptanmadı.

Sonuç: İnternal defibrillator-kardiyoverter takılan hastaların ventriküler uyarı eşiği değerleri antibradikardik pacemaker hasta grubuna göre daha yüksek, ventriküler empedans değerleri antibradikardik pacemaker hasta grubuna göre daha düşüktür. Bu çalışmada KAH ciddiyeti ve EF değeri ile uyarı eşiği ve empedans değerleri arasında bir ilişki saptanmamıştır. *(Anadolu Kardiyol Derg 2012; 12: 208-13)*

Anahtar kelimeler: Koroner arter hastalığı, pacemaker, uyarı eşiği, empedans

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Introduction

The electrical resistance of a circuit is the measure of opposition to the passage of an electric current. Impedance, which is used in pacemaker terminology, is a term that extends the concept of resistance, describing not only the relative amplitudes of the voltage and current, but also the relative phases (1). Pacing threshold is the lowest voltage, which can produce 5 consecutive stimuli (2). Several factors may have an effect on pacing threshold. Factors which have been proven to increase pacing threshold are myocardial ischemia-infarction, hypothermia, hypothyroidism, hyperkalemia, acid-base imbalance, class Ic and class III antiarrhythmics, possibly class Ia, Ib and II antiarrhythmics, severe hypoxia, hyperglycemia over 600mg/dL, hypoglycemia, inhalant anesthetics in dose dependent manner and local anesthetic agents. Factors that decrease pacing thresholds are cathecholamines, stress, anxiety, anticholinergic drugs, glucocorticoids, hyperthyroidism and hypermetabolic state (3).

To our knowledge, there is no published data regarding the effects of severity, and distribution of coronary artery disease (CAD) on pacing thresholds and impedance at the time of implantation.

This study investigated the effect of severity, distribution of CAD and left ventricular ejection fraction (LVEF) on acute ventricular pacing threshold and lead impedance at the time of either antibradycardic pacemaker (PM) or implantable cardiac defibrillator (ICD) implantations in our institution for various indications.

Methods

Study design

This observational study evaluated the effect of CAD severity, distribution and EF on acute ventricular pacing threshold and lead impedance at the time of pacemaker implantation with retrospective analysis of patient charts.

Patients

Patients who received ventricular PM or ICD leads between 2007 and 2010 in İzmir Atatürk Teaching Hospital were retrospectively screened for this observational study. One hundred thirty-two patients who received a PM or an ICD for any indication and whose ventricular leads (steroid eluting with passive fixation mechanism) are located in the right ventricular apex were included. Another inclusion criterion was the presence of a recent coronary angiogram (≤ 3 months) with CAD diagnosis before device implantation. Exclusion criteria were right ventricular leads located in an area other than apex, active fixation mechanism, epicardial leads, patients who receive Vaughan-Williams Class I and III antiarrhythmic drugs and absence of a recent coronary angiography before implantation. Patient charts were reviewed for demographic data, such as diabetes, hypertension, hyperlipidemia, smoking, and echocardiographic LVEF (General Electric, Vivid 3, USA).

PM and ICD measurements

In our institution, ICD leads that were used are of different make and models, but typically bipolar/dual coil, 65 cm, passive fixation, steroid eluting with porous structure. Pacemaker leads are also bipolar/dual coil, 52 cm, passive fixation, steroid eluting with porous structure. Pacing threshold was defined as the lowest voltage, which can produce 5 consecutive stimuli and was measured at pulse duration of 0.4 ms. Pacing thresholds were recorded in volts (V), and impedance values in ohms (Ω) at the time of implantation.

Coronary angiography

Coronary angiograms were reviewed for CAD (Philips, H 3000, Holland). No visible plaques was defined as ‘absence of CAD’, <70% stenosis in left anterior descending artery (LAD), circumflex (Cx), right coronary artery (RCA) or <50% stenosis in left main coronary artery (LMCA) as ‘noncritical CAD’, ≥70% stenosis in any of the three vessels or ≥50% stenosis in LMCA as ‘critical CAD’ in the relevant vessel.

