Reflex responses of venous capacitance vessels in patients with hypertrophic cardiomyopathy

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1. The aim of this study was to determine if there is impaired reflex venoconstriction in patients with hypertrophic cardiomyopathy and whether this is related to a history of syncope or exercise hypotension.

2. Thirty percent of patients with hypertrophic cardiomyopathy have exercise-induced hypotension associated with a failure of arteriolar constriction. Impaired venoconstriction could exacerbate this situation.

3. We evaluated 43 patients with hypertrophic cardiomyopathy and 24 controls. Nuclear venous plethysmography was used to measure forearm venous capacitance during lower body negative pressure, splenic venous volume changes during bicycle exercise and blood pressure responses to treadmill exercise. We assessed any association between abnormal reflex venous control and a history of syncope and exercise hypotension.

4. The percentage reduction in unstressed forearm venous volume during lower body negative pressure was similar in patients and controls (8.9 ± 7.1% versus 9.7 ± 5.9%, P not significant). Patients with a history of syncope demonstrated a less marked percentage reduction in volume than those without (-2.1 ± 6.9% versus -10.6 ± 6.0%, P = 0.001). In three patients with a history of syncope there was a paradoxical increase in forearm venous volume during lower body negative pressure. During exercise there was a substantially smaller decrease in splenic venous volume in patients compared with controls (-20.1 ± 14.0% and -42.6 ± 12.6% respectively, P = 0.0001). Furthermore, there was an association between attenuated splenic vеноconstriction or venodilation and exercise hypotension in patients (P = 0.005).

5. Abnormal reflex control of venous capacitance beds in patients with hypertrophic cardiomyopathy was associated with both syncope and exercise hypotension.

INTRODUCTION

We have previously demonstrated that approximately 30% of patients with hypertrophic cardiomyopathy (HCM) have exercise-induced hypotension which was associated with a failure to constrict resistance vessels [1, 2]. In a prospective study, this abnormality was associated with an adverse outcome suggesting that haemodynamic factors may contribute to sudden death in HCM [3]. Although approximately 50% of sudden deaths are unrelated to exercise, our recent observations show that episodes of hypotension occur during everyday life, therefore abnormal reflex vascular control may result in hypotension in situations other than exercise [4]. We hypothesize that some patients with HCM may show a failure of reflex vеноconstriction during central blood volume unloading and exercise which may contribute to haemodynamic instability.

The aims of this study were:

(1) To assess whether there is abnormal reflex control of veins in patients with HCM.

(2) If so, to assess any association with syncope or exercise hypotension.

(3) To assess any association between abnormal reflex control of veins and:

(i) extent of left ventricular hypertrophy

(ii) presence or absence of outflow tract gradient

(iii) history of chest pain.

MATERIALS AND METHODS

Patient and control populations

The 47 study patients with HCM, who satisfied the inclusion criteria, were selected as follows. Recruitment took place at both the Royal Brisbane Hospital and St George’s Hospital, London. At the former hospital, patients were recruited over an 18 month period. At St George’s Hospital a consecutive series of patients were recruited over a shorter...
but parallel time frame. The diagnosis of HCM was based on typical clinical, echocardiographic and haemodynamic features. All patients had left ventricular hypertrophy (1.4 cm or more) demonstrated on 2-dimensional echocardiography in the absence of other cardiac disease or systemic hypertension (blood pressure >160/90 mmHg) [5]. Patients unable to exercise were excluded. Significant epicardial coronary artery disease had been excluded by coronary angiography in patients greater than 40 years of age and in those with a history of chest pain. Forty-three patients satisfied the above criteria and consented to undertake the study. Twenty-four control subjects were age- and gender-matched to the patient group (Table 1). The control subjects had no history of cardiovascular disease, autonomic neuropathy or syncope and had normal clinical examinations, ECGs and echocardiograms. They were recruited from the gastroenterology re-endoscopy database. None had irritable bowel syndrome.

