Cardiovascular response to coughing: its value in the assessment of autonomic nervous control

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SUMMARY

1. The relationship between blood pressure and heart rate responses to coughing was investigated in 10 healthy subjects in three body positions and compared with the circulatory responses to commonly used autonomic function tests: forced breathing, standing up and the Valsalva manoeuvre.

2. We observed a concomitant intra-cough increase in supine heart rate and blood pressure and a sustained post-cough elevation of heart rate in the absence of arterial hypotension. These findings indicate that the sustained increase in heart rate in response to coughing is not caused by arterial hypotension and that these heart rate changes are not under arterial baroreflex control.

3. The maximal change in heart rate in response to coughing (28 \pm 8 beats/min) was comparable with the response to forced breathing (29 \pm 9 beats/min, \(P > 0.4\)), with a reasonable correlation \((r = 0.67, P < 0.05)\), and smaller than the change in response to standing up (41 \pm 9 beats/min, \(P < 0.01\)) and to the Valsalva manoeuvre (39 \pm 13 beats/min, \(P < 0.01\)).

4. Quantifying the initial heart rate response to coughing offers no advantage in measuring cardiac acceleratory capacity; standing up and the Valsalva manoeuvre are superior to coughing in evaluating arterial baroreflex cardiovascular function.

Key words: baroreflex, blood pressure, cardiovascular autonomic function, forced respiratory sinus arrhythmia, heart rate, standing up, vagal outflow, Valsalva manoeuvre.

Abbreviations: ECG, electrocardiogram; FINAP, finger arterial blood pressure; FRSA, forced respiratory sinus arrhythmia; HR\(_{\text{max}}\), maximum heart rate; \(\Delta HR_{\text{max}}\), maximum heart rate minus control heart rate; IAP, intra-arterial blood pressure; I-E difference, mean difference between maximal and minimal heart rate during each of six consecutive respiratory cycles of forced inspiration and expiration; R\(-R_0\), etc., last R-R interval before the marker pulse, etc.; \(T_{\text{max}}\), time from R\(-R_0\) to HR\(_{\text{max}}\).

INTRODUCTION

Investigation of cardiovascular reflexes is used as a non-invasive bedside test to examine the integrity of autonomic circulatory control in man. Among these tests, the cardiovascular responses induced by deep breathing, standing up and the Valsalva manoeuvre are most commonly used \([1-4]\). Sharpey-Schafer \([5]\) demonstrated in healthy subjects that the mechanical peaks in arterial blood pressure were followed by an undershoot immediately after prolonged coughing, which in certain patients elicited a syncope \([6, 7]\). Wei & Harris \([8]\) reported a reduction in blood pressure after short-lasting coughing in patients. The initial chronotropic response to short-lasting coughing was recently shown to be vagal in origin \([9]\) and proposed to be useful as an assessment of autonomic integrity \([8]\) and cardiac acceleratory capacity \([8-11]\). Maddens \textit{et al.} \([12]\) applied the heart rate response to coughing as an autonomic test in elderly patients. Although a relationship between blood pressure and heart rate responses to coughing was presumed to exist \([8, 9]\), this has not yet been established for the proposed new 'cough'-test.

The present study was designed to investigate the relationship between blood pressure and heart rate responses to coughing in normal subjects and to evaluate in the same subjects coughing as a new autonomic function test in comparison with the commonly used tests forced breathing, standing up and the Valsalva manoeuvre.

METHODS

Subjects

Ten healthy male volunteers participated in the study after informed consent had been obtained. The experimental procedures started at 09:00 hours in a room with a constant ambient temperature of about 21\(^{\circ}\)C. At least 2 h
before the test procedures the subjects consumed a light breakfast without coffee or tea. All subjects were non-smokers, did not use any medication and were within 10% of their ideal body mass index. The mean age of the subjects was 28 (range 22-40) years, mean weight 71.6 (range 62-88) kg and mean resting auscultatory blood pressure 116/69 mmHg (15.5/9.2 kPa) [range 100-128/64-82 mmHg (13.3-17.1/8.5-10.9 kPa)].

Measurements

Instantaneous heart rate was determined from the electrocardiogram (ECG).

