VIA MEDICA

ORIGINAL ARTICLE

Cardiology Journal
2015, Vol. 22, No. 1, 94–100
DOI: 10.5603/CJ.a2014.0025

ISSN 1897–5593

Relationships between P wave dispersion, atrial electromechanical delay, left atrial remodeling, and NT-proBNP levels, in patients with hypertrophic cardiomyopathy

Kamil Tuluce[1], Filiz Ozerkan[1], Selcen Yakar Tuluce[2], Oguz Yavuzgil[1], Cemil Gurgun[1], Murat Bilgin[1], Nihan Kahya Eren[2], Ugur Kocabas[2], Sanem Nalbantgil[1], Cahide Soydas Cinar[1]

[1]Department of Cardiology, Ege University Faculty of Medicine, Izmir, Turkey
[2]Department of Cardiology, Ataturk Training and Research Hospital, Izmir, Turkey

Abstract

Background: *We evaluated the associations among the well-known atrial fibrillation (AF) predictors including P-wave dispersion (PWD), intra- and inter-atrial electromechanical dyssynchrony (EMD), left atrial (LA) phasic functions, and plasma N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) levels, in patients with hypertrophic cardiomyopathy (HCM).*

Methods: *Seventy patients with HCM and age and sex matched 70 subjects were enrolled. PWD, LA total emptying fraction (LATEFr), active emptying fraction (LAAEFr), passive emptying fraction (LAPEFr), expansion index (LAEI) intra- and inter-atrial EMD were calculated. Levels of NT-proBNP of all subjects were determined.*

Results: *Higher PWD ($p = 0.006$), significantly decreased LAEI ($p < 0.001$), LATEFr, and LAPEFr (both p values < 0.001) values and significantly increased inter-atrial ($p < 0.001$), LA ($p = 0.001$), and right atrial dyssynchrony ($p < 0.001$) were observed in the HCM group compared to controls. PWD was negatively correlated with LAEI ($r = –0.236$, $p = 0.005$) and LATEFr ($r = –0.242$, $p = 0.04$), however not with LAPEFr ($p = 0.7$), or LAAEFr ($p = 0.3$). Except for the LA lateral wall PA' ($r = 0.283$, $p = 0.02$), PWD was not correlated with any atrial EMD parameter. Inter-atrial dyssynchrony was related to LAEI ($r = –0.272$, $p = 0.001$), LATEFr ($r = –0.256$, $p = 0.03$), and LAPEFr ($r = –0.332$, $p = 0.006$), but not, however, to LAAEFr ($p = 0.4$). The plasma NT-proBNP levels of patients were not correlated with either PWD ($p = 0.927$) or inter-atrial dyssynchrony ($p = 0.102$).*

Conclusions: *PWD and inter-atrial dysynchrony seem to independently promote AF, although both are associated with LA reservoir function in HCM populations. The NT-proBNP level is not associated with these two AF predictors in patients with HCM. NT-proBNP seems to be a poor marker of atrial electrical remodeling in HCM patients.* (Cardiol J 2015; 22, 1: 94–100)

Key words: hypertrophic cardiomyopathy, atrial dysynchrony, P-wave dispersion, atrial phasic functions, natriuretic peptide

Address for correspondence: Dr Kamil Tuluce, Ege University Faculty of Medicine, Department of Cardiology, 35100, Izmir, Turkey, tel: +090 232 3904001, fax: +090 232 3903287, e-mail: kamiltuluce@gmail.com

Received: 26.12.2013 Accepted: 23.02.2014

The results of this study were presented in EuroEcho-Imaging 2013 Congress.

Introduction

Alterations in left atrial (LA) functions [1], atrial fibrosis [2], and even LA appendage dysfunction [3], have been reported in patients with hypertrophic cardiomyopathy (HCM). Changes in atria may lead to electrical remodeling and affect the conduction properties of the atria, as is true in other cardiac pathologies [4]. Prolongation of atrial conduction can be assessed noninvasively by surface electrocardiography (ECG) measuring P wave duration (Pdur) [5] and and by tissue Doppler imaging (TDI) assessing atrial electromechanical dyssynchrony (EMD) [6]. These parameters and LA phasic functions have been used widely to predict development of atrial fibrillation (AF) episodes in patients with various heart diseases [5–7]. Patients with HCM are more prone to development of AF, which is suggested to be a strong determinant of HCM-related morbidity and is the most common disease variable associated with progressive heart failure [8].