**Study protocols**

Ethics committee approval and written informed consent were obtained before the studies. On three consecutive days subjects arrived at 08.00 hours after fasting from midnight. All cardioactive medications were withdrawn for at least five half-lives before the study, except for amiodarone (five patients). Five patients had been taking β-blockers and seven, calcium-channel blockers before enrolment. None of the control subjects was on any vasoactive medication. Studies were performed as follows:

**Day 1.** Forearm venous capacitance was assessed during application of sub-hypotensive LBNP [6–8], and 3 h later, splenic venous capacitance was assessed during erect cycle exercise [8].

**Day 2.** Changes in forearm vascular resistance were assessed during semi-erect cycle exercise [2, 9, 10].

**Day 3.** Blood pressure responses were assessed during erect treadmill exercise.

**Methodology**

**Blood pressure responses during treadmill exercise.**

In our previous studies [1, 10], exercise-induced hypotension was demonstrated during treadmill rather than bicycle exercise. Furthermore, the association between exercise-induced hypotension and increased risk of sudden death refers to treadmill exercise [3]. Therefore to assess the relation between exercise hypotension and abnormal reflex responses of the venous capacitance beds, symptom-limited treadmill exercise was performed using a Bruce Protocol. Systolic blood pressure was measured at rest and at 1 min intervals during exercise. Exercise-induced hypotension was defined by either of the following standard criteria [11].

1. Systolic blood pressure at peak exercise less than systolic blood pressure at rest.
2. An initial rise in systolic blood pressure followed by a fall ≥20 mmHg but not below baseline.

**Changes in splenic blood volume during erect cycle exercise.** One hour later, the patient was seated on an erect cycle ergometer in a quiet room of constant temperature. Changes in splenic venous volume were assessed by imaging the spleen using a technique which has been previously described [8]. A 3 min resting acquisition was performed. A 5 ml blood sample was drawn before and during the last minute of exercise for subsequent analysis of radioactive counts per ml. Exercise commenced at a 25 W workload and increased by 25 W increments every 4 min until subjects were symptom limited (fatigue,

