Cardiac output measured by transthoracic impedance cardiography at rest, during exercise and at various lung volumes

A. T. EDMUNDS, S. GODFREY* AND MARION TOOLEY
Department of Paediatrics and Neonatal Medicine, Hammersmith Hospital, London

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Summary
1. Cardiac output measured by transthoracic impedance cardiography has been compared with simultaneous measurements made by the indirect Fick CO₂ rebreathing method in nine adults and 14 children. All were healthy normal volunteers. Sixty-six comparisons were made at rest and during steady exercise at work loads up to 100 W.
2. Impedance measurements of cardiac output were consistently higher than indirect Fick measurements of cardiac output, but after application of a correction factor related to packed cell volume there was close correlation between the results obtained by the two methods ($r = 0.94$).
3. The mean coefficient of variation of impedance measurements of cardiac output was 13% at rest and 5% during steady-state exercise.
4. Changes of lung volume due to breath holding or resulting from addition of an expiratory resistance did not affect the measurement of cardiac output by impedance.
5. Transthoracic impedance cardiography is a rapid, non-invasive technique for measurement of cardiac output. It requires very little active co-operation from the subject. The method would probably give reliable results for patients with respiratory illnesses such as acute asthma or bronchiolitis, during which changes of lung volume may be expected to occur.

Key words: cardiac output, exercise, impedance cardiography, indirect Fick, lung volumes.

Introduction
Impedance cardiography is a non-invasive technique which has numerous potential applications in clinical practice. Cardiac output is measured by detection of the changes in transthoracic electrical impedance associated with the cardiac cycle [1]. The method and its potential applications have recently been reviewed by Mohapatra [2]. It relies on the over-simplified assumption that the thorax is a homogeneous column of blood, the volume of which increases by the left ventricular stroke volume during each systole [3]. Because of this the results are largely empirical and measurements made under various physiological conditions must be verified by comparison with established standard methods. Comparison with several other methods has been made in adults and children with various results [3–11]. As far as we are aware cardiac output measured by the impedance technique has not previously been compared with simultaneous measurements made by the indirect Fick CO₂ rebreathing method. We report such a comparison made in normal subjects at rest and during exercise. We have also studied the effects of alteration of lung volume caused by breath holding and by breathing through an expiratory resistance on impedance measurements of cardiac output in normal subjects. This has been done in an attempt to determine the potential value of the impedance method for measuring cardiac output in patients with lung disease.
A. T. Edmunds, S. Godfrey and M. Tooley

TABLE 1. Anthropometric data of 23 subjects
Mean values ± se are shown.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Males</th>
<th>Females</th>
<th>Age (years)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>Surface area (m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>4</td>
<td>5</td>
<td>29 ± 1-1</td>
<td>173 ± 4</td>
<td>64 ± 3</td>
<td>1.75 ± 0.06</td>
</tr>
<tr>
<td>Children</td>
<td>9</td>
<td>5</td>
<td>11.5 ± 0.8</td>
<td>141 ± 4</td>
<td>31 ± 3</td>
<td>1.11 ± 0.06</td>
</tr>
</tbody>
</table>

Methods

Subjects

Comparison of cardiac output measured by impedance with simultaneous indirect Fick CO₂ measurements was made in studies of 23 normal healthy volunteers. Nine were adults (five women and four men), mean age 29 ± 1 years. Fourteen were children (nine boys and five girls), mean age 11.8 ± 0.8 years. Their anthropometric data are shown in Table 1. All consented to participate in the study after full explanation, and were free to withdraw at any stage.

Impedance cardiac output

Impedance cardiac output was measured with the Minnesota Impedance Cardiograph model 304A. This utilizes four disposable aluminized strip electrodes. Two were placed around the neck, one with its lower border at the level of the supra-sternal notch anteriorly and the spinous process of the seventh cervical vertebra posteriorly and one parallel to the latter, but at least 3 cm above it. The lower pair of electrodes was applied horizontally, one with its upper border at the tip of the xiphisternum and the second parallel and at least 3 cm below it. A constant sinusoidal current of 4 mA r.m.s. with a frequency of 100 KHz was applied between the outer two electrodes. The potential difference, $Z_v$, between the two inner electrodes was recorded via a high input impedance linear amplifier. The potential varies during the cardiac cycle. For the calculation of stroke volume the thorax is assumed to be a homogeneous cylinder of blood, the diameter of which changes uniformly during the cardiac cycle. The measured change of potential reflects the increase in volume of the cylinder during systole. This increase in volume, $\Delta V$, can be calculated by using the formula of Kubicek et al. [3].

