

# Bioreactance is a reliable method for estimating cardiac output at rest and during exercise

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## Editor's key points

- Noninvasive cardiac output measurements are useful for risk stratification and improved clinical outcome.
- Bioreactance is a novel method involving thoracic electrical measurements.
- Bioreactance showed good test-retest correlation in monitoring cardiac, which correlated with oxygen consumption.
- Further work is required to demonstrate clinical utility in risk assessment and guiding therapy.

**Background.** Bioreactance is a novel noninvasive method for cardiac output measurement that involves analysis of blood flow-dependent changes in phase shifts of electrical currents applied across the thorax. The present study evaluated the test-retest reliability of bioreactance for assessing haemodynamic variables at rest and during exercise.

**Methods.** 22 healthy subjects (26 (4) yrs) performed an incremental cycle ergometer exercise protocol relative to their individual power output at maximal O<sub>2</sub> consumption (W<sub>max</sub>) on two separate occasions (trials 1 and 2). Participants cycled for five 3 min stages at 20, 40, 60, 80 and 90% W<sub>max</sub>. Haemodynamic and cardiorespiratory variables were assessed at rest and continuously during the exercise protocol.

**Results.** Cardiac output was not significantly different between trials at rest ( $P=0.948$ ), or between trials at any stage of the exercise protocol (all  $P>0.30$ ). There was a strong relationship between cardiac output estimates between the trials (ICC=0.95,  $P<0.001$ ) and oxygen consumption (ICC=0.99,  $P<0.001$ ). Stroke volume was also not significantly different between trials at rest ( $P=0.989$ ) or during exercise (all  $P>0.15$ ), and strong relationships between trials were found (ICC=0.83,  $P<0.001$ ).

**Conclusions.** The bioreactance method demonstrates good test-retest reliability for estimating cardiac output at rest and during different stages of graded exercise testing including maximal exertion.

**Keywords:** cardiac output; exercise test; haemodynamics; monitoring, physiological

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Monitoring of cardiac output has wide clinical application in anaesthesiology, emergency care and cardiology. This can improve outcomes, establish diagnosis, guide therapy and help risk stratification in different clinical groups.<sup>1</sup> Measurement of cardiac output is essential in critically ill, injured and unstable patients as it provides an indication of systemic oxygen delivery and global tissue perfusion.<sup>2</sup> Cardiac output monitoring during surgery is associated with reductions in length of hospital stay and postoperative complications.<sup>3-5</sup> Measurement of cardiac output under pharmacological and physiological stimulations defines overall function and performance of the heart, predicts prognosis and survival in heart failure can help explain the mechanisms of exercise intolerance, and improves risk stratification.<sup>6-10</sup>

Thermodilution and direct Fick<sup>11-13</sup> methods remain the 'gold standard' and reference methods for assessing cardiac output. Whilst 'gold standard', these methods have inherent limitations as they are invasive, costly, require specialist skills and are associated with noteworthy risks and complications

such as catheter-related infections, arrhythmias and bleeding.<sup>14 15</sup> The risk: benefit ratio of these assessment methods has also been questioned.<sup>14</sup> These limitations preclude use of invasive cardiac output monitoring in large number of patients limiting the application of this useful diagnostic and prognostic technique.

Over previous decades several minimally invasive and non-invasive methods for assessing cardiac output have been developed including; transoesophageal Doppler ultrasonography, transpulmonary thermodilution, pulse contour and pulse power analysis, and noninvasive techniques such as CO<sub>2</sub> and inert gas rebreathing, transthoracic Doppler ultrasonography, thoracic bioimpedance cardiography, and electrical velocimetry (modified bioimpedance).<sup>2 16-18</sup> Unfortunately whilst these methods are safe they are associated with certain limitations in accuracy and reliability.<sup>13 19</sup>

Bioreactance, a novel method for continuous noninvasive cardiac output monitoring, has received increased attention in clinical and research practice in the recent years. The

bioreactance method estimates cardiac output by analysing the frequency of relative phase shift of electronic current across the thorax.<sup>20 21</sup> In contrast to impedance cardiography which is based on analysis of transthoracic voltage amplitude changes in response to high frequency current, bioreactance analyses frequency spectra variations of delivered oscillating current.<sup>20</sup> This approach result in improved precision of the bioreactance system as demonstrated by a 100-fold larger signal-to-noise ratio than that of bioimpedance, making it less susceptible to interference from adipose tissue, electrode placement and excessive movement.<sup>20 22</sup>

The ability of bioreactance to monitor rapid changes in blood flow has recently been confirmed by Marik and colleagues.<sup>23</sup> We compared carotid Doppler ultrasonography against bioreactance in patients with unstable cardiac conditions during passive leg raising. A strong correlation was reported in blood flow between the two methods in critically ill patients, with an accelerated response to these volume changes reported by bioreactance. Bioreactance cardiac output monitoring has been used in intensive care, during and after cardiac surgery, patients with chronic obstructive pulmonary disease and healthy individuals.<sup>19 20 22–25</sup> Other studies demonstrated that bioreactance measurements of cardiac output at rest and during exertion can identify cardiovascular function abnormalities, indexing disease severity, help prognosis and risk stratification, and track responses to treatment.<sup>26 27</sup>