| Table 1. Clinical characteristics. Abbreviations: SAM, systolic anterior motion; NS, not significant. |
|-----------------|-----------------|-----------------|
|                 | Patients (n = 43) | Controls (n = 24) | P value |
| Age (years)     | 40.0 ± 15.0      | 41.3 ± 13.7      | NS      |
| Gender          | 17 F / 26 M      | 8 F /16 M        | NS      |
| Family history of HCM | 22            | 0                | 0.0001  |
| Family history of sudden death | 8             | 0                | 0.024   |
| Syncope         | 8                | 0                | 0.024   |
| Presyncope      | 15               | 0                | 0.001   |
| Typical chest pain | 12             | 0                | 0.004   |
| Atypical chest pain | 13           | 0                | 0.003   |
| Palpitations    | 5                | 0/24             | NS      |
| Left ventricular wall thickness (mm) | 21.3 ± 5.6 | 9.3 ± 1.16 | 0.0001 |
| Left ventricular systolic dimension (mm) | 25.3 ± 8.1 | 27.9 ± 4.6 | NS      |
| Left ventricular diastolic dimension (mm) | 42.8 ± 10.5 | 46.2 ± 4.0 | NS      |
| Left atrial dimension (mm) | 38.4 ± 10.4 | 32.2 ± 4.0 | NS      |
| Fractional shortening (mm) | 42.6 ± 9.9 | 37.8 ± 6.3 | NS      |
| Peak gradient < 30 mmHg | 7              | 0                | 0.037   |
| Complete SAM of mitral valve | 7             | 0                | 0.037   |
| Incomplete SAM of mitral valve | 12           | 0                | 0.004   |
| Non sustained ventricular tachycardia <120 beats/min | 10            | 0                | 0.010   |
| Paroxysmal atrial fibrillation | 3             | 0                | NS      |
breathlessness, chest pain or symptomatic hypoten-
sion). Splenic counts were acquired continuously in
30 s epochs and both the blood pressure and the
ECG were monitored.
Assessment of changes in right atrial pressure during
erect cycle exercise. To exclude the possibility that an
attenuated reduction in splenic counts may reflect a
shift in pressure along the same venous volume–
pressure relation, rather than a failure to appro-
priately increase venous tone, we measured mean
right atrial pressure using a fluid-filled catheter.
Pressures, from 12 patients and 5 controls during
maximal erect cycle exercise, were acquired using
the Acq Knowledge data acquisition system on an
Apple McIntosh IICi microcomputer.
Forearm resistance vessel responses during dynamic
leg exercise on a semi-erect cycle. Forearm vascular
resistance during semi-erect cycle exercise (70° to
the horizontal) was measured to assess whether
parallel changes in tone occurred in both the resis-
tance and venous capacitance beds. Forearm blood
flow was measured using a standard mercury in
silastic strain gauge plethysmography technique
which has been described previously [2, 9, 10].
Blood pressure was measured in the opposite arm.
Forearm venous capacitance during sub-hypotensive
LBNP. The subjects lay in a specially constructed
LBNP bed and were allowed to rest for 20 min in a
temperature-controlled (22–24°C) laboratory. Fore-
arm venous capacitance was assessed using a pre-
viously described radionuclide volume–pressure
technique [6-8]. In brief, a cannula was inserted in
the left antecubital vein. Ten minutes after intra-
venous injection of approximately 1.7 mg of stan-
nous pyrophosphate, 5 ml of blood were drawn into
a heparinized syringe and incubated for 20 min with
925 MBq (25 mCi) of Tc-99m pertechnetate before
re-injection. Static images of the region of interest
(elbow to the wrist) were recorded at venous oclud-
ing pressures of 0, 10, 20 and 30 mmHg with step-
wise increases every 90 s. The counts were acquired
in the last 30 s of each interval. These measurements
were repeated during application of −20 mmHg
LBNP (insufficient to induce systemic hypotension).
The count rate in this region of interest obtained
with no occluding pressure and with no LBNP
applied was arbitrarily taken to represent 100% for-
earm blood volume. All subsequent readings
were expressed as a percentage of this value.
Measures of scintigraphic venous volumes (in per-
centage units) at occluding cuff pressures of 0, 10,
20 and 30 mmHg were used to construct venous
volume–pressure plots, after correction for physical
decay.

Data analysis
Splenic counts during erect cycle exercise testing. A
region of interest was drawn around the spleen and
counts were measured within this region of interest.
Resting and peak exercise crude counts were correc-
ted for the counts per gram in the blood samples
taken at rest and at peak exercise in order to assess
changes in splenic venous volume. No correction
was made for difference in tissue attenuation.
Forearm vascular resistance during semi-erect cycl-
ing. Forearm blood flow at rest and at each stage of
exercise was calculated from the mean of three
slopes. Forearm vascular resistance, expressed in
resistance units, was calculated as the quotient of
the mean arterial pressure (mmHg)/forearm blood
flow (ml·min⁻¹·100 ml⁻¹).
Forearm venous capacitance during sub-hypotensive
LBNP. At 0 and at −20 mmHg of LBNP, forearm
counts were assessed at each venous occlusion pres-
sure to give paired venous volume–pressure plots
for each patient. Linear regressions were performed
on each set of data points, to determine if a linear
model described the data. A linear method was
accepted if the correlation coefficient (r) was > 0.8.
We then determined whether the slopes of the two
lines in each set of data were different (i.e. if the
lines were parallel), using a method for testing the
difference between two independent regressions.
Unstressed venous volume, which reflects venous
tone, was defined as the intercept on the volume
axis.

Statistical analysis
Data are expressed as means ± S.D.s. Statistical
analysis was performed using Student's paired and
unpaired t-test, analysis of variance, the χ² test and
by linear regression where appropriate. A P value of
<0.05 was considered significant.

