

Comparison of DDD versus VVIR pacing modes in elderly patients with atrioventricular block

Atriyoventriküler tam bloklü yaşlı hastalarda DDD ve VVIR kalıcı kalp pili modlarının karşılaştırılması

Barış Kılıçaslan, M.D., Fahriye Vatansever Ağca, M.D.,# Esin Evren Kılıçaslan, M.D.,† Ozan Kınay, M.D.,‡ Kürşat Tigen, M.D., Çayan Çakır, M.D.,§ Cem Nazlı, M.D.,§ Oktay Ergene, M.D.§

Department of Cardiology, Medeniyet University Göztepe Training and Research Hospital, İstanbul; #Department of Cardiology, Bahar Hospital, Bursa; †Department of Pschiatry, Erenkoy Pschiatry and Neurology Training and Research Hospital, İstanbul; ‡Department of Cardiology, Tınaztepe Hospital, İzmir; §Department of Cardiology, Atatürk Training and Research Hospital, İzmir

ABSTRACT

Objectives: Dual-chamber pacing is believed to have an advantage over single-chamber ventricular pacing. The aim of this study was to determine whether elderly patients who have implanted pacemakers for complete atrioventricular block gain significant benefits from dual-chamber (DDD) pacemakers compared with single chamber ventricular (VVIR) pacemakers.

Study design: This study was designed as a randomized, two-period crossover study-each pacing mode was maintained for 1 month. Thirty patients (16 men, mean age 68.87±6.89 years) with implanted DDD pacemakers were submitted to a standard protocol, which included an interview, pacemaker syndrome assessment, health related quality of life (HRQoL) questionnaires assessed by an SF-36 test, 6-minute walk test (6MWT), and transthoracic echocardiographic examinations. All of these parameters were obtained on both DDD and VVIR mode pacing. Paired data were compared.

Results: HRQoL scores were similar, and 6MWT results did not differ between the two groups. VVIR pacing elicited significant enlargement of the left atrium and impaired left ventricular diastolic functions as compared with DDD pacing. Two patients reported subclinical pacemaker syndrome, but this was not statistically significant.

Conclusion: Our study revealed that in active elderly patients with complete heart block, DDD pacing and VVIR pacing yielded similar improvements in QoL and exercise performance. However, after a short follow-up period, we noted that VVIR pacing caused significant left atrial enlargement and impaired left ventricular diastolic functions.

ÖZET

Amaç: İki odacıklı uyarı veren kalıcı kalp pillerinin tek odacıklı uyarı verenlere göre belirgin üstünlüğüne inanılmaktadır. Bu çalışmanın amacı, atriyoventriküler (AV) tam blok tanısı ile kalıcı kalp pili takılan yaşlı hastalarda, tek odacıklı ventriküler (VVIR) kalıcı kalp piliyle karşılaştırıldığında iki odacıklı (DDD) kalıcı kalp pillerinin belirgin yararlarının olup olmadığının saptanmasıdır.

Çalışma planı: Bu çalışma randomize, iki periyotlu çapraz ve her kalp pili mod periyodu 1 ay sürecek şekilde tasarlandı. DDD kalp pili takılan otuz hastaya (16 erkek, ortalama yaş 68.87±6.89) standart bir protokol uygulandı. Protokolde karşılıklı görüşme, pacemaker sendromu değerlendirilmesi, sağlıkla ilişkili yaşam kalitesi (SİYK) anketi (SF-36 testi), 6 dakika yürüme testi ve transtoraksik eko-kardiyografik inceleme yapıldı. Bu değişkenlerin tümü her iki DDD ve VVIR modunda uygulandı. Elde edilen veriler karşılaştırıldı.

