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# *Continuous Fick Cardiac Output Compared to Continuous Pulmonary Artery Electromagnetic Flow Measurement in Pigs*

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**A system for continuous Fick cardiac output measurement (CFCO) is described and compared to continuous electromagnetic pulmonary artery flow (EMCO) and intermittent thermodilution (TDCO) measurements. Oxygen consumption was determined from continuous respiratory gas exchange analysis and arterio-venous oxygen difference from fiberoptic oximetry. A computer calculated cardiac output and other variables every 20 s. Seven pigs were monitored for a total of 10 h, during which cardiac output was manipulated by obstructing venous return or infusing epinephrine. 1748 pairs of EMCO and CFCO values were compared. The best correlation was obtained when CFCO was advanced 20 s with respect to EMCO (R = .89, CFCO = .99 EMCO + .16). TDCO was compared to EMCO during periods of steady state (R = .85, TDCO = .89 EMCO + 1.25, N = 139). TDCO was also compared with simultaneous CFCO (R = .87, TDCO = .89 CFCO + 1.01, N = 251). CFCO is recommended as a reliable standard of continuous cardiac output measurement. It is not a real time measurement; the technique has a time lag of approximately 20 s which is the result of the time constant of the $V_{O_2}$ measurement. Sources for error are discussed with suggestions for improving quality control. (Key words: Heart: cardiac output. Measurement techniques: cardiac output; continuous; electromagnetic flow probe; Fick principle; oxygen consumption.)**

GUYTON, IN 1959, described a continuous cardiac output recorder employing the Fick principle for use in animals. The method was found to reliably record dynamic changes in flow.[1] Since then, improvements in gas exchange measurements and continuous oximetry have enabled the development of clinically applicable methods of continuous Fick cardiac output monitoring.[2–4]

We have developed a computer-based monitoring system based upon the Fick principle to update cardiac output, and derived variables every 20 s. Our technique depends on real-time monitoring of mixed venous and arterial oxygen saturation, continuous analysis of gas exchange, and the integration of this information by computer with manually entered hemoglobin concentration. In a previous study, we compared Fick cardiac output to thermodilution cardiac output, and discovered a significant systematic difference in that Fick was 6–14% lower than TDCO.[4] Previous work suggests that thermodilution gives erroneously high cardiac outputs.[5] To investigate the performance of the Fick method in non-steady-state conditions, and to determine its phase relationship to real-time measurement, we compared Fick cardiac output and thermodilution cardiac output to a reliable standard. We chose an electromagnetic flow probe placed around the pulmonary artery of pigs as the best available method of real-time flow measurement with postmortem calibration of the probe on the excised vessel.

## Methods

Seven Yorkshire swine, weighing approximately 40 kg, were anesthetized with intramuscular ketamine 10 $mg \cdot Kg^{-1}$ and Innovar-vet 0.2 $ml \cdot kg^{-1}$ (a mixture containing 25 mg droperidol and 0.4 mg fentanyl per ml). Anesthesia was maintained with Innovar-vet 2 ml per h and a succinylcholine infusion. Intravenous fluids were given at a rate of 8 $ml \cdot Kg^{-1} \cdot hr^{-1}$. A tracheostomy was performed and a Bear I ventilator with initial settings of 12 bpm and 12 $ml \cdot Kg^{-1}$ tidal volume was adjusted to maintain a $Pa_{CO_2}$ of 35–40 torr. A Siemens $O_2$/air blender (Siemens Elema, Elkgrove, IL) was used to power the ventilator and ensure a constant $FI_{O_2}$ in the range of .25 to .35.

Respiratory gas exchange was monitored by a self-contained instrument for measuring oxygen consumption ($V_{O_2}$) and carbon dioxide production ($V_{CO_2}$) (MGM II, Utah Medical Products, Midvale, UT).[6] In this device, expired gas is collected in a mixing chamber, and expired ventilation ($V_E$) measured by an ultrasonic flow transducer. Samples of inspired and mixed expired gas are alternately conducted to the infrared $CO_2$ sensor and zirconium oxide $O_2$ sensors every 10 s. The formula for $V_{O_2} = V_E (FI_{O_2} - FE_{O_2} - (FI_{O_2} \times FE_{CO_2}))/(1 - FI_{O_2})$. $V_E$ is converted to STPD. Calibration of the sensors is performed automatically several times each hour, by the gas exchange analyzer. Before each experiment, a standard reference gas (80% $O_2$, 5% $CO_2$) was used for two-point calibration of the sensors, and the flow transducer was checked with a calibration syringe. The gas collection system was then pressure tested for leaks.

