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Improvement in sympatho-vagal imbalance and heart rate variability in patients with mitral stenosis after percutaneous balloon commissurotomy

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Abstract Elevated sympathetic nerve activity in patients with mitral stenosis (MS) may be an index of the severity of the disease. Percutaneous mitral balloon commissurotomy (PMBC) is now a standard treatment for many patients with symptomatic MS. We aimed to show the effects of PMBC on autonomic nervous system activity in the patients with MS by heart rate variability (HRV) analysis.

Fifty-four consecutive patients with mitral stenosis and sinus rhythm who underwent percutaneous mitral commissurotomy were enroled. Apart from significant haemodynamic improvements, mean heart rate (HR), LF day, LF night, LF/HF day and night significantly decreased and SDNN, RMSSD, PNN50, HF day and night significantly increased in the early period after PMBC and these changes were preserved for up to one month. SDNN was positively correlated with left ventricle ejection fraction (LVEF) but negatively correlated with mean valve area (MVA), left atrial (LA) diameter and pressure, right atrial (RA) pressure; LF/HF day ratio was positively correlated with LA diameter and pressure, mean transmitral gradient and negatively correlated with LVEF; LF/HF night ratio was positively correlated with LA pressure and mean transmitral gradient. The increase in SDNN was correlated with the change in LA and RA pressure. The decrease in LF/HF ratio after PMBC was significantly correlated with the changes in the mean transmitral gradient, LA pressure and RA pressure.

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As a result, the heart rate variability and autonomic nervous system function in patients with mitral stenosis are correlated with the atrial pressures and left ventricular function. These parameters significantly change in the early period after PMBC and are preserved at one month. The improvement in the heart rate variability and sympatho-vagal balance are significantly affected by the early changes in atrial pressures after PMBC.
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Introduction

Mitral stenosis (MS) may increase sympathetic nervous activity by increasing left atrial (LA) pressure that alters pulmonary haemodynamics and reduces cardiac output similar to congestive heart failure [1,2]. Increased sympathetic activity may lead to atrial thrombus formation by precipitating platelet aggregation [3], may promote pulmonary congestion by stimulating renin release from the kidney [4], increase pulmonary arterial resistance [5] and shorten the diastolic filling period by increasing the heart rate [2]. Therefore, elevated sympathetic nerve activity may either be a risk factor for the development of clinical manifestations of MS or an index of the severity of the disease or both. Percutaneous mitral balloon commissurotomy (PMBC) is now a standard treatment for many patients with symptomatic MS [6–8] without any disturbance of the cardiac autonomic nervous system in contrast to surgical mitral commissurotomy.

Heart rate variability (HRV) analysis has been extensively used to evaluate autonomic modulation of sinus node and to identify patients at risk for an increased cardiac mortality [9]. HRV analysis has been shown to reflect sympatho-vagal balance and used previously to define the role of autonomic nervous system activity in certain cardiac disorders [10,11]. In this study, we examined the effects of PMBC on autonomic nervous system activity in the patients with MS by HRV analysis and assessed whether there is a correlation between the haemodynamic changes and the changes in autonomic function.

Materials and methods

Patients

Fifty-four consecutive patients with mitral stenosis and sinus rhythm who underwent successful percutaneous mitral commissurotomy between January 2002 and November 2003 were enroled in the study. All clinical, echocardiographic and HRV analysis data were prospectively collected. Patients with more than mild mitral regurgitation (MMR), significant aortic valve disease, mitral valve prolapse, coronary heart disease, diabetes mellitus, hypertension, thyroid disorders, unsuccessful PMBC were excluded from the study. All the drugs that may affect HRV analysis were withheld for at least 5 half-lives. All the patients were treated with low-dose diuretics and aspirin (300 mg/day) during the whole analysis.