The levels of the amino-terminal portion of pro-BNP (N-terminal prohormone of B-type natriuretic peptide [NT-proBNP]) are elevated in patients with HCM [1]. Studies focusing on atrial functions showed that NT-proBNP levels also reflected LA dysfunction in patients with structural heart disease [9]. Increased levels of NT-proBNP are also known to be related to the AF burden [10].

In the current study, we investigated the associations among well-known AF predictors, including P wave dispersion (PWD), intra- and inter-atrial dyssynchrony, LA phasic functions, and plasma NT-proBNP levels, in patients with HCM.

Methods

Patients with established diagnoses of HCM [11] were enrolled. All patients were in sinus rhythm (SR) and underwent 24-h Holter ECG monitoring before enrollment. Patients with any of the following were excluded: (1) mitral annular calcification; (2) bundle branch block; (3) any wall-motion abnormality or left ventricular (LV) systolic dysfunction; (4) any pulmonary or metabolic disorder; (5) prior pacemaker implantation; (6) moderate to severe valvular disease; (7) prior intervention to alleviate LV outflow obstruction; (8) presence of AF attacks on 24-h Holter ECG monitoring; (9) and treatment with anti-arrhythmic drugs other than beta-blockers or verapamil; (10) history of paroxysmal AF attacks. The study population consisted of 70 patients HCM with no complaint of palpitation who were in SR at the time of recruitment. If a patient took any medication, this was stopped ≥ 48 h before enrollment, when possible. The findings in patients were compared with those of a control group of 70 subjects. The findings in patients were compared with those of a control group of 70 age- and sex-matched healthy volunteered subjects who admitted to our center for medical examination who had normal physical examination findings.

All participants gave written informed consent to participate in the study, which was approved by the hospital Ethic Committee.

Echocardiographic analysis

Echocardiographic assessments were performed using a Sonos 7500 ultrasound machine (Philips Medical Systems, Andover, MA) equipped with a 2.5-MHz transducer, and recorded on VHS videotape. One-lead ECG was recorded continuously during all examinations. Measurements were performed using the criteria of the American Society of Echocardiography [12]. The LA volumes (LAVs) were calculated from the 4- and 2-chamber views, using Simpson's rule. The following LAVs were measured: maximal volume (Vmax) during LV end-systole immediately before mitral valve opening; minimal volume (Vmin) just before mitral valve closure; and LAV before atrial contraction (VpreA) at the onset of the P wave of the simultaneously recorded ECG. Left atrial total emptying fraction (LATEFr) was calculated as [(Vmax – Vmin)/Vmax × 100%]; left atrial active emptying fraction (LAAEFr) as [(VpreA – Vmin)/ /VpreA × 100%]; left atrial passive emptying fraction (LAPEFr) as [(Vmax – Vpre A)/Vmax × × 100%]; and left atrial expansion index (LAEI) as [(Vmax – Vmin)/Vmin × 100%] [13, 14].

The pulsed Doppler sample volume was placed at the lateral and septal sides of the mitral annulus, and the right ventricular (RV) tricuspid annulus, to obtain tissue Doppler velocities. The time interval from the onset of the P wave on surface ECG to the peak of the late diastolic wave (the A' wave), termed PA', was obtained from the lateral mitral annulus (lateral PA'), the septal mitral annulus (the septal PA'), and the RV tricuspid annulus (the tricuspid PA') (Fig. 1) [15]. The difference between the lateral PA' and tricuspid PA' (lateral PA' – tricuspid PA') was defined as the inter-atrial dyssynchrony, while the intra-atrial dyssynchrony was defined as the difference between the septal PA' and the tricuspid PA' (right atrial [RA] dyssynchrony) and the lateral PA' and the septal PA' (LA dyssynchrony) [16]. All echocardiographic measurements were calculated as averages of data from 3 beats.

