Power spectral analysis of heart rate variability in children with aortic stenosis

Osman Küçükosmanoğlu[1], Nazan Özbarlas[1], Ahmet Birand[2], Gulmira Z. Kudaiberdieva[2]
Departments of [1]Pediatrics, and [2]Internal Medicine, Çukurova University Faculty of Medicine, Adana, Turkey

SUMMARY: Küçükosmanoğlu O, Özbarlas N, Birand A, Kudaiberdieva GZ. Power spectral analysis of heart rate variability in children with aortic stenosis. Turk J Pediatr 2002; 44: 109-115.

Aortic stenosis is a progressive disorder and can be the cause of serious arrhythmias and possibly sudden death. Evaluation and follow-up of the autonomic nervous system may provide some useful information for management of the disease. Our study aimed to examine heart rate variability in children with aortic stenosis in the supine position and to detect the changes in autonomic activity during head-up tilt testing. Sixteen patients and 11 healthy controls participated in the study. In the supine position, seven minutes of continuous echocardiographic (ECG) recording was performed, followed by four consecutive ECG recordings, each consisting of seven minutes in 70° tilt position. To obtain power spectrums, the tachograms were taken on the autoregressive mode. The mean RR interval duration, standard deviation of RR interval, central frequencies of low and high frequency oscillations, their powers, total power and percents of normalized low and high frequency powers were accepted for statistics. There were no significant differences between the groups in the supine position. In tilt position, mean RR interval and its standard deviation were decreased in both groups. The central frequency of low freuquency power significantly ($p<0.05$) shifted to left, normalized low frequency power increased and normalized high frequency power decreased in the control group at the beginning of tilt position, but at the second phase of tilt position in the patient group. We conclude from the results that children with mild-to-moderate aortic stenosis reflect delayed response to sympathetic provocation.

Key words: heart rate variability, aortic stenosis, tilt table testing, children.

Analysis of heart rate variability (HRV) is a reliable and noninvasive method for assessing cardiovascular autonomic control[1-4]. Reduced HRV has been found to be related with high cardiovascular mortality including sudden cardiac death in adult patients with myocardial infarction[5-6], chronic heart failure[7], left ventricular hypertrophy[8] and diabetic neuropathy[9]. While HRV became very popular in the field of adult cardiology, there are only a few reports available in pediatric literature[10-12]. Although impairment of HRV was reported in elderly patients with severe aortic stenosis[13,14], to our knowledge cardiovascular autonomic tone in children with mild-to-moderate aortic stenosis has not been studied. Because aortic stenosis is a progressive disorder and can be the cause of serious arrhythmia and possibly sudden death, evaluation and follow-up of the autonomic nervous system may provide some useful information for management of the disease. The aim of our study was to examine HRV in children with aortic stenosis in the supine position and to detect the changes in autonomic activity during the head-up tilt table testing. The head-up tilt table testing was used as a sympathetic provocative technique.

Material and Methods

Subjects

Sixteen patients with aortic stenosis and 11 healthy children participated in the study. One patient who developed syncope at 10th minute of head-up tilt testing was excluded. Therefore, data were analyzed from 15 patients (3 girls,

12 boys) ranging in age from 7 to 15 years (mean 9.7±3.7 years), and 11 healthy controls (4 girls, 7 boys; mean age, 9.3±2.1 years; range 7 to 15 years). All subjects were screened with a detailed history and physical examination. They were not taking any medication prior to the study. The procedures of the study were explained to each child and his or her family, and an informed consent obtained. The patients underwent echocardiographic study before echocardiographic (ECG) recordings and exercise testing afterwards. Echocardiographic study and exercise testing were not performed in the control group.

Echo-Doppler Study

Echo-Doppler studies were done using General Electric RT 6800 echocardiograph with 3.5 and 5 mHz transducers. End-diastolic and end-systolic diameters of the left ventricle and thickness of the interventricular septum and posterior wall were noted in parasternal long-axis window, then ejection fraction and fractional shortening were calculated. Left ventricular outflow tract and the structure of the aortic valve were evaluated by 2-D and M-mode echocardiography. Peak systolic pressure gradient between the left ventricle and aorta were determined by CW Doppler.