RESULTS
Patient characteristics
The clinical characteristics of the patients are
given in Table 1.

Blood pressure responses during erect treadmill exer-
cise testing. All patients and controls satisfactorily
completed the exercise test. The limiting factors in
the patient group were breathlessness (n = 9), chest
pain (n = 8), symptomatic systemic hypotension
(n = 5) and leg fatigue (n = 21). In the control sub-
jects the limiting factors were breathlessness in five
subjects and leg fatigue in the remainder.

Heart rate was similar at rest and at peak exercise
in both groups (Table 2). Systolic blood pressure
was similar at rest in patients and controls but was

| Table 2. Haemodynamic responses during erect treadmill exercise |
|----------------|----------------|----------------|----------------|
|                | Controls       | Patients       |
|                | Rest           | Peak           | Rest           | Peak           |
| Heart rate (beats/min) | 85 ± 14        | 169 ± 16       | 79 ± 15        | 163 ± 23       |
| Systolic blood pressure (mmHg) | 123 ± 14     | 186 ± 17       | 126 ± 22       | 159 ± 43       |
lower at peak exercise in the patients (159 ± 43 versus 186 ± 17 mmHg, \( P = 0.01 \)). Exercise-induced hypotension was only observed in patients (n = 11). Exercise duration was similar in patients with and without exercise hypotension (13.1 ± 4.5 min versus 14.4 ± 5.1 min respectively, \( P \) not significant).

**Splenic volumes during erect cycle exercise testing.** As shown in Table 3 and Figure 1 there was no difference in the resting splenic volumes between controls and patients (98 ± 53 ml and 94 ± 51 ml respectively, \( P \) not significant). However, there was a greater reduction in the splenic volume at peak exercise in controls compared with patients (42 ± 16 versus 66 ± 34 ml) which relates to a greater percentage reduction in splenic volume in controls compared with patients (\( P = 0.0001 \)). Using the definition of an abnormal exercise splenic venous response as a decrease of ≤ 17.4% (i.e. 2 S.D.s below the mean of the control group), 17 patients exhibited an abnormal response. Three patients exhibited an increase in volume during exercise (a response seen in none of the controls).

**Right atrial pressure measurements.** In the 12 patients and 5 controls in whom right atrial pressure was measured at rest and during exercise, the change in central venous pressure during exercise was similar in both groups (0 ± 2 mmHg and 0 ± 3 mmHg respectively, \( P \) not significant).

**Erect cycle exercise data.** All subjects completed the erect cycle exercise test. Resting heart rate and systolic blood pressure and peak heart rate were similar in both groups. At peak exercise systolic blood pressure was significantly lower in patients compared with controls (153 ± 34 versus 191 ± 12 mmHg respectively, \( P = 0.01 \)). Although not significant, exercise duration was marginally shorter in the patient group (14 ± 5.3 min) than in the control group (15.4 ± 4.3 min, \( P \) not significant). This could possibly explain the difference in splenic venous volume. However, after 14 min of exercise (mean for the patient group), the reduction in splenic venous volume in controls (38.2 ± 11%) was still markedly greater than at peak exercise in the patients (20.1 ± 14%).

**Changes in forearm vascular resistance during semi-erect cycle exercise.** As shown in Table 4, forearm vascular resistance increased by 53% in patients and by 97% in controls (\( P = 0.001 \)). Forearm vascular resistance fell during exercise in 12 patients, a response not seen in any of the controls.

