Altered autonomic cardiac control in hypertrophic cardiomyopathy

Role of outflow tract obstruction and myocardial hypertrophy

U. Limbruno, G Strata, R. Zucchi, R. Baglini, G. Mengozzi, A. Balbarini and M. Mariani

Cardiovascular and Pulmonary Department, University of Pisa, Pisa, Italy

Aim The goal of this study was to investigate the role of left ventricular outflow tract obstruction and myocardial hypertrophy on autonomic cardiac function in patients with hypertrophic cardiomyopathy.

Methods and results The sympatho-vagal function was evaluated by spectral analysis of heart rate variability in 28 patients with hypertrophic obstructive cardiomyopathy, 22 patients with hypertrophic non-obstructive cardiomyopathy, 12 with systemic hypertension and left ventricular hypertrophy and 28 healthy subjects. Left ventricular outflow tract pressure gradient in patients with hypertrophic cardiomyopathy was evaluated by echo-Doppler methods and the quantitative assessment of left ventricular hypertrophy was based on an echocardiographic index. At rest, patients with hypertrophic non-obstructive cardiomyopathy showed normal spectral patterns, while in patients with hypertrophic obstructive cardiomyopathy and in patients with systemic hypertension we observed, respectively, a significant reduction and increase in the low frequency component relative to the control (P <0.05). During tilt, the physiological increases in the low frequency component, and in the low to high frequency ratio were markedly blunted, or even reverted, only in patients with hypertrophic obstructive cardiomyopathy. In these patients, the heart rate increase during tilt was delayed in comparison to the other groups. Finally, in the hypertrophic obstructive cardiomyopathy group, the impairment of sympathetic activation (lack of increase in the low frequency component during tilt) was significantly correlated to the echocardiographic index of left ventricular hypertrophy (r = −0.800, P <0.001) rather than to the left ventricular outflow tract pressure gradient (r =0.295, P : ns).

Conclusion Among patients with hypertrophic cardiomyopathy, only those with outflow tract obstruction show spectral signs of altered autonomic cardiac control. Within this group, the autonomic dysfunction appears to be correlated to myocardial hypertrophy rather than to left ventricular outflow tract obstruction (Eur Heart J 1998; 19: 146-153).

Key Words: Spectral analysis, Hypertrophic cardiomyopathy, systemic hypertension, autonomic nervous system.

Introduction

Several data suggest that autonomic dysfunction may play a role in the pathogenesis of hypertrophic cardiomyopathy. In fact, clinical and haemodynamic findings of hypertrophic obstructive cardiomyopathy, such as left ventricular hypercontractility with dynamic outflow tract obstruction, high incidence of ventricular tachyarrhythmias and effectiveness of beta-blocking agents, suggest a possible involvement of the sympathetic nervous system[1-5]. In addition, other studies show reduced parasymathetic cardiac control occurring in hypertrophic obstructive cardiomyopathy[6,7]. In the experimental setting, adrenaline infusion at sub-hypertensive doses induces biventricular hypertrophy[8-10]. Abnormalities in myocardial response to catecholamines, possibly related to altered adrenergic receptor density and/or sensitivity, and reduced norepinephrine reuptake from sympathetic cardiac fibres have also been reported[11,12]. However, the hypothesis of involvement of the autonomic nervous system in the pathogenesis of hypertrophic cardiomyopathy has been questioned and remains controversial[13-16].