Bulgular: SİYK skorları benzer bulundu. Altı dakika yürüme testi sonuçları iki grupta da benzerdi. DDD mod kalp pili ile karşılaştırıldığında, VVIR mod kalp pilinde sol atriyumun genişlediği, sol ventrikül diyastolik fonksiyonlarının bozulduğu saptandı. İki hastada istatistiksel anlama ulaşmayan subklinik pacemaker sendromu saptandı.

Sonuç: AV tam blok tanısı ile kalıcı kalp pili takılan aktif yaşlı hastalarda yaşam kalitesi ve egzersiz performansı açısından DDD ve VVIR mod kalp pili arasında fark saptanmamıştır. Fakat, bir aylık kısa takip süresine rağmen VVIR mod kalp pili ile sol atriyumda genişleme ve sol ventrikül diyastolik fonksiyonlarında bozulma saptanmıştır.

Received: August 01, 2011 Accepted: May 18, 2012

Correspondence: Dr. Barış Kılıçaslan. Manavkuyu Mah., 249/4 Sok., No 2, Altın sitesi A Blok 16, Bayraklı, İzmir, Turkey.
Tel: +90 216 - 566 40 00 e-mail: kilicaslanbaris@yahoo.com

© 2012 Turkish Society of Cardiology

Pacemaker (PM) technology and clinical practice permit the use of either single-chamber ventricular pacemakers (VVIR) or dual-chamber pacemakers (DDD) for patients who require cardiac pacing. Ventricular pacemakers are less expensive, are easier to implant, and have longer service lives than dual-chamber pacemakers. However, dual-chamber pacing has an advantage over single-chamber ventricular pacing in that it more closely resembles cardiac physiology by maintaining atrioventricular (AV) synchrony and dominance of the sinus node.^[1] Because of this, it may reduce cardiovascular morbidity^[2-4] and mortality, and may contribute to survival and improved quality of life (QoL).^[3-5] According to previous data, both DDD and VVIR modes lead to similar improvements in exercise tolerance.^[6-8] Our study was designed to assess the influence of different pacing modes on the health related QoL (HRQoL), 6-minute walk test (6MWT), and echocardiographic parameters in elderly patients with dual chamber pacemakers implanted for AV block.

PATIENTS AND METHODS

We studied 30 consecutive patients aged 68.9 ± 6.9 years (men 69.4 ± 2.2 years; 16 men) that had been referred for permanent pacemaker implantation. Patients were included in the study if they had an electrocardiogram (ECG) that showed sinus rhythm and complete heart block before implantation, and if they had been able to do the daily activity tests described below. Patients with left ventricular dysfunction, acute coronary syndromes, sick sinus syndrome, hypertro-

phic obstructive cardiomyopathy, left ventricular systolic dysfunction, sinus bradycardia with AV block, Mobitz type 1 AV block, supraventricular tachycardia, and transient AV block were excluded from the study. Informed consent was obtained from each patient and the study was approved by the local research ethics committee.

Study design

The study included two periods with crossover comparisons of DDD and VVIR modes. Each mode was maintained for one month. At enrollment, clinical baseline characteristics were assessed and a 12-lead surface ECG was obtained from each patient. After patient selection, a non-permanent transvenous pacemaker was placed and the pacing rate was programmed to 60 beats per minute. Next, a dual chamber pacemaker was implanted and the patient was randomized to either VVIR or DDD modes (mode 1). One month later the patient returned for his/her first visit. A standard protocol was submitted which included PM syndrome assessment (breathlessness, pulsation, dizziness, blackout, wheeze, fatigue, palpitation, and cough), HRQoL questionnaires assessed by an SF-36 test,^[9] 6-minute walk test,^[10] and transthoracic echocardiographic examinations with Doppler

Abbreviations:

AV	Atrioventricular
DDD	Dual-chamber pacemakers
Ea	Early phase of diastole
ECG	Electrocardiogram
E	Peak early velocities
HRQoL	Health related QoL
PM	Pacemaker
QoL	Quality of life
VVIR	Single-chamber ventricular pacemakers