**Forearm venous responses during LBNP.** Forty-one of the forty-three patients consented and completed the LBNP study without complications. As shown in Table 5, heart rate and systolic blood pressure in the two groups were similar at rest and at -20 mmHg. Systolic blood pressure did not fall by more than

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<th>Table 3. Haemodynamic and splenic venous volume changes during erect cycle exercise</th>
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<td>Heart rate (beats/min)</td>
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<td>Systolic blood pressure (mmHg)</td>
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<td>Resting splenic venous volume (ml)</td>
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<th>Table 4. Haemodynamic responses during semi-erect exercise</th>
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<td>Heart rate (beats/min)</td>
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<td>(mmHg/ml·min⁻¹·100 ml⁻¹)</td>
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<th>Table 5. Haemodynamic and forearm venous changes during LBNP in patients and controls. Percentage change in counts indicates percentage change in forearm counts during LBNP. There were no significant differences between patients and controls.</th>
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<td><strong>LBNP (mmHg)</strong></td>
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10 mmHg in any patient (i.e. the LBNP was sub-hypotensive).

The percentage reduction in unstrained volume during application of LBNP was similar in patients and controls (−8.9 ± 7.1% and −9.7 ± 5.9% respectively, \( P \) not significant). However, in three patients, there was an upward shift in the volume–pressure relation of 0.6, 1.8 and 13.9% respectively, indicating venodilation.

**Patients with exercise hypotension.** Eight of the eleven patients who developed exercise hypotension during treadmill exercise, also developed hypotension on the bicycle. Of 17 patients with abnormal splenic responses, 8 had exercise hypotension whereas only 3 out of 26 patients with normal splenic responses had exercise hypotension (\( \chi^2 = 6.6; \ P = 0.01 \)). There was no significant difference in the change in right atrial pressure during exercise for patients with exercise hypotension (fall of 2 ± 3 mmHg) compared with those without exercise hypotension (change of 0 ± 2 mmHg). Although right atrial pressure was only measured in a subset of patients and controls, the splenic venous volume changes for this patient group were representative of the patient group as a whole (24.9 ± 17.7% versus 20.1 ± 14%, \( P \) not significant).

Abnormal forearm vascular responses were associated with exercise hypotension (\( \chi^2 = 4.42; \ P = 0.04 \)).

**Comparison of data with other clinical variables**

Association between forearm venous changes during LBNP and other clinical variables. Patients with a history of syncope demonstrated less marked forearm venaconstriction during LBNP than either controls (−2.1 ± 6.9 compared with −9.7 ± 5.9%, \( P = 0.004 \)) or patients without a history of syncope (−2.1 ± 6.9 compared with −10.6 ± 6.0%, \( P = 0.001 \)). All three patients who demonstrated paradoxical venodilation during LBNP gave a history of syncope. However, the change in forearm venous volume during LBNP was similar in those with a history of exercise-induced hypotension compared with those without (−9.5 ± 6.6% versus −8.62 ± 7.3%, \( P \) not significant).

Forearm venous responses were similar in patients with (−8.3 ± 8%) or without (−9.6 ± 6.4%) a history of chest pain. Likewise, responses were similar in patients with (−7.1 ± 6.2%) or without (−9.5 ± 7.5%) an outflow tract gradient.

**Association between splenic venous changes during exercise and other clinical and echocardiographic variables.** As shown in Table 6, the decrease in splenic venous volume was similar in patients irrespective of chest pain or a history of syncope but was significantly greater in those with a resting outflow tract gradient than in those without (−34.5 ± 14.3% and −17.4 ± 13.1% respectively, \( P = 0.005 \)). Importantly, exercise duration was similar in patients with and without outflow tract gradients (13.2 ± 5.3 min versus 14.2 ± 5.5 min, \( P \) not significant) (Table 7). The decrease in splenic venous volume was inversely related to maximum left ventricular wall thickness (\( r = 0.43 \ P = 0.01 \)).

Relation between venous and resistance vessel responses to exercise and exercise hypotension. In patients there was a weak inverse relationship between percentage reduction in splenic venous volume and percentage increase in forearm vascular resistance during exercise (\( r = 0.33; \ P = 0.048 \)). However, in controls, this was not the case (\( r = 0.18; \ P \) not significant). In the 11 patients with exercise hypotension, forearm vascular responses were normal in two, and splenic venous responses were normal in two. Both of the patients with exercise hypotension and a normal forearm resistance vessel response had abnormal splenic venous responses on exercise.

