Leg crossing, muscle tensing, squatting, and the crash position are effective against vasovagal reactions solely through increases in cardiac output

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METHODS

At the Academic Medical Center Syncope Unit, patients with vasovagal syncope are instructed how and when to apply physical countermeasures during vasovagal reactions provoked by head-up tilting. Usually a symptomatic vasovagal reaction returns after termination of the maneuver. This gives the opportunity to have patients use more than one maneuver to combat a vasovagal reaction and to compare the effects. Table 1 summarizes the maneuvers.

Inclusion. From a consecutive series of 66 patients who developed a vasovagal reaction during tilt table testing, 26 patients were selected who successfully had applied either of the next two combinations of maneuvers: LBMT and LCMT (series A, n = 9) or WBT and LCMT (series B, n = 12). Patients who had squatted or applied HBK constituted series C (n = 14) and series D (n = 9), respectively. Consequently, there was some overlap between the series of patients.

Medical history in all patients (conducted by the senior investigator W. Wieling) consisted of at least one episode of loss of consciousness, with prodromal symptoms such as diaphoresis, pallor, or visual disturbances (“seeing black spots”) in the presence of any of the following triggers: (prolonged) orthostatic stress, pain, or the experience of an unusually strong emotional circumstance. Exclusion criteria for tilt testing were pregnancy or the presence of structural or (possibly) arrhythmogenic heart disease that could lead to syncope.

Tilt protocol and maneuvers. Investigations took place in the morning, at least 1 h after breakfast, in a room with a temperature of 23°C. Patients were strapped by a single torso belt to a manually controlled tilt table with a foot board. After 5 min of supine rest, patients were 60° tilted head up for 20 min. If no vasovagal reaction developed, 0.4 mg of nitroglycerin was administrated sublingually before an additional 15-min tilt (2). Beat-to-beat systolic and diastolic BPs were measured continuously noninvasively by use of Finapres model 5 (TNO Biomedical Instrumentation, Amsterdam, The Netherlands). The finger cuff was applied to the midphalanx of the left

Fig. 1. Top: excerpts from the original (continuous) blood pressure (BP) tracing in a subject (female, 21) from series A, at indicated intervals during the protocol. Bottom 4 panels show derived heart rate (HR), stroke volume (SV), cardiac output (CO), and total peripheral resistance (TPR). SV, CO, and TPR are represented as percentage from baseline [%bl, i.e., mean over the interval 2.5 to 3 min after head-up tilt (HUT)]. LCMT and LBMT, tensing of lower body muscles with and without leg crossing, respectively; HDT, head-down tilt. Vertical gray bars indicate the intervals at which hemodynamic parameters were determined for comparison, as described in METHODS.
middle finger. To avoid hydrostatic level differences, the hand was held at right atrial level in the midaxillary line. Finapres recordings accurately reflect BP changes during orthostatic stress (7). One of the investigators operated a marker pulse to identify the onset and termination of each maneuver. For offline analysis, all signals were digitally stored in a personal computer at a sampling rate of 100 Hz, as well as real-time printed by a thermo-paper writer (Thermal arrayrecorder WR 7700, Graphitec, Solingen, Germany) for direct inspection and annotation.

Before the test patients had practiced the maneuvers that they performed during the vasovagal reaction. Patients were instructed to avoid straining during performance of the maneuvers.

All maneuvers started at the moment of a rapid fall in BP in association with symptoms of impending syncope (Fig. 1). Each maneuver was sustained for 40–60 s. Half of patients in series A started with LBMT and applied LCMT at faint recurrence; the other half performed these in reverse order. In series B, maneuver order was split similarly.

In series C and D, patients were tilted back or had applied one of the muscle tensing maneuvers when a faint was imminent. After a subsequent head-up tilt or a release of the maneuver, they stepped off the tilt table. Standing next to the table, the patients waited until faint recurrence and then squatted in series C and in series D performed HBK. For safety reasons (i.e., risk of collapse when stepping off the table and consequences), in our tilt lab patients aged >55 years are never taught HBK or squatting when a vasovagal reaction is present.

During all testing, patients were closely monitored by two experienced investigators. In case of syncope during or after a maneuver, the tilt table was tilted down immediately or if the patient was standing they were laid down on the bed.

**SV and TPR computation.** From the continuous BP measurement, the arterial pulse wave was analyzed by a pulse wave analysis method, which computes changes in left ventricular SV from the pulsatile systolic area. We used the improved method of Wesseling, as described in detail previously, using the Modelflow program (model-based measurement method based on a nonlinear, 3-element model of the input impedance of the aorta) (8). This methodology tracks rapid changes in SV accurately (compared with gas rebreathing) during leg crossing with and without muscle tensing (23). During conditions with a low systemic BP, the technique provides accurate values for SV and CO (6, 8).