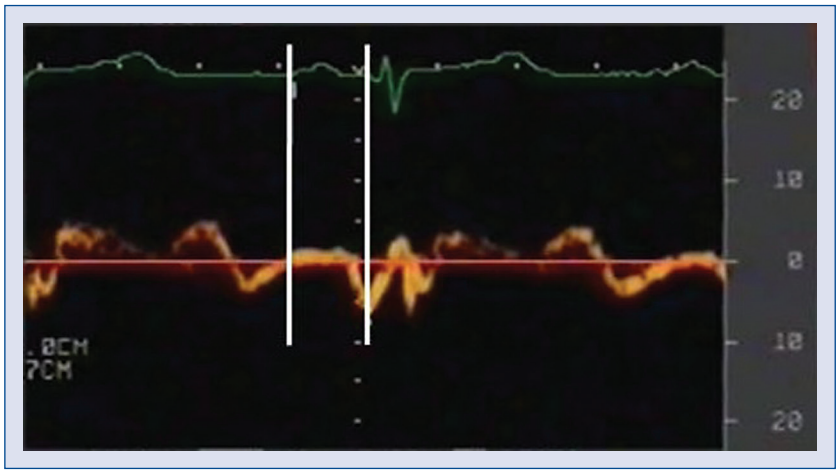

Figure 1. Electromechanical coupling interval from initiation of the P wave on electrocardiography to the peak of the late diastolic tissue Doppler imaging signal (A').

Electrocardiographic analysis

A 12-lead resting surface ECG was obtained from all subjects (lying supine) at a paper speed of 50 mm/s and a signal size of 20 mm/mV, during SR, using a computer-based ECG system. Paper printouts of the averaged data from all 12 ECG leads were scanned using a high-resolution scanner (Samsung SCX-4200 Multifunction, 600 × 600 dpi, Samsung Electronics Co., Ltd., Tokyo, Japan), transferred into computer memory, and opened using a high-performance graphic program (Autodesk AutoCAD 2011, Autodesk, Inc., San Rafael, CA). The P wave was magnified 1,000-fold using Autodesk. The start- and end-points of the P wave were defined as the junction between the P-wave pattern and the isoelectric line. P-wave duration was manually measured from the commencement to the end of the P wave, using digital calipers, on a high-resolution computer screen. Leads with baseline noise > 10 μV and/or a peak-to-peak isoelectric line-P wave amplitude of < 15 μV were excluded from analysis [9]. Subjects with measurable P waves in ≥ 10 ECG leads were included in the study. P wave dispersion was defined as the difference between the maximum (Pmax) and minimum (Pmin) P-wave durations [7].

Statistical analysis

All analyses were performed using SPSS for Windows, version 18.0 (SPSS Inc., Chicago, IL). Results are presented as means ± standard deviations for continuous data or as numbers with percentages for categorical data. NT-proBNP levels were logarithmically transformed. After performing the normality test, continuous variables were analyzed using Student's *t*-test or the Mann-Whitney U test, as appropriate. Categorical data and proportions were analyzed using the χ^2 test. Associations between variables were examined by calculating Pearson correlations or by using the Spearman correlation test, as appropriate. Two-sided p values < 0.05 were considered to indicate statistical significance. The reproducibility of measures of Pmax, PWD, and atrial electromechanical coupling intervals obtained by TDI, was assessed by calculation of coefficients of variation (CV), which were the standard deviations of differences between repeated measurements divided by the average values of those measurements, and are expressed as percentages.

Results

Baseline characteristics of the subjects are presented in Table 1. There were no significant differences between groups in terms of age, gender, heart rate, blood pressure, or body surface area. Clinical features of the HCM group are summarized in Table 2. Thirty-nine (55.7%) patients had obstructive-type HCM. Before the concurrent medications were stopped, 52 of our patients (74.3%) were on beta-blocker therapy while 2 (2.9%) were on calcium-channel therapy. The electrocardiographic and echocardiographic parameters of the two groups are compared in Table 3. The Pmax ($p < 0.001$), Pmin ($p = 0.02$), and PWD ($p = 0.006$) values were significantly higher in HCM patients compared to controls. All PA' values were significantly longer in HCM patients. Comparison of tissue Doppler findings between groups showed a significant increase in inter-atrial ($p < 0.001$),

Table 1. Baseline characteristics of the study population.

