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The Non-invasive Determination of Cardiac Output in Children: A Three-breath Technique

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In this study, the cardiac output of 11 children (5 days to 18 yr of age) was measured following cardiopulmonary bypass. Standard dye dilution cardiac outputs and an indirect Fick-CO_2 technique were simultaneously determined. A rebreathing maneuver is described to estimate the oxygenated mixed venous P_{CO_2} ($PvCO_2$). This estimate of $PvCO_2$ was combined with the end tidal P_{CO_2} and CO_2 production to give a non-invasive Fick estimate of the cardiac output. Non-invasive cardiac outputs correlated well with those measured by dye-dilution (r^2 = 0.94) over a range of cardiac outputs from 490–7280 ml/min. All non-invasive determinations were within 15% of the line of identity, and within 22% of averaged replicate dye-dilution values. Our results agree with previous comparisons of indirect Fick-CO_2 methods with invasive determinations of cardiac output. These data suggest that the indirect Fick-CO_2 technique offers a rapid, non-invasive alternative to invasive monitoring of cardiac output. (Key words: Anesthesia, pediatrics. Measurement technique, cardiac output: non-invasive.)

IN 1956, COLLIER[1] DESCRIBED a rebreathing technique to estimate the mixed venous P_{CO_2}. Collier's "oxygenated" $PvCO_2$ is defined as the mixed venous P_{CO_2} measured in the presence of oxygen saturated hemoglobin. With Collier's technique, a patient rebreathes a gas mixture with a CO_2 partial pressure greater than the estimated $PvCO_2$ to obtain an equilibrium $PvCO_2$ estimate. Defares[2] subsequently reported $PvCO_2$ estimates based on the asymptotic rise in P_{CO_2} during rebreathing. Refinements of the equilibrium and exponential techniques have been used to determine cardiac output by the indirect Fick-CO_2 method.[3–7]

Our initial attempts to reproduce stable estimates of $PvCO_2$ by the equilibrium method were unsuccessful in small (≦5.3 kg) subjects. Equilibration of CO_2 could not be obtained within three breaths, inspired and expired gas varied by more than 1 mmHg, and a plateau could not be sustained for 10 s.[8] On the other hand, these criteria for an adequate equilibrium capnogram were easily replicated in larger subjects.

In this paper, we present a technique to estimate the oxygenated mixed venous P_{CO_2} ($PETCO_2$) in both large and small subjects. To reproducibly determine the $PvCO_2$ in both large and small subjects, we combined a controlled-rebreathing technique described by Fisher,[9] with an equilibrium rebreathing approach. Our modification allows the inspired P_{CO_2} to equilibrate toward the expired P_{CO_2} during rebreathing. In contrast, Fisher's technique rigidly controls the inspired P_{CO_2}. We calculated cardiac output combining the indirect Fick-CO_2 technique with this estimate of $PvCO_2$, the end-tidal P_{CO_2} ($PETCO_2$), and CO_2 production ($\dot{v}CO_2$). These indirect Fick-CO_2 cardiac outputs were compared with simultaneous dye-dilution determinations.

Materials and Methods

The study was approved by the hospital Human Subject Review Committee. We studied 11 patients weighing 2.8–43 kg, aged 5 days–18 yr following elective surgical repair of congenital heart disease. One patient with a residual postoperative left-to-right intracardiac shunt was excluded. All cardiac outputs were measured 1–2 h after patients were transferred to the intensive care unit.

All patients were ventilated by a Siemens 900-C ventilator. We measured $\dot{v}CO_2$ continuously with a Siemens model 930 CO_2 analyzer. This CO_2 analyzer determines $\dot{v}CO_2$ by integrating the product of the instantaneous expiratory flow and the instantaneous expired P_{CO_2}. $\dot{V}CO_2$ was recorded when the $\dot{v}CO_2$ measurement was stable for at least 30 s immediately before the cardiac output determination. Inspiratory and expiratory volumes were compared by a pitot tube flowmeter[10] to assure no endotracheal tube leaks.

A Puritan-Bennett CO_2 analyzer (response time of 200 msec at 150 ml/min flow rate) equipped with a graph recorder was calibrated with dry 5.17% CO_2 before each study. $PETCO_2$ and all rebreathing CO_2 measurements were sampled from a 19-gauge catheter positioned near the distal tip of the endotracheal tube.

