

Influence of posture on the Valsalva manoeuvre

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ABSTRACT

The objective of the present study was to evaluate the influence of posture on the responses of blood pressure (BP) and heart rate (HR) to the Valsalva manoeuvre (VM). Neurohumoral activation, as well as changes in intravascular and intracardiac volumes and pressures, are well known effects of orthostatic stress. These changes are likely to have significant effects on cardiovascular reflexes, such as the response to the VM. However, the influence of posture on the VM has not been intensively evaluated, except for a few studies involving small sex- and age-selected case series. We therefore investigated the effects of posture on the VM in a larger non-selected group of healthy control subjects. In 19 healthy volunteers (ten female/nine male; age range 20–72 years, mean age 43 years), two reproducible VMs (40 mmHg; 15 s) were performed after 10 min of supine rest, 10 min of sitting and 10 min of standing. HR and BP were monitored continuously. End-diastolic volume, total peripheral resistance and cardiac output were calculated at baseline for each position. We found that assuming an upright position resulted in increases in total peripheral resistance and HR, accompanied by decreases in end-diastolic volume and cardiac output. The fall in BP during early phase II and the BP overshoot during phase IV were clearly more pronounced with increasing orthostatic stress, whereas the rise in BP during late phase II remained unchanged; pulse pressure was more compressed during phase II, but higher during phase IV. The Valsalva ratio was not significantly affected, but baroreflex gain (calculated from early phase II) was significantly decreased in the upright position. While a reduced late phase II was observed on one occasion in each of the lying and sitting positions, three abnormal responses were observed during standing. We conclude that posture has a significant influence on BP responses to the VM, probably resulting from changes in the intrathoracic blood volume. Standing results in a lower rate of 'flat-top' responses, but also seems to reduce the specificity of this test. Sympathetic activation in the upright position seems to blunt baroreflexes, leading to similar HR responses in spite of larger changes in BP.

INTRODUCTION

The Valsalva manoeuvre (VM) consists of an abrupt, transient, voluntary elevation of intrathoracic and intra-abdominal pressure caused by blowing against a pneumatic resistance maintaining a predetermined pressure. The changes in arterial blood pressure (BP) and heart rate (HR) that occur during and after the VM reflect not only the mechanical effects on the heart and blood vessels

(phase I, early phase II and phase III), but also ongoing reflex changes in autonomic activity (late phase II and phase IV) [1–5].

The VM has therefore become an important tool in the standard evaluation of autonomic function, providing valuable information about cardiovascular adrenergic and cardiovagal function, and is widely used to assess the degree of autonomic failure in disorders such as multiple system atrophy or autonomic neuropathies [1,2]. How-

Key words: Valsalva manoeuvre, posture, blood pressure, baroreflex.

Abbreviations: BP, blood pressure; BRG, baroreflex gain; CO, cardiac output; EDV, end-diastolic volume; HR, heart rate; PP, pulse pressure; TPR, total peripheral resistance; VM, Valsalva manoeuvre; VR, Valsalva ratio.

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ever, the test conditions – including body position – are by no means standardized [6–8].

A change in posture is well known to cause changes in intravascular and intracardiac volumes and pressures, and in neurohumoral activity [9–12]. These changes are likely to have significant effects on cardiovascular reflexes, such as the responses to the VM. However, this hypothesis has been only sparsely investigated. We therefore sought to evaluate the effects of posture on the responses of BP and HR to the VM in healthy volunteers.

METHODS

Subject selection

A total of 19 healthy volunteers (10 female and nine male), with a mean age of 43 years (range 20–72 years), were selected. All subjects demonstrated normal autonomic nervous system function, as determined by (i) medical history, general clinical and clinical autonomic evaluation; and (ii) standardized autonomic reflex testing, including HR responses to deep breathing, BP and HR responses to the VM, BP and HR responses to 70° head-up tilt, and quantitative sudomotor axon reflex testing (QSART) at four standardized sites [1,2].

Exclusion criteria were as follows. (i) Pregnant or lactating females. (ii) The presence of failure of organ systems or systemic illness that could affect the study results, autonomic function or the patient's ability to cooperate. These included dementia, pheochromocytoma, congestive heart failure, clinically significant coronary artery disease, arrhythmia, renal or hepatic disease, severe anaemia, alcoholism, malignant neoplasms, hypothyroidism, sympathectomy and cerebrovascular accidents. (iii) Therapy with anti-cholinergic agents, α - and β -adrenergic antagonists, vasoactive agents or other medication that could interfere with the testing of autonomic function. If such a drug had to be discontinued, subjects were instructed to stay off medication for at least five half-lives.