Power spectral analysis of heart rate variability has been used extensively for non-invasive assessment of the autonomic nervous control of cardiac function[17-23]. The power spectrum of heart rate in humans contains...
two major components of clinical interest: the low frequency component (approximately centred at 0·1 Hz) and the high frequency component (approximately centred at 0·25 Hz)\textsuperscript{[18,22,24–26]}. These two components show synchronous changes which are closely related to the changes in the autonomic balance\textsuperscript{[27]}. Spectral analysis may thus provide a valuable estimate of the interaction between parasympathetic and sympathetic neural oscillatory structures\textsuperscript{[27]}. The purpose of this study was to investigate: (i) the autonomic modulation of cardiac rhythm, as assessed by spectral analysis of heart rate variability, in patients with hypertrophic cardiomyopathy; (ii) the relationship between the autonomic activity and two major features of this clinical condition, i.e. left ventricular outflow tract obstruction and myocardial hypertrophy. Patients with essential systemic hypertension and secondary left ventricular hypertrophy, a physiopathological setting known to be associated with sympathetic predominance\textsuperscript{[28]}, were also included in the study in order to compare the autonomic changes associated with different types of myocardial hypertrophy.

**Methods**

**Patient population**

We studied 28 patients (18 males, 10 females, mean age 41 ± 16 years) with hypertrophic obstructive cardiomyopathy, and 22 patients (14 males, 8 females, mean age 40 ± 14 years) with hypertrophic non-obstructive cardiomyopathy. Diagnosis was based on the echocardiographic demonstration of a hypertrophied and non-dilated left ventricle in the absence of other cardiac or systemic diseases capable of inducing myocardial hypertrophy\textsuperscript{[29]}. A haemodynamic study (including left ventricular angiography, coronary angiography and endomyocardial biopsy) was also performed in 32 patients with hypertrophic cardiomyopathy (20 obstructive and 12 non-obstructive). Doppler intraventricular peak pressure gradient measured at basal conditions was greater than 25 mmHg in all patients with hypertrophic obstructive cardiomyopathy. In patients with hypertrophic non-obstructive cardiomyopathy, the absence of the intraventricular pressure gradient was confirmed, both at basal conditions and during tilt. The clinical characteristics of the 50 patients with hypertrophic cardiomyopathy are summarized in Table 1. Twelve additional patients (7M, 5F, mean age 41 ± 15 years) affected by essential systemic hypertension (diastolic blood pressure consistently higher than 95 mmHg as assessed by at least five measurements on 3 separate days) were enrolled. All patients with systemic hypertension had echocardiographic evidence of left ventricular hypertrophy (left ventricular mass >134 g.m\textsuperscript{-2}) as calculated by the Penn cube method described by Devereux et al\textsuperscript{[30]}. Patients with clinical and/or instrumental evidence of coexisting overt heart failure, coronary artery disease, diabetes, uraemia or neurological disorders were excluded from the study. Patients with relevant rhythm disturbances, such as marked sinus arrhythmia, atrial fibrillation or flutter, frequent ectopic beats or conduction blocks were also excluded. Twenty-eight healthy subjects (18 males, 10 females, mean age 42 ± 17 years) were considered as controls.

All medications were discontinued 3 days before the study. Beta-blocker drugs were taken by 15 out of 28 patients (54%) with hypertrophic obstructive cardiomyopathy, six out of 22 patients (27%) with hypertrophic non-obstructive cardiomyopathy and five out of 12 patients (42%) with systemic hypertension. No patients were taking (or were previously administered) amiodarone. Consumption of alcoholic or caffeinated beverages and cigarette smoking were avoided in the 12 h preceding the study. All subjects gave their informed consent to the investigation.

**Spectral analysis of heart rate variability**

Spectral analysis was performed according to the standards specified by the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology\textsuperscript{[31]}. The ECGs were recorded between 1000h and 1300h, at least 2 h after a meal in a quiet room with a stable temperature (21–23 °C). After 20 min of rest in a sitting position, each participant was placed in a supine position and connected to a solid-state storage ECG recorder with chest electrodes. Respiratory activity was monitored by a nose-tip thermistor. After the 20 min allowed for stabilization, a 50 min recording period in control conditions was performed. The participants were then positioned at a 60° angle with passive tilt and an additional 40 min recording was performed. Arterial blood pressure was measured by a conventional sphygmomanometer at the end of the rest period, and at minute 1, 20 and 40 of the tilt test period. Three of the authors reviewed all computer displayed ECGs to select from each phase of the