	HCM group (n = 70)	Control group (n = 70)	P
Age [years]	50.54 ± 12.86	49.26 ± 11.6	0.536
Females/males	25/45	24/46	0.86
Body surface area [m^2]	1.87 ± 0.22	1.92 ± 0.19	0.089
Systolic blood pressure [mm Hg]	122.41 ± 15.58	125.8 ± 16.02	0.207
Diastolic blood pressure [mm Hg]	72.1 ± 11.19	71.34 ± 12.16	0.702

Continuous data are expressed as means ± standard deviation; HCM — hypertrophic cardiomyopathy

Table 2. Clinical features of the hypertrophic cardiomyopathy group.

Type of hypertrophy:	
Asymmetric septal hypertrophy	62 (88.6%)
Concentric	4 (5.7%)
Midventricular	3 (4.3%)
Apical	1 (1.4%)
Mitral regurgitation:	
No	10 (14.3%)
Mild	27 (38.6%)
Moderate	33 (47.1%)
Obstruction	39 (55.7%)

LA ($p = 0.001$), and RA dyssynchrony ($p < 0.001$), in the HCM group (Table 3). Assessment of LA phasic functions revealed a significantly decreased LAEI ($p < 0.001$), total LA, and passive emptying fraction (both p values < 0.001), in HCM patients, but no difference with respect to LAAEFr ($p = 0.26$) between the two groups (Table 3). Correlation analysis of the PWD with other parameters revealed that PWD was positively correlated with Vmax ($r = 0.342$, $p = 0.004$), while negatively correlated with LAEI ($r = –0.236$, $p = 0.005$) and LATEFr ($r = –0.242$, $p = 0.04$). Except for the LA lateral wall PA' ($r = 0.283$, $p = 0.02$), PWD was not correlated with any atrial EMD parameter. No associations were detected between PWD and the degree of LV hypertrophy ($p = 0.86$), LAPEFr ($p = 0.7$), or LAAEFr ($p = 0.3$). Inter-atrial dyssynchrony was related to Vmax ($r = 0.276$, $p = 0.02$), LAEI ($r = –0.272$, $p = 0.001$), LATEFr ($r = –0.256$, $p = 0.03$), and LAPEFr ($r = –0.332$, $p = 0.006$), but not, however, to LAAEFr ($p = 0.4$) (Table 4). The median NT-proBNP level was 711.5 pg/mL in the HCM group and 24 pg/mL in the control group. The plasma NT-proBNP levels of patients were correlated with RA dyssynchrony ($r = 0.31$, $p = 0.01$), but not with PWD ($p = 0.927$) or inter-atrial dyssynchrony ($p = 0.102$).

Intra- and inter-observer CVs were 3.8% and 4.9% for Pmax and 3.9% and 4.7% for PWD, respectively. The CVs for intra- and inter-observer variability were 6.1% and 5.3% for lateral PA'; 6.8% and 7.2% for septal PA', and 5.5% and 5.7% for tricuspid PA', respectively.

Discussion

We found that in patients with HCM, the LA total emptying fraction, the LA expansion index, and LA phasic volumes were commonly associated with PWD and inter-atrial dyssynchrony. No correlations were evident between PWD and LA electromechanical coupling intervals, except for the lateral PA'. No associations were detected between plasma NT-proBNP levels, and PWD and inter-atrial dyssynchrony, in patients with HCM.