Echocardiography

The transthoracic studies were performed by a standard technique using a Vingmed System Five with a 2.5-MHz probe one day before and after PMBC and at the one month visit. M-mode measurements were taken according to the recommendations of the American Society of Echocardiography [12]. The mitral valve area was measured by continuous wave Doppler using the pressure half time method. The mean transmitral diastolic pressure gradient was calculated by the diastolic velocity–time integral from the maximal transmitral flow velocity. Left atrial diameter was taken in the parasternal long axis view in M-mode at end systole. The measurements were made of three beats. Mitral regurgitation was graded by colour Doppler echocardiography as recommended by Helmcke et al. [13]. Transoesophageal echocardiography was performed routinely in all patients to evaluate intracardiac thrombus.

Percutaneous mitral balloon commissurotomy

The patients first underwent diagnostic right and left heart catheterization. After biplane left ventriculograms were obtained, PMBC was performed by transvenous (antegrade) approach through the femoral vein using the Inoue et al. technique [6]. Sequential inflation of the Inoue balloon catheter was performed at increasing balloon diameters until the balloon waist disappeared. Right and left

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heart catheterization, left ventriculography were repeated after PMBC. The successful PMBC was defined as the increase in mitral valve area (MVA) by 50% or $>2\,cm^2$ without significant MR ($>2+$) and left to right shunt (>1.5).

Heart rate variability analysis

All patients underwent 3 channel 24-h Holter ambulatory ECG monitoring (Biomedical System Century 2000/3000 Holter System, Version 1.32) three times; one day before PMBC, in the first day and one month after PMBC. Recordings were analyzed by 'Biomedical Systems Century 2000/3000 HRV Package System', following manual adjustment of RR intervals. Patients were instructed to behave in a normal manner with usual daily physical activity. Analog data were digitized at 200 Hz and edited by a cardiologist. The validation procedure consisted of beat labelling and tagging of noisy regions. The continuous series of RR intervals (tachogram) was obtained and all 5 min segments with a maximum of five isolated ectopic beats were retained for spectral analysis. Recordings with <18 h of data or $<85\%$ of qualified sinus beats were excluded. The time and frequency-domain analysis of HRV were performed according to the recommendation of the European Society of Cardiology task force [9]. The mean heart rate, standard deviation of all NN intervals (SDNN), root mean square of successive differences (RMSSD), number of NN intervals that differed by more than 50 ms from adjacent interval divided by the total number of all NN intervals (PNN50) were measured in the time domain analysis of HRV. A reduced SDNN has been considered to reflect a diminished vagal and an increased sympathetic modulation of sinus node [9]. The power spectrum of HRV was measured using fast-Fourier transform analysis in four frequency bands: <0.0033 (ultra low frequency, ULF), 0.0033—0.04 (very low frequency, VLF), 0.04—0.15 (low frequency, LF) and 0.15—0.40 Hz (high frequency, HF). HF was used as a marker of the parasympathetic nervous system and LF was used as a marker of sympathetic activity [6]. The power of these components was stated as normalized units (nu). The normalization procedure is crucial for the interpretation of data [14]. We also measured the ratio of low—high frequency power (LF/HF) reflecting the sympatho-vagal balance. High values (>2) were considered to reflect a shift of sympatho-vagal balance towards sympathetic predominance [14]. For frequency-domain parameters three circadian periods were considered, the complete 24 h, the diurnal and the nocturnal periods defined on the basis of patient diaries. Diurnal periods covered lengths of at least 6 h to a maximum of 10 h; nocturnal periods covered a minimum of 4 h to a maximum of 6 h. Normalized LF and HF components were defined dividing the corresponding raw power by total power minus the power in the VLF band [$LF(nu) = LF/(TP - VLF)$].

Statistical analysis

Continuous variables are presented as mean $\pm$ SD and discrete variables are expressed as frequencies and percentages. Paired *t*-test was used to compare the continuous variables before and after PMBC. Pearson's correlation analysis was performed to show the correlation between haemodynamic, echocardiographic variables and HRV parameters before PMBC. Linear logistic regression and correlation analysis were performed to define the correlation between changes in echocardiographic, haemodynamic parameters and heart rate variability after PMBC.