$$\Delta V = P \times \frac{L^2}{Z_0} \times \left(\frac{dZ}{dt}\right)_{\text{max}} \times T$$

where $\Delta V$ represents stroke volume (ml), $P$ is the resistivity of blood (ohm/cm), $L$ is the mean distance between the recording electrodes, $Z_0$ is the basal thoracic impedance (ohm), $(dZ/dt)_{\text{max}}$ is the maximum rate of fall of impedance in ohms/s and $T$ is the ventricular ejection time (s). In this study the outputs taken from the impedance cardiograph were $Z_v$, $dZ/dt$, an ECG trace and a phonocardiogram trace. A typical record is illustrated in Fig. 1.

$P$ was calculated according to packed cell volume from the data of Mohapatra et al. [12]. Packed cell volume was measured on finger-prick blood specimens spun for 3 min on a Hawksley haematocrit centrifuge. $L$ was calculated as the mean of the distances between the lower edge of the upper and upper edge of the lower recording electrodes in the mid-line anteriorly and posteriorly, $Z_0$ was taken as the mean of the maximum and minimum values on the digital display during the period of the record. The subjects breathed freely during measurements. Therefore the baseline for the measurement of $(dZ/dt)_{\text{max}}$ was taken as the start of the steep upstroke irrespective of its position relative to the calibration zero [2, 10]. $T$ was calculated as the time between the start of the steep upstroke and the start of the second heart sound, which coincides with the lowest point on the $dZ/dt$ trace. Beats were analysed only if there was no obvious movement artifact. Traces from subjects at rest, during treadmill walking and during moderate exercise on the bicycle ergometer were rarely distorted, and most could be analysed without difficulty. At the highest workloads movement of the baseline in association with respiration became more prominent and a proportion of the traces were not suitable for analysis. When this happened the measurement was immediately repeated, while the steady-state exercise was continued unaltered.

Cardiac output was calculated from the mean stroke volume measured over 8-12 consecutive beats during one or more complete respiratory cycles:

$$\text{Cardiac output} = \text{Mean } \Delta V \times \text{HR}$$

where HR is heart rate (beats/min).
Impedance cardiography

Indirect Fick CO₂ rebreathing cardiac output

Measurements of cardiac output by the indirect Fick CO₂ rebreathing method were made as described by Godfrey [13]. As the subjects were all normal, end-tidal CO₂ concentration was measured and assumed to have a partial pressure equal to that of arterial blood (Paco₂). Subjects breathed through a low resistance, low dead space (50 ml) valve. Inspired ventilation was measured with a dry gas meter and the expired gas flushed through a 4 litres mixing chamber. Gas was continuously sampled either from the mouthpiece or from the outlet of the mixing chamber. It was passed through an infrared analyser to measure the concentration of CO₂, and a paramagnetic oxygen analyser to measure the concentration of O₂. The analysers were calibrated frequently during study periods with gases of known concentration, which had been analysed chemically by means of the Haldane technique. Data were continuously recorded on an ink jet recorder. CO₂ rebreathing was performed with a sliding valve assembly. By means of this the subject could be switched instantaneously from breathing air through the valve, to rebreathe from a previously prepared bag of CO₂ in O₂. The bag CO₂ concentration was made slightly higher than the predicted mixed venous CO₂ concentration (PvCO₂) and the volume was adjusted according to the subject's tidal volume to ensure good equilibration with alveolar gas in less than one circulation time. PvCO₂ was measured as the plateau concentration of CO₂ achieved. If no satisfactory plateau was recorded it was estimated by using the extrapolation method of Denison [13, 14]. In the calculation of cardiac output, measured values of PvCO₂ were used for all subjects with no correction for the down-stream effect described by Jones et al. [15].

Measurements of steady-state oxygen consumption (Vo₂) and cardiac output were made with the subject seated at rest on a bicycle ergometer and performing exercise at one or more workloads ranging from 16.5 to 100 W. Impedance cardiograph recordings were made during the measurement of steady-state Vo₂ immediately before the performance of the CO₂ rebreathing manoeuvre, so that comparison of paired measurements could be made.

