Assessment of beat to beat changes in cardiac output during the Valsalva manoeuvre using electrical bioimpedance cardiography

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Summary
1. Beat to beat changes in cardiac output during standardized Valsalva's manoeuvres were recorded using electrical bioimpedance cardiography in 13 normal subjects.
2. Cardiac output increased by 12±5% after 1 s of straining solely because of an increase in heart rate. Subsequently, cardiac stroke volume and cardiac output fell during the strain to lows of -40±6% and -21±3% respectively at 15 s.
3. There was a sustained increased in cardiac output (maximum +17±4%) in the late post strain period.
4. The mean coefficient of variation in impedance measurements of cardiac output was 6.8% during all parts of Valsalva's manoeuvre, with no single value exceeding 10%.

Key words: cardiac output, heart rate, impedance cardiography, stroke volume, Valsalva's manoeuvre.

Abbreviations: CO, cardiac output; HR, heart rate; MBP, mean intra-arterial blood pressure; PVR, peripheral vascular resistance; SV, stroke volume; VEPT, volume of electrically participating tissue.

Introduction
The circulatory changes that occur during and after the Valsalva's manoeuvre have been used for many years to investigate the integrity of neural cardiovascular control mechanisms in a variety of clinical conditions [1-5]. These changes are mediated by complex interacting mechanisms which include activation of sino-aortic and cardio-pulmonary baro-reflexes and alterations in intrathoracic pressure, venous return and aortic impedance. Changes occur very rapidly, particularly immediately after the beginning and after the end of the strain. Thus in order to fully characterize the circulatory effects of Valsalva's manoeuvre it is necessary to know beat to beat values not only for heart rate and blood pressure, but also for central haemodynamic parameters.

Continuous recordings of heart rate and intra-arterial blood pressure during Valsalva's manoeuvre were first made in 1936 [6]. However, beat to beat estimation of cardiac output (CO) has proved difficult. Standard indicator dilution techniques for measurement of CO take several seconds to perform and are not applicable on a beat to beat basis. Previous studies have either used these methods or inferred blood flow from pressure data [7, 8].

Measurement of changes in electrical bioimpedance during the cardiac cycle has been used to estimate beat to beat changes in CO [9, 10]. The technique is safe, non-invasive and simple to perform. It has been applied and validated in the investigation of changes in CO under anaesthesia [11] and during dynamic exercise [12, 13].

The present investigation was undertaken to determine (1) whether analysis of changes in thoracic electrical bioimpedance can be used to determine beat to beat changes in CO during Valsalva's manoeuvre, and (2) to characterize the profile of these changes in a small group of normal individuals.

Methods
Subjects
Thirteen normal Caucasian volunteers were recruited from the staff of our department. They had
no past history of cardiovascular disease, diabetes mellitus or any other illness likely to influence the outcome of the study. Three were smokers, but none had a history of excessive alcohol consumption and none had received drug therapy of any kind for at least 1 month before the study.

Details of sex, age, weight, height and resting casual blood pressure are given in Table 1.

**Electrical bioimpedance cardiography**

The technique depends upon mathematical conversion of changes occurring in impedance during each cardiac cycle into blood flow information.

Kubicek et al. [14] empirically derived the following formula to calculate pulse volume:

\[ SV = \frac{R \times L' \times T \times (dz/dt)_{\text{max.}}}{Z_0^2} \]  

where \( SV \) is stroke volume (in ml), \( R \) is the specific resistivity of blood (in ohms/cm), \( L' \) is the distance between the recording electrodes (in cm), \( T \) is the ventricular ejection time (in s), \( Z_0 \) is the thoracic base impedance (in ohms) and \( (dz/dt)_{\text{max.}} \) is the maximum rate of impedance change during the systolic upstroke (in ohms/s).

Sramek has modified this formula by inserting a 'personal constant':

\[ SV = \frac{VEPT \times T \times (dz/dt)_{\text{max.}}}{Z_0} \]  

where \( VEPT \) is volume of electrically participating tissue (in ml).