Results

Fifty-four patients (12 male and 42 female with an average age of 30.6 ± 6.7 years) who underwent successful PMBC were included in this study. The mitral valve area (MVA) ranged between 0.8 and $1.3\,cm^2$, transmitral mean gradient was 13.2 ± 2.5 mmHg (range 8—21), systolic pulmonary arterial pressure (SPAP) was 48.8 ± 11.6 mmHg (range 35—70), left atrial (LA) diameter was 4.4 ± 0.2 cm (range 3.8—4.9) and left ventricle ejection fraction (LVEF) was $62.6 \pm 3.1\%$ (range 55—68). Mitral regurgitation was present in 30 (56%) of all patients: in 6 (20%) of them, MR was $1+$, and in the remainder there was only minimal regurgitation.

Mitral valve area and LVEF were significantly increased and transmitral mean gradient, SPAP, LA diameter, mean LA pressure, mean right atrial (RA) pressure were significantly decreased after PMBC. At the one month visit, the increased MVA and LVEF, the decrease in mean transmitral gradient, LA diameter and SPAP were seen to persist (Table 1). Regarding HRV parameters, mean HR, LF day, LF night, LF/HF day and night significantly decreased and SDNN, RMSSD, PNN50, HF day and night significantly increased one day after PMBC and these changes were shown to be preserved at one month (Table 1). All the patients were totally asymptomatic at the one month follow-up visit.

Pearson's correlation analysis revealed that some HRV parameters were correlated with the

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Table 1 Echocardiographic, haemodynamic variables and heart rate variability parameters before and after percutaneous mitral balloon commissurotomy

	Before PMBC	After PMBC	
		One day	One month
Echocardiographic variables			
Mitral valve area (cm^2)	1.03 ± 0.2	1.9 ± 0.2*	1.9 ± 0.3*
Transmitral mean gradient (mmHg)	13.2 ± 2.5	2.4 ± 1.2*	3.0 ± 1.4*
Systolic PAP (mmHg)	48.8 ± 11.6	33.0 ± 7.3*	34.4 ± 6.5*
Left atrial diameter (cm)	4.4 ± 0.2	4.2 ± 0.2*	4.2 ± 0.3*
Left ventricular EF (%)	62.6 ± 3.1	64.3 ± 2.5*	65.2 ± 3.4*
Haemodynamic variables			
Left atrial pressure (mmHg)	23.1 ± 2.6	12.1 ± 1.9*	
Right atrial pressure (mmHg)	7.7 ± 2.4	6.6 ± 1.9*	
HRV parameters			
Mean heart rate (beats/min)	82.7 ± 9.5	72.5 ± 6.9*	75.4 ± 9.4*
SDNN (ms)	101.0 ± 34.1	138.1 ± 67.8*	136.6 ± 56.6*
RMSSD (ms)	32.8 ± 13.7	55.6 ± 28.5*	54.4 ± 22.5*
PNN50 (%)	9.0 ± 7.3	18.6 ± 15.6*	16.8 ± 9.8*
LF day (nu)	77.7 ± 8.4	56.5 ± 8.5*	58.2 ± 7.3*
HF day (nu)	22.5 ± 6.5	43.6 ± 6.9*	42.1 ± 7.2*
LF/HF day	3.9 ± 1.6	1.4 ± 0.4*	1.5 ± 0.3*
LF night (nu)	60.1 ± 14.7	44.7 ± 9.6*	47.7 ± 6.8*
HF night (nu)	40.3 ± 11.5	53.6 ± 10.3*	54.3 ± 9.8*
LF/HF night	1.8 ± 1.1	1.0 ± 0.3*	1.1 ± 0.3*

PAP: pulmonary arterial pressure, HRV: heart rate variability, PMBC: percutaneous mitral balloon commissurotomy; *: $P < 0.001$ compared with before PMBC. SDNN, RMSSD, PNN50, LF and HF are defined in the text.

