

Similar pattern of diastolic function adaptation of both ventricles to programmed atrioventricular interval modification in patients with DDD pacing

DDD pacing`li hastalarda programlanmış atriyoventriküler intervalin modifikasyonuna her iki ventrikülün benzer diyastolik fonksiyon adaptasyon paterni

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ABSTRACT

Objective: To evaluate both left ventricular (LV) and right ventricular (RV) diastolic performance adaptation to variable atrioventricular interval (AVI), in patients with DDD pacing for complete heart block and to investigate a possible interaction between LV and RV in this specific cohort of patients.

Methods: We studied 22 consecutive patients (mean age 65.2 ± 14.3) who underwent DDD pacemaker implantation following admission for complete heart block. One day following implantation, patients were paced at 3 different pacing modes, under the same programmed heart rate and a different AVI (100, 150 and 200 ms respectively). Standard Doppler echocardiography of mitral and tricuspid valve inflow was performed to evaluate LV and RV diastolic function, during each pacing mode.

Results: Left ventricular and RV diastolic performance adaptation to variable AVI modifications was similar, showing a progressive increase of late diastolic filling velocities and a subsequent decrease of E/A wave ratios following AVI prolongation. A short AVI of 100 or 150 ms was associated with improved LV and RV diastolic filling dynamics.

Conclusions: In elderly patients with complete heart block and unimpaired systolic function undergoing DDD pacemaker implantation, both ventricles share a similar pattern of diastolic function adaptation to AVI modifications and that might be the reflection of ventricular interaction under this specific pacing mode. (*Anadolu Kardiyol Derg 2006; 6: 243-7*)

Key words: DDD pacing, diastole, AVI, adaptation, ventricular interaction

ÖZET

Amaç: Bu çalışmanın amacı tam atriyoventriküler (AV) blok nedeni ile DDD pacemaker takılan hastalarda değişen AV interval'e (AVI) hem sol (LV) hem sağ (RV) ventrikül diyastolik fonksiyonların adaptasyonunu değerlendirmek ve bu spesifik hasta grubunda LV ile RV arasındaki olası etkileşimi araştırmaktır.

Yöntemler: Tam AV blok nedeni ile kliniğe kabul sonrası DDD pacemaker implantasyonu yapılan 22 ardışık hasta (ortalama yaş 65.2 ± 14.3 yıl) çalışmaya alındı. İmplantasyon'dan 1 gün sonra hastalar 3 farklı pacing modda aynı programlanmış kalp hızında ve farklı AVI de (100 ms, 150 ms ve 200 ms, sırası ile) pacing edildi. Her pacing modda, LV ve RV diyastolik fonksiyonları değerlendirmek amacı ile mitral ve triküspid akımları standart Doppler ekokardiyografi ile incelendi.

Bulgular: Değişen AVI'lere LV ve RV diyastolik performansların adaptasyonu benzer idi, her AVI uzaması sonunda geç diyastolik doluş hızları progresif olarak artmıştır ve takiben E/a oranları azalmıştır. Kısa AVI (100 ms veya 150 ms) LV ve RV diyastolik doluş dinamiklerinin iyileşmesine neden olmuştur.

Sonuçlar: Tam AV blok'lu ve korunmuş sistolik fonksiyonu olan DDD pacemaker takılan yaşlı hastalarda, her iki ventrikül AVI modifikasyonlara benzer diyastolik fonksiyonun adaptasyon paterni paylaşmaktadır ve bu spesifik pacing modda her iki ventrikülün etkileşiminin göstergesi olabilir. (*Anadolu Kardiyol Derg 2006; 6: 243-7*)

Anahtar kelimeler: DDD pacing, diyastol, AVI, adaptasyon, ventriküler etkileşim

Introduction

In patients receiving a dual chamber DDD pacemaker, atrioventricular interval (AVI) is a critical parameter to increase hemodynamics since an appropriately timed atrial systole can imp-

rove left ventricular filling and stroke volume according to the Frank-Starling law. Previous reports have been focused mainly on LV diastolic function optimization following DDD pacemaker implantation demonstrating a large inter-individual variability of the optimal AVI (1-3). In contrast, reports evaluating right ventri-

cular diastolic function adaptation to different AVIs following DDD pacemaker implantation are sparse and limited (4,5).