Study protocol

Patients were first divided into PM and ICD groups. Ventricular pacing thresholds, impedance values and ejection fractions of the two groups were compared. Both groups were further divided into two subgroups according to LVEF (≥50% and <50%). Pacing thresholds and impedance values of the subgroups (LVEF≥50% vs. <50%) were compared. Later critical and noncritical CAD subgroups of each group were compared for pacing threshold and impedance values. Critical and noncritical CAD subgroups of each group were also compared for pacing threshold and impedance values according to involved coronary artery separately. Lastly, for each coronary artery, patients with totally occluded coronary arteries were compared with patients without total occlusion in terms of pacing threshold and impedance values.

Statistical analysis

Statistical Package for Social Sciences (SPSS for Windows, Chicago, IL, USA) version 16 was used for statistical analysis. Quantitative data of the two groups were compared by means of independent samples t-test. A p value of <0.05 was considered as significant.

Results

Patients

Seventy-seven (58%) of 132 subjects were male. Mean age of all subjects was 65±12 years. The ICD group was comprised of 43 subjects (30 male, mean age: 58±12; 13 women, mean age: 67±10). The PM group included 89 subjects (47 male, mean age: 65±13 years; 42 women, mean age: 68±8 years). Patients in PM group were not receiving any antiarrhythmic drug during measurement of pacing parameters. In contrast, 74% of patients (n=32) in the ICD group were receiving beta-blocker treatment.

PM and ICD indications

ICD indications were ischemic cardiomyopathy in 18, non-ischemic cardiomyopathy in 6, sudden death survival in 5, hypertrophic cardiomyopathy in 7, other indications in 7 patients. Antibradycardic pacemaker indications were complete atrioventricular block (AV) block in 55, sick sinus syndrome in 15, second-degree AV block in 13, atrial fibrillation with slow ventricular response in 5, symptomatic trifascicular block in 1 patient.

Pacing threshold and impedance values

Ventricular pacing thresholds were significantly higher, impedance values and ejection fractions were found significantly lower in the ICD group, compared with the PM group (p<0.05), (Table 1).

There was no statistically significant difference in threshold and impedance values between the normal and low LVEF subgroups of ICD and PM groups (p>0.05) (Table 2). Comparison of impedance and threshold values between ICD and PM groups both in low and normal LVEF subgroups also did not reveal any significant difference (Table 2).

Effect of coronary artery disease severity

Both groups were divided into two subgroups according to the severity of CAD (noncritical and critical CAD subgroups). No statistically significant difference was found between the subgroups in terms of pacing thresholds and impedance (p>0.05) (Table 3).

When patients in both ICD and PM groups were analysed separately for each vessel (i.e. LAD, Cx and RCA), for the presence or absence of critical CAD, no statistically significant difference was found in terms of pacing threshold and impedance values (p>0.05), (Table 4).

Lastly, for each coronary artery, pacing threshold and impedance values of patients with totally occluded coronary arteries were compared with patients without total occlusion in ICD and PM groups. In ICD group, no statistically significant difference was found in terms of pacing threshold and impedance values (p>0.05) (Table 5). In the pacemaker group, a tendency for higher impedance values was observed if coronary artery was totally occluded. Impedance values were found significantly higher only if LAD is occluded (p<0.05). High pacing impedance values more than 1400 Ohm were measured especially in some patients with total occlusion of LAD, Cx and RCA as seen in Table 5. On the other hand, pacing thresholds were not significantly affected by the location of total occlusion (Table 5).

When patients were grouped for myocardial infarction (MI) location on the surface ECG, no statistically significant difference was found for pacing threshold and impedance values according to MI location in ICD and PM groups (p>0.05).

Table 1. Comparison of EF, pacing threshold and impedance values in ICD and PM groups

Variables	ICD Group (n=43)	PM Group (n=89)	*p
EF, %	34.1±16.4	47.2±8.8	0.000
Impedance, ohm	903.3±213.6	996.7±309.4	0.046
Threshold, volt	0.5±0.2	0.4±0.1	0.032

Continuous variables are expressed as mean±SD
*Independent samples t-test
EF - ejection fraction, ICD - implantable cardiac defibrillator, PM - pacemaker

Table 2. Comparison of impedance and threshold values in relation to EF in ICD and PM groups

Groups	Parameters	EF≥50% (n)	EF<50% (n)	*p
ICD group	Impedance, ohm	896.4±222.5 (11)	923.5±194.0 (32)	NS
	Threshold, volt	0.5±0.3 (11)	0.5±0.2 (32)	NS
PM group	Impedance, ohm	904.3±302.6 (16)	1013.4±311.7 (73)	NS
	Threshold, volt	0.4±0.2 (16)	0.4±0.1 (73)	NS