| Table 1 Clinical characteristics of patients with hypertrophic cardiomyopathy |
|-----------------------------|-----------------------------|
|                             | HOCM (n=28) | HNCM (n=22) |
| Age (years)                     | 41 ± 16     | 40 ± 14     |
| Male sex                         | 18 (64%)    | 14 (64%)    |
| Family history of HCM           | 15 (53%)    | 9 (41%)     |
| Family history of PSD           | 6 (21%)     | 5 (23%)     |
| Syncope or pre-syncope          | 7 (25%)     | 3 (14%)     |
| Exertional chest pain           | 11 (39%)    | 7 (32%)     |
| Exertional dyspnoea             | 5 (18%)     | 5 (23%)     |

HCM = hypertrophic cardiomyopathy; HNCM = hypertrophic non-obstructive cardiomyopathy group; HOCM = hypertrophic obstructive cardiomyopathy group; PSD = premature sudden cardiac death.

† New York Heart Association class II in all cases.
protocol at least 5–7 series of approximately 512 consecutive R R intervals of stationary sinus rhythm. An autoregressive model was used to estimate the power spectrum of the heart rate variability[20,25,31]. The autoregressive coefficients were automatically calculated by the computer program, while the model order which minimized A kaike’s final prediction error figure of merit was chosen[32]. Each spectral component was then identified by the centre frequency and quantified by its power. The latter was expressed in normalized units (n.u.) obtained by dividing the absolute power (ms × ms) of the individual component by the total variance after having subtracted from it the DC component — this ratio multiplied by 100. The use of normalized units facilitates comparison of spectra with large differences in total variance[22]. Only components with an individual power greater than 5% of the total power were considered to be significant. Those at 0·04–0·15 Hz were defined as low frequency components and those at 0·15–0·40 Hz as high frequency components; the R R interval variance and the low to high frequency ratio, the latter having been reported to be an index of sympato-vagal balance[25,27], were also calculated.

**Colour Doppler echocardiography**

All patients were studied by 2D colour Doppler echocardiography using a commercial machine (Toshiba SSH-16) equipped with 2·5 and 3·75 M Hz probes within a few hours from the execution of spectral analysis.

The entity and extent of left ventricular hypertrophy in patients with hypertrophic cardiomyopathy and systemic hypertension was evaluated by means of an echocardiographic index of left ventricular hypertrophy as described by Spirito et al.[33,34]. Left ventricular walls were visualized in the parasternal short axis view at the level of both the mitral valve and the papillary muscles. The left ventricle was then subdivided in four segments (anterior and posterior interventricular septum and the lateral and posterior left ventricular free walls) and the index was obtained by adding the maximal end-diastolic wall thickness measured (at either mitral valve or papillary muscle level) in each of the four segments. Spectral CW Doppler was used to measure the intraventricular peak pressure gradient at clinostatism and during 60° passive tilt. The ultrasonic beam was aligned to the blood flow as guided by the colour Doppler signal.

**Statistical analysis**

Data were expressed as mean ± SD. The significance of differences between rest and tilt was tested with the Student’s paired t-test. The significance of differences between groups was tested by the analysis of variance with the Newman–K euls test[35]. The significance of differences between groups as regards total variance, low frequency component power density, high frequency component power density and low to high frequency ratio was also evaluated by non-parametric analysis (M ann–Withney test) [36]. Linear regression analysis was performed between spectral and echo-Doppler parameters. A P value of less than 0·05 was considered significant.

**Results**

Table 2 shows the main spectral parameters obtained in hypertrophic obstructive cardiomyopathy, hypertrophic non-obstructive cardiomyopathy, essential systemic hypertension and control groups. At rest (supine position), the low frequency component was slightly, although significantly, reduced in the hypertrophic obstructive cardiomyopathy group with respect to the control group, whereas in patients with systemic hypertension the low frequency component showed a significant increase. In hypertrophic non-obstructive cardiomyopathy, systemic hypertension, and control groups, the tilt manoeuvre induced a significant decrease in the high frequency component, an increase in the low frequency component and a marked increase in the low to high frequency ratio, all of which reflect the physiological shift of the autonomic balance towards a sympathetic dominance. Patients with hypertrophic obstructive cardiomyopathy, however, did not show the tilt-mediated increase in the low frequency component and low to high frequency ratio.