Doppler echocardiography is a well-established modality for the evaluation of LV diastolic filling patterns in normal population and in various types of pacing and remains up to date the standard method for the assessment of the optimal AVI in DDD pacing mode (2). In normal subjects, standard Doppler-derived LV filling indexes correlate significantly to those of the RV, demonstrating the close interaction between the two ventricles (6,7). This observation might be the reflection of ventricular interdependence phenomenon, described almost four decades ago (8). Anyway, patients with complete heart block are usually old and ventricular interdependence might not exist.

We have recently published a paper assessing LV diastolic function and atrial natriuretic peptide levels adaptation to variable AVIs in patients with complete heart block and normal LV and RV systolic function undergoing DDD pacing (9). In the same population we sought to investigate the effects of the variation of AVI on both RV and LV diastolic Doppler indices. On these grounds, the present study was performed in order to elucidate two major issues. The first one is if both ventricles exhibit a similar pattern of diastolic function adaptation to variable programmed AVI during DDD pacing, demonstrating indirectly the presence of ventricular interaction in elderly patients, while the second issue addresses the need for RV diastolic filling assessment in this cohort of patients, when optimizing the AVI.

Methods

Study patients

We studied prospectively 22 consecutive patients (mean age 65.2 ± 14.3 years, 12 male) with complete AV block and normal LV and RV systolic function and without any medical history (9). All patients were in NYHA functional class I and underwent a DDD pacemaker implantation following detection of third degree AV block. Atrial and ventricular leads had been positioned in the right atrial appendage and in the right ventricular apex respectively. Exclusion criteria were determined as a poor echocardiographic window, spontaneous rhythm at rest and the presence of significant systolic dysfunction, valve disease or pulmonary disease.

Pacing protocol

All patients were assessed the day following pacemaker implantation and they were evaluated under the same protocol as previously described (9). They were examined in the supine position and the pacemaker was programmed to a rate of 80 beats / min in order to ensure a sequential AV pacing. Patients were then paced for 3 successive continuous pacing periods of 30 minutes duration, using 3 selective AVIs (100, 150 and 200 ms) respectively in a randomized fashion. During each specific pacing period, LV and RV diastolic performances were evaluated by Doppler echocardiography.

Blood pressure was evaluated before and at the end of each pacing period in order to secure diastolic function assessment under the same haemodynamic conditions. The data collected, were categorized in three groups according to the specific AVI of DDD pacing under which they were obtained. To evaluate the effect of each specific AVI on LV and RV diastolic filling dynamics, we compared the data obtained under the 3 different stimulation modes.

Echocardiography

All patients underwent complete transthoracic echocardiography and Doppler study before pacemaker implantation, 24 hours later (before pacing protocol initiation) and at 1 year follow-up. Additionally LV and RV Doppler systolic and diastolic indices were recorded during the 3 variable predefined AVIs according to the methodology of the study. All antihypertensive medications were withdrawn before any echocardiographic evaluation.

Transthoracic M-mode, 2-D and spectral Doppler (pulsed and continuous wave) echocardiographic studies were performed with a SIGMA "IRIS" apparatus (Kontron Instruments, France) equipped with 2.8-3.5 MHz transducers. Standard M-mode measurements were obtained from the left parasternal long axis view according to the recommendations of the American Society of Echocardiography (10) and left ventricular fractional shortening was obtained. LV and RV diastolic indices were accessed from the apical four-chamber view by positioning a sized 2-4 mm sample volume at the tips of mitral and tricuspid leaflets accordingly, during diastole and at end expiration. The following RV and LV diastolic indices were calculated: peak velocity of E wave, representing early filling; peak velocity of A wave, representing late filling; ratio of peak early to peak late velocity (E/A); deceleration time of E wave (DTE); and finally filling time (FT). Furthermore, from the apical 5-chamber view and by positioning a sized 2-4 mm sample volume at the LV outflow tract, the LV outflow tract velocity time integral was assessed (LVOT VTI). All Doppler indices were measured at six consecutive beats and their values were averaged.

Echocardiographic studies were recorded on SVHS videotape and were analyzed offline by two experienced operators, blinded to the clinical data. Intraobserver variability was established by having one observer to measure echocardiographic data on at least two occasions in 10 subjects selected at random from the patient population under study ($r=0.94$). Interobserver variability was determined by having a second operator to measure independently the same parameters in these subjects ($r=0.89$).

Follow-up

All patients were followed for 1 year in the outpatient pacemaker clinic. Patients were reevaluated by echocardiography 1 year following implantation and the echocardiographic examination was performed under the baseline (implantation) conditions (same AVI, pacing at 80 bpm for at least 30 minutes).