CO was computed as SV times heart rate (HR), and TPR was calculated as mean BP (MBP) divided by CO. MBP was obtained as the integral of pressure over one beat divided by the corresponding interbeat interval.

**Analysis.** As baselines, BP, HR, SV, CO, and TPR were averaged over the intervals 4.5 to 5 min supine rest and 2.5 to 3 min head-up tilt, respectively. The same parameters were then determined 1) right after start of each maneuver, 2) after 10–40 s, and 3) after duration of each maneuver (Tables 3 and 4). For the comparison of maneuvers, the changes from baseline were calculated and tested for significance.

**Table 2. Patient characteristics and baseline values per series**

<table>
<thead>
<tr>
<th></th>
<th>Series A</th>
<th>Series B</th>
<th>Series C</th>
<th>Series D</th>
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<tbody>
<tr>
<td></td>
<td>LBMT vs. LCMT</td>
<td>WBT vs. LCMT</td>
<td>SQT vs. HBK</td>
<td>WBT vs. LCMT</td>
</tr>
<tr>
<td><strong>n</strong></td>
<td>12</td>
<td>9</td>
<td>14</td>
<td>9</td>
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<tr>
<td><strong>Patient characteristics</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Age, yr</strong></td>
<td>46 (18–80)</td>
<td>37 (16–71)</td>
<td>27 (16–52)</td>
<td>28 (16–38)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td>7 f/5 m</td>
<td>4 f/5 m</td>
<td>9 f/5 m</td>
<td>7 f/2 m</td>
</tr>
<tr>
<td><strong>Height, meters</strong></td>
<td>1.75±0.12</td>
<td>1.76±0.89</td>
<td>1.74±0.11</td>
<td>1.73±0.63</td>
</tr>
<tr>
<td><strong>Weight, kg</strong></td>
<td>81±9</td>
<td>72±8</td>
<td>81±11</td>
<td>84±10</td>
</tr>
<tr>
<td><strong>No. of syncopal episodes in 1 year</strong></td>
<td>2 (1–10)</td>
<td>2 (1–20)</td>
<td>3 (1–30)</td>
<td>5 (1–30)</td>
</tr>
<tr>
<td><strong>No. of syncopal episodes, life time</strong></td>
<td>6 (1–40)</td>
<td>10 (1–40)</td>
<td>10 (1–35)</td>
<td></td>
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<tr>
<td><strong>5-Min supine rest</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>SBP, mmHg</strong></td>
<td>116±16</td>
<td>105±12</td>
<td>120±17</td>
<td>123±14</td>
</tr>
<tr>
<td><strong>DBP, mmHg</strong></td>
<td>63±9</td>
<td>56±8</td>
<td>63±10</td>
<td>66±8</td>
</tr>
<tr>
<td><strong>MBP, mmHg</strong></td>
<td>81±9</td>
<td>72±8</td>
<td>81±11</td>
<td>84±10</td>
</tr>
<tr>
<td><strong>HR, beats/min</strong></td>
<td>73±10</td>
<td>73±11</td>
<td>71±11</td>
<td>73±14</td>
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<tr>
<td><strong>3-min head-up tilt</strong></td>
<td></td>
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<tr>
<td><strong>SBP, mmHg</strong></td>
<td>118±15</td>
<td>113±18</td>
<td>123±18</td>
<td>124±15</td>
</tr>
<tr>
<td><strong>DBP, mmHg</strong></td>
<td>73±11</td>
<td>67±14</td>
<td>75±11</td>
<td>74±12</td>
</tr>
<tr>
<td><strong>MBP, mmHg</strong></td>
<td>88±11</td>
<td>80±14</td>
<td>89±12</td>
<td>89±12</td>
</tr>
<tr>
<td><strong>HR, beats/min</strong></td>
<td>88±19</td>
<td>91±21</td>
<td>89±12</td>
<td>89±15</td>
</tr>
</tbody>
</table>

Age and number of syncopal episodes are given as median and range. Systolic (SBP), diastolic (DBP), and mean (MBP) blood pressure and heart rate (HR) are given as means and SD.
before the start of the maneuver over an interval of 3–5 beats and 2) over an interval after onset of each maneuver of 30 s when a stable BP was reached (Fig. 1). SV, CO, and TPR were expressed in percentage of head-up tilted baseline values (%bl).

