Long-term safety and efficacy of right ventricular outflow tract pacing in patients with permanent pacemakers

Kalıcı kalp pili olan hastalarda sağ ventrikül çıkış yolu uyarı yerinin uzun dönem etkinliği ve emniyeti

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ABSTRACT

Objective: The aim of the present study was to investigate long-term safety and change in pacing parameters of right ventricular outflow tract (RVOT) pacing.
Methods: This prospectively designed controlled clinical study comprised patients in Group 1 (n= 16) and Group 2 (n= 16) who were paced in RVOT and right ventricular apex (RVA), respectively, and were selected from patients with permanent pacemakers who were routinely followed up at our pacemaker clinic. Commercially available active fixation leads were used in all patients. Pacing parameters were compared at implant and long-term follow-up visits. Statistical analyses were performed using Pearson Chi-Square, nonparametric Mann-Whitney U and Wilcoxon Signed Ranks tests.
Results: The mean duration of follow-up was 38.3±18.0 months for RVOT and 30.4±20.0 months for RVA (p=0.255). Impedance values, pacing thresholds and R wave amplitudes measured at implant and last pacemaker check did not significantly differ between RVOT and RVA pacing groups. There was no lead dislodgment or any other procedure related complication during follow-up.
Conclusion: Right ventricular outflow tract pacing site is safe and pacing impedance and threshold values are comparable with conventional RVA pacing in the long-term. *(Anadolu Kardiyol Derg 2008; 8: 350-3)*
Key words: Right ventricular outflow tract, pacing, sensing, impedance, complication, threshold

ÖZET

Amaç: Kalıcı kalp pili olan hastalarda sağ ventrikül çıkış yolu uyarı yerinin uzun dönem etkinliğini ve emniyetini araştırmak.
Yöntemler: Prospektif, kontrollü bu klinik çalışmada kalp pili polikliniğinde takip edilen ve sağ ventrikül çıkış yoluna ventrikül elektrodunun yerleştirildiği 16 hasta (Grup 1) ile apikal pozisyona yerleştirilen 16 hasta (Grup 2) karşılaştırıldı. Tüm hastalarda çeşitli firmaların aktif elektrodu kullanılmıştı. Grup içi ve gruplar arası eşik değerleri, direnç ölçümleri ve R dalga boyları implantasyon esnasında ve geç dönemde karşılaştırıldı. İstatistiksel analiz Ki-kare, Mann-Whitney U ve Wilcoxon Rank testleri ile yapıldı.
Bulgular: Uzun dönem takip süreleri Grup 1'de ortalama 38.3±18.0 ay ve Grup 2'de 30.4±20.0 ay olarak bulundu (p=0.255). Eşik değerleri, direnç ölçümleri ve R dalga boyları her iki grup arasında erken ve geç dönemde benzer bulundu. Uzun dönemde işleme bağlı komplikasyon ve elektrod problemi gözlenmedi.
Sonuç: Uzun dönem takipte kalıcı kalp pili olan hastalarda sağ ventrikül çıkış yolu uyarı yeri emniyetli gözükmekte ve apikal uyarı yeriyle karşılaştırıldığında da benzer eşik ve direnç ölçüm değerleri göstermektedir. *(Anadolu Kardiyol Derg 2008; 8: 350-3)*
Anahtar kelimeler: Sağ ventrikül çıkış yolu, kalp pili, eşik, direnç, komplikasyon

Introduction

Right ventricular apex (RVA) for pacing lead position has been traditionally used for many years because of its established safety, stability and easy accessibility. However, recent studies revealed that RVA pacing is associated with asynchronous activation of the left ventricle and resulted in impaired hemodynamic function related to myocardial perfusion defects, especially when pacing duration increased (1, 2). Right ventricular outflow tract (RVOT) pacing has been proposed as an alternative pacing site and resulted in hemodynamic benefits as well as improved myocardial perfusion by enabling synchronous

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activation of the left ventricle (1-4). Although previous work related to RVOT pacing reported its short-term safety and hemodynamic benefit, long-term safety and efficacy of RVOT pacing remains to be confirmed given the paucity of long-term follow-up data (5, 6).