This formula has been carefully validated by thermodilution and magnetic flowmeter techniques in animals and humans [15].

**Study protocol**

The study was performed in a quiet laboratory with a constant ambient air temperature of 22°C. The subjects were asked to refrain from smoking and taking coffee or alcohol from midnight of the previous day. After measurement of weight and height they rested supine for 10 min before blood pressure assessment using a standardized sphygmomanometer.

Ten, low contact impedance, self-adhesive electrodes (Red Dot) were positioned for injecting the constant current and recording the electrocardiogram and electrical bioimpedance signals (Fig. 1). Impedance cardiac output was measured using a commercially available machine (BoMed, model NCCOM3). This device injects the current and performs on-line analysis of a digitally converted impedance signal using Sramek’s equation [15]. Adjustment is automatically made for respiration. A beat by beat printout of \( Z_0, (dz/dt)_{\text{max.}}, T, \) heart rate (HR), \( SV \) and CO can be obtained using the machine's RS 232 interface.

Standardized Valsalva’s manoeuvres were performed according to a strictly controlled protocol. The subjects, whilst recumbent at 45 degrees, were asked to take a shallow inspiration and to blow into a anaeroid manometer to maintain a pressure of 30 mmHg for 15 s. A 22 gauge needle was inserted into the circuit to provide a small air leak, preventing subjects maintaining manometer pressure by occluding the mouthpiece. One investigator was solely responsible for observing the manometer reading and timing the strain. The subjects were asked to breath normally, avoiding excessively deep respirations, at the end of the strain.

After instruction in the technique, and several practice runs, two standardized Valsalva’s manoeuvres were performed by each subject. HR,
SV and CO for every beat were recorded from 5 s before the strain until 20 s after the end of the strain.

The procedure was repeated in one subject (male, age 30 years, weight 76 kg, height 185 cm, resting blood pressure 125/68 mmHg) on four occasions to assess the reproducibility of the technique.

A fourteenth subject (male, age 36 years, weight 88 kg, height 177 cm, resting blood pressure 156/95 mmHg) completed the study whilst being investigated for labile hypertension. A brachial arterial cannula had been inserted (part of our routine investigative protocol for such patients) allowing beat to beat measurement of intra-arterial blood pressure. He proved not to be hypertensive on 24 h ambulatory intra-arterial blood pressure recording [16] with an average pressure of 111/63±10/8 mmHg. However, his data were not included with those from the normal subjects for statistical analysis because of his high casual blood pressure reading. Results for this subject will be presented separately.

Analysis of results and statistical methods

CO was calculated for each cardiac cycle by multiplying SV by HR.

Estimates of peripheral vascular resistance (PVR) in one subject (kPa l⁻¹ s) were made using the formula:

\[ \text{PVR} = \frac{\text{MBP}}{\text{CO}} \times 80 \]

where MBP is mean intra-arterial blood pressure (in mmHg).

The reproducibility of the method was determined by calculation of the coefficient of variation.

Data are presented as the means ± SEM. Statistical significance of observed differences was determined by standard methods of analysis of variance and paired Student’s t-tests. The 95% limits of probability were considered significant.

Results

Data from both Valsalva’s manoeuvres were analysed in all 13 subjects. Absolute values for HR, SV and CO were obtained for three control beats and for beats occurring at or around 1, 2, 3, 6, 9, 12 and 15 s during the strain and 1, 2, 4, 7, 10, 15 and 20 s after release. Percentage change was calculated by comparing observed values for each beat with the mean value from the three beats immediately preceding the start of the strain.

Resting CO, taken from the three beats immediately preceding the strain, was 6.58 ± 0.43 litres/min, SV was 85.6 ± 5.4 ml and HR was 77.8 ± 9.5 beats/min.