The right carotid artery and internal jugular vein were

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TABLE 1. Equations Used in the Program

$$Ca_{O_2} = [(Hb \times 1.34 \times Sa_{O_2}) + (.003 \times Pa_{O_2})]10 \text{ mls/L}^{10}$$

$$C\bar{v}_{O_2} = [(Hb \times 1.34 \times S\bar{v}_{O_2}) + (.003 \times P\bar{v}_{O_2})]10 \text{ mls/L},$$

where

$$PA_{O_2} = (Pb - P_{H_2O})FI_{O_2} - \frac{Pa_{CO_2}}{RQ}^{10},$$

$$Hb = Hb\,Total\left(\frac{1 - (\%\,COHb + \%\,MetHb)}{100}\right)$$

and

$$Pa_{O_2} = \frac{1}{\left(\left(\frac{.015}{Sa_{O_2}}\right) - .00015\right)}.370370370^{11}$$

Similarily, $P\bar{v}_{O_2}$ is calculated from $S\bar{v}_{O_2}$

$$CO = \frac{\dot{V}_{O_2}}{Ca_{O_2} - C\bar{v}_{O_2}}$$

$$\dot{V}_{CO_2} = V_E \times FE_{CO_2}{}^{6}$$

$$\dot{V}_{O_2} = V_E \frac{(FI_{O_2} - FE_{O_2} - (FI_{O_2} \cdot FE_{CO_2}))}{I - FI_{O_2}}{}^{6}$$

exposed, and catheter introducers were inserted. Arterial pressure and continuous $Sa_{O_2}$ were obtained from a fiberoptic catheter (Opticath, Oximetrix Inc., Mountain View, CA) placed in the carotid artery. A second fiberoptic catheter was flow directed to the pulmonary artery to give continuous $Sv_{O_2}$ and pressure readings. A third flow-directed catheter was placed in the right atrium *via* a femoral vein cut down to provide a suitable injection site for thermodilution measurements.

A sternotomy was performed to expose the pulmonary artery and aorta, and a 14 mm electromagnetic flow probe (In Vivo Metric, PO Box 249, Healdsburg, CA) was placed around the pulmonary artery. A flowmeter (FM 501, Carolina Medical Electronics, King, NC) gave a mean signal of cardiac output (EMCO).

Linen tape was looped around the inferior vena cava; traction on the tape produced a reduction in venous return which caused controllable step changes in cardiac output. An epinephrine infusion was used to further increase cardiac output after restoration of venous return.

TABLE 2. Correlation Coefficients of CFCO against EMCO for Seven Animals

| | CFCO | CFCO-20 | CFCO-40 | CFCO-60 | CFCO-80 |
|---|---|---|---|---|---|
| R ± S.D. | .86 ± .08 | .89 ± .06 | .82 ± .12 | .77 ± .12 | .7 ± .15 |

The simultaneously measured and time advanced CFCO by 20–80 s are analyzed to determine the time lag of CFCO relative to EMCO. The correlation is best when CFCO is advanced 20 s with respect to EMCO.

Mixed venous and arterial blood samples were taken every 20 min. Hb, $Sa_{O_2}$, $Sv_{O_2}$, and blood gases were measured with an oximeter and blood gas analyzer (IL 282 CO-oximeter and IL 813 BGA, Instrumentation Laboratory, Lexington, MA). Fractional saturation from the CO-oximeter was converted to functional saturation of the fiberoptic system by the relationship: Functional sat. = Fractional sat. (100/100 − (COHb + MetHb)). The oximeters were recalibrated if there was a discrepancy of greater than 2%.

Thermodilution cardiac output (TDCO) was estimated by the injection of 10 ml ice-cold saline into the right atrium by pneumatic gun at end expiration. A cardiac output computer (9520A, Edwards Laboratories, PO Box 11150, Santa Ana, CA) was used, and thermodilution curves conforming to an acceptable shape were retained.§

Continuous Fick cardiac output (CFCO) was calculated, using the equations presented in table 1, and recorded to disc by a portable IBM personal computer. The analogue output of the EM flowmeter was connected to the A-D converter, and was sampled and, also, recorded to disc by the computer.