Therefore, the present clinical study aimed to find out first, whether the implanted leads in the RVOT are stable and safe in the long-term and second, whether chronic pacing parameters with RVOT pacing are within the acceptable range or at least as effective and comparable as with RVA pacing site.

Methods

Patients and study protocol

The present study was a prospective controlled clinical study. Patients who underwent pacemaker implantation for indications such as symptomatic bradycardia without a reversible etiology, high-degree and complete atrioventricular block were evaluated during the last routine pacemaker check. Among all patients who were regularly followed up at the pacemaker clinic we detected that ventricular leads were implanted in the RVOT site in 16 patients according to fluoroscopic views taken at implant and electrocardiogram (ECG) tracings that showed positive QRS complexes in inferior leads. Those patients with RVOT leads (Group 1, n=16) were regularly being followed-up at our pacemaker clinic with all their pacing data available. Age and sex matched subjects (Group 2, n=16) who have apically positioned right ventricular leads determined by fluoroscopic views taken at implant were randomly selected according to implant dates matched with RVOT implants without being aware of measured pacing parameters. All patients gave written informed consent for pacemaker implantation before the procedure. The study protocol was approved by the local Ethics Committee of our institution.

Pacemaker follow-up

All patients underwent routine pacemaker check by an experienced technician who was unaware of patients' demographic data and lead position. Seven patients had DDDR pacemakers (Medtronic, n= 4; Vitatron, n=1; Biotronik, n=2) and 25 patients had VVIR pacemakers (Medtronic, n=13; St. Jude, n=5; Vitatron, n=2; Guidant, n=3; Biotronik, n=2). All patients had active bipolar ventricular leads (Medtronic 5076, n=18; St. Jude 1488T and 1688T, n=6; Vitatron ICF09, n=3; Guidant 4096 and 4097, n=3; Biotronik Elox, n=2) positioned either in the RVOT or RVA.

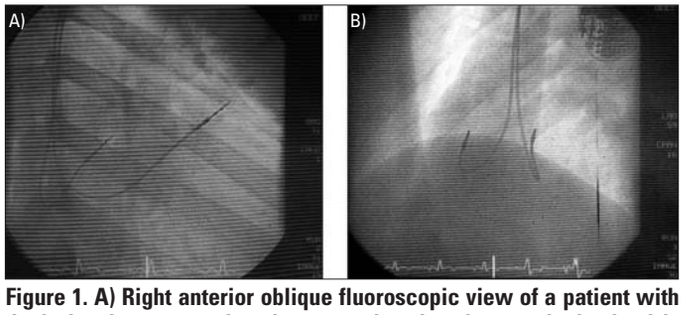

Figure 1. A) Right anterior oblique fluoroscopic view of a patient with dual chamber pacemaker demonstrating that the ventricular lead is positioned high in the right ventricular outflow tract
B) Left anterior oblique fluoroscopic view of a patient with dual chamber pacemaker clearly shows the right ventricular outflow tract lead is directed superiorly and anteriorly reflecting a free wall insertion site.

Implantation technique

Positioning of the RVOT lead performed by two experienced operators at our institution was guided by fluoroscopy, intracardiac signals and surface ECG. After the lead was advanced high into the pulmonary artery with an S-curve shaped stylet, it was withdrawn until the tip fell into the RVOT pointing at 2 or 3 o'clock in the antero-posterior projection. At the same time, the appropriate position was confirmed by 12-lead surface ECG that showed high positive R waves in inferior leads. If the lead tip was stable, it was screwed on the wall of the RVOT. When the pacing threshold was >1.5 V, the lead was repositioned. Figure 1a and 1b show right anterior and left anterior oblique views of a ventricular lead positioned on the free wall of RVOT. Unfortunately, it is not always possible to implant the lead on the true high septal region in every patient because it is more time consuming and requires certain maneuvers. Therefore, we attempted to fix the leads either on the free or anterior wall of RVOT. Sometimes, the maneuver of the lead in RVOT produced frequent ectopy and nonsustained ventricular tachycardia episodes that unfortunately prohibited safe implantation of the lead in RVOT. If fixing the lead in RVOT did not easily go, it was then inserted in RVA. All pacing and sensing parameters were measured at implant using specific pacing system analyzer.