Study design

A prospective study was performed to evaluate the effects of posture on responses of BP and HR to the VM. The study protocol was approved by the Institutional Review Board, and has been carried out in accordance with the Declaration of Helsinki (1989) of the World Medical Association. Subjects gave informed consent before entering the study.

A total of 19 healthy volunteers recruited from Rochester/Minnesota participated in the study. All recordings were done in the morning between 09.00 and 11.00 hours (2 h after a light breakfast) at controlled ambient room temperature (23 °C). No caffeine or nicotine was allowed for 24 h before the study.

Two reproducible VMs were performed in each of three body positions: lying, sitting and standing, in randomized order. Each position was assumed at least 10 min before performing the manoeuvre, in order to allow the cardiovascular system to reach a steady state.

The manoeuvres in the lying position were performed with the subjects resting comfortably on their backs in the horizontal position on a table equipped with an inflatable air mattress. For the sitting position, subjects sat on adjustable chairs with back support. The height of the seat was adjusted so that the angle of hip and knee joints was 90°. For the standing position, subjects were instructed to stand free with the feet slightly apart, aiming for an equal weight distribution between left and right feet.

When performing the VM, subjects were instructed to breathe in and then to blow into a bugle, maintaining an expiratory pressure of 40 mmHg for 15 s [2]. For that purpose, the expiratory pressure was displayed on a large mercury column. The connection between bugle and mercury column had an air leak to ensure an open glottis during the manoeuvre [2].

Primary end-points were: (i) influence of posture on changes in BP and pulse pressure (PP) during the VM; and (ii) influence of posture on cardiovagal indices [Valsalva ratio (VR) and baroreflex gain (BRG)]. Secondary end-points were the influence of posture on baseline HR, cardiac output (CO), end-diastolic volume (EDV) as an estimate for pre-load and total peripheral resistance (TPR) as an estimate for afterload.

Data acquisition

Photoplethysmographic determination of BP

Beat-to-beat BP was recorded continuously using the digital photoplethysmographic volume-clamp method (Finapres Model 2300; Ohmeda, Englewood, CO, U.S.A.), which provides a reliable non-invasive estimate of intra-arterial BP during both short- and long-term recordings [13,14]. The analogue BP signal was sampled at 250 Hz, and the maximal and minimal points that occur between the QRS pulse derived as systolic and diastolic BP. Mean BP was calculated using the formula:

$$\text{Mean BP} = \text{diastolic BP} + (\text{systolic BP} - \text{diastolic BP})/3.$$

Recording of HR

Instantaneous HR was calculated from the RR-interval using continuous three-lead ECG recordings and a specialized cardioteach board with 2 ms resolution.

Impedance cardiography

Changes in thoracic impedance during the cardiac cycle reflect changes in thoracic fluid volume and velocity, with a major contribution of the thoracic aorta [15].

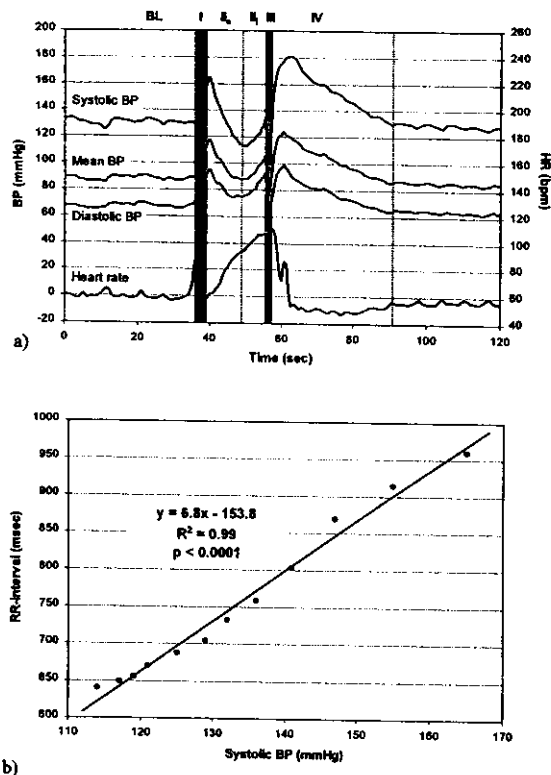


Figure 1 HR and BP responses to the VM (a) and BRG calculated from early phase II (b)

BL, baseline; I, phase I; II_e, early phase II; II_l, late phase II; III, phase III; IV, phase IV.