Interaction between PWD and atrial dyssynchrony

P-wave dispersion [5] on surface ECG and atrial EMD [6] have been reported as risk factors for development of AF in various heart diseases. However, only a few studies have evaluated the relationship between PWD and atrial dyssynchrony. A positive correlation between inter-atrial electromechanical delay and PWD was shown in patients with mitral stenosis [17]. A strong correlation between the signal-averaged P-wave duration and total atrial activation time (defined as the time interval from the beginning of the P-wave on the ECG until the peak of the tissue A'-wave in the lateral LA wall) was found by Merckx et al. [18] in subjects during SR. A recent study focusing on the relationship between Pdur and atrial EMD in patients with sinus node disease, who were in different atrial pacing modalities, found that, upon univariate analysis, all parameters, except for RA dyssynchrony, correlated positively with the Pdur while, upon multivariate analysis, Pdur was associated only with the electromechanical delay in the lateral LA wall [19]. The lateral LA

Table 3. Comparison of baseline electrocardiographic and echocardiographic findings between groups.

	HCM group	Control group	P
Echocardiographic findings			
IVS thickness [cm]	2.02 ± 0.45	0.95 ± 0.13	< 0.001
Posterior wall thickness [cm]	1.07 ± 0.27	0.81 ± 0.09	< 0.001
LV mass index [g/m^2]	143.3 ± 47.03	67.56 ± 12.87	< 0.001
Ejection fraction [%]	66.69 ± 6.76	65.30 ± 5.45	0.181
LAV preA [mL]	64.8 ± 27.2	31.8 ± 11.3	< 0.001
LAV minimum [mL]	39.5 ± 22.2	18.2 ± 7.4	< 0.001
LAV maximum [mL]	82.23 ± 33.04	47.08 ± 14.23	< 0.001
Electrocardiographic findings			
Heat rate [bpm]	68.27 ± 11.26	69.56 ± 9.25	0.46
P maximum [ms]	126.21 ± 14.1	116.57 ± 12.81	< 0.001
P minimum [ms]	85.57 ± 18.23	79.64 ± 10.19	0.02
P wave dispersion [ms]	43.5 ± 16.29	37.07 ± 10.61	0.006
Electromechanical coupling interval (PA') [ms]			
Lateral PA'	150.07 ± 23.59	124.21 ± 11.59	< 0.001
Septal PA'	132.64 ± 23.45	110.14 ± 12.54	< 0.001
Tricuspid PA'	109.93 ± 23.81	96.57 ± 14.36	< 0.001
Inter-atrial asynchrony	42.29 ± 17.87	27.64 ± 12.27	< 0.001
LA dyssynchrony	20.43 ± 14.13	13.93 ± 8.42	0.001
RA dyssynchrony	25.43 ± 17.33	13.57 ± 8.43	< 0.001
LA phasic functions [%]			
LA expansion index	129.7 ± 57.2	174.5 ± 60.9	< 0.001
LA total emptying fraction	54.47 ± 11.46	62.01 ± 8.25	< 0.001
LA passive emptying fraction	21.45 ± 10.07	33.05 ± 10.43	< 0.001
LA active emptying fraction	40.78 ± 14.41	43.25 ± 10.55	0.26

Continuous data are expressed as means ± standard deviation; IVS — interventricular septum; LA — left atrium; LV — left ventricular; LAV — left atrial volume; LAV preA — left atrial volume before atrial contraction; PA' — time interval from the onset of the P wave on surface ECG to the peak of the late diastolic wave; RA — right atrium

Table 4. Correlation of P-wave dispersion and inter-atrial dyssynchrony with other parameters.

Variables	P wave dispersion r (p value)	Inter-atrial dyssynchrony r (p value)
Log NT-proBNP	–0.012 (0.927)	0.203 (0.102)
LV mass index	–0.078 (0.86)	0.232 (0.053)
LA maximum	**0.26 (0.024)**	**0.286 (0.013)**
LAV preA	**0.328 (0.006)**	**0.373 (0.002)**
LAV minimum	**0.301 (0,01)**	**0.337 (0.004)**
LAV maximum	**0.342 (0.004)**	**0.276 (0.02)**
LA expansion index	**–0.236 (0.005)**	**–0.272 (0.001)**
LA total emptying fraction	**–0.242 (0.04)**	**–0.256 (0.03)**
LA passive emptying fraction	–0.046 (0.7)	**–0.332 (0.006)**
LA active emptying fraction	–0.137 (0.3)	–0.095 (0.4)
Lateral PA'	**0.283 (0.02)**	**0.412 (< 0.001)**
Septal PA'	0.218 (0.07)	0.07 (0.5)
Tricuspid PA'	0.144 (0.2)	**–0.454 (<0.001)**
LA dyssyncrony	0.165 (0.2)	**0.441 (< 0.001)**
RA dyssyncrony	0.02 (0.9)	**0.556 (< 0.001)**
Inter-atrial dyssyncrony	0.107 (0.38)	–
P wave dispersion	–	0.107 (0.38)