Follow-up period

During the last visit for routine pacemaker check, all devices were interrogated. Measured values regarding pacing parameters at implant and last pacemaker check were compared between RVOT and RVA pacing. All pacing threshold measurements were performed by a constant pulse width at 0.5 ms. None of the patients was on any anti-arrhythmic medication and electrolytes were within normal limits. All pacemaker interrogations were performed by an experienced physician and technician.

Statistical analysis

All statistical analysis were performed by using SPSS for Windows version 10.0 software (SPSS Inc. Chicago, IL, USA). Data are presented as mean±SD. Categorical variables were analyzed by Pearson Chi-Square test. Comparisons of continuous variables between groups were analyzed by using Mann-Whitney U test. Comparisons of continuous and successive variables within group were analyzed by using Wilcoxon Signed Ranks test. A p value <0.05 was considered significant.

Results

Demographic variables are shown in Table 1. Patients in both RVOT and RVA pacing groups showed similar pacing rates of 92.4% and 84.7%, respectively (p=0.171). Mean duration of follow-up period between implant and last pacemaker check were 38.3±18.0 months in RVOT vs 30.4±20.0 months in RVA (p=0.255). As expected, mean impedance values were significantly decreased with time in both groups. However, comparisons between impedance values of RVOT vs RVA pacing at implant and final interrogation revealed no significant change (Table 1). R wave amplitudes did not significantly change with time in each group and were also similar in both groups measured at implant and last follow-up interrogation. None of the patients in both groups developed lead dislodgment or revision during follow-up.

Discussion

In contrast to previous studies that compared pacing parameters at implant and hemodynamic parameters at different time intervals between RVOT vs RVA, the present study aimed to investigate long-term safety of RVOT pacing and compare pacing parameters between RVOT and RVA stimulation sites at a mean follow-up period of 38 months. None of the patients experienced lead dislodgement or any other lead related problem at implant and follow-up in both groups. Capture thresholds, R waves and impedances at implant as well as at long-term follow-up were similar in both RVOT and RVA pacing sites.

A number of studies comparing RVOT with RVA pacing established the benefits of RVOT stimulation site over RVA in terms of improved hemodynamic performance of the left ventricle and less frequent occurrence of myocardial perfusion defects. However, most of them were short-term studies with follow-up periods lasting 3 to 6 months and did not directly compare pacing parameters between RVOT and RVA pacing sites (2-4, 7, 8). Table 2 summarizes published reports in the literature that have directly compared changes in pacing and sensing parameters between both pacing sites. Barin et al. (6) only reported comparison of chronic pacing threshold values at most recent follow-up, as it was indicated. In their report, they did not provide comparative data about chronic sensing and impedance values between RVOT and RVA pacing sites. They reported that there was only one lead dislodgment in RVOT position. Another long-term study published by Vlay SC (5) reported that there was no difference in R wave sensing, pacing threshold and lead impedance between the two pacing sites. Late dislodgment of the RVOT lead occurred 6 days after the implantation in a patient with severe pulmonary hypertension. There were no increased thresholds requiring repositioning either acutely or chronically. In addition to those studies, our present study with a mean follow-up period of 38 months provides important information about the safety and efficacy of RVOT pacing in the long-term. We were not able to detect any significant change in chronic pacing and sensing parameters within RVOT group as well as when compared with RVA pacing. In contrast to above mentioned two studies we did not observe any lead dislodgement in the long-term. Therefore, we may conclude that RVOT pacing site can be considered at least as safe and effective as the apical pacing site in terms of lead stability and pacing parameters. Right ventricular apical pacing by causing left ventricular dysfunction, regional myocardial perfusion defects, increased morbidity and mortality is currently not the ideal target for pacing stimulation site (1, 2, 8-11). Although Erdogan et al. (12) suggested that RVOT pacing might also be responsible for myocardial perfusion defect, it is currently considered as an alternative site instead of RVA pacing given its

Table 1. Comparison of pacing parameters of ventricular leads in the right ventricular outflow tract (RVOT, Group 1) vs right ventricular apical (RVA, Group 2) positions