**DISCUSSION**

In this study, we have demonstrated that the average increase in forearm venous capacitance was similar in patients and controls during LBNP. However, patients with a history of syncope exhibited less venaconstriction than patients without a history of syncope or controls, and three patients with a history of syncope exhibited paradoxical venodilation. We have also shown that there was impaired venaconstriction or even venodilation during exercise in patients with HCM, this abnormal pattern being associated with exercise hypotension.

We have previously reported that exercise-induced hypotension occurred in approximately 30% of a large consecutive series of patients with HCM [1]. It was associated with an exaggerated fall in systemic vascular resistance, a peak exercise cardiac output which was marginally greater in patients with
hypotension [1], and impaired constriction or even vasodilation of the forearm resistance vessels [2]. In the present study, the attenuated reduction in splenic venous volume during exercise (and the increase in three patients) supports the suggestion that impaired venoconstriction may contribute to exercise-induced hypotension. This abnormality is not simply a reflection of differences in arterial perfusion, since Wang et al. [12] have shown that unstimulated venous volume as assessed by this technique is not changed by arterial perfusion. We also observed that the abnormal resistance and capacitance vessel responses may not necessarily occur in the same patients. Thus, two patients with exercise-induced hypotension had a normal increase in forearm vascular resistance during exercise but there was a failure of splenic venoconstriction. Importantly, abnormal splenic venous responses were associated with exercise-induced hypotension. The observation of impaired venoconstriction during LBNP in patients with a history of syncope, together with our previous observation of impaired constriction of resistance vessels during LBNP [13], may also provide a substrate for the development of profound hypotension during postural stress via a vasovagal mechanism.

The potential importance of these observations is underscored by the association between a history of syncope and risk of sudden death [14], and our recent observation in a prospective study of an association between abnormal blood pressure responses on exercise and increased risk of sudden death [3]. In their everyday life patients do not however commonly undertake the levels of physical activity associated with maximum treadmill exercise. A recent ambulatory BP study demonstrated that such patients develop hypotension in their everyday lives, often unassociated with exercise [4]. It is possible that a failure of venoconstriction during postural stress may be contributory.

Control of venous capacitance and resistance vessels

The mechanism of splanchnic and splenic venoconstriction during leg exercise is uncertain. It is likely that the central command reflex and skeletal muscle metaboreceptors are involved. In animal studies, cardiac distension increases splanchnic venous capacitance, presumably due to ventricular mechanoreceptor activation [15-17]. Intestinal venous capacitance is also increased by intracoronary prostacyclin; this effect is blocked by vagotomy suggesting mediation via cardiac chemoreceptors [18]. A recent study demonstrated splanchic venodilation during the ‘vasovagal’ phase (phase 2) of severe haemorrhage [19]. Phase 2 in this model appears to be partly (but not completely) due to left ventricular mechanoreceptor activation [20, 21]. Thus, ventricular mechanoreceptor or chemoreceptor activation may contribute to impaired venoconstriction or vasodilation in patients with HCM. In the present study, however, patients exhibited a weak inverse relation between the increase in forearm vascular resistance during exercise and the decrease in splenic venous volume. This was not the case with the control subjects. It is possible that the reflex mechanisms responsible for control of the resistance and venous beds in patients on exercise may be different. These findings should be interpreted with caution since the changes in the resistance and venous capacitance beds were assessed during slightly different forms of exercise (70° to the horizontal and erect).