Table 2 Correlation between heart rate variability parameters and echocardiographic, haemodynamic variables before PMBC

		MVA	LA diameter	LVEF	RA pressure	LA pressure	SPAP	Mean gradient
HR		$r = -0.05$	$r = 0.1$	$r = 0.2$	$r = 0.06$	$r = 0.2$	$r = 0.2$	$r = 0.15$
		$P = 0.6$	$P = 0.1$	$P = 0.3$	$P = 0.6$	$P = 0.1$	$P = 0.1$	$P = 0.3$
SDNN		$r = -0.5$	$r = -0.3$	$r = 0.6$	$r = -0.3$	$r = -0.5$	$r = 0.13$	$r = 0.15$
		$P = 0.005$	$P = 0.01$	$P = 0.006$	$P = 0.01$	$P = 0.03$	$P = 0.4$	$P = 0.3$
RMSSD		$r = -0.1$	$r = 0.09$	$r = 0.2$	$r = -0.7$	$r = -0.6$	$r = 0.14$	$r = 0.4$
		$P = 0.4$	$P = 0.5$	$P = 0.2$	$P = 0.001$	$P = 0.001$	$P = 0.3$	$P = 0.001$
PNN50		$r = -0.5$	$r = 0.02$	$r = 0.2$	$r = -0.6$	$r = -0.5$	$r = 0.1$	$r = 0.4$
		$P = 0.005$	$P = 0.9$	$P = 0.3$	$P = 0.001$	$P = 0.001$	$P = 0.5$	$P = 0.007$
Day	LF	$r = -0.2$	$r = 0.6$	$r = -0.6$	$r = 0.3$	$r = 0.5$	$r = 0.3$	$r = 0.2$
		$P = 0.1$	$P = 0.001$	$P = 0.01$	$P = 0.04$	$P = 0.001$	$P = 0.04$	$P = 0.2$
	HF	$r = 0.3$	$r = 0.1$	$r = 0.5$	$r = -0.3$	$r = -0.2$	$r = -0.3$	$r = -0.2$
		$P = 0.07$	$P = 0.4$	$P = 0.001$	$P = 0.03$	$P = 0.3$	$P = 0.03$	$P = 0.1$
	LF/HF	$r = -0.2$	$r = 0.2$	$r = -0.4$	$r = 0.1$	$r = 0.4$	$r = 0.1$	$r = 0.3$
		$P = 0.1$	$P = 0.02$	$P = 0.01$	$P = 0.4$	$P = 0.01$	$P = 0.4$	$P = 0.04$
Night	LF	$r = -0.1$	$r = 0.05$	$r = -0.4$	$r = 0.2$	$r = 0.2$	$r = 0.2$	$r = 0.2$
		$P = 0.95$	$P = 0.7$	$P = 0.8$	$P = 0.3$	$P = 0.1$	$P = 0.3$	$P = 0.2$
	HF	$r = -0.1$	$r = -0.08$	$r = 0.03$	$r = -0.2$	$r = -0.4$	$r = -0.2$	$r = -0.4$
		$P = 0.9$	$P = 0.6$	$P = 0.08$	$P = 0.2$	$P = 0.004$	$P = 0.2$	$P = 0.002$
	LF/HF	$r = -0.1$	$r = 0.2$	$r = 0.2$	$r = 0.1$	$r = 0.5$	$r = 0.1$	$r = 0.3$
		$P = 0.5$	$P = 0.2$	$P = 0.2$	$P = 0.4$	$P = 0.01$	$P = 0.4$	$P = 0.04$

MVA: mitral valve area, SPAP: systolic pulmonary arterial pressure, LA: left atrium, HR: heart rate, LVEF: left ventricle ejection fraction. SDNN, RMSSD, PNN50, LF and HF are defined in the text.

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echocardiographic and haemodynamic variables before PMBC (Table 2). The factors affecting the symptomatic status of the patients before PMBC were mean HR ($\beta = 0.5$, $P = 0.03$), SDNN ($\beta = 0.6$, $P = 0.02$), LF/HF ratio ($\beta = 0.5$, $P = 0.01$), MVA ($\beta = -0.3$, $P = 0.03$) and mean gradient ($\beta = 0.4$, $P = 0.007$). The symptomatic improvement at one month after PMBC was found to be correlated with the increase in SDNN ($\beta = 0.5$, $P = 0.01$), the decrease in LF/HF ($\beta = -0.5$, $P = 0.002$) and the decrease in mean transvalvular gradient ($\beta = -0.4$, $P = 0.004$).