Continuous variables are expressed as mean±SD
*Independent samples t-test - differences are nonsignificant for comparison between ICD and PM groups and EF subgroups
EF - ejection fraction, ICD - implantable cardiac defibrillator, NS - not significant, PM - pacemaker

Table 3. Comparison of threshold and impedance values according to severity of CAD in ICD and PM groups

Groups	Variables	Non-critical CAD (n)	Critical CAD (n)	*p
ICD Group	Impedance, ohm	895.3±198.7 (20)	910.3±230.0 (23)	NS
	Threshold, volt	0.5±0.3 (20)	0.4±0.2 (23)	NS
PM Group	Impedance, ohm	982.3±298.1 (61)	1027.9±336.1 (28)	NS
	Threshold, volt	0.4±0.1 (61)	0.4±0.1 (28)	NS

Continuous variables are expressed as mean±SD
*Independent samples t-test
CAD - coronary artery disease, ICD - implantable cardiac defibrillator, NS - not significant, PM - antibradycardic pacemaker

Patients, who needed revascularization because of critical CAD, underwent revascularization procedure following device implantation. Sixteen patients treated with primary coronary intervention (PCI), 5 patients with coronary bypass surgery (CABG), and 7 patients with medical treatment in PM group. In ICD group, 11 patients treated with PCI, 2 patients with coronary bypass surgery (CABG), 2 patients with hybrid approach, and 8 patients with medically.

Discussion

In this study, data of 132 patients who received ventricular PM or ICD leads between 2007 and 2010 were retrospectively screened. We investigated the effect of severity, distribution of coronary artery disease and LVEF on acute ventricular pacing threshold and lead impedance at the time of pacemaker implantation. Patients with ventricular ICD lead had higher pacing thresholds but lower pacing impedance values comparing with PM group. This study did not find any significant relationship between pacing parameters at implantation and EF, severity, and distribution of CAD.

In addition to reflecting electrophysiological properties of the heart, threshold and impedance values affect battery longevity, and may indicate pacemaker dysfunction. To our knowledge, there is no published study, which investigates the effect of severity and distribution of coronary artery disease on pacing thresholds and impedance values. Some studies point to the effects of left ventricular ejection fraction on the lead impedance (4). Distribution of coronary artery lesions in patients with permanent pacemakers and severe conduction disturbances reported previously (5-7).

Schuchert et al. (4) investigated impedance values during implantation and compared clinical characteristics of patient groups with low and high impedance. They found no difference between the groups in terms of age, gender, arterial hypertension, but discovered that low impedance is more prevalent in those with previous history of heart disease. They comment that coexistent heart disease lowers impedance values. Another study by Schuchert et al. (8) compared the atrial sensing and pacing parameters of CRT patients with dual chamber pacemaker patients. They found that pacing impedance did not differ between the groups at implantation but CRT patients showed significantly lower impedance values during follow-up. They conclude that CRT recipients have ‘less good’ electrical characteristics in the atrium.

A study by Stambler et al. (9) examined whether changes in RV pacing impedance correlate with changes in LVEF and NYHA functional class during follow-up in PM recipients. The study included 67 patients, in NYHA class II or III, and with a mean LVEF of 29±8% at implantation. At implant, impedance values were similar in RV outflow tract and apex. Between implant and 3 months, mean impedance values decreased at both locations. Changes in RV apex impedance correlated with changes in LVEF. Right ventricular apex impedance also decreased significantly, as NYHA class increased from I to IV. Conversely, there was no correlation between impedance values measured at the right ventricular outflow tract and LVEF or NYHA class.

In the light of the aforementioned data, impedance values tend to be low in coexistent heart disease and this situation may adversely affect battery life. Our study does not confirm any relationship between impedance values and LVEF, severity and distribution of CAD, but finds the impedance values to be significantly low in the ICD cohort. When groups are analysed separately, same relation does not hold true between LVEF and

Table 4. Comparison of pacing threshold and impedance values according to the severity and localization of coronary lesions in ICD and PM groups