Recording and Analysis of the ECG Signals

All subjects were studied between 10:00 a.m.-12 noon after a light breakfast free of caffeine. The room was quiet, with dim lighting and a comfortable temperature (22°C). The subjects were loosely strapped to the tilt table that had a foot-broad support and was electrically driven. To avoid emotional stress, we did not perform any vascular intervention or blood pressure measurement during the study. The subjects were asked to breathe normally. After at least a 10-minute adaptation period in the supine position, seven minutes of continuous ECG recording was performed. At the end of supine recording, we rotated the table to head-up right tilt position with an angle of 70°, and four consecutive ECG recordings (tilt phase 1 to 4), each of seven minutes, duration, were done. Therefore, a total of 35 minutes continuous ECG recording (seven minutes in supine, 28 minutes in tilt position) were performed.

All recordings were done using a personal computer based high resolution ECG system (Kardiosis® Ars-LP). Bipolar X, Y and Z leads (0.5-340 Hz) and common-mode line interference signal on the body surface were recorded simultaneously. All signals were sampled at a rate of 1,000 samples/second and digitized using a 12-bit A/D converter. To obtain power spectrums, the tachograms were taken on the autoregressive mode with order 6, and power spectral densities were calculated. Very low frequencies (<0.03 MHz) were filtered before calculation. The mean RR interval duration, standard deviation of RR interval, central frequencies of low frequency (LF) and high frequency (HF) oscillations, their powers (LFP and HFP), total power (TP), normalized LFP and HFP were accepted for statistics.

Exercise Testing

After ECG recordings, all patient underwent exercise testing using Marquette 2000 tread-mill with Bruce Protocol. Tread mill stopped when desired maximal heart rate was attained or patient fatigued or when ST segment changes were observed on ECG monitor.

Statistical Analysis

Statistical analysis was done using SPSS for Windows Release 6.0 Data are presented as mean±SD. If the ±SD is near or higher than mean value, data are presented as mean ±SD (median). Wilcoxon matched-pairs signed-ranks test was used for comparing supine and tilt position results of each group. Mann-Whitney U-Wilcoxon rank sum W test was used for comparing counter groups. A p-value <0.05 was considered significant.

Results

The mean weights of the patient and control groups were found similar (29.4±11.2 kg vs 33.5±10.2 kg). There was also no significant difference in the mean heights of the patient and control groups (130.0±21.2 cm vs. 136.8±10.6 cm).

Ejection fraction and fractional shortening were found in normal ranges in all patients (74.0±3.9 and 42.5±3.7%, respectively). 2-D echocardiography showed subvalvular membranous aortic stenosis in two patients and valvular aortic stenosis in others. Color Doppler showed first-degree aortic insufficiency in five patients and second-degree in one patient. The peak systolic

transvalvular aortic gradients which were measured with CW Doppler were found ranging between 20-50 mmHg (mean 34.8±9.5 mmHg).

All patients completed at least three stages (nine minutes) of exercise testing with Bruce protocol. No patient developed chest pain or significant ST change on ECG monitor.

HRV Analysis

There were no significant differences between RR tachograms (mean RR interval and standard deviation of mean RR interval) and power spectral analysis (central frequency of LF and HF, their powers, total power, normalized LFP and HFP) results of patients and control groups in the supine position (Table I).

The changes in HRV parameters during tilt position are summarized in Table II (patient group) and Table III (control group). Figure 1 shows typical examples of power spectral analysis graphics of the supine position and first phase of tilt recordings.

The RR tachogram showed similar changes in both groups by tilting: mean RR interval and its standard deviation were decreased and remained stable during whole tilt testing.

The central frequency of LF shifted to left (decreased) by tilting in both groups. however, this shift became significant in the second period of tilt testing in the patient group, but in the first period of tilt testing in the control group.

The central frequency of HF did not change significantly during tilt testing in the control group, but it decreased in the fourth (last) period of tilt testing in the patient group.

In both groups, the power of LF decreased in the first period, then increased in the second period and remained stable, slightly under supine values.