For each maneuver we compared all parameters before and during the maneuver, using Student’s paired t-tests. In series A and B, we compared the parameters during each of the two maneuvers in each series, also using paired t-tests. P values <0.05 were considered statistically significant.

RESULTS

Patient characteristics and hemodynamic baseline values are given in Table 2.

On the basis of the nadir values and the presence of prodromal symptoms, at the start of each maneuver, all patients had a vasovagal reaction with imminent syncope if no measures were taken. BP, HR, and derived parameters before start of each maneuver are given in Tables 3 and 4.

All maneuvers caused an increase in BP (Tables 3 and 4, Fig. 2) varying from a rise in systolic blood pressure (SBP) from 77 ±8 to 104 ±18 mmHg (P<0.05) in series A during LBMT to a rise from 70 ±10 to 123 ±9 mmHg (P<0.05) in series B during LCMT. With the onset of each maneuver, BP started to increase after ~3 s and in all patients stabilizing BP took less than 15 s. HR increased in LBMT, LCMT, and WBT (P<0.05). In HBK HR decreased from 99 ±14 to 78 ±12

<table>
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<th>Table 4. Effects of maneuvers in series C and D</th>
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<tr>
<td>SQT</td>
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<tr>
<td>SBP, mmHg</td>
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<tr>
<td>DBP, mmHg</td>
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<tr>
<td>MAP, mmHg</td>
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<tr>
<td>HR, beats/min</td>
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<tr>
<td>SV, %bl</td>
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<tr>
<td>CO, %bl</td>
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<tr>
<td>TPR, %bl</td>
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Values are means and SD. SV, CO, and TPR are given as percentage baseline, i.e. after 2.5–3 min head up-tilt. *Significant difference, P<0.05.

Fig. 2. Effects of the various maneuvers on mean blood pressure (MBP), HR, SV, CO, and TPR. SV, CO, and TPR are represented as percentage from baseline (%bl, i.e., mean over the interval 2.5 to 3 min after head-up tilt). Each line represents the indexes at the start of and during the maneuver. The dashed lines with the white plotting-dot represent the group means. The graphs on LCMT combine all subjects in series A and B. *Significant change at P<0.05; NS, nonsignificant. WBT, whole body tensing; HBK, head bent between knees. See Table 1 for further description of maneuvers.
beats/min ($P < 0.05$). All maneuvers elicited an increase in CO ($54 \pm 12\%$ baseline to $94 \pm 21$ in WBT to a rise from $65 \pm 17$ to $110 \pm 22$ in LCMT in \textit{series A}) without significant changes in TPR. The hemodynamic effects of maneuver per group are given in Tables 3 and 4 and Fig. 2.

In \textit{series A}, SBP rose to $104 \pm 18$ mmHg in LBMT, whereas in LCMT SBP stabilized at $120 \pm 13$ mmHg ($P < 0.05$). In \textit{series B} WBT showed slightly less effective on BP than LCMT: SBP was $123 \pm 19$ vs. $115 \pm 23$ mmHg ($P < 0.05$). CO was lower during LBMT than during LCMT ($95 \pm 17$ to $110 \pm 22$, $P < 0.05$). All other values (including HR) within both series did not differ. In Fig. 3, MBP, HR, SV, CO, and TPR during the two compared maneuvers in \textit{series A} and \textit{B} are plotted.

**DISCUSSION**

This study shows that the circulatory effect of various physical countermaneuvers during vasovagal reactions is exclusively due to an increase in CO rather than any consistent effect on TPR. The small differences between the BP effects of LCMT and LBMT, respectively, WBT do not seem clinically relevant. The study also documents the efficacy of squatting and the crash position as countermaneuvers to increase BP immediately during vasovagal reactions.

*Effects of physical countermaneuvers on CO and peripheral resistance.* There are remarkable resemblances between the effects of the physical countermaneuvers in the present study on CO and those when inflating an antigravity suit at the onset of an impending vasovagal faint (26). CO rises by a factor of 1.3–1.7 in our maneuvers (Tables 3 and 4) and 1.4 during suit inflation (26). In both experiments, CO increased to $\sim 100\%$ of baseline upright values (Tables 3 and 4, Ref. 26). In another study in two healthy individuals, squatting caused a factor 1.6 increase in CO measured by dye dilution (11).

In the classical study by Weissler and coworkers (26), inflation of an antigravity suit during an impending vasovagal faint induced an instantaneous increase in central venous pressure. More recently, it was shown that leg muscle tensing during upright free standing also increased central venous pressure instantaneously (24). These observations document the rapid effect of these interventions on right ventricular filling pressure. However, an effect on systemic BP was observed with a latency of $\sim 3$ s (9, 26). The explanation for this latency is straightforward and was likely due to the time it took to translocate the venous blood from the right ventricle through the pulmonary circulation to the left ventricle and the systemic circulation (27).