During all manoeuvres arterial blood pressure was measured from a continuous recording of finger arterial blood pressure (FINAP) by means of a TNO model 4 Finapres (now commercially available as the Ohmeda 2300 Finapres NIBP monitor). This instrument is based on the volume clamp technique of Penaz et al. [13]. Its recording of finger blood pressure accurately reflects intrabrachial blood pressure changes [13-15], as was recently shown for the Valsalva manoeuvre [14]. To assess the reliability of the Finapres device during coughing, finger blood pressure and intra-arterial blood pressure (IAP) were recorded simultaneously in three of the 10 participants in the sitting position. IAP was measured by means of a Teflon cannula inserted into the brachial artery from the opposite arm using the Seldinger technique. The cannula was attached to a Hewlett-Packard 1290A transducer and monitor (Hewlett-Packard, Palo Alto, CA, U.S.A.). The IAP transducer and the FINAP cuff were held at heart level in order to avoid hydrostatic level errors.

Respiratory phase was determined using a nose thermistor (Nihon Kohden) and Valsalva strain by means of an electrical LED-bar and checked by the investigator. Care was taken to prevent deep breathing before and immediately after release of the strain [19].

Coughing. The values of the blood pressure peaks and valleys during coughing were separately derived from the individual tracings. The means of the three peaks and three valleys were averaged to one peak and one valley and expressed as the differences from control systolic and diastolic blood pressure, respectively. Control heart rate was subtracted from the maximum heart rate response (HRmax) to coughing and was defined as ΔHRmax. The time from R-R0 to when HRmax was reached was defined as Tmax.

Forced respiratory sinus arrhythmia (FRSA). The so-called 'I–E difference' was computed as the mean difference between the maximal and minimal heart rate during each of six consecutive respiratory cycles of forced inspiration and expiration and was expressed in beats/min [16].

Standing up and the Valsalva manoeuvre. Control heart rate was subtracted from HRmax on standing up and the Valsalva manoeuvre and defined as ΔHRmax [1, 3, 16].

Statistical analysis. All values are given as means ± sd. Comparison was performed with a non-parametric analysis of variance technique (Kruskal–Wallis). If significant differences were established, the two-tailed Wilcoxon matched-pairs signed-ranks test was used. To compare the heart rate responses to the four manoeuvres, correlation coefficients were computed using multiple regression techniques between the ΔHRmax of coughing on the one hand and the I–E difference for FRSA and ΔHRmax for standing up and the Valsalva manoeuvre on the other hand.

RESULTS

Blood pressure and heart rate responses to coughing

Recordings of IAP and FINAP in three subjects are shown in Fig. 1, demonstrating the similarity between the
signals during the manoeuvres. The mean values of the three intra-cough peaks and valleys are given as differences from control blood pressure in Table 1. Individual post-cough blood pressure responses did not show a consistent pattern but varied from a rise to a fall or an absence of changes in blood pressure (Fig. 1). Apart from the intra-cough peaks we observed no changes in blood pressure when the subjects were supine. The heart rate response to supine coughing was characterized by a rapid increase 5 s after the onset of coughing, followed by a plateau phase and a sluggish decrease to baseline values by 20 s. The sustained elevation of post-cough heart rate was independent of either the presence or direction of change in post-cough blood pressure. \( \Delta HR_{\text{max}} \) was 28 ± 8 beats/min with \( T_{\text{max}} \) at 5.7 ± 2.4 s.

Influence of body position on blood pressure and heart rate responses to coughing

Resting blood pressure values differed significantly between the three body positions for diastolic but not for systolic pressure (Table 1). Control heart rate increased from the supine to the sitting and from the sitting to the standing position (Table 2). Post-cough diastolic blood pressure showed a slight, but consistent, decrease in the sitting and the standing position (Table 1). By varying body position the pattern of the heart rate responses to cough differed mainly in that \( HR_{\text{max}} \) was reached later in the sitting position (7.1 ± 2.9 s) and in the standing position (9.5 ± 3.1 s; Table 2).

Relationship between onset of coughing and the initial heart rate response

In eight out of 10 subjects R-R\(_{-1}\) did not differ from R-R\(_{-2}\) but R-R\(_{0}\) was significantly shorter than R-R\(_{-1}\) (\( P < 0.01 \)). The inspiration before the first cough started, on average, in R-R\(_{-1}\) (range R-R\(_{-3}\) to R-R\(_{0}\)).

Comparison of the magnitude of heart rate responses to coughing, FRSA, standing up and the Valsalva manoeuvre.