Total power and the power of HF decreased at the beginning of tilt testing and remained stable until the end of testing in both groups. The percentage of normalized LFP increased significantly, while the percentage of normalized HFP was decreasing by tilting. These changes became significant in the second phase of tilt testing in the patient group, but in the first phase in the control group (Fig. 2). The LF/HF ratio was not significantly different in patient and control groups during supine position. In the first phase of tilt position, LF/HF ratio of the patient group was significantly lower than of the control group ($p<0.05$), but this difference disappeared in the 2nd, 3rd and 4th phases of tilt position.

Table I. HRV parameters of control and patient groups in supine position

Variable	Units	Patient mean±SD (median)	Control mean±SD (median)	p
CF1	Hz	0.102±0.027	0.105±0.018	>0.05
CF2	Hz	0.322±0.037	0.308±0.043	>0.05
LFP	ms^2	1907±1376 (1462)	1727±1185 (1433)	>0.05
HFP	ms^2	990±1232 (560)	1490±1986 (882)	>0.05
TP	ms^2	2898±2265 (2609)	3218±2279 (2316)	>0.05
NLFP	%	70±15 (73)	64±20 (63)	>0.05
NHFP	%	30±15 (27)	36±20 (36)	>0.05
MRR	ms	711.32±97.74	693.73±87.65	>0.05
MRRSD	ms	59.73±23.46	62.41±22.78	>0.05

HRV : Heart rate variability.
CF1 : Central frequency of low frequency oscillation.
CF2 : Central frequency of high frequency oscillation.
LFP : Low frequency power.
HFP : High frequency power.
TP : Total power.
NLFP : Normalized LFP.
NHFP : Normalized HFP.
MRR : Mean R-R interval.
MRRSD : Standard deviation of MRRR.
Hz : Hertz.
ms : millisecond.
* $p<0.05$.

Table II. Comparison of supine and tilt results of patient group [Mean±SD (median)]

Variable	Units	Supine	Tilt 1st phase	Tilt 2nd phase	Tilt 3rd phase	Tilt 4th phase
CF1	Hz	0.102±0.027	0.092±0.022	0.088±0.015*	0.086±0.013*	0.091±0.016
CF2	Hz	0.322±0.037	0.297±0.053	0.298±0.047	0.293±0.051	0.275±0.041*
LFP	ms²	1907±1376 (1462)	1159±808* (936)	1449±1173 (936)	1387±1012 (1085)	1480±1060 (1266)
HFP	ms²	990±1232 (560)	548±934* (166)	412±729* (164)	432±822* (195)	375±536* (174)
TP	ms²	2898±2265 (2609)	1708±1556* (1285)	1861±1805* (1100)	1819±1677* (1183)	1841±1492* (1269)
NLFP	%	70±15	75±15	84±10*	82±12*	84±10*
NHFP	%	30±15	25±15	16±10*	18±12*	15±10*
MRR	ms	711±97	632±82*	625±75*	616±67*	615±73*
MRRSD	ms	59±23	47±19*	47±19*	46±18*	46±18*

CF1 : Central frequency of low frequency oscillation.
CF2 : Central frequency of high frequency oscillation.
LFP : Low frequency power.
HFP : High frequency power.
TP : Total power.
NLFP : Normalized LFP.
NHFP : Normalized HFP.
MRR : Mean R-R interval.
MRRSD : Standard deviation of MRRR.
Hz : Hertz.
ms : millisecond.
* $p<0.05$.

Table III. Comparison of supine and tilt results of control group [Mean±SD (median)]

Variable	Units	Supine	Tilt 1st phase	Tilt 2nd phase	Tilt 3rd phase	Tilt 4th phase
CF1	Hz	0.105±0.018	0.088±0.019*	0.086±0.015*	0.087±0.009*	0.087±0.012*
CF2	Hz	0.308±0.043	0.293±0.045	0.294±0.053	0.277±0.043	0.281±0.037
LFP	ms²	1727±1185 (1433)	1063±687* (1048)	1212±617 (1096)	1379±505 (1443)	1262±914 (1115)
HFP	ms²	1490±1986 (882)	213±170* (164)	192±159* (146)	183±124* (186)	225±220* (104)
TP	ms²	3218±2779 (2316)	1267±808* (1238)	1405±715* (1267)	1562±589* (1556)	1488±1068* (1241)
NLFP	%	64±20	83±9*	86±8*	89±6*	86±10*
NHFP	%	36±20	16±9*	14±8*	11±6*	14±10*
MRR	ms	693±87	573±51*	573±40*	565±44*	564±41*
MRRSD	ms	62±22	42±11*	42±10*	43±9*	43±14*

