Impedance Cardiography Accurately Measures Cardiac Output During Exercise in Children With Cystic Fibrosis*

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**Objectives:** After validation of impedance cardiography (ICG) in healthy children, this same device was tested in children with cystic fibrosis (CF) to validate its capability of measuring cardiac output (Q) in this population.

**Design:** Comparative study of ICG vs the indirect Fick (CO2) method.

**Setting:** Tertiary care children’s teaching hospital.

**Patients:** Twenty-one CF children with mean FEV1 of 77±21% predicted.

**Measurements:** ICG results were compared with CO2 rebreathing (RB) measurements of Q with sampling of capillary blood gases at two levels of exercise (0.5 and 1.5 W/kg). ICG measurements were made each minute, and duplicate RB measurements from 6 to 8 min at each workload. Q was regressed against oxygen uptake and results by each method were compared.

**Results:** Mean bias (QRB-QICG) was −0.09±0.94 L/min. The largest deviation of QICG from QRB was +33%, and 83% of corresponding QICG values were within ±20% of QRB result.

**Conclusions:** This device gives rapid, accurate, noninvasive Q measurements in children with CF. (CHEST 1997; 111:333-37)

**Key words:** cardiac output; cystic fibrosis; exercise; impedance

**Abbreviations:** CF=cystic fibrosis; ICG=impedance cardiography; Q=cardiac output; QICG=impedance cardiac output; QRB=rebreathing cardiac output; RB=CO2 rebreathing; VO2=oxygen uptake

Cardiac output (Q) during exercise in patients with cystic fibrosis (CF) is usually measured by the indirect Fick (CO2) method, either with or without blood sampling to measure arterial PCO2. As the latter method is unreliable in this population and in patients with chronic obstructive lung disease, a technique for measuring Q repeatedly and noninvasively would be a very useful tool for evaluating stroke volume during exercise and elaborating factors affecting it in CF patients. Work in this laboratory has already validated impedance cardiographic (ICG) measurement of Q with the ICG-M401 (ASK Ltd; Budapest, Hungary) against the CO2 rebreathing (RB) method in healthy children. The present study was designed to extend these findings to include patients with CF over the entire spectrum of severity of airway obstruction. Validation of this method would permit its application during progressive exercise, to evaluate the stroke volume response to exercise further, and obviate the need for repeated blood sampling.

**Materials and Methods**

This study received approval from the University of Manitoba Faculty of Medicine Committee for Use of Human Subjects in Research and informed, written consent was obtained from parents and patients alike. The protocol was identical to our study done in healthy children, except that children with CF from the Children’s Hospital of Winnipeg CF Clinic were recruited for the present study. Routine spirometry was performed on a portable spirometer (model AT-6; Schiller AG; Baar, Switzerland) and expressed as percent of predicted. Exercise was performed on an electrically braked cycle ergometer (Excalibur; Quinton Instruments; Seattle) at two work rates: 0.5 and 1.5 W/kg. Subjects pedaled for 4 min before gas exchange measurements commenced, starting with blood gas sampling, followed by mixed expired gas collection for 2 min, and ending with duplicate RB maneuvers. Total duration of work at each load was approximately 8 min. Expired ventilation was measured on a spirometer (Transferscreen II; Erich Jaeger Co; Wurzburg, Germany) equipped with a heated pneumotachograph, calibrated before and after tests using a volumetric syringe. Mixed expired gases
were collected in gas collection bags and analyzed with zirconium oxide O₂ and infrared CO₂ analyzers (S-3A/1, CD-3A, respectively; Ametek Inc; Pittsburgh). Analyzers were calibrated with reference gases (room air; 5% CO₂, 15% O₂, balance N₂; and 15% CO₂, balance O₂) before and after testing. Arterialized capillary blood was obtained from a finger warmed by wrapping in a heating pad, stored on ice, and analyzed within 30 min on a blood gas analyzer (Radiometer ABL500; Copenhagen) to measure pH and PaCO₂. Hemoglobin (g/L) was also measured from these samples (on a Radiometer Hemoximeter OSM 3). The rebreathing bag was filled with an appropriate mixture of CO₂ (10 to 15%) in O₂, with the volume of the rebreathing mixture approximating the subject’s vital capacity. At end-expiration, the subject was switched into the rebreathing bag for a period of approximately 15 s. This maneuver was attempted in duplicate with at least 1 min between each, and if both trials resulted in an equilibrium plateau, the mean mixed venous PCO₂ was used, incorporating the “downstream” corrected CO₂ partial pressure. Maneuvers that did not achieve a plateau in the PCO₂ tracing were discarded. Signals were recorded in real time on a thermal chart recorder (Gould TA2000; Cleveland).