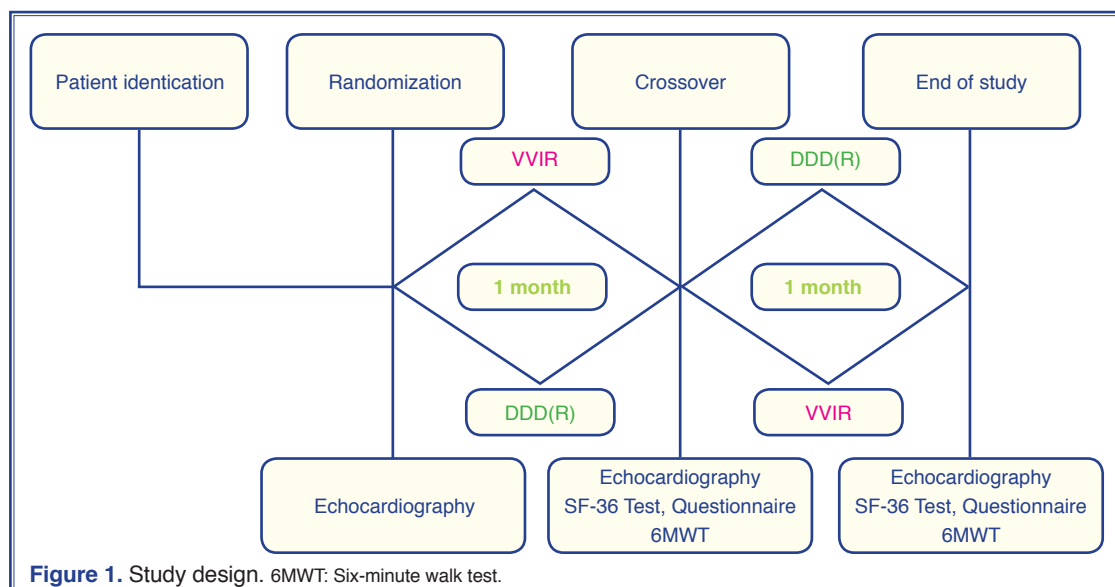


Figure 1. Study design. 6MWT: Six-minute walk test.

Table 1. Basic demographic data

	Male			Female			Total		
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD
Patients	16	53.3		14	46.6		30	100	
Age			69.4±2.2			68.5±1.1			68.9±6.9
Left ventricular ejection fraction			58.6±3.5			62.1±4.4			60.2±4.2
Hypertension	10	62.5		8	57.1		18	60	
Coronary artery diseases	4	25		2	14.3		6	20	
Type II diabetes mellitus	5	31.2		4	28.5		9	30	

tissue imaging (DTI) measurements. Atrial fibrillation (AF) was detected by asking patients for new-onset palpitations and by either analysing the pacemakers rhythm memory or by a 24 h rhythm holter ECG. After data were collected, the patients' pacemaker modes were reprogrammed to the alternative modes (mode 2). One month later, patients were reevaluated. The same protocol as previously described was once again performed on the patients. After this period, the study was stopped and all patients were returned to DDD pacing (Fig. 1).

Pacemaker programming

In all modes the lower and upper rates were set at 60 and 120 beats/minute, respectively. The range of a-v delay was set as 120-150 ms. In VVIR mode, the rate response threshold was set at medium, and the curve was set between 6 and 8.