An informed consent has been obtained from all patients, which comprised the study population. The study complied with the Declaration of Helsinki and was approved by the Institutional Committee on human research of our hospital.

Statistical analysis

Results are expressed as mean values \pm SD. For all variables (except deceleration time of E wave) ANOVA for repeated measurements (multivariate approach) was performed. For paired comparisons "t-test" was implemented, verified by the "Tukey's honest significant difference". A linear regression model was used in order to correlate diastolic and systolic Doppler indices obtained during the 3 different stimulation modes. Values of $p < 0.05$ were considered to be statistically significant.

Results

Of the total 22 patients, 20 were discharged on DDD pacing mode with an AVI of 100 ms, while in 2 an AVI of 150 ms, was selected due to a more favorable echocardiographic diastolic filling

performance. There was no AVI modification throughout the follow-up period. That means all patients were under the baseline implantation conditions (same AVI, pacing at 80 bpm for at least 30 minutes) when evaluated by echocardiography 1 year following implantation. Four patients were lost during follow-up period, while none of the rest complained of any symptom during this period.

The effect of DDD pacing on heart rate and LV ventricular systolic and both ventricular diastolic echocardiographic indices throughout the follow-up period, are presented in Table 1. Left ventricular fractional shortening showed no change throughout the period of evaluation, meaning that DDD pacing did not offer an analogous to diastolic filling improvement in LV systolic performance. Both ventricular sizes, reflected by end-diastolic diameter remained unchanged between implantation date and 12

Table 1. Heart rate and echocardiographic data in patients with DDD pacing before, after and one year following pacemaker implantation

Variables	Baseline (N=22)	24 hours (N=22)	1 year (N=18)
Heart rate, bpm	41 ± 4	78 ± 8*	73 ± 5*
LVFS, %	37.23 ± 3.75	37.27 ± 3.72	36.88 ± 3.52
RVEDD, cm	2.3 ± 0.8	2.2 ± 0.6	2.3 ± 0.9
LVEDD, cm	6.1 ± 1.3	5.8 ± 1.0	6.1 ± 0.9
LVOT VTI, cm	-	24.28 ± 3.16	25.65 ± 2.36
MV-E/A	-	0.57 ± 0.22	0.65 ± 0.26
TV-E/A	-	1.02 ± 0.29	1.02 ± 0.26
MV-DTE, sec	-	0.149 ± 0.03	0.150 ± 0.02
TV-DTE, sec	-	0.158 ± 0.02	0.161 ± 0.02

* denotes statistically significant difference (p<0.05), between baseline and 24 h post implantation

+ denotes statistically significant difference (p<0.05), between baseline and 1 year post implantation

LVEDD- left ventricular end-diastolic diameter, LVFS- left ventricular fractional shortening, LVOT VTI- left ventricular outflow tract velocity time integral, MV-DTE- left ventricular deceleration time, MV-E/A- left ventricular ratio of peak early to peak late velocity, RVEDD- right ventricular end-diastolic diameter, TV-E/A- right ventricular ratio of peak early to peak late velocity, TV-DTE- right ventricular deceleration time

months later, while both LV and RV Doppler diastolic indices stayed unaffected as well (Table 1).

LV and RV diastolic function adaptation to variable AVI modification

Table 2 presents Doppler diastolic indices of both LV and RV, during DDD pacing under the 3 different selected AVIs. We noticed that both ventricles shared a similar pattern of diastolic performance adaptation to programmed AVI modification, consisting in a progressive greater contribution of late diastole to ventricular filling together with a decrease of E/A ratio and filling time, following prolongation of AVI.

In addition, we observed that LV diastolic filling velocities always prevailed over RV ones, while differences in E/A ratios, DTE and FT did not reach statistical significance. It must be emphasized that LV and RV DTE evaluation under an AVI of 200 ms, was not feasible due to the fusion effect of E and A waves under this specific AVI.

Evidence of ventricular interaction during DDD pacing

Figure 1 represents a statistically significant positive correlation between LV and RV E/A ratios obtained under an AVI of 100 ms. This finding in addition to a statistically significant positive correlation between RV E/A ratio (TV E/A ratio, RV diastolic function index) and LVOT VTI (LV stroke volume index) obtained during all 3 different pacing protocols (Figure 2), demonstrates the physiologic ventricular interaction in patients with DDD pacing.

AVI selection

Our findings suggested that the shortest AVI of 100 ms or 150 ms compared to 200 ms, exerted the most beneficial effect on diastolic filling dynamics of both ventricles (Table 2) and was associated with a more favorable LV stroke volume index (LVOT VTI) (Table 2).