LA — left atrium; LV — left ventricul; LAV — left atrial volume; LAVpreA — left atrial volume before atrial contraction; PA' — time interval from the onset of the P wave on surface ECG to the peak of the late diastolic wave; RA — right atrium

wall PA' estimates total atrial activation time [20] and has been shown to predict maintenance of SR after cardioversion in patients with persistant AF [21]. In the present study, PWD was related only to the lateral LA wall PA', thus not to intra- and inter-atrial dyssynchrony, in patients with HCM. This suggests that inter--atrial dyssynchrony is explained not only by LA structural and electrical remodeling, but also by the time elapsing from electrical activation in the atrium to atrial myocardial contraction. The observed lack of correlation between PWD and inter-atrial dysynchrony may indicate that these 2 parameters are relatively independent in terms of promoting AF in HCM populations.

Relationships of PWD and atrial EMD to LA phasic volumes

The LAV is known to be a predictor of AF in patients with HCM [22]. In our study, both PWD and inter-atrial dyssynchrony were correlated with all phasic LAVs. Our findings are similar to those of previous studies evaluating patients with mitral stenosis [17], and sinus node disease without structural heart disease [19]. The positive correlation between phasic LAVs, and PWD and atrial dyssynchrony, may suggest that these two AF predictors are affected by LA structural remodeling. Chronic elevation of LV filling pressure in patients with HCM may cause secondary atrial myopathy [1], contributing to atrial dyssynchrony and prolongation of PWD.

Relationships of PWD and atrial EMD to LA phasic functions

No relationship between LA phasic functions and PWD and atrial EMD has yet been shown. In the present study, we found negative correlations between LA reservoir functions (the LA expansion index and the LA total emptying fraction), and PWD and atrial dyssynchrony; however, the LA active emptying fraction was not associated with these 2 parameters. Schneider et al. [23] investigated atrial deformation properties in an effort to predict maintenance of SR in patients undergoing catheter ablation for AF, and showed that LA reservoir function parameters, rather than LA contractile functions, were the best predictors of maintenance of SR in such patients. In another study, the presence of atrial dyssynchrony during the reservoir period, but not during the atrial contraction period, was associated with future development of AF in patients with congestive heart failure [24]. The LA active emptying fraction in the HCM population has been shown to follow the Frank-Starling mechanism [1], so an increase in LA preload up to a certain point contributes to enhanced LA booster pump function, which might explain why this function does not predict development of AF. On the other hand, LA reservoir function parameters are affected mostly by atrial compliance [25], and show advanced remodeling rather than LA enlargement. This may explain the value of this function in predicting AF [26].

Relationships of PWD and atrial EMD to NT-proBNP levels

A recent study showed a direct correlation between plasma NT-proBNP levels and the AF burden [10]. Elevation of plasma NT-proBNP levels, despite the absence of obvious structural heart disease, was evident in patients with chronic AF, and no relationship was found between plasma NT-proBNP levels and intra-atrial conduction time (measured as the filtered Pdur) after cardioversion, in a previous study [27]. Evaluation of patients with persistent AF found that the baseline plasma BNP level and the magnitude of the decrease thereof after successful cardioversion, predicted AF recurrence [28]. In contrast, a prospective study found similar BNP levels in patients with AF and SR, suggesting that the peptide was not associated with AF [29]. Thus, the relationship between BNP level, and the chronicity or burden of AF, remains controversial. In our study, NT-proBNP levels were elevated in patients with HCM, but were not associated with either PWD or atrial dyssynchrony. The stimulus for BNP release is myocyte stretching rather than the transmural pressure load [30]. For this reason, NT-proBNP seems to be a poor marker of atrial electrical remodeling induced by chronic pressure loading.