Groups	CA	Pacing parameter	Non-critical CAD (n)	Critical CAD (n)	*p
ICD Group (n=43)	LAD	Impedance, ohm	898.8±213.3 (18)	910.2±220.6 (15)	NS
		Threshold, volt	0.5±0.3 (18)	0.5±0.2 (15)	NS
	RCA	Impedance, ohm	907.3±215.5 (22)	890.2±218.2 (10)	NS
		Threshold, volt	0.5±0.2 (22)	0.5±0.3 (10)	NS
	CX	Impedance, ohm	919.18±190.5 (26)	843.6±291.2 (8)	NS
		Threshold, volt	0.5±0.26 (26)	0.51±0.33 (8)	NS
PM Group (n=89)	LAD	Impedance, ohm	994.1±299.6 (52)	1004.5±344.7 (17)	NS
		Threshold, volt	0.3±0.1 (52)	0.4±0.1 (17)	NS
	RCA	Impedance, ohm	990.3±311.4 (45)	1023.6±308.4 (14)	NS
		Threshold, volt	0.4±0.1 (45)	0.4±0.1 (14)	NS
	CX	Impedance, ohm	989.7±309.6 (54)	1067±319.0 (15)	NS
		Threshold, volt	0.4±0.1 (54)	0.3±0.2 (15)	NS

Continuous variables are expressed as mean±SD
*Independent samples t test
CA - coronary artery, CAD - coronary artery disease, CX - circumflex artery, ICD - implantable cardiac defibrillator, LAD - left anterior descending artery, NS - not significant, PM - antibradycardic pacemaker, RCA - right coronary artery

Table 5. Comparison of pacing threshold and impedance values according to presence or absence of total occlusion of coronary arteries in ICD and PM groups

Group	CA	Pacing parameter	Total occlusion absent (n)	Total occlusion present (n)	*p
ICD group (n=43)	LAD	Impedance, ohm	894.2±226.2 (34)	937.7±163.6 (9)	NS
		Threshold, volt	0.5±0.3 (34)	0.4±0.1 (9)	NS
	RCA	Impedance, ohm	922.0±176.3 (36)	807.2±353.8 (7)	NS
		Threshold, volt	0.5±0.2 (36)	0.4±0.3 (7)	NS
	CX	Impedance, ohm	888.9±205.4 (39)	1044±274.4 (4)	NS
		Threshold, volt	0.5±0.2 (39)	0.26±0.1 (4)	NS
PM group (n=89)	LAD	Impedance, ohm	977.1±300.3 (85)	1412.5±202.5 (4)	0.005
		Threshold, volt	0.4±0.1 (85)	0.35±0.1 (4)	NS
	RCA	Impedance, ohm	993.6±290.9 (81)	1027.6±485.0 (8)	NS
		Threshold, volt	0.4±0.1 (81)	0.5±0.1 (8)	NS
	CX	Impedance, ohm	993.2±302.0 (84)	1054.6±456.5 (5)	NS
		Threshold, volt	0.4±0.1 (84)	0.4±0.1 (5)	NS

Continuous variables are expressed as mean±SD
*Independent samples t-test
CA - coronary artery, CAD - coronary artery disease, CX - circumflex artery, ICD - implantable cardiac defibrillator, LAD - left anterior descending artery, NS - not significant, PM - anti-bradycardic pacemaker, RCA - right coronary artery

impedance. Low impedance seems to be due to other electrical properties of the myocardium rather than purely LVEF in ICD patients. Impedance difference between the ICD and PM leads may also be explained by different lead structures.

In a study by Kostiainen et al. (10) the long-term stimulation thresholds were evaluated and were found significantly higher in the cases of enlarged heart and in the age group less than 50 years than in those with a heart of normal size and in the age group greater than 70 years.

Tse et al. (11) studied the effect of LVEF on LV pacing and sensing thresholds in patients with coronary sinus lead. The LV pacing and sensing thresholds, and lead impedance were compared between patients with LVEF <40% and patients with LVEF >40%. At implant, LV pacing thresholds were similar between the groups, however, at 3-month follow-up, stimulation thresholds increased significantly in patient group with low LVEF (<40%). They concluded that LV systolic function has a significant impact on LV pacing threshold, which is remarkable in the long-term.

In the abovementioned study by Schuchert et al. (8) the atrial pacing threshold was found significantly higher in the CRT group than the PM group at implantation, then the groups equalized at 1 month and CRT group had significantly higher values again after 3 and 6 months.