The ICG-M401 employs a tetrapolar lead system with paired inner electrodes placed on either side in the supraclavicular fossa just above the level of the suprasternal notch and along the midaxillary line at the level of the xiphoid. The outer electrodes are placed 6 cm cephalad and caudal, respectively. The phonocardiogram was recorded by a proprietary microphone attached with double-sided adhesive and placed along the left sternal border at a site where the second heart sound was loudest. The software program used a modification of the Kubicek equation7 based on empirical corrections for body habitus.

\[ SV = r \left( \frac{L^2}{Z_0^2} \right) \left[ \text{VET} \frac{dZ}{dt} \right] \]

where SV = stroke volume (mL), r = blood resistivity (assumed constant 135 Ω/cm), L = distance between inner electrodes (measured), Z₀ = baseline thoracic impedance (Ω), VET = ventricular ejection time (s), and dZ/dt = maximum value of first time derivative of impedance. The three types of body habitus were ectomorph, mesomorph, and endomorph, which we defined for use in children as percent ideal weight for height <85, 85 to 120, and >120, respectively. Thoracic length was measured while the subject was seated on a stool after electrode placement, and verified later with the subject seated on the ergometer. The mean of these (nearest centimeter) was entered as “L” into the computations. Subjects also underwent duplicate measurement of anteroposterior and lateral chest diameters at the level of the xiphoid. The ratio of these two diameters (thoracic index) was also calculated.

A single measurement of impedance cardiac output was made once each minute from all cardiac cycles over an 8-s interval, by computing beat by beat stroke volume and multiplying by heart rate. Unlike the experience in healthy children, obtaining good

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**Figure 1.** Graphic output of waveforms processed by the ICG M401. Upper trace is ECG; second from the top is dZ/dt; third trace is the phonocardiogram (PCG); and lower trace is the thoracic electrical bioimpedance (ICG). The calculated numeric value of dZ/dt is shown for three individual heartbeats, one of which (No. 3) is distorted by artifact. Below is a list of beat-by-beat computations of stroke volume for these beats, in which one can readily appreciate the error inherent in including such a beat (eg, beat 3) in the stroke volume calculation for that sampling interval.
analog signals for impedance and phonocardiogram was difficult in some CF patients. The ICG-M401 saves all raw signals for
subsequent review, permitting manual elimination of beats in
which the computer algorithm had erroneously determined
dVldt; because the signal contained too much motion artifact
(Fig 1). In practice, the phonocardiographic signal did not cause
any beats to be discarded, but in six patients up to seven cardiac
cycles were omitted from stroke volume calculations, leaving no
fewer than 10 beats from which to compute stroke volume during
any given minute. Impedance measurements from the fourth or
fifth to eighth minutes of work were averaged to provide a single
value for heart rate and Q.

Values of Q obtained by both methods were regressed against
oxygen uptake (V02). Measurements of Q by the two methods
were compared by the following: (1) regression of impedance
cardiac output (QICG) on rebreathing cardiac output (QRB); (2)
by the method of Bland and Altman8; and (3) by paired t test of
the difference between results (QRB−QICG). The ratio of QICG/QRB
was regressed against thoracic index to test the appropri¬
ateness of Kubicek's equation in patients with varying degrees of
barrel-chest deformity.

RESULTS

Anthropometric characteristics of the 21 patients
(8 male, 13 female) were as follows (mean, [range]):
age, 12 (8 to 16) years; height, 146 (120 to 164) cm;
weight, 41 (21 to 87) kg; and percent ideal body
weight, 105 (83 to 180). Chest length, ie, interelec-
trode distance, averaged 19 (16 to 24) cm, while
thoracic index averaged 0.82 (0.69 to 0.96). Pulmo¬


in the CO2 rebreathing

\[ Q = 1.96 + 6.15V02, \quad r^2 = .88 \]

\[ Q = 3.06 + 4.88V02, \quad r^2 = .73 \]

Figure 2. Plots of Q measured by thoracic electrical impedance
and RB vs V02.

largest deviation of QICG from QRB being +33%.
Eighty-three percent of QICG values were within
±20% of the corresponding QRB result. It is clear
from this figure that severity of pulmonary disease
bore no relationship to the accuracy of ICG mea¬
surements of Q.