The heart rate increase during tilt was quantitatively similar in hypertrophic obstructive cardiomyopathy, hypertrophic non-obstructive cardiomyopathy, systemic hypertension and control groups (40 ± 13%, 31 ± 10%, 33 ± 10% and 34 ± 13%, P: ns). Nevertheless, the rate of increase was markedly reduced in the first group, and a new steady-state heart rate was reached later (time to 80% of peak heart rate: 8 ± 1 vs 1 ± 1, 1 ± 1 and 1 ± 1 min, P <0·001) (Fig. 1).

In patients with hypertrophic obstructive cardiomyopathy the intraventricular peak pressure gradients at rest and during tilt were not significantly correlated with the tilt-induced variation of the low frequency component (at rest: r=0·295, P: ns; during tilt: r=0·260, P: ns) and low to high frequency ratio (at rest: r=0·036, P: ns; during tilt: r=0·197, P: ns).

Table 3 reports the regional distribution of myocardial hypertrophy in patients with hypertrophic obstructive and non-obstructive cardiomyopathy. The mean values of the echocardiographic index of left ventricular hypertrophy were similar in patients with hypertrophic obstructive cardiomyopathy, hypertrophic non-obstructive cardiomyopathy and systemic hypertension (66 ± 8, 69 ± 16 and 64 ± 8 mm, P: ns). In the hypertrophic obstructive cardiomyopathy group, the index of left ventricular hypertrophy was significantly correlated with the tilt-induced change in the low frequency component (r = −0·800, P <0·001) (Fig. 2(a)) and the low to high frequency ratio (r = −0·671,
Table 2  Heart rate variability in control, hypertrophic obstructive cardiomyopathy, hypertrophic non-obstructive cardiomyopathy and essential systemic hypertension groups