CF1 : Central frequency of low frequency oscillation.
CF2 : Central frequency of high frequency oscillation.
LFP : Low frequency power.
HFP : High frequency power.
TP : Total power.
NLFP : Normalized LFP.
NHFP : Normalized HFP.
MRR : Mean R-R interval.
MRRSD : Standard deviation of MRRR.
Hz : Hertz.
ms : millisecond.
* $p<0.05$.

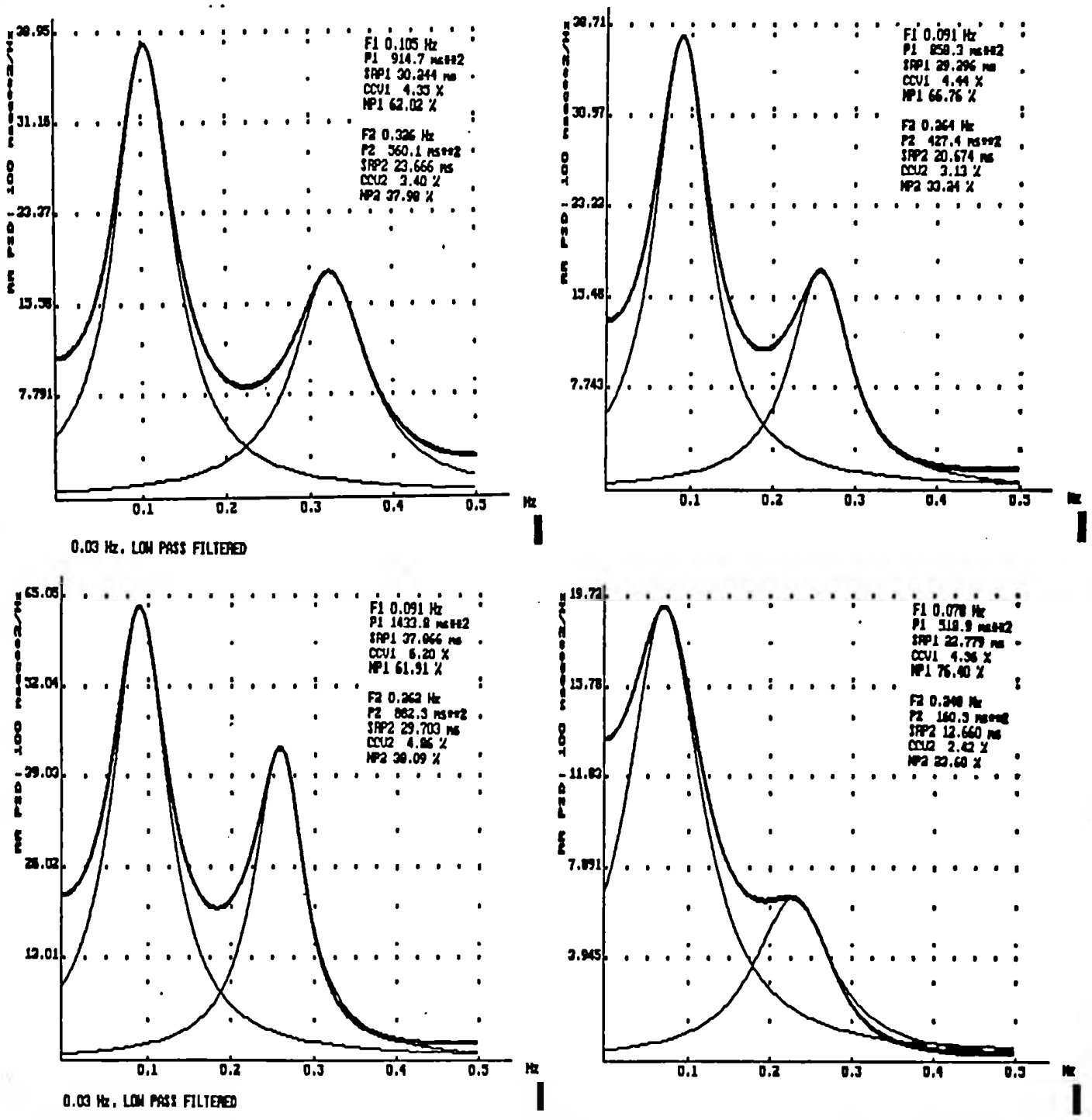

Fig. 1. Typical graphics of power spectral analysis; top left: patient supine, top right: patient first phase of tilt, bottom left: control supine, bottom right: control first phase of tilt. F1: Central frequency of low frequency, P1: Power of low frequency, NP1: % of normalized low frequency power, F2: Central frequency of high frequency, P2: Power of high frequency, NP2: % of normalized high frequency power.

Discussion

Power spectral analysis of heart rate variability has been accepted as a reliable, noninvasive tool for the assessment of sympathetic and parasympathetic control of the cardiovascular system in children as well as in adults[15-17]. To our knowledge, this is the first study which investigates HRV in children with aortic stenosis in supine and tilt positions. Dobutamine and isoproterenol are used in adults as sympathetic provocatives in stress echocardiography[18,19]. In the supine position, we did not find any significant difference between heart rate tachograms and power spectral analysis of HRV of children with aortic stenosis and of healthy controls. Some previous studies showed impairment of HRV in adult patients with severe aortic stenosis[13-14], and autonomic dysfunction tends to normalize within the first year of valve replacement[20]. Therefore, we can say that