Effects of change of lung volume and addition of expiratory resistance

The effect of change of lung volume on the measurement of cardiac output by impedance was determined in seven resting subjects. Measurements were made during breath holding with glottis open at functional residual capacity (FRC), total lung capacity (TLC) and at residual volume (RV). For each subject vital capacity was first measured by spirometry. During the experiment the subject breathed through a mouthpiece and three-way tap with outlets to room air and to a water-sealed spirometer. Cardiac output was measured first at FRC, then at TLC and finally
at RV after a maximum expiratory manoeuvre into the spirometer.

The effect of breathing against an expiratory resistance on the measurement of cardiac output by impedance was determined in six normal adults. With the subject seated in a constant-pressure whole-body plethysmograph and breathing in time with a metronome, a variable expiratory resistance was adjusted until FRC increased by 50% of the resting inspiratory capacity. Subsequently outside the plethysmograph, again with the subject breathing in time with the metronome, a steady-state resting cardiac output was measured by impedance and indirect Fick methods. The measurements were then repeated with the previously determined resistance in the expiratory line between the mouthpiece and the mixing chamber.

The reproducibility of the measurement of cardiac output by impedance was determined in 11 subjects and during steady-state treadmill walking in three subjects. Six to ten measurements were made over a period of half an hour and the coefficient of variation was calculated.

Results

The linear relationship between the data obtained by simultaneous measurements of cardiac output by indirect Fick CO₂ rebreathing and by impedance is shown in Fig. 2. The data for nine adults and 14 children are plotted separately.

Impedance measurements of cardiac output were consistently higher than indirect Fick measurements of cardiac output. This difference was more marked for adults than for children. The ratio of impedance cardiac output values to indirect Fick values was significantly related to packed cell volume (Fig. 3). This relationship could be used as a correction factor to reduce the calculated values of impedance cardiac output. From the regression line in Fig. 3 the impedance cardiac output/Fick cardiac output ratio was determined according to the measured packed cell volume. Impedance cardiac output was then divided by this ratio, which was used as the correction factor. The relation between indirect Fick cardiac output and impedance cardiac output for all subjects after correction for packed cell volume in this way is shown in Fig. 4. There was a linear relationship between VO₂ and cardiac output measured by both methods, as shown in Fig. 5.

The reproducibility of the measurement of cardiac output by impedance cardiography in 11 subjects sitting at rest and in three subjects during steady-state treadmill walking is shown in Table 2. The mean coefficient of variation at rest was 13% and during exercise was 5%. Analysis of variance demonstrated that after removal of the difference between subjects the standard
deviation of the residual differences for the resting measurements was 10%. For the measurements during steady-state exercise it was 4.9%. Thus the 95% confidence limits for measurement of cardiac output by impedance cardiography were ±10% during moderate steady-state exercise.

Comparison of 19 paired estimates of cardiac output made in seven subjects breath holding at TLC and RV is shown in Fig. 6. A paired t-test showed no significant differences between the measurements made at the two lung volumes (P > 0.05). Comparison of paired measurements in six subjects made at rest and while breathing against an expiratory resistance is shown in Fig. 7. Again a paired t-test showed no significant difference between measurements made at rest and those made while breathing through the resistance (P > 0.05).

Discussion

In early studies of impedance cardiography a constant value of 150 ohm/cm was assumed for P [3–6, 9]. More recently various values of P, related to the subjects' packed cell volume, have been used [7, 8, 10, 11]. A number of different relationships between P and packed cell volume have been reported [11]. We have used the relationship reported by Mohapatra et al. [12] because it was obtained with fresh specimens of capillary blood from normal newborn babies, children and adults. Costeloe et al. [10] found this gave an overestimation of cardiac output in infants, and derived a correction factor related to packed cell volume to bring their impedance measurements into line with simultaneous measurements of pulmonary capillary flow obtained by the nitrous oxide rebreathing method. Many factors including chest shape and the resistivity of tissue must affect measurement of cardiac output by impedance. Hence it is unlikely that the same correction factor would apply to newborn babies and to older children or adults. We therefore derived a new correction factor for our subjects. It is again related to packed cell
A. T. Edmunds, S. Godfrey and M. Tooley