When the data is taken on the whole, it can be said that low LVEF is correlated with high stimulation threshold. In our study, differences in ICD and PM groups in terms of stimulation threshold and impedance also hold true for LVEF. When groups are analysed separately, LVEF alone does not have significant effect on stimulation threshold and impedance. This may also be explained by different lead structures. The lack of relatioship between high stimulation threshold and systolic dysfunction suggests that factors other than mechanical dysfunction may apply. The connection between threshold and impedance and LVEF may be fairly indirect rather than straight, via complex mechanisms in which ventricular electrical properties and instability may also play a part. Therefore, we think that further studies are needed to investigate the predictive value of stimulation threshold and impedance values for ventricular arrhythmias.

In an animal model, the effect of global ischemia of different degrees of severity and reperfusion was studied. Four levels of ischemia were induced by reducing the coronary flow for 30 minutes. After severe ischemia, loss of contractility was irreversible and pacing threshold increased. Following moderate ischemia, contractility fully recovered and the pacing threshold did not increase (12). The effect of ischemia on pacing thresholds changes depending on the location of ischemia and myocardial contact region of the pacemaker lead. Resting membrane potential increases in case of acute myocardial ischemia (13). Delmar et al. (14) proved that the amount of current needed to stimulate the myocardium increased, at all pulse widths under metabolic blockage with 2-4 dinitrophenol. Therefore pacing threshold is expected to increase if the lead tip is in the ischemic territory. The increase may be more dramatic in case of a more severe ischemia or infarction. This reality is manifested by 'acute loss of capture' in a clinical scenario of acute inferior myocardial infarction, accompanied by right ventricular involvement in a patient with a previously implanted permanent pacemaker. If the lead tip is, by chance, located in a nonischemic region, pacing threshold may even decrease due to sympathetic stimulation in a patient with myocardial infarction (13). The achievement of a pacing threshold well less than 1V/0.4ms is, in general, more difficult (sometimes after testing several different positions around RV apex) in patients with ischemic cardiomyopathy than in patients without structural heart disease.

Our study does not yield any relationship between pacing threshold values and severity and distribution of CAD. Considering the previous published data which indicate a correlation between presence and severity of ischemia and pacing threshold, lack of this relation in our study may be explained with reduced ischemia in study subjects owing to maximal antiischemic therapy or absence of active ischemia. Another explanation may be that all pacemaker electrodes may have been implanted in relatively nonischemic or noninfarcted myocardium, in an effort to reach the ideal or the most acceptable threshold values in these patients. For this reason, we believe the findings of this study may not be accepted as a conflict with the previously published data. We also investigated the effect of total coronary occlusions on pacing threshold and impedance values. Comparison of pacing threshold and impedance values according to presence or absence of total occlusion of LAD, Cx and RCA in the ICD group revealed a nonsignificant difference. But in the pacemaker group, impedance values were significantly higher if LAD is occluded; on the other hand pacing thresholds were not significantly affected by the location of total occlusion in this group. This study's finding of a significant effect of LAD total occlusions on pacing impedance values only in the pacemaker group, in our opinion, is clinically irrelevant because of small number of patients with LAD total occlusion (n:4).

Study limitations

This study investigated the effect of CAD severity, distribution and LVEF on acute ventricular pacing threshold and lead impedance at the time of pacemaker implantation. Future studies are needed to demonstrate the effect of CAD and LVEF on these pacing parameters during long term follow-up. Future studies should also consider serum electrolyte levels and thyroid function of patients during measurement of pacing parameters. In our institution, pacemaker and ICD leads that were used are of different make and models. Different pacing threshold and impedance values may be obtained with different lead models and multiple lead models are another limitation of this study. Lastly, in this study, the number of patients with total coronary occlusion is too small to make a clinically relevant comparison and larger studies are needed.

Conclusion

To conclude, this study did not find any significant relationship between pacing parameters at implantation and LVEF, severity, distribution of CAD. Ventricular pacing thresholds were found significantly higher ICD group compared with PM group. ICD leads usually have higher impedance values comparing with PM leads. In our study, ventricular PM leads had slightly higher impedance values comparing with ICD leads with a borderline significance. This finding should also be noted. Different lead structures may be responsible for this difference between the ICD and PM leads. Different electrical pacing parameters may also be due to other electrical properties of the myocardium rather than merely EF in ICD patients. Ventricular pacing threshold and impedance values may reflect dissimilar electrical properties of ventricles in both groups. Future studies are needed to investigate correlation between pacing threshold, pacing impedance and electrical properties of diseased ventricles.

Conflict of interest: None declared.

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