Impedance cardiography (BoMed NCCOM3 R-7; BoMed Medical Manufacturing, Irvine, CA, U.S.A.) uses these dynamic changes in thoracic bioimpedance (sampled at 500 Hz) together with ECG and BP recordings for a beat-to-beat calculation of EDV, TPR and CO. Derived beat-to-beat values were transferred serially to a personal computer.

Respiration

Respiratory excursion was measured using a nasal thermistor. The respiratory signal was sampled at 250 Hz, and the data point occurring coincident with the QRS pulse was written to file.

All data were acquired and displayed at real time by a Pentium II 350 MHz personal computer using specially developed software.

Data analysis

For each body position, systolic, mean and diastolic BP, PP, HR, EDV, TPR and CO were analysed and averaged for the 1 min baseline periods preceding the VM, in order to detect changes in cardiovascular factors that may have a possible impact on the responses to the VM.

A typical response to the VM is shown in Figure 1(a).

The minimum values of systolic, mean and diastolic BP during early phase II, the maxima during late phase II and the maxima during phase IV were determined, and the following changes were calculated: fall during early phase II compared with baseline, increase during late phase II compared with early phase II, and overshoot during phase IV compared with baseline. Similarly, the minimum value of PP during phase II and the maximum during phase IV were determined, and the maximal PP compression during phase II and the maximal PP expansion during phase IV were derived (compared with baseline).

The BP response to the VM was considered abnormal if the rise during late phase II did not reach baseline levels [2].

There is a variant of the typical BP response to the VM. In some subjects, the systolic BP does not fall below baseline levels during phase II. This variant is referred to as a 'flat-top' response [16]. Typically, these patients also have a reduced or absent phase IV. Some authors call this phenomenon a 'square-wave' response [17,18].

The VR was calculated as the maximum HR generated by the VM divided by the lowest HR occurring within 30 s of the peak HR [2]. BRG was calculated as the slope of the linear relationship between the change in systolic BP (in mmHg) and the RR-interval (in ms) during early phase II of the VM (Figure 1b) [2,3].

All data are expressed as means \pm S.D. The paired two-tailed Student *t*-test was used for statistical comparisons between body positions. Significance was accepted at the 5% level.

RESULTS

Influence of body position on baseline parameters

Changes in body position from lying to sitting and to standing resulted in significant changes in baseline parameters (Table 1, Figure 2). Increases in HR and TPR were accompanied by decreases in EDV and CO. HR was 61.2 ± 4.8 beats/min supine, 67.2 ± 7.6 beats/min sitting and 79.4 ± 12.5 beats/min standing ($P < 0.001$ for each of supine compared with sitting, sitting compared with standing and supine compared with standing). CO was 6.94 ± 1.94 litres supine, 5.78 ± 1.27 litres sitting and 5.44 ± 1.28 litres standing (supine compared with sitting, $P < 0.001$; sitting compared with standing, $P < 0.05$; supine compared with standing, $P < 0.001$). TPR was 1183 ± 417 $\text{m}^2 \cdot \text{min} \cdot \text{mmHg} \cdot \text{l}^{-1}$ supine, 1240 ± 379 $\text{m}^2 \cdot \text{min} \cdot \text{mmHg} \cdot \text{l}^{-1}$ sitting and 1407 ± 367 $\text{m}^2 \cdot \text{min} \cdot \text{mmHg} \cdot \text{l}^{-1}$ standing (supine compared with sitting, not significant; sitting compared with standing, $P < 0.001$; supine compared with standing, $P < 0.01$). EDV was 183.7 ± 47.5 ml supine, 153.7 ± 27.7 ml sitting and

Table 1 Baseline parameters, changes in BP and PP during the VM, and cardiovagal indices derived from the VM for different body positions

Units for the various parameters are as follows: HR in beats/min; CO in litres; EDV in ml; TPR in $\text{m}^2 \cdot \text{min} \cdot \text{mmHg}^{-1}$; systolic BP (SBP), mean BP (MBP), diastolic BP (DBP) and PP in mmHg; YR and BRG in units. ns, not significant.