\( \Delta HR_{\text{max}} \) for coughing in the supine position (28 ± 8 beats/min) was smaller than after standing up (41 ± 9 beats/min, \( P < 0.01 \)) and during the Valsalva manoeuvre (39 ± 13 beats/min, \( P < 0.01 \)) (Fig. 2) and did not differ significantly from the I-E difference for FRSA (29 ± 9 beats/min, \( P > 0.4 \)). \( \Delta HR_{\text{max}} \) for coughing showed a reasonable correlation with the I-E difference for FRSA (\( r = 0.67, P < 0.05 \)); the addition of \( \Delta HR_{\text{max}} \) for standing up to the multiple regression analysis only resulted in an increase in \( r \) to 0.87 (\( P > 0.1 \)) and the improvement obtained by the further addition of \( \Delta HR_{\text{max}} \) for the Valsalva manoeuvre was negligible (\( r = 0.87, P > 0.4 \)).

DISCUSSION

Blood pressure and heart rate responses to coughing: beat-to-beat relationship

The magnitude and time course of the heart rate responses to coughing are in accordance with the studies of Cardone et al. [9] and Wei et al. [8, 10]. In an attempt to unravel blood pressure and heart rate responses to coughing and their possible beat-to-beat relationship, the periods before, during and after coughing will be considered separately.

Before the onset of coughing. An instantaneous heart rate increase preceded the coughing manoeuvre by one interval in all but one subject with, usually, a simultaneous inspiration in that interval. Since the latency to cardio-acceleration after an inspiration is less than 1 s [19], these findings point to a causal relationship between deep inspiration and the early onset of the instantaneous heart rate increase. Supine blood pressure started to rise a number of beats before the onset of coughing (Table 1,

![Fig. 1](image-url)  
**Fig. 1.** Responses during the cough manoeuvre in three subjects. Blood pressure recordings are shown for three forceful coughs spaced over about 3 s. Note the similarity between non-invasive finger and invasive brachial pressures. The response of post-cough blood pressure differed between the three subjects and increased (a), decreased (c) or remained unchanged (b) compared with control values. To convert mmHg to kPa, divide by 7.5.
Table 2. Magnitude and timing of peak heart rate changes in coughing

Values are means ± SD. Statistical significance: *supine vs sitting and standing \( P<0.01 \), sitting vs standing \( P<0.01 \), supine vs sitting \( P<0.05 \), supine vs standing \( P<0.01 \), sitting vs standing \( P<0.05 \). Abbreviation: NS, not significant.

<table>
<thead>
<tr>
<th></th>
<th>Control heart rate (beats/min)</th>
<th>( \Delta HR_{\text{max}} ) (beats/min)</th>
<th>( T_{\text{max}} ) (s)</th>
</tr>
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<tbody>
<tr>
<td>Supine</td>
<td>58 ± 10</td>
<td>28 ± 8</td>
<td>5.7 ± 2.4</td>
</tr>
<tr>
<td>Sitting</td>
<td>67 ± 12</td>
<td>26 ± 10</td>
<td>7.1 ± 2.9</td>
</tr>
<tr>
<td>Standing</td>
<td>80 ± 10</td>
<td>21 ± 8</td>
<td>9.5 ± 3.1</td>
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Fig. 2), suggesting mental involvement in anticipation of the onset of the manoeuvre [20].

During coughing. A cough is produced by a rapid inspiration, followed by closure of the glottis and a strong contraction of thoracic and abdominal muscles resulting in a rise in intrathoracic pressure. This pressure is transmitted to the pulmonary vascular bed, by which an amount of blood may be squeezed through the heart, acting as a conduit into the arterial vascular tree [21].

The large increments in arterial blood pressure during coughing are accompanied by an immediate and rapid increase in heart rate (Fig. 2) and were found to be vagal in origin by Cardone et al. [9]. However, the simultaneous increments in both heart rate and blood pressure render arterial baroreflex heart rate control during coughing unlikely. A possible explanation for the absence of an expected baroreflex-mediated slowing of heart rate is that baroreflex slowing of the heart is inhibited by muscle contractions [19]. Hence the immediate heart rate acceleration may represent an exercise-induced response [9, 22].