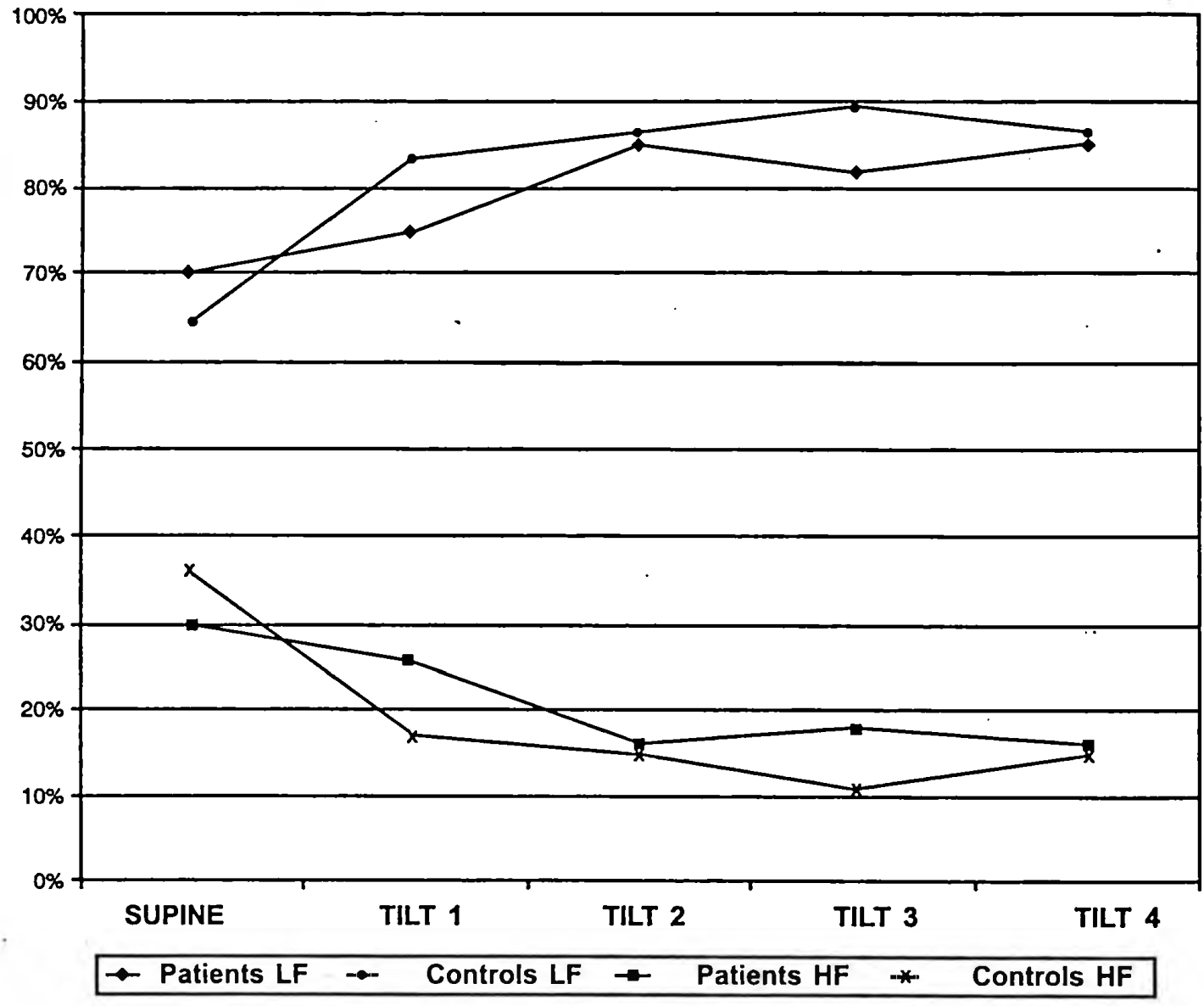

Fig. 2. Comparison of the percentages of normalized low frequency (LF) power and percentages of normalized high frequency (HF) power during tilt position phases. LF increased and HF decreased significantly by the first phase of tilt position in the control group and by the second phase of tilt in the patient group.

impairment of HRV is related to severity and duration of aortic stenosis.

Head-up tilt testing has become a widely accepted tool in the clinical evaluation of patients presenting with syncopal symptoms[21-23]. Head-up tilt position has been known to cause sympathetic excitation, vagal withdrawal and related heart rate changes[16-17]. In our study, both patients and controls showed similar response to tilt position: shifting of central frequency of LF to the left, decreased HF and total powers, and increase in normalized LF power and decrease in normalized HF power, thus an increase in normalized LF/HF ratio. However, there were some important differences between the groups in the timing of response to tilt testing. The patient group showed significantly delayed shifting of central frequency and also showed delayed increase in normalized F/HF ratio. It reflects that children with mild-to-moderate aortic stenosis have delayed response to sympathetic provocation. Previous studies have shown that LF/HF ratio is the best predictor of sympathovagal balance[2,4]. While LF has been found to be related with both the sympathetic and vagal limb of the autonomic nervous system, HF is accepted to be related only with vagal activity. The physiological