Parameter	Supine (1)	Sitting (2)	Standing (3)	<i>P</i>		
				1 versus 2	2 versus 3	1 versus 3
Baseline parameters						
HR	61.2 ± 4.8	67.2 ± 7.6	79.4 ± 12.5	< 0.001	< 0.001	< 0.001
CO	6.94 ± 1.94	5.78 ± 1.27	5.44 ± 1.28	< 0.001	< 0.05	< 0.001
EDV	183.7 ± 47.5	153.7 ± 27.7	133.2 ± 23.6	< 0.001	< 0.001	< 0.001
TPR	1183 ± 417	1240 ± 379	1407 ± 367	ns	< 0.001	< 0.01
Changes in BP and PP during early phase II						
SBP	-12.6 ± 17.3	-18.8 ± 20.1	-28.2 ± 15.5	ns	ns	< 0.001
MBP	1.5 ± 10.6	-1.6 ± 13.7	-8.9 ± 10.7	ns	ns	< 0.001
DBP	8.9 ± 8.6	6.7 ± 11.3	0.9 ± 10.2	ns	ns	< 0.01
PP	-21.4 ± 13.2	-25.6 ± 12.2	-29.1 ± 12.7	ns	ns	< 0.05
Changes in BP during late phase II						
SBP	23.1 ± 16.0	27.0 ± 19.0	26.3 ± 12.5	ns	ns	ns
MBP	22.3 ± 14.2	23.2 ± 13.1	22.4 ± 11.2	ns	ns	ns
DBP	21.7 ± 13.7	21.4 ± 10.7	20.2 ± 11.2	ns	ns	ns
Changes in BP and PP during phase IV						
SBP	35.1 ± 15.0	43.7 ± 19.3	59.7 ± 29.9	< 0.05	< 0.05	< 0.01
MBP	23.1 ± 10.3	24.8 ± 10.6	30.3 ± 15.7	ns	ns	ns
DBP	19.3 ± 8.9	18.5 ± 8.6	20.2 ± 11.7	ns	ns	ns
PP	15.8 ± 8.9	25.2 ± 14.2	39.5 ± 22.1	< 0.01	< 0.05	< 0.001
Cardiovagal indices						
YR	1.98 ± 0.45	2.06 ± 0.48	2.04 ± 0.53	ns	ns	ns
BRG	5.33 ± 2.68	4.20 ± 1.37	3.02 ± 1.59	ns	< 0.01	< 0.001

133.2 ± 23.6 ml standing ($P < 0.001$ for each of supine compared with sitting, sitting compared with standing and supine compared with standing).

Influence of body position on changes in BP and PP during the VM

Changes in BP

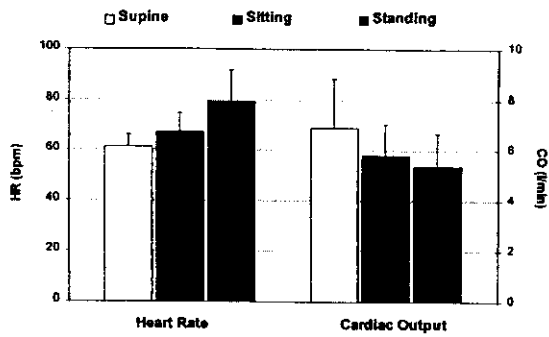
The fall in BP during early phase II increased with increasing orthostatic stress. Compared with baseline, systolic BP dropped by 12.6 ± 17.3 mmHg in the supine position, 18.8 ± 20.1 mmHg in the sitting position and 28.2 ± 15.5 mmHg in the standing position (supine compared with sitting and sitting compared with standing, not significant; supine compared with standing, $P < 0.001$). Postural differences in changes in mean and diastolic BP during early phase II showed a similar pattern, but were less pronounced (Table 1, Figure 3).