Discussion

The present study demonstrates that DDD pacing mode in patients with complete heart block and a relatively preserved LV and RV systolic functions, is associated with a similar pattern of diastolic function adaptation of both ventricles to various AVI modifications and that might be the reflection of ventricular interaction du-

Table 2. Doppler diastolic filling indices and LV stroke volume index (LVOT VTI) adaptation to variable AVI

	AV delay 100 ms	AV delay 150 ms	AV delay 200 ms	p 100 vs 150 ms AV delay	p 100 vs 200 ms AV delay	p 150 vs 200 ms AV delay
MV-PVE, m/s	0.60 ± 0.10	0.55 ± 0.10	0.46 ± 0.10	NS	0.002	0.007
MV-PVA, m/s	0.69 ± 0.10	0.77 ± 0.10	0.87 ± 0.10	0.003	0.0005	0.002
MV- E/A	0.90 ± 0.20	0.72 ± 0.10	0.53 ± 0.10	0.012	0.0005	0.0005
MV-FT, sec	0.40 ± 0.00	0.37 ± 0.00	0.33 ± 0.00	0.003	0.0005	0.0005
MV-DTE, sec	0.15 ± 0.00	0.14 ± 0.00	NA	NS	NA	NA
TV-PVE, m/s	0.46 ± 0.10	0.42 ± 0.10	0.37 ± 0.10	0.001	0.0005	0.0005
TV-PVA, m/s	0.43 ± 0.10	0.46 ± 0.10	0.51 ± 0.10	NS	0.0005	0.002
TV- E/A	1.10 ± 0.30	0.94 ± 0.20	0.74 ± 0.10	0.001	0.0005	0.0005
TV-FT, sec	0.42 ± 0.10	0.40 ± 0.10	0.36 ± 0.10	0.001	0.0005	0.0005
TV-DTE, sec	0.15 ± 0.00	0.14 ± 0.00	NA	NS	NA	NA
LVOT VTI, cm	26.88 ± 3.60	26.26 ± 2.90	24.76 ± 2.50	NS	0.0005	0.0005

LVOT VTI- left ventricular outflow tract velocity time integral, MV-DTE- left ventricular deceleration time, MV-E/A- left ventricular E/A ratio, MV-FT- left ventricular filling time, MV-PVA- left ventricular A wave peak velocity, MV-PVE- left ventricular E wave peak velocity, NS- non significant, NA- non applicable, TV-DTE- right ventricular deceleration time; TV-E/A- right ventricular E/A ratio, TV-FT- right ventricular filling time, TV-PVA- right ventricular A wave peak velocity, TV-PVE- right ventricular E wave peak velocity

ring this pacing mode. Thus, we concluded that in this specific cohort of patients there might be no justification for RV diastolic function assessment during AVI programming and the routinely used LV diastolic filling evaluation is sufficient for AVI optimization.

Right ventricular in contrast to LV adaptation to different DDD pacing modes, has not been widely investigated yet (4,5). Standard Doppler echocardiography is the more established technique for AVI optimization in different kinds of pacing (1,3,6). This modality that shares simplicity, accessibility and lower cost compared to novel Doppler techniques was used in the present study to assess diastolic function adaptation of both ventricles to different DDD pacing stimulations. We have shown that in both ventricles there were a progressive greater contribution of late diastole to ventricular filling together with a decrease of E/A ratio and filling time, following prolongation of AVI. Our results are consistent with the findings of D' Andrea et al. who evidenced an analogous ventricular adaptation, using both Doppler echocardiography and tissue Doppler imaging (4). Additionally, we observed the strong positive correlation between LV and RV E/A ratios as well as between TV E/A ratio and LVOT VTI, displayed quite sufficiently physiologic ventricular interaction. This association first described in an experimental setting almost 4 decades ago (8) has been proved to occur in normal subjects using standard Doppler echocardiography (6,7). Elderly patients with DDD pacing have not been widely evaluated yet for the presence of this phenomenon.