interpretation of very low frequency component is not well known[2-3], thus we filtered very low frequency (<0.03 Hz) before power spectral analysis. In our study, we showed that augmentation of normalized LF/HF ratio is mainly due to decreased HF. The

major question that must be answered is why children with aortic stenosis showed a delayed response to sympathetic provocation. As is known, parasympathetic activity of the autonomic nervous system increases the fibrillation threshold and appears to protect against malignant ventricular tachyarrhythmias and related sudden cardiac death, while sympathetic activity decreases the threshold and predisposes to ventricular tachyarrhythmias[4]. We believe that in children with mild-to-moderate aortic stenosis, sympathovagal balance (LF/HF ratio) is well preserved and remains stable at the first phase of tilt position for protection against sudden predominance of sympathetic activity and related ventricular tachyarrhythmias. Although there was no statistically significant difference between control and patient groups in the supine position, a slight sympathetic predominance was detected in the patient group, and this chronic sympathetic activity could be the cause of delayed response to tilt position. When patients with aortic stenosis age, aortic stenosis becomes more severe and physical activity diminishes due to cardiac failure, rendering the protecting mechanism inadequate and increasing the risks of serious ventricular tachyarrhythmias and sudden cardiac death. Further studies with larger groups and wider symptomatology are needed to clarify our hypothesis.