Thoracic length averaged 13.2±1% of body height. With thoracic index as an independent pre¬
dictor, and the QICG/QRB ratio as dependent vari¬
able, univariate analysis showed no effect (p=0.22)
on measurement of Q by ICG.

DISCUSSION

This study has demonstrated that thoracic electrical
bioimpedance using the ICG-M401 provides
simple, accurate, reliable measurements of \( \dot{Q} \) during exercise in children with CF over a wide range of severity of airflow limitation. Edmunds et al.\(^{10} \) studied ICG in healthy subjects breathing with external resistive loads during exercise and concluded that the method was not influenced by the presumed greater pleural pressure swings and chest wall excursions caused by loaded breathing. Results of the present study support and extend their observations. Chest wall configuration, another factor that could conceivably alter thoracic electrical bioimpedance measurements, likewise did not seem to alter the accuracy or reliability of impedance determination of \( \dot{Q} \). Although not formally tested in pediatric patients with other diseases characterized by airway obstruction such as asthma or bronchopulmonary dysplasia, one should have no reservations in generalizing findings in the present study to children with these disorders.

Technical difficulty arose in obtaining signals sufficiently free of artifact to yield consistent results. Stroke volume appeared to fall in a few patients with minimal spirometric abnormalities in heavy, compared with light, exercise. Although the proprietary software did not “ensemble-average” the impedance waveforms, this was not necessary and, indeed, was less desirable than a feature that allowed exclusion of noise-ridden data rather than averaging such signals with relatively noise-free results. Ensemble averaging of such signals would have likely resulted in acceptance of such an apparent fall in stroke volume in these patients as a true measurement, when there was no physiologic basis for this finding. The ICG-M401 allows determination of \( \dot{Q} \) based on cardiac cycles over 8- or 16-s intervals and stores raw data collected over the chosen interval. The frequency of measurements per minute is largely dependent on the capability of the person computer to which the ICG-M401 is connected, but up to two determinations per minute are possible. Based on the initial experience with healthy control children,\(^{5} \) the 8-s interval once per minute was found to give very acceptable results for comparison purposes. \( \dot{Q}_{ICG} \) values obtained each minute during the interval over which \( \dot{Q}_{RB} \) was being measured in duplicate were averaged. However, problems were encountered with the indirect Fick (\( \dot{CO}_2 \)) method and resulted in unsuccessful measurement on a few occasions, related to blood sampling and to obtaining acceptable rebreathing maneuvers.

The potential applications of this technique open new doors to investigating exercise pathophysiology in children with obstructive lung disease. \( \dot{Q} \) can now be measured rapidly without disturbing the subject, allowing minute-by-minute measurements during progressive exercise, obviating the need for blood sampling.\(^{3} \) Thus, one will be able to characterize the
stroke volume response to exercise more readily and draw conclusions on what factors limit exercise performance in patients with CF.\textsuperscript{11} Faster computers permit calculation of $Q$ up to four or five times per minute, permitting one to study the kinetics of the $Q$ response to exercise in children with lung disease and compare this with healthy subjects. The effects of loaded or unloaded breathing on $Q$ can now be studied to assess the mechanical effect of airway obstruction on cardiac performance,\textsuperscript{12} without requiring the lungs to measure $Q$. The technique is even simpler to use at rest, and though no comparisons of impedance and indirect Fick ($CO_2$) measurements at rest were done, there should be little hesitation in extrapolating the conclusions of the present study to resting conditions. ICG can also measure other valuable parameters besides $Q$, such as systolic time intervals\textsuperscript{13} and indexes of diastolic function\textsuperscript{14} that may provide clues to putative changes in myocardial function in CF.\textsuperscript{15,16}

In conclusion, this study has demonstrated that ICG employing the ICG-M401 gives accurate and reproducible measurements of $Q$ during exercise in children with CF, extending our previous findings in healthy children. The rapid, noninvasive method has the added advantage of providing accurate measurements at rest, and thus readily lends itself to a variety of clinical and research applications in the pediatric population.

REFERENCES

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