Limitations of the study

Our study had a few limitations. We did not perform follow-up. Our results should be validated in a follow-up study identifying the relationships of AF predictors not only to each other but also to clinical endpoints including AF. Phasic volumetric assessment of LA could be performed using 3-dimensional echocardiography.

Conclusions

PWD and inter-atrial dysynchrony seem to independently promote AF, although both are associated with LA reservoir function in HCM populations. The NT-proBNP level is not associated

with these 2 AF predictors in patients with HCM. Analysis of all 3 markers in terms of predicting AF development might yield useful information on HCM patients with a propensity toward development of AF. Further studies of the power of using all 3 parameters together to predict AF in HCM populations are needed.

Acknowledgements

This study was supported by a grant from Ege University (11-TIP-044) and we would like to thank to Dr Raika Durusoy for her guidance in statistical analysis.

Conflict of interest: None declared

References

1. Tuluce K, Yakar Tuluce S, Yavuzgil O et al. The left atrial phasic functions and the relationship with plasma N-terminal pro-B-type natriuretic peptide levels and symptomatic states in patients with hypertrophic cardiomyopathy. Anadolu Kardiyol Derg, 2014; 14; 719–727.
2. Varnava AM, Elliot PM, Sharma S et al. Hypertrophic cardiomyopathy: The interrelation of disarray, fibrosis, and small vessel disease. Heart, 2000; 84: 476–482.
3. Yakar Tuluce S, Kayikcioglu M, Tuluce K et al. Assessment of left atrial appendage function during sinus rhythm in patients with hypertrophic cardiomyopathy: Transesophageal echocardiography and tissue doppler study. J Am Soc Echocardiogr, 2010; 23: 1207–1216.
4. Sanders P, Morton J, Davidson N et al. Electrical remodeling of the atria in congestive heart failure. Electrophysiological and electroanatomical mapping in humans. Circulation, 2003; 108: 1461–1468.
5. Köse S, Aytemir K, Sade E et al. Detection of patients with hypertrophic cardiomyopathy at risk for paroxysmal atrial fibrillation during sinus rhythm by P-wave dispersion. Clin Cardiol, 2003; 26: 431–434.
6. Sakabe K, Fukuda N, Fukuda Y et al. Interatrial dyssynchrony on tissue Doppler imaging predicts progression to chronic atrial fibrillation in patients with non-valvular paroxysmal atrial fibrillation. Heart, 2009; 95: 988–993.
7. Dilaveris PE, Gialafos EJ, Chrissos D et al. Detection of hypertensive patients at risk for paroxysmal atrial fibrillation during sinus rhythm by computer-assisted P wave analysis. J Hypertens, 1999; 17: 1463–1470.
8. Melacini P, Basso C, Angelini A et al. Clinicopathological profiles of progressive heart failure in hypertrophic cardiomyopathy. Eur Heart J, 2010; 31: 2111–2123.
9. Prastaro M, Paolillo S, Savarese G et al. N-terminal pro-b-type natriuretic peptide and left atrial function in patients with congestive heart failure and severely reduced ejection fraction. Eur J Echocardiogr, 2011; 12: 506–513.
10. Plitt DC, Chung EH, Mounsey JP et al. Relation of atrial fibrillation burden and N-terminal pro-brain natriuretic peptide. Am J Cardiol, 2013; 111: 1315–1318.
11. Maron BJ, McKenna WJ, Danielson GK et al. American college of cardiology/european society of cardiology clinical expert consensus document on hypertrophic cardiomyopathy: A report of the american college of cardiology foundation task force on clinical expert consensus documents and the european society of cardiology committee for practice guidelines. Eur Heart J, 2003; 24: 1965–1991.
12. Lang RM, Bierig M, Devereux RB et al. Recommendations for chamber quantification: A report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr, 2005; 18: 1440–1463.