<table>
<thead>
<tr>
<th></th>
<th>Control (n=28)</th>
<th>HOCM (n=28)</th>
<th>HN CM (n=22)</th>
<th>SH (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>rest</td>
<td>tilt</td>
<td>rest</td>
<td>tilt</td>
</tr>
<tr>
<td>Variance (ms × ms)</td>
<td>1534 ± 1061</td>
<td>1752 ± 1454</td>
<td>1428 ± 812</td>
<td>1554 ± 1072</td>
</tr>
<tr>
<td>LF (ms × ms)</td>
<td>363 ± 313</td>
<td>516 ± 435†</td>
<td>290 ± 156</td>
<td>220 ± 152*¶</td>
</tr>
<tr>
<td>Ln (ms × ms)</td>
<td>5.63 ± 0.70</td>
<td>5.90 ± 0.85</td>
<td>5.54 ± 0.52</td>
<td>5.16 ± 0.72†</td>
</tr>
<tr>
<td>(n.u.)</td>
<td>45 ± 10</td>
<td>62 ± 13†</td>
<td>38 ± 9*</td>
<td>30 ± 9†</td>
</tr>
<tr>
<td>HF (ms × ms)</td>
<td>215 ± 163</td>
<td>155 ± 130†</td>
<td>185 ± 127</td>
<td>129 ± 110†</td>
</tr>
<tr>
<td>Ln (ms × ms)</td>
<td>5.09 ± 0.78</td>
<td>4.72 ± 0.82†</td>
<td>4.99 ± 0.70</td>
<td>4.51 ± 0.89†</td>
</tr>
<tr>
<td>(n.u.)</td>
<td>27 ± 11</td>
<td>19 ± 7†</td>
<td>22 ± 8</td>
<td>16 ± 7†</td>
</tr>
<tr>
<td>LF/HF</td>
<td>1.9 ± 1.0</td>
<td>3.8 ± 2.2†</td>
<td>1.9 ± 0.9</td>
<td>2.1 ± 0.8*¶</td>
</tr>
<tr>
<td>SAP (mmHg)</td>
<td>115 ± 3</td>
<td>112 ± 3</td>
<td>116 ± 3</td>
<td>108 ± 3‡</td>
</tr>
<tr>
<td>DAP (mmHg)</td>
<td>76 ± 2</td>
<td>78 ± 1</td>
<td>79 ± 1</td>
<td>76 ± 2</td>
</tr>
</tbody>
</table>
| Values are mean ± SD. Centre frequencies for the LF component at rest were 0.10 ± 0.04, 0.09 ± 0.03, 0.10 ± 0.03 and 0.10 ± 0.03 Hz for the Control, HOCM, HNCM and SH groups. Centre frequencies for the LF component during tilt were 0.09 ± 0.04, 0.10 ± 0.04, 0.10 ± 0.04 and 0.09 ± 0.03 Hz. Centre frequencies for the HF component at rest were 0.25 ± 0.05, 0.26 ± 0.07, 0.26 ± 0.04 and 0.27 ± 0.05 Hz. Centre frequencies for the HF component during tilt were 0.27 ± 0.09, 0.27 ± 0.08, 0.28 ± 0.06 and 0.27 ± 0.07 Hz. Control: control group; DAP = diastolic arterial pressure; HF = high frequency component; HNCM = hypertrophic non-obstructive cardiomyopathy group; HOCM = hypertrophic obstructive cardiomyopathy group; LF = low frequency component; SAP = systolic arterial pressure; SH = essential systemic hypertension group. *P <0.05 vs Control; †P <0.05 vs HOCM; ‡P <0.05 vs HNCM (Newman–Keuls test); ¶P <0.05 vs Control (non-parametric analysis, Mann–Whitney test). ††P <0.05 vs rest.

Table 3 Analytical echocardiographic data on left ventricular wall thickness in patients with hypertrophic cardiomyopathy

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>aIVSTd</th>
<th>pIVSTd</th>
<th>INFWTd</th>
<th>LATWTd</th>
<th>ILVH</th>
</tr>
</thead>
<tbody>
<tr>
<td>HOCM</td>
<td>28</td>
<td>18 ± 4</td>
<td>19 ± 3</td>
<td>14 ± 2</td>
<td>16 ± 3</td>
<td>66 ± 8</td>
</tr>
<tr>
<td>HNCM</td>
<td>22</td>
<td>20 ± 6</td>
<td>18 ± 6</td>
<td>13 ± 4</td>
<td>18 ± 4</td>
<td>69 ± 16</td>
</tr>
</tbody>
</table>

Data are expressed in mm, mean ± SD. aIVSTd=end-diastolic thickness of the anterior interventricular septum; pIVSTd=end-diastolic thickness of the posterior interventricular septum; HOCN=hypertrophic non-obstructive cardiomyopathy group; ILCVH=index of left ventricular hypertrophy; INFWTd=end-diastolic thickness of the inferior wall; LATWTd=end-diastolic thickness of the lateral wall; ILVH was calculated as follows: ILVH = aIVSTd + pIVSTd + INFWTd + LATWTd.