As can be seen in Fig. 2, we observed a small increase in CO at the start of the strain (+ 12 ± 5%, \( P < 0.05 \)) due almost entirely to an increase in HR (+ 7 ± 2%, \( P < 0.05 \)) with little change in SV. This increase, although small, reached statistical significance because it occurred in all patients. HR then briefly fell below control levels before gradually increasing to a maximum of +29 ± 4% \( (P < 0.0001) \) at 15 s. There was a rapid fall in SV and CO throughout the strain with the lowest values (SV -40 ± 6%, \( P < 0.0005 \), CO -21 ± 3%, \( P < 0.0005 \)) occurring at 15 s. After release HR increased further at 1 s and then rapidly fell to below control levels at 4 s. SV increased progressively to a maximum of +47 ± 5% \( (P < 0.0005) \) at 10 s. This rise was sufficient to give a significant increase in cardiac output at 10, 15 and 20 s despite the reduced heart rate.

The coefficients of variation for CO results were calculated in one subject over eight Valsalva’s manoeuvres at control and at fixed times during and after the strain (Table 2). The mean coefficient of variation was 6.8%.

Fig. 3 shows changes in mean HR, MBP, SV, CO and PVR in the subject with an arterial line. The pattern of HR, SV and CO responses to Valsalva’s manoeuvre were similar to those seen in the normal group. The MBP responses showed the classical four phases initially described by Hamilton et al. in 1936 [6]. Estimated PVR increased rapidly during
TABLE 2. Reproducibility of measurements of cardiac output by electrical bioimpedance cardiography at various times during Valsalva’s manoeuvre in one subject.  

Results are shown as means ± SD.

<table>
<thead>
<tr>
<th>Time (s)</th>
<th>No. of observations</th>
<th>Cardiac output (l/min)</th>
<th>Coefficient of variation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>24</td>
<td>7.9±0.8</td>
<td>9.6</td>
</tr>
<tr>
<td>Strain 1</td>
<td>8</td>
<td>9.5±0.8</td>
<td>8.1</td>
</tr>
<tr>
<td>Strain 2</td>
<td>8</td>
<td>10.5±0.9</td>
<td>8.7</td>
</tr>
<tr>
<td>Strain 3</td>
<td>8</td>
<td>9.6±0.5</td>
<td>5.0</td>
</tr>
<tr>
<td>Strain 6</td>
<td>8</td>
<td>8.2±0.4</td>
<td>5.3</td>
</tr>
<tr>
<td>Strain 9</td>
<td>8</td>
<td>7.4±0.2</td>
<td>2.7</td>
</tr>
<tr>
<td>Strain 12</td>
<td>8</td>
<td>6.7±0.3</td>
<td>3.7</td>
</tr>
<tr>
<td>Strain 15</td>
<td>8</td>
<td>5.6±0.4</td>
<td>6.6</td>
</tr>
<tr>
<td>Post 1</td>
<td>8</td>
<td>5.5±0.5</td>
<td>10.0</td>
</tr>
<tr>
<td>Post 2</td>
<td>8</td>
<td>5.5±0.2</td>
<td>4.1</td>
</tr>
<tr>
<td>Post 4</td>
<td>8</td>
<td>7.5±0.7</td>
<td>9.9</td>
</tr>
<tr>
<td>Post 7</td>
<td>8</td>
<td>8.4±0.7</td>
<td>7.8</td>
</tr>
<tr>
<td>Post 10</td>
<td>8</td>
<td>10.4±0.6</td>
<td>5.9</td>
</tr>
<tr>
<td>Post 15</td>
<td>8</td>
<td>11.0±0.7</td>
<td>6.3</td>
</tr>
<tr>
<td>Post 20</td>
<td>8</td>
<td>9.9±0.8</td>
<td>8.3</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td>9.6</td>
<td>6.8</td>
</tr>
</tbody>
</table>

FIG. 3. Percentage change in heart rate (HR), mean intra-arterial blood pressure (MBP), stroke volume (SV), cardiac output (CO) and estimated peripheral vascular resistance (PVR) during and after a standardized Valsalva’s manoeuvre in one subject with labile hypertension.