Abnormal localized left ventricular wall stress during exercise is presumed to be responsible for left ventricular mechanoreceptor activation, which may be due to abnormal cardiac architecture. This may be related to the myofibrillar disarray characteristic of HCM. A recent study reported abnormal desmosome disposition in patients with HCM in areas of myofibrillar disarray which might provide an explanation for mechanical anisotropy [22]. Other potential factors may include the development or exacerbation of left ventricular outflow tract gradients, or exercise-induced myocardial ischaemia. Analysis of the data from the present study did not support a role for either of these factors. Indeed the reduction in splenic venous volume during exercise in the patients with resting outflow tract gradients was comparable to the control group but was markedly impaired in the patients without outflow tract gradients. The degree of impairment of splenic venoconstriction, however, was weakly related to maximum left ventricular wall thickness, consistent with the concept of disruption of cardiac architecture as the mechanism. We have recently reported that patients with vasovagal syncope demonstrate similar impairment of resistance vessel and venous capacitance vessel constriction during exercise to those demonstrated in the present study in patients with HCM [8, 9]. In fact, in our series, reflex venous abnormalities were found on exercise in patients with HCM irrespective of a history of syncope, even though only 18% gave a history of syncope. In our previous study [8], splenic venous volume fell by 15.8% in patients with vasovagal syncope compared with 20.1% in the entire HCM population. This implies a similar abnormality of reflex control mechanisms during exercise in patients with HCM (irrespective of a history of syncope) and in vasovagal syncope. It is not clear why such abnormalities should occur during exercise in vasovagal syncope.

Study limitations

A potential limitation of this study was the inability to directly measure the splenic venous volume–pressure relation. The right atrial pressure changes in subsets of patients and controls, however, support a primary abnormality in venous tone. Con-
versely, while we can accurately measure changes in the venous volume-pressu...

We used different protocols to assess changes in splenic venous volume and document exercise-induced hypotension. We felt it important to demonstrate blood pressure responses during erect treadmill exercise because of the association of abnormal blood pressure responses during this form of exercise and an adverse prognosis [3]. Splenic venous volume could not be assessed during treadmill exercise for technical reasons. However, we have previously noted that while hypotension is less marked during erect cycle exercise than treadmill exercise, such patients nevertheless have very flat blood pressure responses during erect cycle testing. In the present study, of the 11 patients with hypotension during treadmill testing, 8 exhibited hypotension on the erect cycle. Right atrial (and hence splenic venous) pressure is likely to be marginally higher during semi-erect versus treadmill exercise.

In order to standardize the protocol, all studies were performed at 08.00 hours after fasting from midnight. Thus our observations may not necessarily reflect those which would occur in the postprandial state [23]. The patients were not volume depleted.

The stimulus for deactivation of cardiopulmonary mechanoreceptors during application of LBNP is of course not the LBNP itself but the effects this stimulus has on cardiac wall strains. Since left ventricular mechanoreceptors are probably the principal receptor field involved in reflex control of the forearm vessels, changes in wall strain in the left ventricle are the most pertinent. Such changes cannot be accurately judged by changes in right atrial pressure and, despite the limitations, most authors have used the magnitude of LBNP to assess reflex stimulus response relationships [24, 25].

**Significance of the findings**

This study has documented impaired forearm venoconstriction during LBNP in patients with HCM presenting with a history of syncope. This is consistent with an earlier study demonstrating an association between a positive tilt table response and a history of syncope [26]. The observed impairment of splenic venoconstriction during exercise also supports the concept of abnormal reflex control of venous capacitance vessels in these patients. These findings suggest that abnormal reflex control of venous tone may play an important role in the haemodynamic response to upright tilt and exercise in patients with HCM. Abnormal exercise blood pressure responses are associated with an increased risk of sudden death [3].

**CONCLUSIONS**

We have demonstrated that some patients with HCM have, in certain circumstances, an impairment of reflex venoconstriction. As a group, patients with HCM exhibit a normal increase in forearm venous tone during sub-hypotensive LBNP. However, the response was not homogeneous. Patients with a history of syncope, demonstrated impaired forearm venoconstriction during LBNP and three such patients exhibited venodilation. Attenuated venoconstriction or venodilation of the spleen occurred during exercise in patients with HCM and this pattern is associated with exercise-induced hypotension, an abnormality previously shown to be associated with an increased risk of sudden death.

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**REFERENCES**