At the conclusion of each experiment, the animal was killed by bleeding or intravenous KCL injection. At postmortem, the calibration settings of the electromagnetic flowmeter were checked by pumping blood through the excised pulmonary artery with attached flow probe using a pulsatile flow pump calibrated by timed collections.

Paired values of the three methods of cardiac output measurement were obtained. Electromagnetic flow (EMCO) was compared to CFCO by linear regression of the CFCO variable matched in time and advanced 20, 40, 60, and 80 s in order to evaluate the time delay of the CFCO measurement. Individual TDCO measurements were compared to simultaneous CFCO and EMCO values. The paired values were analyzed by linear regression and paired student *t* test. $P < 0.05$ was considered significant.

## Results

The means of all paired values of cardiac output were significantly different by *t* test ($P < .001$).

The mean correlation coefficients of CFCO against EMCO at the four different phase relationships of CFCO are shown in table 2. There were a total of 1748 paired estimates of cardiac output in seven animals representing 10 h of continuous monitoring with cardiac output ranging from 1.5–8 l/min. The correlation was greatest at CFCO lead by 20 s, where the mean coefficient of correlation was 0.89 with a standard deviation of .06.

§ Levett JM, Replogle RL: Thermodilution cardiac output: A critical analysis and review of the literature. Format of Surgical Research 27: 392–404, 1979.

TABLE 3. Comparison of the Three Different Methods of Cardiac Output Estimation (CFCO *vs.* EMCO was Analyzed for Individual Animals and Then Averaged)

| | N | R | SEE | Slope | Intercept |
|---|---|---|---|---|---|
| CFCO *vs.* EMCO (mean + S.D.) | 1748 | .89 ± .06 | .57 ± .09 | .99 ± .09 | .16 ± .39 |
| TDCO *vs.* EMCO (pooled data) | 139 | .86 | .96 | .89 | 1.25 |
| TDCO *vs.* CFCO (pooled data) | 251 | .87 | .85 | .89 | .99 |

The results of linear regression of the three different methods are presented in table 3 and figures 1, 2, and 3.

The performance of the EM flow probe against the known pulsatile flow produced by the calibrated pump is presented in figure 4. There was a slight alinear response with EM flow under reading at progressively increasing flows above 6 l/min; the alinearity contributed to the discrepancy between CFCO and EMCO in the 6–8 l/min range.

## Discussion

The continuous cardiac output measurements, CFCO and EMCO, were collected automatically from the beginning to the end of the experiments in all animals with no data rejection. CFCO and EMCO correlated more closely with one another than either did with steady state TDCO values. The continuous methods, furthermore, allowed data collection throughout the manipulations of cardiac output, where CFCO directly followed even small trends in EMCO with a time delay of about 20 s. The correlation was poorer in the high range where our EM flow probe had a flattened response at flows above 6 l/min, bringing into question the reliability of our "gold" standard, at least in that range of flow.

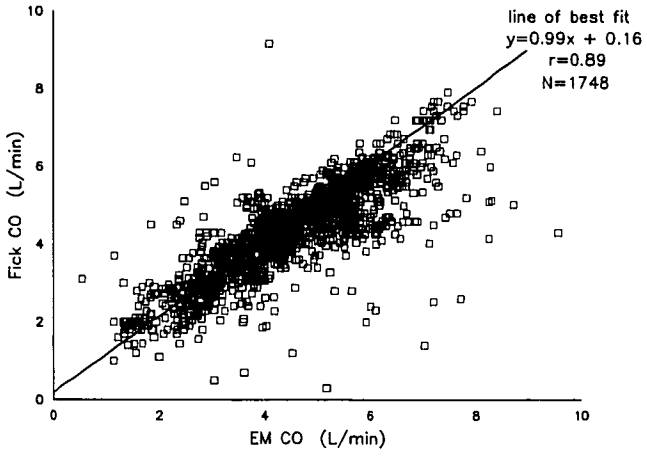


FIG. 1. Fick cardiac output advanced 20 s against electromagnetic pulmonary artery flow.