The increase in BP during late phase II was basically the same for all body positions. Compared with early phase II, the increases in systolic BP were 23.1 ± 16.0 mmHg (supine), 27.0 ± 19.0 mmHg (sitting) and 26.3 ± 12.5 mmHg (standing) (no significant

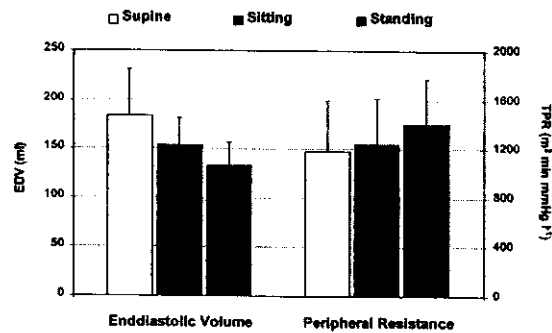
differences). The differences were even smaller for mean and diastolic BP (Table 1, Figure 3).

The BP overshoot during phase IV increased significantly when the body position was changed from lying to sitting and standing. Compared with baseline, systolic BP increased by 35.1 ± 15.0 mmHg in the supine position, 43.7 ± 19.3 mmHg in the sitting position and 59.7 ± 29.9 mmHg in the standing position (supine compared with sitting and sitting compared with standing, $P < 0.05$; supine compared with standing, $P < 0.01$). Posture-related differences in the phase IV overshoot of mean and diastolic BP showed a similar pattern, but again were less pronounced (Table 1, Figure 3).

The influence of posture on changes in BP during the VM resulted in an increased rate of abnormal responses (reduced late phase II) with increased orthostatic stress: one subject (5.3%) in the supine position, one subject (5.3%) in the sitting position and three subjects (15.8%) in the standing position. On the other hand, the frequency of 'flat-top' responses decreased with increasing orthostatic stress. There were five subjects (26.3%) with this variant in the supine position, three subjects (15.8%) in the sitting position and none in the standing position.



a)



b)

Figure 2 Baseline parameters for the different body positions

Changes in PP

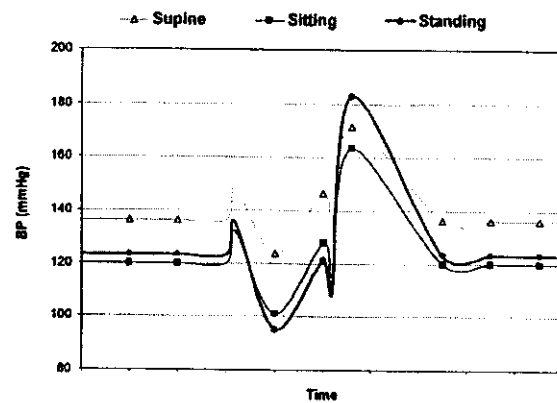
PP compression during phase II was greater in the upright position. Maximal PP compression compared with baseline was 21.4 ± 13.2 mmHg in the supine position, 25.6 ± 12.2 mmHg in the sitting position and 29.1 ± 12.7 mmHg in the standing position (supine compared with sitting and sitting compared with standing, not significant; supine compared with standing, $P < 0.05$) (Table 1).

On the other hand, there was a significant increase in PP expansion during phase IV with increasing orthostatic stress. Maximal PP expansion compared with baseline was 15.8 ± 8.91 mmHg in the supine position, 25.2 ± 14.2 mmHg in the sitting position and 39.5 ± 22.1 mmHg in the standing position (supine compared with sitting, $P < 0.01$; sitting compared with standing, $P < 0.05$; supine compared with standing, $P < 0.001$) (Table 1).

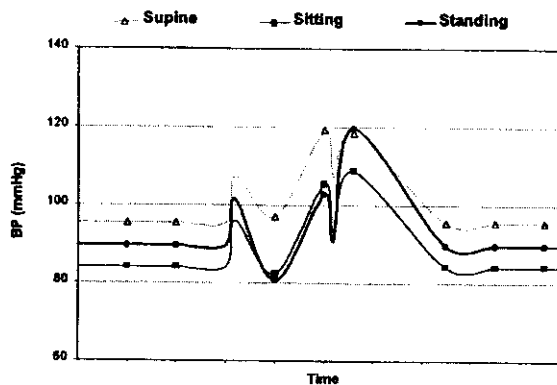
Influence of body position on cardiovascular indices