In the above-mentioned antigravity suit experiment, the effects of the intervention were solely explained by an increase in CO (determined by the dye-dilution method) (26). No effects were observed on peripheral vascular resistance, and the vasovagal faints reoccurred after deflation of the antigravity suit. Accordingly, none of the physical countermaneuvers in the present study had any significant effect on TPR, and vasovagal reactions reoccurred after release of muscle tensing. The lack of an effect of physical countermaneuvers on vascular resistance may be surprising, but it is not when the time course of the effects of skeletal muscle tensing on sympathetic outflow and systemic vascular resistance under similar circumstances is considered. During preparation and initiation (first minute of upright leg-cycling exercise in healthy volunteers, muscle sympathetic nerve activity is decreased, suggesting facilitation of increased muscle blood flow (4). During the first minute of sitting static leg exercise (at 30% of maximal voluntary power), muscle sympathetic nerve traffic was also found to decrease. One of the explanations given by the authors is loading of the cardiopulmonary baroreceptors due to the rapidly increased thoracic blood volume (13). In their study, muscle sympathetic activity only started to increase after 1 min of exercise (13). This increase in sympathetic nerve activity is mediated by the muscle chemoreflex, which is activated after $\sim 1–2$ min of static muscle exercise (14).
In our study, skeletal muscle tensing was only sustained for 40–60 s. Thus an increase in muscle sympathetic outflow and peripheral resistance is not to be expected. Previous observations that show that lower body muscle tensing during orthostatic stress increases orthostatic tolerance but does not increase peripheral vascular resistance (21) and that isolated hand gripping has only a trivial effect on orthostatic tolerance (9) are in excellent agreement with this explanation of the event.

The observation that isometric handgrip does not increase orthostatic tolerance (9) seems in conflict with the observation by Brignole et al. (3) that forceful isometric arm counterpressure maneuvers during free standing are effective to combat vasovagal reactions. We attribute this difference to leg and abdominal contractions that are inevitable during maximal isometric arm exercise in the upright position to stabilize the body.

So far we have attributed the rise in BP during muscle tensing maneuvers to mechanical effects on CO and not to reflex effects. The HR response, however, documents that reflex effects are involved as well. The instantaneous increase in HR at the onset of muscle tensing (Fig. 1, Ref. 9) is a reflex effect by a combination of central command and the muscle-heart reflex (1, 14). Reflex sympathetic stimulation of cardiac contractility at the onset of exercise may have contributed to the increased CO. In contrast to the muscle tensing maneuvers, the crash position (where no skeletal muscle tensing is involved but only passive abdominal compression) subsequently does not increase HR.

In squatting, where compression of arteries would be expected most prominently, TPR also did not change significantly, indicating that mechanical effects on arterial conductance play a minor role in the efficacy of the maneuvers. This corresponds to an earlier study that was unable to show an effect of squatting on TPR (11).

**Limitations.** A potential limitation of our study is that we did not objectify levels of skeletal muscle tension. Although we took care that the different maneuvers were performed with comparable effort in all subjects at all times, the lack of its measurement makes muscle tension an uncontrolled variable in the study. We also did not measure possible changes in intraabdominal and intrathoracic pressure. Especially in whole body tensing, unintentionally increasing intrathoracic pressure (closing the glottis when commencing whole body tensing) may have impaired venous return, thereby not fully effecting the maneuver’s potential.

A potential limitation of generalizability lays in our protocol in which we used nitroglycerine to induce a vasovagal reaction. Although this method is widely used and considered by many as a satisfactory model for vasovagal episodes outside the laboratory (2), there are indications that this provocation leads as a satisfactory model for vasovagal episodes outside the laboratory (2). Among vasovagal episodes outside the laboratory, there are indications that this provocation leads. The crash position is especially appropriate when syncope occurs while sitting or for patients who have motor disabilities that would prevent squatting or make them more vulnerable in case of collapse. Recognition of prodromal signs is pivotal in the timely institution of any of the maneuvers, and thus the maneuvers do not apply to the relatively small subset of patients who experience syncope without warning. The range of maneuvers in this study could, however, offer physicians and the mainstay of their patients a means of tailoring therapy to the individual patient’s needs. By having a short list of readily accomplishable maneuvers, patients could increase control over their symptoms and potentially improve the quality of their lives.

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