Linear regression and correlation analysis revealed that the increase in SDNN was independently affected by age, the change in LA pressure and RA pressure (Table 3). The increase in RMSSD was correlated with the change in RA pressure ($\beta = -0.3$, $P = 0.04$) and the change in MVA ($\beta = 0.3$, $P = 0.009$). The independent variables affecting the increase in PNN50 after PMBC were the changes in MVA ($\beta = 0.3$, $P = 0.02$) and SPAP ($\beta = -0.4$, $P = 0.02$). The decrease in LF/HF ratio after PMBC was significantly correlated with the changes in the mean transmitral gradient, LA pressure and RA pressure (Table 4). The independent variables affecting the increase in HF after PMBC were the changes in MVA ($\beta = 0.4$, $P = 0.03$) and SPAP ($\beta = -0.4$, $P = 0.04$) however, the decrease in LF was significantly affected by the increase in MVA ($\beta = -0.4$, $P = 0.009$) and the decrease in RA pressure ($\beta = 0.5$, $P = 0.01$).

Table 3 The variables affecting the change in SDNN one day after PMBC

Variables	S.E.	β	t	P
Age	1.2	0.5	4.1	0.001
Gender	21.4	0.4	2.6	0.1
ΔLA diameter	44.9	−0.1	−0.9	0.4
ΔLVEF	6.9	0.002	0.2	0.9
ΔMVA	36.8	−0.09	−0.7	0.5
ΔMean gradient	9.6	−0.7	−1.8	0.09
ΔLAP	1.3	−0.3	−2.1	0.03
ΔRAP	1.8	−0.7	−1.5	0.01
ΔSPAP	8.7	0.3	0.9	0.4

LA: left atrium, LVEF: left ventricle ejection fraction, MVA: mitral valve area, LAP: left atrial pressure, RAP: right atrial pressure, SPAP: systolic pulmonary arterial pressure, Δ: the difference between pre-PMBC and post-PMBC values (one day after), S.E.: standard error, β: standardized coefficient.

Table 4 Factors affecting the change in LF/HF ratio one day after PMBC

Variables	S.E.	β	t	P
Age	0.03	−0.2	−1.4	0.2
Gender	0.6	−0.07	−0.5	0.7
ΔLA diameter	1.2	0.07	0.5	0.7
ΔLVEF	0.2	−0.05	−0.3	0.8
ΔMVA	1.0	0.2	1.4	0.2
ΔMean gradient	0.08	0.4	3.4	0.001
ΔLAP	0.2	0.4	1.9	0.02
ΔRAP	0.3	0.4	3.2	0.002
ΔSPAP	0.03	0.1	0.9	0.4

Abbreviations as for Table 3.

Discussion

The major findings in our study can be summarized as; (1) The HRV parameters reflecting autonomic nervous system function in patients with MS are correlated with some haemodynamic variables such as atrial pressures, LA dimension and MVA, (2) These HRV parameters as well as some haemodynamic variables are related to the symptomatic status of the patients with MS, (3) After PMBC, there is a striking decrease in sympathetic activity and an increase in parasympathetic activity which are also correlated with the changes in haemodynamic parameters, (4) The symptomatic improvement in the patients with MS at one month after PMBC is correlated with the changes in HRV parameters.

Autonomic nervous system dysfunction in patients with MS may be associated with, (1) *Reduction in cardiac index*: a significant decrease in stroke index in patients with congestive heart failure has been related to sympathetic activation in these patients [15,16] and a similar mechanism may play a role in patients with MS [2], (2) *Increased atrial or pulmonary arterial pressure*: the increase in left atrial or pulmonary arterial pressure may alter sympathetic activity through cardiopulmonary mechanisms [2], (3) *Atrial stretch*: stretching the right atrium produces a definite increase in sympathetic activity [17] whereas left atrial stretch causes a biphasic response: an initial sympathetic nerve inhibition followed by sympathetic activation [17,18], (4) *Hormonal factors*: plasma noradrenaline (nor-epinephrine) (NE) concentrations were increased in patients with MS and decreased after PMBC [2]. However, in addition to the relative insensitivity of NE as an index of sympathetic activity [19,20], the effects of other hormones such as atrial natriuretic peptide (ANP) [21–23], brain natriuretic peptide (BNP) [21,24] and vasopressin [25] on sympathetic activity are contradictory. As a result, it is reasonable to consider that the improvement in autonomic nervous system function after PMBC would be produced by the changes in these factors after