Discussion

Although heart rate variability has been extensively studied during the last decade, little is known about heart rate variability in patients with hypertrophic cardiomyopathy. In this study we evaluated autonomic cardiac function at rest and during tilt manoeuvre in patients with hypertrophic cardiomyopathy and, for comparison, in patients with left ventricular hypertrophy secondary to systemic hypertension. The main findings of the present study areas follows: (1) Patients with hypertrophic non-obstructive cardiomyopathy showed normal spectral patterns, both at rest and during tilt; (2) In patients with hypertrophic obstructive cardiomyopathy, the reduction in the low frequency component at rest and the lack of increase in the low frequency component and low to high frequency ratio during tilt are consistent with a dysfunction in afferent and/or efferent sympathetic activity. The significant delay in heart rate acceleration during tilt also supports the hypothesis of an impairment in autonomic cardiac responsiveness to the complex reflexes elicited by tilt manoeuvre. Circulating catecholamines may play a compensatory role in sustaining a quantitatively normal, although delayed, increase in heart rate (Fig. 1); and (3) In agreement with previous findings, patients with myocardial hypertrophy secondary to systemic hypertension showed a significant increase in the low frequency component at rest.

Previous studies assessed heart rate variability on long-term (24 h) electrocardiographic recordings during normal daily activities in patients with hypertrophic cardiomyopathy. Fei et al. observed a decrease in the low frequency component and low to high frequency ratio, as well as an increase in the high frequency component. Aljiki et al. found no significant alterations in heart rate variability during the day, although the autonomic balance did not show the physiological shift towards parasympathetic dominance during the night. However, the interpretation of spectral components averaged over 24 h is difficult since these averages may obscure information about autonomic modulation of RR intervals. In this regard, the use of short-term recordings and of the tilt test seems preferable.

In our study, the impairment of sympathetic function and responsiveness is specifically related to the obstructive form of hypertrophic cardiomyopathy. In fact, the spectral patterns observed in these patients are substantially different from those observed in patients with hypertrophic non-obstructive cardiomyopathy (normal patterns) or left ventricular hypertrophy secondary to systemic hypertension (significant increase
at rest in the low frequency component, physiological response to tilt). Although it may appear contradictory, the impairment of sympathetic responsiveness during tilt in patients with hypertrophic obstructive cardiomyopathy was not quantitatively related to the entity of left ventricular outflow tract obstruction (which is the most obvious factor distinguishing these patients from those with non-obstructive hypertrophic cardiomyopathy), but rather to the extent of myocardial hypertrophy (Fig. 2(a)). On the contrary, we found no relationship between the extent of myocardial hypertrophy and the tilt-induced changes in spectral parameters in patients with hypertrophic non-obstructive cardiomyopathy and in hypertensive patients (Fig. 2(b) and (d)). These data suggest that: (1) impaired autonomic responsiveness is not associated with every type of myocardial hypertrophy, but is a specific feature of hypertrophic obstructive cardiomyopathy; (2) in this group, the impairment in autonomic responsiveness is not quantitatively related to the entity of outflow tract obstruction; and (3) although a significant relationship exists between myocardial hypertrophy and autonomic dysfunction in patients with obstructive hypertrophic cardiomyopathy, it is unlikely that a direct causal link exists. On the other hand, each of the two factors might be related to the severity of the disease which in turn may explain their reciprocal relationship.

A different field of speculation suggests that increased adrenergic activity may actually induce the development of myocardial hypertrophy in hypertrophic cardiomyopathy. This hypothesis was based on investigations dealing with different aspects of the adrenergic system, namely cardiac sympathetic nerve endings, circulating catecholamines, affinity and density of myocardial adrenergic receptors, and the intracellular transduction systems of the adrenergic signal. Prolonged norepinephrine infusion at subhypertensive doses induced hypertrophy and disarray in cultured rat myocardial cells[8] and in conscious dogs[10]. Pearse et al.[13] found increased intramyocardial levels of catecholamines, although further studies failed to demonstrate such an increase[39,40]. Beta-1 receptor density and affinity, as well as the adenylate cyclase response to adrenergic agonists, did not show significant alterations[16]. Other findings were consistent with a defect in cardiac sympathetic nervous fibres. In fact, Brush et al.[12] observed a remarkable reduction in norepinephrine reuptake by cardiac nerve endings, while Shimizu et al.[41] found abnormalities of regional myocardial sympathetic nerve iodine-123 metaiodobenzylguanidine uptake which corresponded to the hypertrophied portion of the left ventricular wall. Our findings in patients with hypertrophic obstructive cardiomyopathy are consistent with reduced sympathetic activity and
altered autonomic responsiveness to the tilt manoeuvre. However, spectral analysis is not a measure of the global sympathetic activity, but rather reflects the rhythmic release of the synaptic mediator in the sinus atrial node. Therefore, our hypothesis is that a defect in cardiac sympathetic nerve fibres might occur in the obstructive form of hypertrophic cardiomyopathy so determining: (1) a reduction in noradrenaline reuptake that could in turn increase interstitial noradrenaline concentration (not detected by spectral analysis, which is mainly affected by phasic changes in the adrenergic mediator release); (2) altered uptake of iodine-123 metaiodobenzylguanidine; and (3) an abnormal response to the tilt manoeuvre, accounting for the results reported in the present study.