Echocardiography

All echocardiographic studies were performed by two experienced operators using a commercially available system (GE Vivid 3, General Electrics, USA). Two-dimensional and M-mode measurements were performed according to the recommendations of the American Society of Echocardiography, working together with the European Association of Echocardiography.^[11] Patients were examined while lying in the left lateral supine position. Echocardiography was performed twice during the study: it was repeated at the end of each one month period prior to reprogramming of pacing parameters. The left ventricular ejection fraction (LVEF) was determined using the modified Simpson's method (area-length). Left atrial areas and dimensions were obtained from apical four chamber, parasternal long axis, and apical two chamber views. Left atrial volumes were calculated with

the ellipsoid formula. Transmitral flow patterns were recorded from apical four-chamber views with a 3-5 mm pulsed-sample Doppler volume placed between mitral valve tips in diastole during five consecutive cardiac cycles. Mitral inflow (at end expiration) peak early velocities (E) were recorded.^[12] The tissue Doppler program was set in pulsed-wave Doppler mode. A 3-5 mm sample volume was placed at both the lateral and septal corners of the mitral annulus. The early phase of diastole (Ea) was recorded.^[13] In order to calculate the E/Ea ratio, the average of the velocities of the septal and lateral mitral annulus was used.

Statistical analyses

Analyses were performed using an SPSS 14.0 for Windows package program and all hypothesis testing was performed at the level of $\alpha=0.05$ significance. Parameters normally distributed were compared with the paired Student's t-test. Analyses of variance for repeated measures ANOVA and Fisher's Full Probability Test (Fisher's Exact Test) were used. For pairwise comparisons the Bonferroni test was used.

RESULTS

The mean age of the patients was 68.8±6.9 years. The average ejection fraction was measured to be 60.2±4.2 by the ellipsoid formula. Eighteen patients had hypertension, six had coronary artery disease (CAD), and nine had type II diabetes mellitus. Basic demographic data are presented in Table 1. The first pacing mode (DDD or VVIR) and the order of implantation did not affect our study results (Table 2).

Average walking distances were found to be similar between the two groups; 419±102 m for the VVIR group and 419±93 m for the DDD group ($p=0.86$) (Table 2). We evaluated 8 different parameters for the

Table 2. Quality of life test (SF-36), six-minute walk and echocardiography results

	Group 1 (VVIR) Mean±SD	Group 2 (DDD) Mean±SD	p	p*
Physical function	86±20	84±14	0.39	0.32
Physical role	65±44	66±43	0.95	0.51
Emotional role	92±27	85±29	0.27	0.23
Pain	93±14	87±18	0.04	0.14
General health	67±13	64±17	0.43	0.58
Energy	60±28	67±14	0.13	0.14
Social function	94±10	89±17	0.08	0.41
Mental health	71±13	72±12	0.86	0.54
Six-minute walk test	419±102	419±93	0.49	0.21
Left atrial volume	38.5±14.3	34.0±13.9	0.01	0.79
E/Ea	7.5±2.0	7.1±1.8	0.01	0.52

p<0.05; *Repeated measures ANOVA (Analyses of the order effect). E: Peak early velocities; Ea: Early phase of diastole.

physical function subscale and the physical role subscale of SF-36. There were no significant differences in these scores between the ventricular- pacing and the dual-chamber-pacing groups. Only parameters of pain scores were found to be higher with DDD pacing ($p=0.05$) (Table 2). Echocardiographic data were available in 28 patients. We excluded two patients who had inadequate echocardiographic image quality. The left atrial volume was found to be smaller within the DDD pacing group (VVIR group 38.5 ± 14.3 vs. DDD group 34.0 ± 13.9 , $p=0.03$) (Table 2). The E/Ea ratio was significantly lower in the DDD pacing group (VVIR group 7.5 ± 2.0 and DDD group 7.1 ± 1.8 , $p=0.01$).

Symptoms of PM syndrome were observed in two patients during VVIR stimulation. However, this was not statistically significant ($p=0.48$).

DISCUSSION

Our elderly population with dual-chamber pacemakers inserted for complete AV block benefited equally from both modes of pacing that were tested. However, some echocardiographic parameters improved with DDD pacing more than with VVIR pacing.