When assessing cardiac output at rest or during physiological challenge, it is essential that methods demonstrate acceptable reliability, (i.e. test-retest reliability which refers to reproducibility of a variable when measured in the same subject twice). This is important because even small changes in cardiac output and stroke volume can have significant clinical implications when evaluating the effect of pharmacological and non-pharmacological interventions and risk stratification. The test-retest reliability of bioreactance, as a novel and potent method for noninvasive continuous cardiac output monitoring, has not been evaluated. Based on its higher signal-to-noise ratio and improved performance,<sup>19 20</sup> we hypothesize that bioreactance demonstrates acceptable test-retest reliability for evaluating cardiac output at rest and during physiological stimulation such as graded exercise testing. Additionally, we evaluated the association between cardiac output and oxygen consumption at peak exercise.

## Methods

Experimental procedures were approved by the Faculty's Research Ethics Committee in accordance with the Declaration of Helsinki. In all subjects, after being informed of the benefits and potential risks of the investigation all subjects completed a standardized health-screening questionnaire, undertook a resting electrocardiogram and gave their written informed consent.

Twenty two healthy subjects (10 male, 12 female) participated. All were non-smokers and free from any cardiac and respiratory disorders. Subjects attended the exercise laboratory

on 2 separate days: day 1 involved an initial assessment of maximal aerobic capacity ( $\dot{V}_{O_{2max}}$ ) and day 2 required 2 visits consisting of an incremental exercise cycle ergometer protocol at individual pre-determined workloads based on power output at  $\dot{V}_{O_{2max}}$  (Wmax). Subjects abstained from eating for a >2 h before each test and from vigorous exercise 24 h prior. Subjects were instructed not to consume alcohol or caffeine containing foods and beverages on test days.

Subjects completed a maximal progressive exercise test on an electromagnetically braked recumbent cycle ergometer (Corival, Lode, Groningen, Netherlands). Subjects began cycling against a resistance of 40 W, this increased continually throughout the test  $15 \text{ W min}^{-1}$ . The assessment ceased when subjects reached volitional exhaustion or were unable to maintain a cadence of 60–70 revolutions  $\text{min}^{-1}$ . Maximal effort was achieved if subjects met any two of the following criteria: i) a change in  $\dot{V}_{O_2} < 2 \text{ ml kg}^{-1} \text{ min}^{-1}$  across two stages of the incremental test; ii) a respiratory exchange ratio of  $\geq 1.15$  or greater, or iii)  $\geq 90\%$  age predicted maximum heart rate ( $220 - \text{age}$ ).<sup>28</sup> Expired gases were measured via online metabolic gas exchange system (Cortex metalyser 3B, Leipzig, Germany) and heart rate was measured via short range telemetry (Polar RS400, Finland). Peak oxygen consumption was defined as the average oxygen uptake during the last minute of exercise. Wmax was defined as the power output expressed in W at the point at which subjects reached their individual  $\dot{V}_{O_{2max}}$ .

Exercise protocol was performed twice on study day 2 with  $\geq 3 \text{ h}$  interval between trials 1 and 2. Subjects were required to complete five 3 min stages (equating to 15 min of cycling) at intensities relative to 20, 40, 60, 80 and 90% Wmax. Cardiac and haemodynamic responses including cardiac output, cardiac index, stroke volume and stroke volume index, and heart rate were recorded at rest and throughout the incremental exercise protocol using a noninvasive bioreactance system (NICOM<sup>®</sup>, Cheetah Medical, Delaware, USA). Simultaneously, respiratory and gas exchange measurements were recorded (Cortex metalyser 3B, Leipzig, Germany).

The bioreactance system comprises of a radiofrequency generator that creates a high frequency current across the thoracic cavity. The NICOM<sup>®</sup> has been described previously.<sup>19 20 25</sup> It analyses the relative phase shift of current across the thorax using four dual surface electrodes. The skin was prepared by shaving where required and using adhesive paper to ensure an optimal signal from the electrodes. Two electrodes were placed over the trapezius muscle on either side of the upper torso and two on the lower posterior torso lateral to the margin of the latissimus dorsi musculature. The right and left sensors of the device generate independent signals that are subsequently integrated to generate the final signal analysed. Blood present in the thoracic cavity absorbs electrons, which results in a delay in the signal proportional to the volume of blood flow. This is called a phase shift that is translated to blood flow. The signal is then processed separately and averaged after digital processing at 30 or 60 s intervals. The signal processing unit of the NICOM<sup>®</sup> determines the relative phase shift ( $\Delta\phi$ ) between input signals relative to the output

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