Parameters	Group 1	Group 2	p
Patients, n	16	16	
Age, years	69.7±8.9 71 (54-85)	70.3±9.7 73 (5-85)	0.866
Male gender, n (%)	10 (63)	12 (75)	0.446
Pacing time, months	38.3±18.0 44 (2-64)	30.4±20.0 23 (7-72)	0.255
Pacing rate, %	92.4±10.0 88 (78-100)	84.7±18.1 76 (50-100)	0.171
Initial impedance, Ohm	809.3±195.4* 831 (372-1100)	913.8±304.9¶ 910 (513-1560)	0.257
Final impedance, Ohm	569.8±137.6 548 (280-771)	633.8±182.1 583 (400-983)	0.271
Initial R wave, mV	11.5±5.4** 11 (6.4-19.3)	13.7±4.5¶¶ 14 (7-19.7)	0.254
Final R wave , mV	10.6±6.2 13 (3-16.7)	11.2±2.6 11 (7.5-15.7)	0.792
Initial pacing threshold, V	0.5±0.2*** 0.5 (0.4-1)	0.6±0.2¶¶¶ 0.6 (0.4-1)	0.073
Final pacing threshold, V	0.8±0.8 0.6 (0.3-2.6)	1.0±0.8 0.9 (0.5-1.2)	0.073
Lead models, n			
Medtronic 5076	8	10	
St Jude 1488 and 1688 T	4	2	
Biotronik Elox (non-steroid)	2	0	
Guidant 4096 and 4097	0	3	
Vitatron ICF09	2	1	

Categorical data are expressed as proportions/percentages and continuous variables are expressed as mean ± SD, med ian (minimum-maximum) values.
Group 1 (initial vs final): * p= 0.001 ; **p= 0.686; ***p=0.093. Group 2 (initial vs. final): ¶ p=0 .006; ¶¶ p=0.5 ; ¶¶¶ p=0.007
Categorical data (gender) were analyzed by Pearson Chi-Square test. Between groups comparisons of continuous variables were analyzed by Mann-Whitney U test. Comparisons of continuous and successive variables within groups were analyzed by using Wilcoxon Signed Ranks test

Table 2. Overview of both short and long-term studies comparing chronic pacing and sensing parameters in right ventricular outflow tract (RVOT) and right ventricular apical (RVA) stimulation sites in patients with permanent pacemakers

Study (Ref)	Patients, n		Follow-up, months	Fixation site		R-Wave, mV		Threshold, V / 0.5ms		Impedance, ohm	
	RVOT	RVA		RVOT	RVA	RVOT	RVA	RVOT	RVA	RVOT	RVA
(6)	20	13	73	Act	Act	-	-	0.13±0.2	0.15±0.2 †	-	-
(2)	12	12	6	Act	Pass	9±5	13±6	1.4±0.7	1.2±0.5	587±174	560±175
(7)*	16	16	7	Act	Pass	-		1.3±0.4	0.9±0.3	571±171	961±225
(5)	52	21	20	Act	Act	12±6	12±6	0.7±0.3	0.9±0.4	598±185	611±234

* - Bifocal RVA and RVOT, † - pulse width at 5 V

effectiveness and proven benefits. In addition, patients with heart failure requiring biventricular pacing in whom coronary sinus pacing is not successful, bifocal pacing at RVA and RVOT can be considered as an alternative technique (13). This issue was investigated in a single center, blinded, randomized, crossover study (BRIGHT study) in patients eligible for cardiac resynchronization therapy. Compared with baseline, bifocal pacing significantly improved ejection fraction, functional class, the 6-minute walk test and the Minnesota Living with Heart Failure scores. In contrast, no significant changes in any parameters were observed in the control group (14). Pacing in the RVOT is safe and results in comparable pacing and sensing values with RVA in the long-term. However, which specific site in the RVOT is most appropriate for establishing better clinical and hemodynamic benefits, remains to be established by further studies. According to a new definition proposed by Mond et al. (15), RVOT was divided into four anatomical regions such as free, anterior, posterior and septal wall areas according to right and left anterior oblique fluoroscopic views. They emphasized that the true septal region of RVOT should be considered as the ideal target for placing the lead. They also established a new maneuver and technique to implant the lead on the true septal region. However, both septal and free wall sites were usually preferred by previous authors as the implantation sites of the RVOT leads.