Ouali et al.^[14] demonstrated that elderly patients (over 70 years) with DDD pacing had a better QoL than did patients with VVIR pacing. CTOPP and MOST showed that pacing itself had a significant benefit on QoL. This significant benefit could be achieved with pacing and with the restoration of chronotrop-

ic competence. In both trials, pacing mode was not found to be important.^[9,15,16] In our study, seven SF-36 test parameters were similar in both groups. Only the sub-parameter of pain was better in the VVIR group. However, this finding was not considered to be important.

Previous studies have demonstrated similar exercise tolerance results in both pacing modes.^[7,14,17,18] We also observed that exercise performance assessed by the 6MWT was not significantly influenced by the pacing mode.

Höjjer et al.^[19] found smaller left atrial end-systolic diameters with DDDR pacing than with VVIR pacing. Ouali et al.^[14] showed that VVIR pacing elicited significant enlargement of the left atrium despite a relatively short follow-up period of 3 months. In our study, left atrial volume was significantly smaller with DDD pacing as compared to VVIR pacing. Previous studies have suggested that LA enlargement was one of the major risk factors for AF.^[20,21] As a consequence of atrial enlargement, it might be speculated that AF may develop more frequently with VVI pacing as compared to DDD. However, in our study AF was not detected in any of our patients. Left atrial volumes were different between groups. However, these differences were not found to be predictors of health status (QoL) or exercise capacity of the patients. The follow-up period of our study was restricted to one month. With a longer follow-up period, the volume

differences may reflect electrocardiographic and echocardiographic parameters. E/Ea ratios are indicators of LV filling pressures.^[22] In our study, E/Ea ratios were significantly smaller with DDD pacing. Therefore, we can conclude that LV filling pressures with DDD pacing are smaller than those with VVIR pacing. This finding might suggest that DDD pacing is more physiological than VVIR pacing. On the other hand, DDD pacing also provided better left ventricular diastolic functions in our study.

According to previous data, PM syndrome was found in 5-15% of patients with VVI pacing.^[23] The MOST study demonstrated that the frequency of patients who were switched to DDD pacing due to PM syndrome was 1% per year; all of these patients began with VVIR pacing.^[9] Sulke et al.^[15] found that subclinical PM syndrome occurred in 75% of patients after switching from DDD to VVI pacing mode. In our study, two patients reported fatigue and tiredness with VVIR pacing that improved after switching to DDD pacing. The 6MWT and QoL tests of these patients were not different from those of the others. This finding was considered as subclinical PM syndrome, however, it did not reach statistical significance.

Today, in clinical practice, patients who receive a PM are usually over 60 years old.^[24-26] Hemodynamic studies have revealed the importance of atrial contribution to ventricular filling with advancing age.^[27,28] In our study, although it was a short follow-up period, left atrial volumes were calculated to be significantly larger, and left ventricular diastolic functions were observed to be impaired with VVIR pacing. As a consequence to atrial enlargement, AF may develop in a longer term of follow-up. In elderly patients with complete heart block, efforts should be made to maintain AV synchrony, and DDD pacing should be the preferred pacing mode.

Limitations

Patients with permanent cardiac PM may develop PM syndrome over a long period of time. Our follow-up period was one month for each mode. In order to perform more accurate monitoring of PM syndrome, a longer term of follow-up is needed.

Conclusion

Our study revealed that in active elderly patients with complete heart block, DDD pacing and VVIR pac-

ing might yield to similar improvements in QoL and exercise performance. However, after a short follow-up period, VVIR pacing caused significant left atrial enlargement and impaired diastolic functions, which could increase the risk of AF and PM syndrome in these patients.