13. Blume GG, Mcleod CJ, Barnes ME et al. Left atrial function: physiology, assessment, and clinical implications. Eur J Echocardiogr, 2011; 12: 421–430.
14. Wang WH, Hsiao SH, Lin KL et al. Left atrial expansion index for predicting atrial fibrillation and in-hospital mortality after coronary artery bypass graft surgery. Ann Thorac Surg, 2012; 93: 796–803.
15. De Vos CB, Weijs B, Crijns HJ et al. Atrial tissue Doppler imaging for prediction of new-onset atrial fibrillation. Heart, 2009; 95: 835–840.
16. Dabrowska-Kugacka A, Lewicka-Nowak E, Ruciński P et al. Atrial electromechanical sequence and contraction synchrony during single-and multisite atrial pacing in patients with brady-tachycardia syndrome. Pacing Clin Electrophysiol, 2009; 32: 591–603.
17. Ozer N, Yavuz B, Can I et al. Doppler tissue evaluation of intra-atrial and interatrial electromechanical delay and comparison with P-wave dispersion in patients with mitral stenosis. J Am Soc Echocardiogr, 2005; 18: 945–948.
18. Merckx KL, De Vos CB, Palmans A et al. Atrial activation time determined by transthoracic Doppler tissue imaging can be used as an estimate of the total duration of atrial electrical activation. J Am Soc Echocardiogr, 2005; 18: 940–944.
19. Dąbrowska-Kugacka A, Lewicka-Nowak E, Ruciński P, Zagożdżon P, Raczak G, Kutarski A. Relationship between P-wave duration and atrial electromechanical delay assessed by tissue Doppler echocardiography. Pacing Clin Electrophysiol, 2011; 34: 23–31.
20. Omi W, Nagai H, Takamura M et al. Doppler tissue analysis of atrial electromechanical coupling in paroxysmal atrial fibrillation. J Am Soc Echocardiogr, 2005; 18: 39–44.
21. Park SM, Kim YH, Choi JI, Pak HN, Kim YH, Shim WJ. Left atrial electromechanical conduction time can predict six-month maintenance of sinus rhythm after electrical cardioversion in persistent atrial fibrillation by Doppler tissue echocardiography. J Am Soc Echocardiogr, 2010; 23: 309–314.
22. Tani T, Tanabe K, Ono M et al. Left atrial volume and the risk of paroxysmal atrial fibrillation in patients with hypertrophic cardiomyopathy. J Am Soc Echocardiogr, 2004; 17: 644–648.
23. Schneider C, Malisius R, Krause K et al. Strain rate imaging for functional quantification of the left atrium: Atrial deformation predicts the maintenance of sinus rhythm after catheter ablation of atrial fibrillation. Eur Heart J, 2008; 29: 1397– 409.
24. Cho GY, Jo SH, Kim MK et al. Left atrial dyssynchrony assessed by strain imaging in predicting future development of atrial fibrillation in patients with heart failure. Int J Cardiol, 2009; 134: 336–341.
25. Suga H. Importance of atrial compliance in cardiac performance. Circ Res, 1974; 35: 39–43.
26. Abhayaratna WP, Fatema K, Barnes ME et al. Left atrial reservoir function as a potent marker for first atrial fibrillation or flutter in persons > or = 65 years of age. Am J Cardiol, 2001; 101: 1626–1629.
27. Okumura Y, Watanabe I, Ashino S et al. Electrophysiological properties of the atrium after cardioversion of chronic atrial fibrillation: Relation to the plasma brain natriuretic peptide level. Int Heart J, 2007; 48: 485–496.
28. Ari H, Binici S, Ari S et al. The predictive value of plasma brain natriuretic peptide for the recurrence of atrial fibrillation six months after external cardioversion. Turk Kardiyol Dern Ars, 2008; 36: 456–460.
29. Rossi A, Enriquez-Sarano M, Burnett JC Jr, Lerman A, Abel MD, Seward JB. Natriuretic peptide levels in atrial fibrillation: A prospective hormonal and Doppler-echocardiographic study. J Am Coll Cardiol, 2000; 35: 1256–1262.
30. Wiese S, Breyer T, Dragu A et al. Gene expression of brain natriuretic peptide in isolated atrial and ventricular human myocardium: Influence of angiotensin II and diastolic fiber length. Circulation, 2000; 102: 3074–3079.