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valvuloplasty. According to our results, although LVEF was an important determinant for SDNN, LF, HF and LF/HF before PMBC, the improvements in these parameters in the early period after PMBC were greatly affected by the decrease in atrial pressures but not with the increase in LVEF. Therefore, chronic atrial stretch and the decrease in atrial pressures in early period after PMBC may explain the sympathetic overactivity in patients with MS and the decrease after PMBC, respectively.

Ashino et al. [2] initially demonstrated that arterial and cardiopulmonary baroreflex are impaired in patients with mitral stenosis and this impaired baroreflex sensitivity is normalized one week after mitral balloon valvuloplasty. They concluded that central sympathetic outflow to the skeletal muscle was increased mainly due to a reduction in cardiac output that decreases afferent activity from the baroreceptors. The decrease in sympathetic nerve activity significantly correlates with the increase in cardiac index and stroke index and with the decrease in total peripheral resistance index but not with the changes in pulmonary arterial pressure, pulmonary vascular resistance index and left atrial pressure. Later, Yuasa et al. also found that muscle sympathetic activity and plasma NE concentrations are significantly decreased and cardiopulmonary baroreflex sensitivity is improved again one week after PMBC [26] in accordance with Ashino et al. However, there was no significant correlation between cardiopulmonary baroreflex sensitivity and haemodynamic parameters such as arterial pressure, heart rate, cardiac output, mean capillary wedge pressure, right atrial pressure and left ventricular enddiastolic pressure. They claimed that a functional rather than anatomical abnormality is more likely to be important in the pathogenesis of cardiopulmonary baroreflex abnormalities and improvement in cardiopulmonary baroreflex sensitivity may contribute to the attenuation of sympathetic activity after mitral valvuloplasty.

As a result, the heart rate variability and autonomic nervous system function in patients with mitral stenosis are correlated with atrial pressures and left ventricular function. These parameters significantly change in the early period after PMBC and are well-preserved at one month. The improvement in heart rate variability and sympatho-vagal balance is significantly correlated with the early changes in atrial pressures after PMBC. Sympathetic overactivity may be a risk factor for the development of clinical findings in MS and the decrease in sympathetic overactivity after PMBC in these patients may partly account for the improvement in symptomatic status.

The adrenergic activation associated with MS is the result of the complex interaction of several neural reflexes originating from different reflexogenic areas in addition to non-neural mechanisms. Unfortunately, HRV analysis does not allow the appraisal of individual mechanisms involved but provides adequate evidence of the final results of such interactions. Lack of plasma noradrenaline, ANP and BNP measurements is the most significant limitation of this study.

References

[1] Cohn JN, Levine TB, Olivari MT, et al. Plasma norepinephrine as a guide to prognosis in patients with chronic congestive heart failure. N Engl J Med 1984;311:819—23.

[2] Ashino K, Gotoh E, Sumita S, Moriya A, Ishii M. Percutaneous transluminal mitral valvuloplasty normalizes baroreflex sensitivity and sympathetic activity in patients with mitral stenosis. Circulation 1997;96:3443—9.

[3] Clayton S, Cross MJ. The aggregation of blood platelets by cathecolamines and by thrombin. J Physiol 1963;169:82—3.

[4] Keeton TK, Campbell WB. The pharmacologic alteration of renin release. Pharmacol Rev 1980;32:81—227.

[5] Pace JB. Sympathetic control of pulmonary vascular impedance in anesthetized dogs. Circ Res 1971;29:555—68.

[6] Inoue K, Owaki T, Nakamura T, Kitamura F, Miyamoto N. Clinical application of transvenous mitral commissurotomy by a new balloon catheter. J Thorac Cardiovasc Surg 1984; 87:394—402.