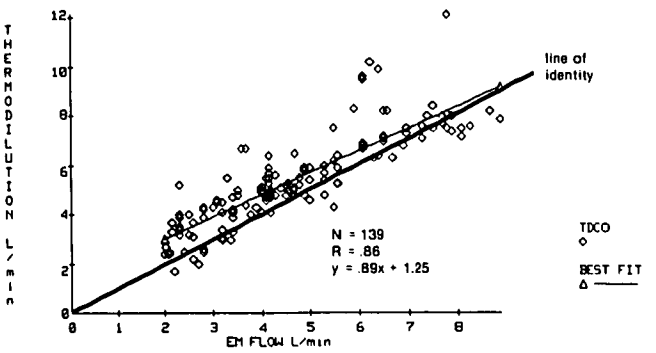


FIG. 2. Thermodilution cardiac output *versus* simultaneously measured electromagnetic pulmonary artery flow.

Paired values of TDCO and CFCO were compared in an analogous fashion to our previous study in intensive care unit patients.[4] The results of both the human and animal comparisons with thermodilution are very similar with an almost identical regression equation and coefficient of correlation. They indicate that TDCO overestimates cardiac output. The likely reason is loss of thermal indicator from blood during its passage from the injectate port to the thermistor. Thermal indicator loss into tissues along the right side of the heart may be expected to vary with flow and temperature gradient. It does seem to be a predictable error, and should be correctable by an adjustment to the computation factor.[5]

Our original hypothesis was that arterio-venous oxygen content difference could be measured over the same time frame as the oxygen uptake measurement, and should give an accurate reflection of the mean cardiac output during that sample period. Because oxygen is being taken up by the lungs and arterio-venous oxygen difference is measured on either side of the lungs, the technique must measure mean pulmonary blood flow. The limiting factor in the use of this technique for continuous changes is the obligatory time delay involved in $V_{O_2}$ measurement. CFCO would be best served by determining alveolar gas

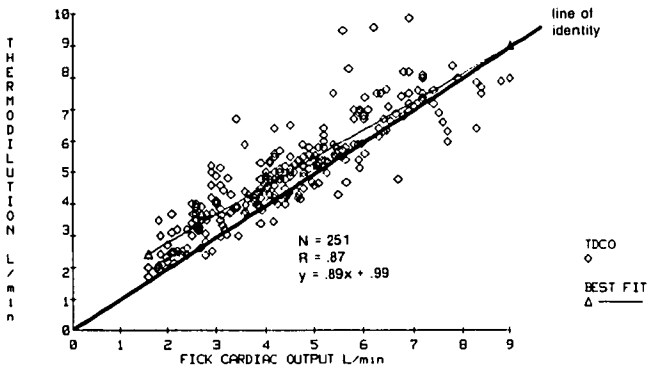


FIG. 3. Thermodilution *versus* Fick cardiac output.

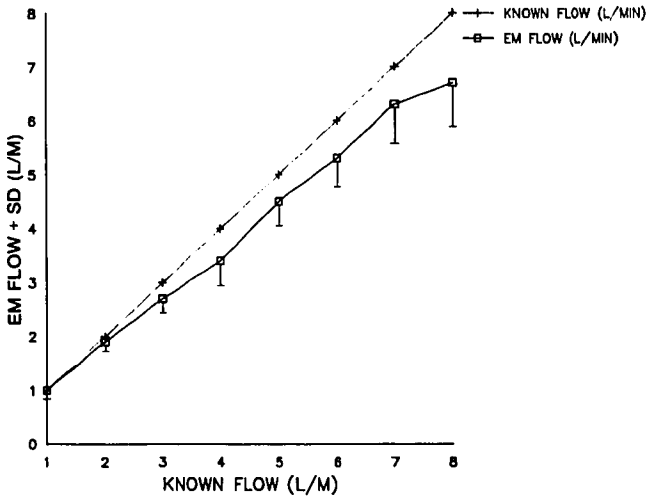


FIG. 4. Results of post-mortem calibration of the EM flow probe against a known flow from a pulsatile pump.

exchange, but we only have access to expired gas. Changes in alveolar gas concentrations will be reflected by changes in airway gas concentrations with a time constant of volume (FRC plus circuit) divided by minute ventilation. Breath by breath $V_{O_2}$ measurement offers the shortest possible time constant of $FRC/V_E$, but may introduce noise due to disturbances of ventilatory pattern,[7] and inaccuracy due to the difficulty of phase matching gas flow and concentration measurements.[8] Our system employs a mixing chamber technique of $V_{O_2}$ measurement. It has a time constant of (mixing chamber volume + FRC)/$V_E$. Assuming FRC = 1 l, mixing chamber volume = 3 l, and a minute ventilation of 8 l/min, the $V_{O_2}$ measurement time constant would be approximately 30 s.