An alternative explanation for our findings in hypertrophic obstructive cardiomyopathy is provided by the observation that anomalous autonomic reflexes may be elicited in the presence of a dynamic left ventricular obstruction. In fact, excessive stimulation of left ventricular mechanoreceptors due to a decrease in left ventricular volume in the presence of vigorous contraction is known to trigger a vasovagal reflex with hypotension and bradycardia, and may play a role in several clinical settings including hypertrophic obstructive cardiomyopathy[42–44]. In this disease the tilt manoeuvre may actually determine excessive stimulation of ventricular mechanoreceptors with consequent reflex bradycardia/hypotension associated with marked reduction in left ventricular dimensions and outflow tract velocity[42]. Nevertheless, some observations do not support this hypothesis. First, no patient showed symptomatic hypotension during tilt. Second, during tilt the heart rate increased, although slowly, in all hypertrophic obstructive cardiomyopathy patients, while the high frequency component of the spectrum (an index of vagal activity) decreased. Neither finding is consistent with the activation of a vagal reflex. Finally, in hypertrophic obstructive cardiomyopathy the bradycardia/hypotension syndrome is associated with marked reduction in left ventricular dimensions and outflow tract velocity[42]. However, none of our patients showed a decrease in the outflow tract velocity during tilt, and the tilt-induced variation of the low frequency component, or low to high frequency ratio, was not correlated with the intraventricular peak pressure gradient measured at rest or during tilt (see Results). These observations do not support the hypothesis of a mechanoreceptor-mediated vagal activation although the occurrence of a failure in the initial vagal withdrawal and persistence of a phasic vagal input during tilt may not be excluded.

Study limitations

The impairment of tilt-induced sympathetic cardiac activation might also be attributed to the beta-blocker therapy, which was assumed by 15 out of 28 hypertrophic obstructive cardiomyopathy patients. In fact, although a 72 h therapy washout was applied in each case, we cannot exclude the persistence of adrenergic receptor dysregulation. However, this interpretation seems unlikely since the impairment of tilt-induced sympathetic activation was also observed in 13 hypertrophic obstructive cardiomyopathy patients who were not treated with beta-blockers while it was preserved in patients with hypertrophic nonobstructive cardiomyopathy or systemic hypertension who were taking beta-blockers (see Results).

Finally, a word of caution must be spent in interpreting data on the entity of myocardial hypertrophy and outflow tract obstruction as obtained by means of echo-Doppler measurements[30,33,34] the accuracy of which is still being questioned.

Conclusions

The present study shows that there is clear evidence, as assessed by spectral analysis, of altered autonomic cardiac control in the obstructive form of hypertrophic cardiomyopathy. This alteration seems to be specific for the obstructive form of hypertrophic cardiomyopathy since it is absent in the non-obstructive hypertrophic cardiomyopathy group and qualitatively different in hypertensive patients. Within the hypertrophic obstructive cardiomyopathy group the autonomic dysfunction is correlated with myocardial hypertrophy rather than with left ventricular outflow tract obstruction.

References


Altered autonomic cardiac control in hypertrophic cardiomyopathy