[7] Reyes VP, Raju BS, Wynne J, et al. Percutaneous balloon valvuloplasty compared with open surgical commissurotomy for mitral stenosis. N Engl J Med 1994;331:961—7.

[8] Iung B, Cormier B, Ducimetiere P, et al. Functional results 5 years after successful percutaneous mitral commissurotomy in a series of 528 patients and analysis of predictive factors. J Am Coll Cardiol 1996;27:407—14.

[9] Task force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability, standards of measurement, physiogical interpretation and clinical use. Circulation 1996;93: 1043—65.

[10] Ozdemir O, Soylu M, Demir AD, et al. Increased sympathetic nervous system activity as a cause of exercise-induced ventricular tachycardia in patients with normal coronary arteries. Tex Heart Inst J 2003;30:100—4.

[11] Demir AD, Soylu M, Balbay Y, Ozdemir O, Korkmaz S. Assessment of autonomic function in subjects with early repolarization. Am J Cardiol 2002;89:990—2.

[12] Sahn DJ, DeMaria A, Kisslo J, et al. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurement. Circulation 1978;58:1072—83.

[13] Helmcke F, Nanda N, Hsiung M, et al. Color Doppler assessment of mitral regurgitation with orthogonal planes. Circulation 1987;75:175—83.

[14] Pagani M, Lombardi F, Guzzetti S, et al. Power spectral analysis of heart rate and arterial pressure variabilities as a marker of sympatho-vagal interaction in man and conscious dog. Circ Res 1986;59:178—93.

[15] Ferguson DW, Berg WJ, Sanders JS. Clinical and haemodynamic correlates of sympathetic nerve activity in normal humans and patients with heart failure: evidence from

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microneurographic recordings. J Am Coll Cardiol 1990;16: 1125—34.
[16] Ando S, Dajani HR, Floras JS. Frequency domain characteristics of muscle sympathetic nerve activity in heart failure and healthy humans. Am J Physiol 1997; 273:R205—12.
[17] Kollai M, Koizumi K, Yamashita H, Brooks CM. Study of cardiac sympathetic and vagal efferent activity during reflex responses produced by stretch of the atria. Brain Res 1978;150:519—32.
[18] Koizumi K, Nishino H, Brooks CM. Centers involved in the autonomic reflex reactions originating from stretching of the atria. Proc Natl Acad Sci U S A 1977;74:2177—81.
[19] Hoeldtke RD, Cilmi KM, Reichard Jr GA, Borden G, Owen OE. Assessment of norepinehrine secretion and production. J Lab Clin Med 1983;101:772—82.
[20] Davis D, Baily R, Zelis R. Abnormalities in systemic norepinephrine kinetics in human congestive heart failure. Am J Physiol 1988;254:E760—6.
[21] Nakamura M, Kawata Y, Yoshida H, et al. Relationship between plasma atrial and brain natriuretic peptide concentration and haemodynamic parameters during percutaneous transvenous mitral valvulotomy in patients with mitral stenosis. Am Heart J 1992;124:1283—8.
[22] Abramson BL, Ando S, Notarius CF, Rongen GA, Floras JS. Effect of atrial natriuretic peptide on muscle sympathetic activity and its reflex control in human heart failure. Circulation 1999;99:1810—5.
[23] Butler GC, Senn BL, Floras JS. Influence of atrial natriuretic factor on heart rate variability in normal men. Am J Physiol 1994;267:H500—5.
[24] Brunner-La Rocca HP, Kaye DM, Woods RL, Hastings J, Esler MD. Effects of intravenous brain natriuretic peptide on regional sympathetic activity in patients with chronic heart failure as compared with healthy control subjects. J Am Coll Cardiol 2001;37:1221—7.
[25] Suzuki S, Takeshita A, Imaizumi T, et al. Central nervous system mechanisms involved in inhibition of renal sympathetic nerve activity induced by arginine vasopressin. Circ Res 1989;65:1390—9.
[26] Yuasa T, Takata S, Terasaki T, et al. Percutaneous transluminal mitral valvuloplasty improves cardiopulmonary baroreflex sensitivity in patients with mitral stenosis. Auton Neurosci 2001;94:117—24.

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