With multiple step changes in cardiac output, we were able to identify the time constants of the subsequent measurements: EMCO and blood pressures were the most rapidly responding parameters, followed 20 s later by a sharp drop in $V_{O_2}$ and the computed CFCO value. Slightly later, a decrease in $Sv_{O_2}$ occurs, causing a subsequent $V_{O_2}$ increase. Oxygen uptake is preserved, but only after the decrease in cardiac output had caused an increase in peripheral oxygen extraction. The time constant for changes in $Sv_{O_2}$ with cardiac output are expected to be blood volume/cardiac output (for 30 kg pigs; 2.1 l/2–3 l/min; approximately 60–80 s). This time delay should not be a factor, because the technique only considers the inputs and outputs to the pulmonary circulation; the lungs become, in practice, a black box.

The availability of a standard of continuous cardiac output measurement remains a problem. We used an electromagnetic flow probe which has to be calibrated outside the body in totally different circumstances to its *in vivo* position. The probe is sensitive to position changes, vessel tension, and electrical and grounding interferences. It is difficult and highly invasive to apply requiring thoracotomy and eventual sacrifice of the animal. Previous workers, recognizing the problems of calibrating a pulmonary artery flow probe after placement in the animal, have used other methods of cardiac output measurement (*e.g.*, dilution or Fick) to calibrate the flowmeter *in situ*. The calibration data of the EM flow probe suggests that EMCO was underestimating cardiac output, particularly at higher flows. Attempts to increase the gain of our particular instrument resulted in overreading at lower flows.

We are left with very few options if accurate continuous cardiac output measurements are required. We recommend CFCO as the best available method, providing the time lag due to $V_{O_2}$ measurement is understood. The derived values will be as accurate as the measurements of the individual inputs of the Fick equation; $V_{O_2}$, $Sa_{O_2}$, $Sv_{O_2}$, and Hgb. To continuously calculate blood oxygen content, *in vivo* fiberoptic oximetry was employed. A standard deviation of 2% of saturation over periods of up to 24 h have been reported for Oximetrix instruments.[9] Our experience supports this claim. Hemoglobin must be accurately measured, and changes must be detected and updated. The oxygen binding capacity of hemoglobin has been variously estimated to be 1.34–1.39 ml/gm, depending on it being a measured value (Van Slyke 1.34) or a value derived from molecular structure (1.39), a 3.5% discrepancy.[10] The contribution of dissolved oxygen to content is less than 2%, and we suggest calculating $P_{O_2}$ from saturation by the Hill equation.[11] Errors resulting from inaccuracy in $P_{O_2}$ are relatively insignificant.

Percentage errors of content estimation apply to the difference rather than the total oxygen content; it follows that a decreasing arterio-venous oxygen content difference will produce a greater standard deviation; likewise, a higher oxygen extraction will improve accuracy.

Quality control of $V_{O_2}$ measurement is a complex issue, and several studies deal with this problem in detail.[12] The gas sensors must be well-calibrated and capable of accuracy of 0.1%. Commonly available gas flow transducers can be accurate to within 5%, as was the case with the ultrasonic flow transducer in our system. All expired gas must be measured and, therefore, leaks in the gas collection system must be eliminated. Overall, the gas exchange monitor used in our experiments is capable of 1.5–1 1% accuracy.[6] An increasing $FI_{O_2}$ produces increasing error until the system becomes unreliable with $FI_{O_2} > 0.8$.[12] In these circumstances, the best compromise to achieve continuity of measurement would be to simply assume a respiratory quotient and use $V_{CO_2}$ divided by RQ to estimate $V_{O_2}$.

A theoretical standard deviation of 0.68 l/min for the normal range of 5 l/min was predicted for Fick cardiac

output assuming 2% standard deviations for $Sa_{O_2}$, $Sv_{O_2}$, and hemoglobin, and a 22 ml/min standard deviation for $V_{O_2}$.

This system has previously been described in detail for use in the intensive care unit, where the same system was used with a pulse oximeter for the $Sa_{O_2}$ measurement.[4] There are added advantages in monitoring the components of the Fick equation which must not be overlooked: continuous monitoring of oxygen demand and oxygen extraction gives a much more complete physiological picture than does monitoring of cardiac output alone.

In conclusion, CFCO is recommended as a reliable standard of continuous cardiac output measurement. There is a time delay which is a function of the time constant of the method of $V_{O_2}$ measurement.

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