Discussion

We have reservations about the absolute values for CO obtained by bioimpedance cardiography in our subjects. The mean resting CO was almost certainly higher than would have been obtained using dye dilution techniques. This is probably because Sramek’s formula depends upon estimation of VEPT from a nomogram based upon weight and height which was devised from measurements made in ‘a large number’ of healthy subjects. This must be regarded as a possible deficiency in the formula as it relies on precise electrode positioning and the assumption that all subjects are anatomically similar. However, as VEPT remains constant in any individual at a single recording session any errors would be proportionately constant for each calculation. Absolute values for SV may be inaccurate but percentage change of SV will be correct.

Direct comparison with dye dilution techniques were not possible in our study because they are invasive and cannot be performed quickly enough to allow beat by beat analysis. Repeated studies in one patient on four different occasions showed that the technique gave reproducible results. The coefficients of variation were less than 10% during all parts of Valsalva’s manoeuvre, indicating that our standard method for performing the manoeuvre gave consistent haemodynamic changes and that the electrical bioimpedance method for measuring CO was reproducible in this situation.

Our results for the changes in SV, CO and HR during Valsalva’s manoeuvre are in accord with those reported previously using bolus dye dilution techniques [7, 8]. They are also consistent with a study using pressure–flow relationships to extrapolate aortic flow on a beat to beat basis in patients with mild hypertension [17]. These studies, however, did not provide detailed data early in the strain and post strain periods. In addition, these techniques are invasive and thus are not suitable for routine use.

Non-invasive studies using two-dimensional echocardiography [3] and praecordial accelerocardiology [2] have concentrated on changes in left ventricular function during Valsalva’s manoeuvre rather than CO. We are aware of a previous study which used Kubicek’s method, thoracic electrical bioimpedance cardiography, during Valsalva’s manoeuvre [18]. However, data were pre-
sented only at 5, 10 and 15 s during the strain and no data were presented from the post strain period.

The most significant new findings were an initial increase in CO at 1 s and a sustained increase in CO in the post strain period. The initial increase was due almost entirely to changes in HR with virtually no change in SV. The HR change is not abolished by β-blockade, and is absent in cardiac transplant recipients (unpublished work). It is thus likely to be due to withdrawal of parasympathetic tone. The change in heart period occurs too quickly to be mediated by direct effects of the strain on aortic or cardiopulmonary baroreceptors. We feel that it may be due to synchronization of the normal sinus arrhythmia because of the voluntary inspiration which precedes the Valsalva strain. An alternative explanation is that it could be due to an alerting reaction, such as that seen at the onset of hand gripping. The initial rise in blood pressure during Valsalva's manoeuvre was originally attributed to an increase in CO caused by 'squeezing' of blood from the heart and lungs into the systemic circulation [6]. This was later refuted by Sharpey-Schafer [19], who attributed the effect to direct transmission of intrathoracic pressure to the great vessels. Our data suggest that an increase in CO may in fact still have some part to play in the initial pressure rise.

The increased CO in the late post strain period has not previously been described. This was due to an increase in SV of greater magnitude than was needed to compensate for the reduced heart rate. Increased left ventricular contractility after the strain has been described [20] and may be part of the explanation. However, we demonstrated in one patient that estimated PVR may be reduced at this time. This could increase CO by reducing afterload.

We are aware of the limitations of our estimation of CO and SV and the possibility that respiratory errors by instructing our subjects to take only a small inspiration before and after the strain could have introduced a systematic error by producing unidirectional changes in $Z_o$. The best way to conclusively prove the reliability of impedance cardiography during Valsalva's manoeuvre would be to simultaneously perform another method of beat to beat assessment of central haemodynamics and compare the results.

In conclusion, we have used electrical bioimpedance to measure beat to beat changes in CO during and after Valsalva's manoeuvre. The results were consistent with those from earlier studies. New findings included an initial increase in CO due to increased HR and prolonged overshoot of CO after the strain. The technique was reproducible and well tolerated. This method may be of value for investigating the mechanisms of abnormal Valsalva responses seen in cardiovascular disease states.

References

the Valsalva manoeuvre in normal subjects, patients with mitral stenosis, and autonomic nervous system alterations. *Circulation*, 9, 511-520.