Table 2. Reproducibility of measurements of cardiac output by impedance cardiography in 11 subjects at rest and three subjects during steady-state exercise

<table>
<thead>
<tr>
<th>Subject no.</th>
<th>No. of observations</th>
<th>Mean cardiac output (l/min)</th>
<th>Coefficient of variation (%)</th>
<th>Mean coefficient of variation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At rest</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>8</td>
<td>3.9 ± 0.7</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>4.2 ± 0.4</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>3.0 ± 0.3</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>9</td>
<td>6.0 ± 0.4</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>9</td>
<td>6.2 ± 0.7</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>8</td>
<td>2.7 ± 0.7</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>9</td>
<td>5.9 ± 0.6</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>8</td>
<td>5.4 ± 0.2</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>8</td>
<td>8.0 ± 0.4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>8</td>
<td>3.9 ± 0.4</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>8</td>
<td>5.4 ± 0.6</td>
<td>11</td>
<td></td>
</tr>
</tbody>
</table>

| Treadmill walking | | | | |
| 12              | 10               | 7.8 ± 0.4                   | 5                             |                                  |
| 13              | 10               | 13.5 ± 0.6                  | 4                             |                                  |
| 14              | 10               | 13.2 ± 0.6                  | 5                             |                                  |

FIG. 6. Relation between 19 paired measurements of impedance cardiac output (\(\dot{Q}\)) made at residual volume and total lung capacity in seven subjects at rest. ———, Line of identity; 20% limits are shown by unbroken lines.

volume and, probably because the range of packed cell volume in our subjects was relatively small, it could be expressed in linear form. After applying the above correction there was very close correlation (\(r = 0.94\)) between the simultaneous measurements of cardiac output made by the impedance and the indirect Fick methods (Fig. 4). This demonstrates that impedance cardiography can provide measurements of cardiac output in normal subjects at rest and during moderate exercise which are as accurate as those obtained with the indirect Fick \(\dot{CO}_2\) rebreathing method. This accuracy was further confirmed by the finding of the expected linear relationship between cardiac output and \(\dot{V}O_2\) (Fig. 5). The equations for the regression lines of cardiac output related to \(\dot{V}O_2\) for both adults and children obtained by impedance cardiography and by indirect Fick \(\dot{CO}_2\) rebreathing were similar to previously published equations derived from direct Fick measurements [16], indirect Fick
measurements [13] and dye-dilution measurements [16, 17]. The scatter of the indirect Fick results about the regression line was very similar to that in previous studies [13, 18] and that of the impedance data was only slightly greater. Analysis of variance demonstrated that between individual subjects there were significant differences in the slope of the relationship between impedance cardiac output and indirect Fick CO₂ rebreathing measurements of cardiac output. These differences were accounted for by the increasing scatter of measurements at the highest workloads on the bicycle ergometer. This scatter was not greater than expected when the coefficient of variation of the impedance measurements was taken into account. Therefore all data have been used in the calculation of the regression equations in Figs. 4 and 5. The mean coefficient of variation of impedance measurements at rest was 13% with 95% confidence limits of ±20%. This is similar to previously published values [3, 6]. During steady-state treadmill walking the mean coefficient of variation was reduced to 5% with 95% confidence limits for the measurement of ±10%. This compares favourably with published values for reproducibility for O₂ direct Fick [19], dye-dilution [19, 20] and CO₂ rebreathing indirect Fick measurements [21]. The reproducibility of measurements of impedance cardiac output was not determined at the highest workloads on the bicycle ergometer, but movement of the baseline was prominent in this situation and a proportion of the tracés could not be analysed because of movement artifact. Thus the 95% confidence limits would almost certainly have been greater than ±10%.

Change of lung volume as a result of breath holding or induced by breathing against an expiratory resistance did not materially affect the measurement of cardiac output by impedance (Figs. 6 and 7). Thus impedance cardiography would probably be reliable for both clinical and experimental purposes in patients with respiratory illnesses such as acute asthma or bronchiolitis, during which changes of lung volume may be expected to occur. It has the added advantage that it is rapid, non-invasive and it can easily be carried out at the bedside.

Acknowledgments

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References