Currently there is increased evidence that the determination of the optimal AVI for each patient should be individualized as it has been proposed during the last decade (1-3,11,12). We have demonstrated that an AVI of 100 ms in the majority of the patients tested, resulted to a more favorable RV and LV diastolic filling performances. Interestingly this effect remained consistent throughout the follow-up period, compared to longer AVIs. In addition, differences in the parameters tested were consistently more significant when shorter AVIs were compared with the longer AVI of 200 ms, while they were less significant when the shorter AVIs (100 vs 150 ms) were compared together. Thus we concluded that this beneficial and sustained effect of a short AVI on myocardial performance might be attributed to the similar pattern of diastolic function improvement of both ventricles, under this specific AVI and not only to the LV diastolic function optimization alone. This

statement of course stands for patients with complete heart block, normal or near normal LV systolic function with no evidence of coronary artery disease or conditions affecting RV performance. In contrast, in patients with RV dysfunction and disturbed systolic and diastolic function there might be a need for evaluating RV diastolic filling dynamics during AVI optimization for DDD pacing. This could be performed using the standard Doppler echocardiography or tissue Doppler myocardial imaging modality.

There are some limitations in the study design that must be taken into account. First, the number of the patients was relatively small. Second, in the present study all echocardiographic measurements were performed at a programmed heart rate (80 beats per min) at rest and supine position and no evaluation of diastolic function adaptation was performed during physical exercise that might improve the reliability of our findings. Third and possibly most important, diastole is a complex phenomenon and diastolic filling patterns, may be influenced by a number of factors such as autonomous nervous system, preload and afterload variations. In accordance we evaluated diastolic function under relatively stable haemodynamic conditions for all patients, which anyhow served as their own control. All measurements of diastolic function indices were assessed at the end-expiration. Additionally, although these indices might be influenced by load variations and respiration, those could not affect our results due to the inter-individual method of assessment (paired comparisons) and furthermore due to the synchronous LV and RV diastolic function evaluation. Nevertheless, this remains a compromise and a limitation of the study. Novel modalities, such as automatic border detection (13), assessment of RV myocardial performance index (14) and especially Doppler tissue imaging (4,5,15,16) have emerged as promising tools in the evaluation of RV diastolic function and are currently under validation.

Conclusions

The results of the present study suggest that in elderly patients with complete heart block and normal RV and LV systolic function, RV adapts to DDD pacing mode and AVI modifications in an analogous and sustained manner to the LV and this finding exhibits a mode of ventricular interaction.

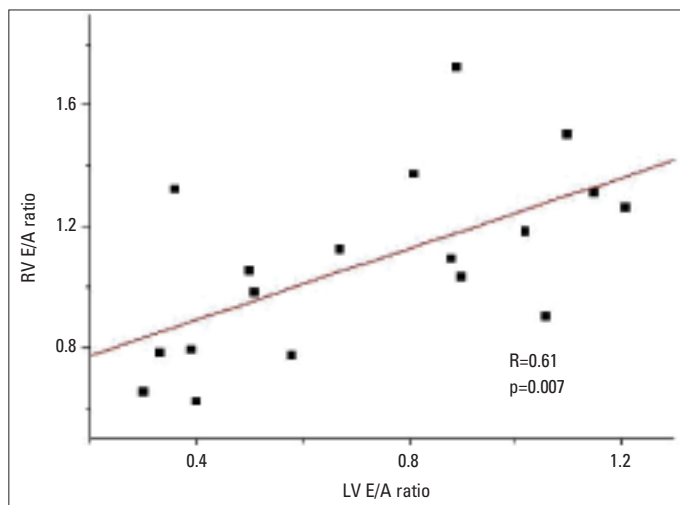


Figure 1. Correlation between RV and LV E/A ratios during pacing with an AVI of 100 ms

AVI- atrioventricular interval, RV E/A ratio- right ventricular ratio of peak early to peak late velocity, LV E/A ratio- left ventricular ratio of peak early to peak late velocity

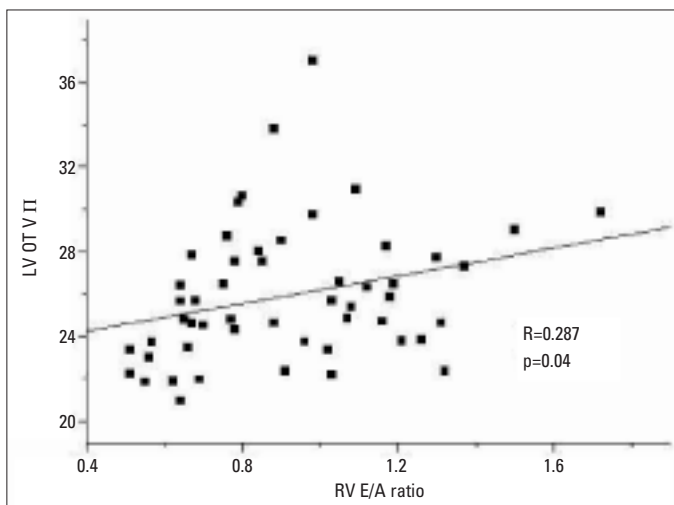


Figure 2. Correlation between RV E/A ratio and LVOT VTI values obtained during all 3 stimulation modes