After cessation of coughing. In our study of healthy subjects we could not confirm earlier observations in patients [8] that supine arterial blood pressure falls after 3 s of coughing. We found, on average, no fall in blood pressure after supine coughing (Table 1). The sustained elevation of heart rate after cessation of coughing was earlier believed to be associated with post-cough hypotension on all occasions [9]. In contrast, we found in some subjects that the post-cough increase in heart rate is accompanied by a slight rise in blood pressure (Fig. 1a). This suggests that the sustained elevated post-cough heart rate is not mediated by the arterial baroreflex. Although an exercise response must be considered, during muscle contractions comparable in length of time with the cough manoeuvre, as for instance handgrip, heart rate increases instantaneously and decreases almost directly after stopping the manoeuvre in contrast to the sustained tachycardia after coughing [Fig. 2] [4, 9, 22]. Stimulation of cardiac and pulmonary afferents could be a possible cause. It has been well documented that during coughing the increment in cardiac filling pressures closely parallels aortic pressure changes [21, 23, 24]. A brisk increase in cardiac filling pressure may be expected to enhance the stimulus to mechanoreceptors in the low-pressure side of the central
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Fig. 2. Blood pressure (systolic and diastolic) and heart rate responses (averaged over 10 subjects) to coughing (a) compared with standing up (b) and the Valsalva manoeuvre (c). The relationship between blood pressure and heart rate responses as observed for standing up and the Valsalva manoeuvre is absent for coughing. Note the difference between the baroreflex-mediated slowing of heart rate during the onset of Valsalva strain (c) and the heart rate acceleration on coughing (b) during a rise in blood pressure of comparable magnitude and timing. To convert mmHg to kPa, divide by 7.5.

circulation. However, since changes in intrathoracic pressure during cough are concurrently transmitted to both intra- and extra-vascular thoracic compartments, they do not simply reflect the transmural vascular wall pressure changes [25] or the net influence on cardiac and pulmonary afferents. Thus, the afferent input profile to the central nervous system during and after coughing is complex and remains to be defined.

Influence of body position on the blood pressure and heart rate responses to coughing

The influence of gravity on cardiovascular reflex activity in manoeuvres like coughing has not been studied in detail and is complex. Gravity affects pre-test baseline neurohumoral activity [26, 27]. Moreover, central blood volume is reduced in the upright position as compared with the supine position [28]. This may be assumed to exaggerate reflexes by manoeuvres that involve a reduction in venous return, such as coughing, standing up and the Valsalva manoeuvre. Efferent sympathetic vasomotor activity increases on transition from the supine to the upright position [28]. In our subjects diastolic blood pressure in the sitting and standing position was increased by 30% compared with the supine position (Table 1), with concomitant increments in heart rate from the supine to the sitting and the standing positions (Table 2). All these factors could be involved in the slight post-cough fall in blood pressure in the sitting and the standing, but not in the supine, positions.

Coughing as a test for cardiovascular autonomic function: comparison with FRSA, standing up and the Valsalva manoeuvre

The heart rate response to coughing was recently proposed [8, 9] and applied [12] as a new and simple test for investigating autonomic function. The relationship between blood pressure and heart rate during standing up and the Valsalva manoeuvre (Fig. 2) points to the arterial baroreflex as their main common reflex-mechanism [19]. The baroreflex-mediated slowing of heart rate during the onset of Valsalva strain is a typical example of this relation [19] (Fig. 2); it contrasts with the combined rise in blood pressure and heart rate during coughing (Fig. 2). Absence of a baroreflex-mediated relationship between changes in blood pressure and heart rate during and after coughing (Fig. 2) allows us to conclude that this manoeuvre provides no information on the integrity of the arterial baroreflex. Since determination of the site of the lesion on the baroreflex arc is the mainstay in classifying patients with autonomic failure, standing up and the Valsalva manoeuvre are superior to coughing in evaluating baroreflex cardiovascular function.

We quantified the heart rate response to coughing (Table 2) and compared it with the magnitude of the
maximal heart rate changes in response to FRSA, standing up and the Valsalva manoeuvre. The magnitude of $\Delta HR_{\text{max}}$ for coughing was equal to the $I-E$ difference for FRSA with a reasonable correlation ($r=0.67$, $P<0.05$). Therefore we conclude that $\Delta HR_{\text{max}}$ for coughing gives similar information to the $I-E$ difference for FRSA. The heart rate response to FRSA is, however, usually easier to analyse, since muscle artefacts associated with forceful coughing often impede scoring heart rate from the ECG.

HR$_{\text{max}}$ induced by standing up and the Valsalva manoeuvre was larger than that induced by coughing. However, the magnitude of a response cannot be used as a simple criterion of its power to separate health from disease and both inter- and intra-individual variability should be taken into account. We did not study this issue.

REFERENCES


