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# Evaluation of Noninvasive Cardiac Output Methods During Exercise

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#### Introduction

Cardiac output is a measure of the ability of the heart to meet the demands imposed by physical activity. The gold standard used for determination of cardiac output is the direct Fick method. This method requires sampling of both arterial and mixed venous (right heart or pulmonary arterial) blood and is impractical to perform on human subjects, particularly during activity. Several noninvasive techniques of cardiac output estimation have been developed. These techniques include:

- carbon dioxide rebreathing
- prolonged single breath carbon dioxide measurements
- rebreathing of a physiologically inert gas such as acetylene or nitrous oxide
- impedance changes in the thoracic cavity due to fluid output of the left ventricle
- measurement of ascending aortic blood flow velocity and aortic diameter using Doppler and two dimensional echocardiography.

Measurement of cardiac output during exercise is proposed for future studies during manned space flight missions. Each method is associated with at least one drawback that makes it less than optimal for use in flight. Two examples of viable methods and their limitations are: (1) Doppler echocardiographic estimates of cardiac output, which require a substantial amount of technician training for the results to be reliable; and (2) rebreathing methods, which require extra mass to store the rebreathing gas and a more complex gas analysis system than that necessary for routine metabolic monitoring. No one method has an advantage with regard to in-flight technical feasibility. Thus, it is logical to compare each of the techniques to determine if they are suited for use on the basis of consistent measurement error. This comparison has not been conducted to date.

The purpose of this investigation was to develop a data base from published literature regarding cardiac output responses to graded exercise. The data base will be used to determine which of the noninvasive methods yielded values most comparable to those obtained by the direct Fick technique.

## Methods

A literature search was conducted to identify published data regarding the use of noninvasive techniques to measure cardiac output during exercise. Over 100 published papers were identified. Studies reporting cardiac output and exercise values of each subject are included in the data base. Studies with only group mean cardiac output data are not included in the data base. Forty studies were identified that met these criteria, representing 2,196 separate estimates of steady-state exercise cardiac outputs. Exercise heart rate responses were used to group exercise intensities. Three exercise levels were defined as 33-64, 65-72, and 72-100% HRmax.

Examinations of the mean cardiac output responses to exercise levels were conducted using a 3x6 ANOVA to compare all noninvasive methods to the Fick technique. The correlation of each noninvasive method to exercise level was compared to the relationship between the direct Fick technique and exercise level. This comparison was made to determine if the rate of increase in cardiac output for any of the noninvasive methods was significantly different than the rate of increase in cardiac output measured by the Fick technique.

#### **Results/Discussion**

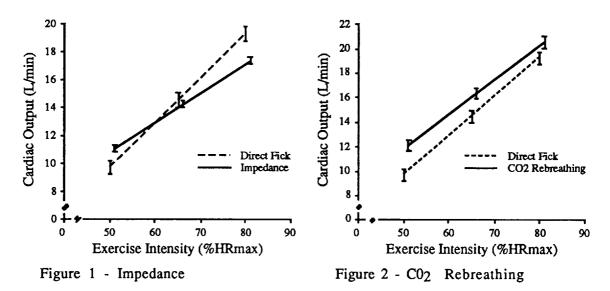
None of the mean values for resting or exercise cardiac output determined by the noninvasive methods differed significantly from the values obtained with the direct Fick technique. This finding may reflect that the methods estimated cardiac output well, or could be due to the method by which exercise intensity was coded.

The expected increase in cardiac output with exercise intensity was observed, regardless of the method.

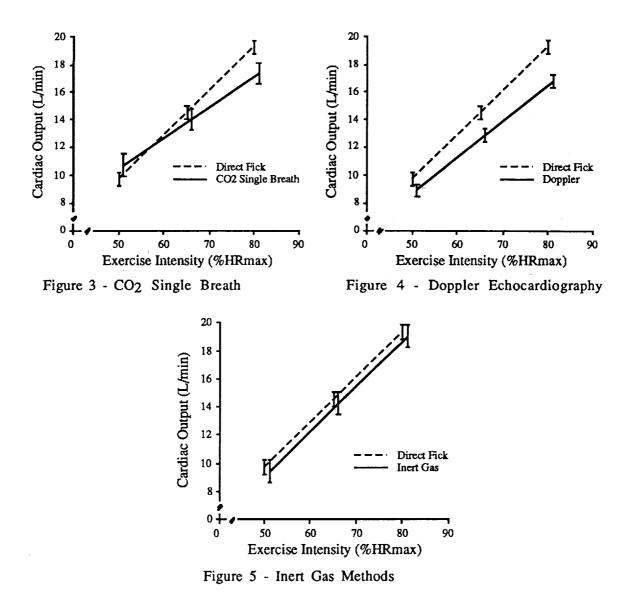
The correlations between cardiac output and exercise intensity for the impedance method (Figure 1) and the CO<sub>2</sub> rebreathing method (Figure 2) were significantly different (p<0.01) than the correlation between the direct Fick technique and exercise intensity. The impedance method overestimated cardiac output at lower levels of exercise (33-64%  $HR_{max}$ ) and underestimated cardiac output at higher (74-100%  $HR_{max}$ ) levels. The CO<sub>2</sub> rebreathing method

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overestimated cardiac output at all levels. These findings indicate that impedance and  $CO_2$  rebreathing methods are not candidates of choice.



The correlations between cardiac output and exercise intensity for the CO<sub>2</sub> single breath, Doppler, and inert gas methods were not significantly different than the correlation between the direct Fick technique and exercise intensity (Figures 3-5). The inert gas estimates were most similar to those obtained by the direct Fick technique with regard to slope and intercept of relationship. The Doppler and CO<sub>2</sub> single breath methods had the lowest sample sizes of those in the literature data base (with 15 and 18 data points, respectively). These small sample sizes may have introduced bias (by violation of the central limit theorem) into the statistic used. Thus, more information is needed on the Doppler and CO<sub>2</sub> single breath methods before firm conclusions can be drawn.



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#### Conclusions

The ANOVA results indicate no evidence to suggest that the noninvasive methods used to estimate exercise cardiac output were different than direct Fick measurements.

The inert gas method best expressed the expected relationship (correlational analyses) between exercise intensity and cardiac output. Both the  $CO_2$  single breath and Doppler methods were not significantly different than the Fick technique; however, the small sample sizes reported on these two methods make this finding preliminary at best.

The impedance and CO<sub>2</sub> rebreathing methods did not demonstrate a similar relationship to exercise intensity as that obtained using the direct Fick technique. Therefore, although the mean values obtained by these methods did not significantly differ from those of the direct Fick technique, refinement of these methodologies may be merited. These methods currently cannot be recommended for use during space flight.

#### Future Directions

A retrospective literature search is a useful procedure to address methodology concerns in that it can identify inherent problems not specific to individual laboratories. A stronger approach is to conduct a study comparing the methods of cardiac output estimation to each other and to the direct Fick method.

The literature data base will be continually updated to resolve which of the noninvasive methods yield the best estimates of cardiac output during exercise.

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<sup>13.</sup> ABSTRACT (Maximum 200 words) Noninvasive techniques to estimate cardiac output (Qc) will be used during future space flight. This retrospective literature survey compared the Qc techniques of carbon dioxide rebreathing (CO2-R), CO2 single breath (CO2-S), Doppler (DOP), impedance (IM) and inert gas (IG: acetylene or nitrous oxide) to direct (DIR) assessments measured at rest and during exercise.				
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