Conflict-of-interest issues regarding the authorship or article: None declared

REFERENCES

1. Stewart WJ, Dicola VC, Harthorne JW, Gillam LD, Weyman AE. Doppler ultrasound measurement of cardiac output in patients with physiologic pacemakers. Effects of left ventricular function and retrograde ventriculoatrial conduction. *Am J Cardiol* 1984;54:308-12. [\[CrossRef\]](#)
2. Lamas GA, Pashos CL, Normand SL, McNeil B. Permanent pacemaker selection and subsequent survival in elderly Medicare pacemaker recipients. *Circulation* 1995;91:1063-9.
3. Lamas GA, Orav EJ, Stambler BS, Ellenbogen KA, Sgarbossa EB, Huang SK, et al. Quality of life and clinical outcomes in elderly patients treated with ventricular pacing as compared with dual-chamber pacing. *Pacemaker Selection in the Elderly Investigators. N Engl J Med* 1998;338:1097-104. [\[CrossRef\]](#)
4. Connolly SJ, Kerr CR, Gent M, Roberts RS, Yusuf S, Gillis AM, et al. Effects of physiologic pacing versus ventricular pacing on the risk of stroke and death due to cardiovascular causes. *Canadian Trial of Physiologic Pacing Investigators. N Engl J Med* 2000;342:1385-91. [\[CrossRef\]](#)
5. Toff WD, Camm AJ, Skehan JD; United Kingdom Pacing and Cardiovascular Events Trial Investigators. Single-chamber versus dual-chamber pacing for high-grade atrioventricular block. *N Engl J Med* 2005;353:145-55. [\[CrossRef\]](#)
6. Oldroyd KG, Rae AP, Carter R, Wingate C, Cobbe SM. Double blind crossover comparison of the effects of dual chamber pacing (DDD) and ventricular rate adaptive (VVIR) pacing on neuroendocrine variables, exercise performance, and symptoms in complete heart block. *Br Heart J* 1991;65:188-93.
7. Menozzi C, Brignole M, Moracchini PV, Lolli G, Bacchi M, Tesorieri MC, et al. Inpatient comparison between chronic VVIR and DDD pacing in patients affected by high degree AV block without heart failure. *Pacing Clin Electrophysiol* 1990;13:1816-22. [\[CrossRef\]](#)
8. Sulke N, Chambers J, Dritsas A, Sowton E. A randomized double-blind crossover comparison of four rate-responsive pacing modes. *J Am Coll Cardiol* 1991;17:696-706. [\[CrossRef\]](#)
9. Newman D. Relationships between pacing mode and quality of life: evidence from randomized clinical trials. *Card Electrophysiol Rev* 2003;7:401-5. [\[CrossRef\]](#)
10. Solway S, Brooks D, Lacasse Y, Thomas S. A qualitative systematic overview of the measurement properties of functional walk tests used in the cardiorespiratory domain. *Chest* 2001;119:256-70. [\[CrossRef\]](#)

11. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Recommendations for chamber quantification. *Eur J Echocardiogr* 2006;7:79-108. [\[CrossRef\]](#)
12. Quiñones MA, Otto CM, Stoddard M, Waggoner A, Zoghbi WA; Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. Recommendations for quantification of Doppler echocardiography: a report from the Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. *J Am Soc Echocardiogr* 2002;15:167-84. [\[CrossRef\]](#)
13. Oki T, Tabata T, Yamada H, Wakatsuki T, Shinohara H, Nishikado A, et al. Clinical application of pulsed Doppler tissue imaging for assessing abnormal left ventricular relaxation. *Am J Cardiol* 1997;79:921-8. [\[CrossRef\]](#)
14. Ouali S, Neffeti E, Ghouli K, Hammas S, Kacem S, Gribaa R, et al. DDD versus VVIR pacing in patients, ages 70 and over, with complete heart block. *Pacing Clin Electrophysiol* 2010;33:583-9. [\[CrossRef\]](#)
15. Newman D, Lau C, Tang AS, Irvine J, Paquette M, Woodend K, et al.; CTOPP Investigators. Effect of pacing mode on health-related quality of life in the Canadian Trial of Physiologic Pacing. *Am Heart J* 2003;145:430-7. [\[CrossRef\]](#)
16. Lamas GA, Lee KL, Sweeney MO, Silverman R, Leon A, Yee R, Marinchak RA, et al. Ventricular pacing or dual-chamber pacing for sinus-node dysfunction. *N Engl J Med* 2002;346:1854-62. [\[CrossRef\]](#)
17. Channon KM, Hargreaves MR, Cripps TR, Gardner M, Ormerod OJ. DDD vs. VVI pacing in patients aged over 75 years with complete heart block: a double-blind crossover comparison. *Q J Med* 1994;87:245-51.
18. Hargreaves MR, Channon KM, Cripps TR, Gardner M, Ormerod OJ. Comparison of dual chamber and ventricular rate responsive pacing in patients over 75 with complete heart block. *Br Heart J* 1995;74:397-402. [\[CrossRef\]](#)
19. Höijer CJ, Brandt J, Willenheimer R, Juul-Möller S, Boström PA. Improved cardiac function and quality of life following upgrade to dual chamber pacing after long-term ventricular stimulation. *Eur Heart J* 2002;23:490-7. [\[CrossRef\]](#)
20. Schotten U, Verheule S, Kirchhof P, Goette A. Pathophysiological mechanisms of atrial fibrillation: a translational appraisal. *Physiol Rev* 2011;91:265-325. [\[CrossRef\]](#)
21. Neuberger HR, Schotten U, Blaauw Y, Vollmann D, Eijsbouts S, van Hunnik A, et al. Chronic atrial dilation, electrical remodeling, and atrial fibrillation in the goat. *J Am Coll Cardiol* 2006;47:644-53. [\[CrossRef\]](#)
22. Gottdiener JS, Bednarz J, Devereux R, Gardin J, Klein A, Manning WJ, et al. American Society of Echocardiography recommendations for use of echocardiography in clinical trials. *J Am Soc Echocardiogr* 2004;17:1086-119. [\[CrossRef\]](#)
23. Heldman D, Mulvihill D, Nguyen H, Messenger JC, Rylaarsdam A, Evans K, et al. True incidence of pacemaker syndrome. *Pacing Clin Electrophysiol* 1990;13:1742-50. [\[CrossRef\]](#)
24. Bayata S, Yeşil M, Arıkan E, Postacı N, Berilgen R, Ceylan Ö ve ark. Bir kardiyoloji kliniğinde ardışık 2 ayrı dönemde takılan 1650 kalıcı kalp pilinin retrospektif karşılaştırmalı incelemesi. *Anadolu Kardiyoloji Dergisi* 2010;10:130-4. [\[CrossRef\]](#)
25. Kiliçaslan F. Does our permanent pacemaker implantation practice change?. *Anadolu Kardiyol Derg* 2010;10:135-6.
26. Erdinler İ. Türkiye’de kalıcı kalp pili implantasyonunun durumu. *Türk Kardiyol Dem Arş* 2004;32:115-6.
27. Frielingsdorf J, Dür P, Gerber AE, Vuillomenet A, Bertel O. Physical work capacity with rate responsive ventricular pacing (VVIR) versus dual chamber pacing (DDD) in patients with normal and diminished left ventricular function. *Int J Cardiol* 1995;49:239-48. [\[CrossRef\]](#)
28. Kuo LC, Quiñones MA, Rokey R, Sartori M, Abinader EG, Zoghbi WA. Quantification of atrial contribution to left ventricular filling by pulsed Doppler echocardiography and the effect of age in normal and diseased hearts. *Am J Cardiol* 1987;59:1174-8. [\[CrossRef\]](#)

Key words: Aged; cardiac pacing, methods; cross-over studies; DDD pacing; heart block/therapy; pacemaker, artificial; quality of life; VVIR pacing.

Anahtar sözcükler: Yaşlı; pacemaker, yöntemler; çapraz çalışma; DDD kalp pili; kalp bloğu/tedavi; kalp pili; yaşam kalitesi; VVIR kalp pili.