VR

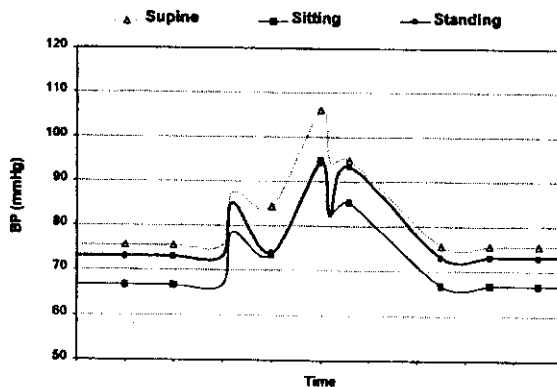
There were no significant differences in the VR between the three tested body positions: supine, 1.98 ± 0.45 ;



a)



b)



c)

Figure 3 Changes in systolic (a), mean (b) and diastolic (c) BP during and after the VM for different body positions

sitting, 2.06 ± 0.48 ; standing, 2.04 ± 0.53 (Table 1, Figure 4).

BRG

BRG was significantly decreased in the upright position. BRG values were: supine, 5.33 ± 2.68 $\text{ms} \cdot \text{mmHg}^{-1}$; sitting, 4.20 ± 1.37 $\text{ms} \cdot \text{mmHg}^{-1}$; standing, $3.02 \pm$

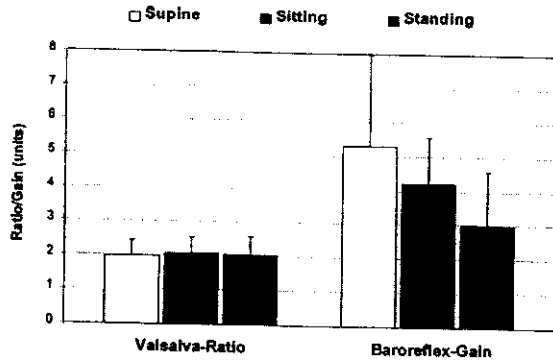


Figure 4 Cardiovascular indices for different body positions

$1.59 \text{ ms} \cdot \text{mmHg}^{-1}$ (supine compared with sitting, not significant; sitting compared with standing, $P < 0.01$; supine compared with standing, $P < 0.001$) (Table 1, Figure 4).

Unpublished normative data on BRG derived from early phase II of the VM suggest this parameter to be abnormal if its value less than $2 \text{ ms} \cdot \text{mmHg}^{-1}$ (K. Juhasz, W. Singer and P. A. Low, unpublished work). This was the case in one subject (5.3%) for each of the supine and sitting positions, and in five subjects (26.2%) for the standing position.

DISCUSSION

Assuming the upright posture is accompanied by a vertical displacement of blood below heart level [19]. When humans stand up from the supine position, it is estimated that 300–800 ml of blood is shifted from the chest to the venous capacitance bed within seconds [20–22]. In addition, slow transcapillary fluid shifts from vessels below the hydrostatic indifference level in the surrounding tissues reduce plasma volume over several minutes by about 10% [23,24]. These changes result in a decline in venous return and stroke volume [19,22]. Our findings of decreased EDV as an index of preload with a consequent decrease in CO in the standing position are concordant with these reports.

A significant fall in BP can be prevented by a complex regulatory system comprising a series of neurohumoral mechanisms and cardiovascular reflexes that regulate peripheral vascular resistance and capacitance, stroke volume and HR, with BP as the controlled variable [17]. The baroreceptor reflex plays a key role in this [25–28].

A fall in BP leads to unloading of baroreceptors located in the carotid sinus and aortic arch, resulting in reduced traffic in glossopharyngeal and vagal afferents to the nucleus of the tractus solitarius [26,29–32]. Sympathetic outflow is activated via the caudal ventrolateral medulla, the rostral ventrolateral medulla and the inter-mediolateral cell column, thus increasing arterial vascular

resistance, venous tone, CO and plasma catecholamine levels [25,29,33]. Cardiovascular neurons of the nucleus ambiguus are inhibited, and HR increases [29,34,35]. Our findings of graded increases in HR and TPR with increasing orthostatic stress reflect some of these mechanisms.

The main purpose of the present study was to answer the question of whether these well known effects of posture have a significant influence on the responses of BP and HR to the VM. There are only few published studies addressing this question, all of which are selective for age and gender, as they include only young men [36–39]. However, it has been shown that age and gender have significant effects on cardiovascular responses to the VM and on autonomic function in general [1–3,16]. In addition, most of the reported case series are rather small, are focused on certain aspects of the manoeuvre or are limited to HR analysis, without investigating the effects on BP. We therefore evaluated the effects of posture on both HR and BP responses to the VM in a larger, non-selected group of healthy volunteers.