RV E/A ratio- right ventricular ratio of peak early to peak late velocity, LVOT VTI- left ventricular outflow tract velocity time integral

References

1. Ritter P, Padeletti L, Gillio-Meina L, Gaggini G. Determination of the optimal atrioventricular delay in DDD pacing. *Europace* 1999; 1: 126-30.
2. Porciani CM, Fantini F, Musilli N, Sabini A, Michelucci A, Colella A, et al. A perspective on Atrioventricular Delay Optimization in Patients with a Dual Chamber Pacemaker. *PACE* 2004; 27: 333-8.
3. Leonelli FM, Wang K, Youssef M, Hall R, Brown D. Systolic and diastolic effects of variable atrioventricular delay in patients with complete heart block and normal ventricular function. *Am J Cardiol* 1997; 80: 294-8.
4. D'Andrea A, Caso P, Galderisi M, Ducceschi V, Scherillo M, Sarubi B, et al. Ventricular interdependence in patients with dual-chamber pacing: a Doppler tissue imaging study. *Echocardiography* 2002; 19: 289-97.
5. D'Andrea A, Ducceschi V, Caso P, Galderisi M, Mercurio B, Liccardo B, et al. Usefulness of Doppler tissue imaging for the assessment of right and left ventricular myocardial function in patients with dual-chamber pacing. *Int J Cardiol* 2001; 8: 75-83.
6. Yu CM, Sanderson JE. Right and left ventricular diastolic function in patients with and without heart failure: Effect of age, sex, heart rate, and respiration on Doppler-derived measurements. *Am Heart J* 1997.
7. Zoghbi WA, Habib GB, Quinones MA. Doppler assessment of right ventricular filling in a normal population. Comparison with left ventricular filling dynamics. *Circulation* 1990; 82: 1316-24.
8. Santamore WP, Lynch PR, Meier G, Heckman J, Bove AA. Myocardial interaction between the ventricles. *J Appl Physiol* 1976; 4: 362-8.
9. Styliadis IH, Gouzoumas NI, Karvounis HI, Papadopoulos CE, Efthimiadis GK, Karamouzis M, et al. Effects of variation of atrioventricular interval on left ventricular diastolic filling dynamics and atrial natriuretic peptide levels in patients with DDD pacing for complete heart block. *Europace* 2005; 7: 576-83.
10. Sahn D, De Maria A, Kisslo J, Weyman A. The Committee on M-mode Standardizations of the American Society of Echocardiography. Recommendations regarding quantitation in M-mode echocardiography: Results of a survey of echocardiographic measurements. *Circulation* 1978; 58: 1072-83.
11. Nishimura RA, Hayes DL, Holmes DR Jr, Tajik AJ. Mechanism of hemodynamic improvement by dual-chamber pacing for severe left ventricular dysfunction: an acute Doppler and catheterization hemodynamics study. *J Am Coll Cardiol* 1995; 25: 281 - 8.
12. Meluzin J, Novak M, Mullerova J, Krejci J, Hude P, Eisenberger M, et al. A fast and simple echocardiographic method of determination of the optimal atrioventricular delay in patients after biventricular stimulation. *Pacing Clin Electrophysiol* 2004; 27: 58-64.
13. Maeda M, Yamakado T, Nakano T. Right ventricular diastolic function in patients with hypertrophic cardiomyopathy-an invasive study. *JPN Circ J* 1999; 63: 681-7.
14. Eidem BW, O'Leary PW, Tei C, Seward JB. Usefulness of the myocardial performance index for assessing right ventricular function in congenital heart disease. *Am J Cardiol* 2000; 86: 654-8.
15. Caso P, Galderisi M, Cicala S, Cioppa C, D'Andrea A, Lagioia G, et al. Association between myocardial right ventricular relaxation time and pulmonary arterial pressure in chronic obstructive lung disease: Analysis by pulsed Doppler tissue imaging. *J Am Soc Echocardiogr* 2001; 14: 970-7.
16. Bolca O, Hobikoğlu G, Norgaz T, Asiltürk R, Dayi SU, Gürkan U, et al. The prediction of pulmonary artery systolic pressure and vascular resistance by using tricuspid annular tissue Doppler imaging. *Anadolu Kardiyol Derg* 2002; 4: 302-6.