Study limitations

Limitations of the present study were first, it was not a randomized study and second, it included limited number of patients in both groups. Accordingly, further large based prospective clinical studies are definitely needed for better clarifying the safety and efficacy of RVOT leads and pacing site.

Conclusion

The present study showed that RVOT pacing is as safe and effective as RVA pacing in terms of stable pacing parameters and lead stability in the long-term. Hence, we would like to emphasize again the importance of RVOT stimulation site in chronic pacing and recommend it to be considered as an alternate site of fixing the ventricular leads.

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References

1. De Cock CC, Giudici MC, Twisk JW. Comparison of the hemodynamic effects of right ventricular outflow tract pacing with right ventricular apex pacing: A quantitative review. Europace 2003; 5: 275-8.
2. Tse HF, Yu C, Wong KK, Tsang V, Leung YL, Ho WY, et al. Functional abnormalities in patients with permanent right ventricular pacing. J Am Coll Cardiol 2002; 40: 1451-8.
3. Giudici MC, Thornburg GA, Buck DL, Coyne EP, Walton MC, Paul DL, et al. Comparison of right ventricular outflow tract and apical lead permanent pacing on cardiac output. Am J Cardiol 1997; 79: 209-12.
4. De Cock CC, Meyer A, Kamp O, Visser CA. Hemodynamic benefits of right ventricular outflow tract pacing: comparison with right ventricular apex pacing. Pacing Clin Electrophysiol 1998; 21: 536-41.
5. Vlay SC. Right ventricular outflow tract pacing: Practical and beneficial. A 9-year experience of 460 consecutive implants. Pacing Clin Electrophysiol 2006; 29: 1055-62.
6. Barin ES, Jones SM, Ward DE, Camm AJ, Nathan AW. The right ventricular outflow-tract as an alternative permanent pacing site: long-term follow-up. Pacing Clin Electrophysiol 1991; 14: 3-6.
7. Res JC, Bokern MJ, Vos DH. Characteristics of bifocal pacing: right ventricular apex versus outflow tract. An interim analysis. Pacing Clin Electrophysiol 2005; 28 Suppl 1: S36-38.
8. Schwaab B, Frohlig G, Alexander C, Kindermann M, Hellwig N, Schwerdt H, et al. Influence of right ventricular stimulation site on left ventricular function in atrial synchronous ventricular pacing. J Am Coll Cardiol 1999; 33: 317-23.
9. Wilkoff BL, Cook JR, Epstein AE, Greene HL, Hallstrom AP, Hsia H, et al. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: the Dual Chamber and VVI Implantable Defibrillator (DAVID) Trial. JAMA 2002; 288: 3115-23.
10. Andersen HR, Nielsen JC, Thomsen PE, Thuesen L, Mortensen PT, Vesterlund T, et al. Long-term follow-up of patients from a randomised trial of atrial versus ventricular pacing for sick-sinus syndrome. Lancet 1997; 350: 1210-6.
11. O'Keefe JH Jr, Abuissa H, Jones PG, Thompson RC, Bateman TM, McGhie AI, et al. Effect of chronic right ventricular apical pacing on left ventricular function. Am J Cardiol 2005; 95: 771-3.
12. Erdoğan O, Altun A, Durmuş-Altun G, Özbay G. Inferolateral myocardial perfusion defect caused by right ventricular outflow tract pacing. Pacing Clin Electrophysiol 2004; 27: 808-11.
13. Vlay SC. Alternatives when coronary sinus pacing is not possible. Pacing Clin Electrophysiol 2003; 26: 4-7.
14. Res JC, Bokern MJ, de Cock CC, van Loenhout T, Bronzwaer PN, Spierenburg HA; on behalf of the BRIGHT investigators. The BRIGHT study: bifocal right ventricular resynchronization therapy: a randomized study. Europace 2007; 9: 857-61.
15. Mond HG, Hillock RJ, Stevenson IH, McGavigan AD. The right ventricular outflow tract: The road to septal pacing. Pacing Clin Electrophysiol 2007; 30: 482-91.