We could demonstrate significant effects of posture on BP responses to the VM. The magnitude of the fall in BP during early phase II and in the BP overshoot during phase IV were lowest in the supine position, and increased with increasing orthostatic stress. The changes were most pronounced for systolic BP, but were also present for mean and diastolic BP. These results agree with the findings of Ten Harkel et al. [39], who investigated the effects of posture on the VM in ten healthy men and also reported larger BP responses when the subjects were standing. In accordance with findings of Luster et al. [36], we found the increase in BP during late phase II to be uninfluenced by posture.

The greater fall in BP during early phase II could be explained on the basis of a reduced intrathoracic blood pool in the upright position, lessening the subject's ability to compensate for the additional decrease in venous return, secondary to the increased intrathoracic pressure during the VM.

It is known that late phase II represents a progressive increase in TPR due to heightened sympathetic vasoconstrictor activity in response to the fall in BP during early phase II, as reflected by increased efferent sympathetic nervous outflow to limb muscles and increased concentrations of plasma noradrenaline [40–42]. It seems likely that the additional decrease in the intrathoracic blood volume in the upright position requires greater vascular adrenergic activation to compensate for the reduced venous return during the VM and in order to achieve a similar rise in BP during late phase II.

The BP overshoot during phase IV of the VM is thought to be due in part to an overshoot of arteriolar vasoconstriction during late phase II [2,40]. Another important mechanism appears to be cardiac adrenergic activation, since phase IV can be significantly blunted by

β -blockade [2,5]. The greater phase IV overshoot in the upright position is therefore likely to be due a combination of the two mechanisms, reflecting an overall higher adrenergic activation.

The influence of body position on changes in BP during the VM resulted in an increased number of responses that showed a reduced late phase II, from one subject (5%) in the supine and sitting positions to three subjects (16%) in the standing position. This suggests that the upright posture may reduce the specificity of this test.

Another effect of posture was a progressive decrease in the number of flat-top responses from the supine (26%) to the sitting (16%) to the standing (0%) position. Ten Harkel et al. [39] also reported an incidence of 30% square-wave responses in healthy volunteers in the supine position, which changed to sinusoidal responses on changing to either the sitting or the standing position in all subjects. The flat-top/square-wave response was originally linked to patients with congestive heart failure [17,43,44], but can also, according to these data, be frequently seen in healthy subjects during a supine or sitting VM. It therefore appears that this type of response is not necessarily indicative of congestive heart failure, but can be a normal variant, especially when the VM is performed with the subject in a lying or sitting position.

From a practical standpoint, we therefore recommend that the VM should be routinely performed in the lying position. If a flat-top response occurs, the subject should repeat the manoeuvre in the sitting position and, if necessary, also in the standing position. The manoeuvre should only be called abnormal if the response does not change to a sinusoidal response following a change of posture. A reduced late phase II should only be considered abnormal if the manoeuvre was performed with the subject in the supine position.

The influence of posture on changes in BP during the VM also affected PP. PP compression during phase II was greater in the upright position, as was PP expansion during phase IV. The explanation for these findings can again involve the additional reduction of venous return and the greater stimulation of adrenergic responses.

Even though Ten Harkel et al. [39] reported an increased VR in the standing position, we did not find the VR to be significantly altered by posture. On the other hand, BRG decreased significantly with increasing orthostatic stress, which agrees with the findings of Luster et al. [36], who reported an effect of posture on the $\Delta HR/\Delta MAP$ (mean arterial pressure) coefficient of early phase II. Based on normative data of BRG derived from early phase II of the VM (K. Juhasz, W. Singer and P. A. Low, unpublished work), we found one subject to have a mildly reduced BRG both in the supine and the sitting positions, compared with five subjects in the standing position. We propose that sympathetic activation in the upright position blunts baroreflexes, resulting in similar

HR responses in spite of greater changes in BP. Therefore assessment of baroreflex sensitivity should not be performed under conditions of orthostatic stress.

In conclusion, the findings of the present study suggest that posture has significant effects on cardiovascular responses to the VM. Knowledge of these effects and standardization of the body position for this manoeuvre are necessary in order to avoid misinterpretation.

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