REFERENCES

1. Akselrod S, Gordon D, Ubel FA, et al. Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat to beat cardiovascular control. Science 1981; 213: 220-222.
2. Malik M. Heart rate variability: standards of measurement, physiological interpretation, and clinical use. Circulation 1996; 93: 1043-1065.
3. Malliani A, Lombardi F, Pagani M. Power spectrum analysis of heart rate variability: a tool to explore neural regulatory mechanisms. Br Heart J 1994; 71: 1-2.
4. van Ravenswaaij-Arts CM, Kollee LA, Hopman JC, et al. Heart rate variability. Ann Intern Med 1993; 118: 436-447.
5. Casolo GC, Stroder P, Signoinin C, et al. Heart rate variability in the acute phase of myocardial infarction. Circulation 1992; 85: 2073-2079.
6. Wolf MM, Varigos GA, Hunt D, Sloman JG. Sinus arrhythmia in acute myocardial infarction. Med J Aust 1978; 52-53.
7. Casolo GC, Balli E, Taddei T, et al. Decreased spontaneous heart rate variability in congestive heart failure. Am J Cardiol 1989; 64: 1162-1167.
8. Mandawat MK, Wallbridge DR, Pringle SD, et al. Heart rate variability in left ventricular hypertrophy. Br Heart J 1995; 73: 139-144.
9. Malpas SC, Maling TJ. Heart rate variability and cardiac autonomic function in diabetes. Diabetes 1990; 39: 1177-1181.
10. Akıncı A, Çeliker A, Baykal E, Teziç T. Heart rate variability in diabetic children: sensitivity of the time and frequency domain methods. Pediatr Cardiol 1993; 14: 140-146.
11. Gordon D, Herrera VL, McAlpine L, et al. Heart-rate spectral analysis: a noninvasive probe of cardiovascular regulation in critically ill children with heart disease Pediatr Cardiol 1997; 9: 69-77.
12. Massin M, Bernuth G. Normal ranges of heart rate variability during infancy and childhood. Pediatr Cardiol 1997; 18: 297-302.
13. Airaksinen KE, Ikaheimo MJ, Koistinen MJ, Takkunen JT. Impaired vagal heart rate control in aortic valve stenosis. Eur Heart J 1988; 9: 1126-1130.
14. Jung J, Heisel A, Tscholl D, et al. Factors influencing heart rate variability in patients with severe aortic valve disease. Clin Cardiol 1997; 20: 341-344.
15. Goto M, Nagashima M,m Baba R, et al. Analysis of heart rate variability demonstrates effects of development on vagal modulation of heart rate in healthy children. J Pediatr 1997; 130: 725-729.
16. Vybiral T, Bryg RJ, Maddens ME, Boden WE. Effect of passive tilt on sympathetic and parasympathetic components of heart rate variability in normal subjects. Am J Cardiol 1989; 63: 1117-1120.
17. Yeragani VK, Pohl R, Berger R, et al. Relationship between age and heart rate variability in supine and standing postures: a study of spectral analysis of heart rate. Pediatr Cardiol 1994; 15: 14-20.
18. Takeda S, Rimington H, Chambers J. The relation between transaortic pressure difference and flow during dobutamine stress echocardiography in patients with aortic stenosis. Heart 1999; 82: 11-14.
19. Bermejo J, Antoranz JC, Garcia-Fermandez MA, Mareno MM, Delcan JL. Flow dynamics of stenotic aortic valves assessed by signal processing of Doppler spectrograms. Am J Cardiol 2000; 85: 611-617.
20. Vukosavic JL, Florenzano F, Adriazola P, Escobar E. Heart rate variability in severe aortic stenosis. J Heart Valve Dis 1999; 8: 143-148.
21. Alehan D, Lenk MK, Özmek S, Çeliker A, Özer S. Comparison of sensivitiy and specificity of tilt protocols with and without isoproterenol in children with unexplained syncope. PACE 1997; 20: 1769-1776.
22. Lenk MK, Alehan D, Özme S, Çeliker A, Özer S. Vasovagal syncope: asystole provoked by head-up tilt testing under sertraline therapy. Turk J Pediatr 1997; 39: 573-577.
23. Lenk M, Alehan D, Özme S, Çeliker A, Özer S. The role of serotinin re-uptake inhibitors in preventing recurrent unexplained childhood syncope a preliminary report. Eur J Pediatr 1997; 156: 747-750.