Pulmonary blood flow (PBF) was determined from the Fick equation:

$$PBF(ml/min) = \frac{\dot{v}CO_2(mlCO_2/min)}{CvCO_2 - CaCO_2(mlCO_2/ml)},$$

where $\dot{v}CO_2$ = production of CO_2, $CvCO_2$ = CO_2 content of mixed venous blood, and $CaCO_2$ = CO_2 content of arterial blood. Distal $PETCO_2$ measurements were used to estimate arterial P_{CO_2} ($PaCO_2$).[11] If arterial

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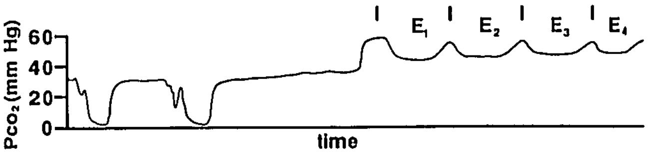

FIG. 1. Capnograph of a single rebreathing maneuver in a 7.2-kg child. $PICO_2$ = 60 mmHg. The plateau after the third expired breath (E_3) was used to calculate P_vCO_2 as described in the text. The discontinuity in the ventilated breath at the left of the figure resulted from a brief ventilator disconnection and an attempt at spontaneous ventilation by the patient.

blood gases were not available, a Nellcor® pulse oximeter was used to measure O_2 saturation.

To measure $PvCO_2$, a closed 2-liter reservoir bag was filled from an anesthesia machine equipped with Quantiflex® CO_2 and O_2 flowmeters. The P_{CO_2} of the delivered mixture ($PICO_2$) was analyzed immediately before the rebreathing maneuver. The endotracheal tube of each patient was disconnected from the ventilator and the patients were allowed to rebreathe for at least four breaths a test gas of 6–9% CO_2 in oxygen. During rebreathing, the ventilator frequency and volume was manually approximated. The expired P_{CO_2} ($PEXCO_2$) following the second, third, and fourth breaths was recorded (fig. 1). This rebreathing maneuver was repeated two to five times with different concentrations of test gas, allowing at least 1 min before repetition. When $PEXCO_2$-$PICO_2$ was plotted as a function of $PICO_2$, a least-squares linear regression was obtained (fig. 2). The x-intercept ($PEXCO_2 = PICO_2$) was used as an estimate of $PvCO_2$. This modification of Fisher's technique allows the $PICO_2$ to equilibrate toward $PvCO_2$ during the rebreathing trial.

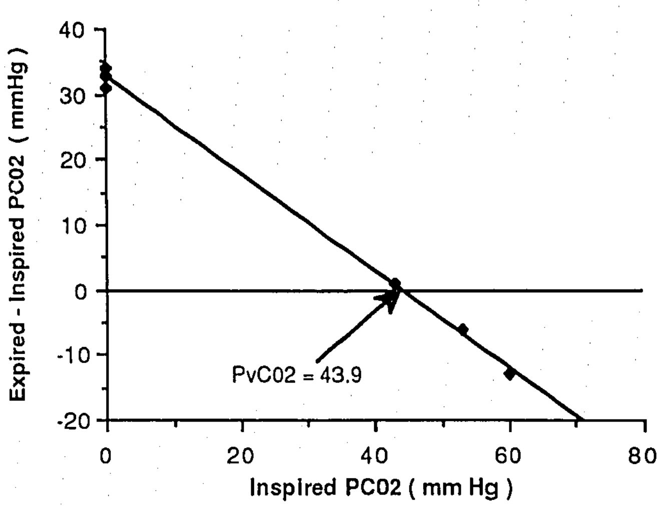

FIG. 2. P_vCO_2 estimation in a 7.2-kg child. A least-squares regression line is shown. Three separate rebreathing maneuvers produced the three points at the right of the figure. The $PETCO_2$ (where $PICO_2$ = 0) is shown on the ordinate.

CO_2 contents were calculated from McHardy's[12] mathematical derivation of the CO_2 dissociation curve. Corrections were applied for O_2 saturation and hemoglobin concentration.

$$CvCO_2 - CaCO_2 = 11.02(PvCO_2^{0.396} - Pa_{CO_2}^{0.396}) - 0.015(PvCO_2 - Pa_{CO_2})(15 - Hb) - 0.064(95 - SaO_2),$$

where $CvCO_2 - CaCO_2$ is the mixed venous-arterial CO_2 content difference in ml of CO_2/100 ml of blood, $PvCO_2$ is the oxygenated mixed venous tension of CO_2 in mmHg, Pa_{CO_2} is approximated by $PETCO_2$, SaO_2 is the percent O_2 saturation of arterial blood, and Hb is the hemoglobin concentration in gm/100 ml blood.

Dye dilution cardiac outputs were determined immediately after the indirect-Fick cardiac outputs. Cardiogreen dye (1.25–5.0 mg) was rapidly injected into a superior vena caval catheter or left atrial catheter at end-exhalation. A Waters COR-10 cardiac output computer continuously analyzed arterial blood and integrated the resultant dye-dilution curves. Indirect Fick-CO_2 cardiac outputs and dye-dilution outputs were compared by linear regression analysis.

In a parallel study, the oxygenated $PvCO_2$ was determined in 12 subjects (2.8–84 kg) using both the equilibrium technique[8] and our three-breath method.

Results

Table 1 shows the demographic profile of our patients, including indirect-Fick and dye-dilution cardiac output determinations. The two-, three-, and four-breath cardiac outputs were calculated from the $PvCO_2$-$PETCO_2$ gradient as described using $PEXCO_2$ after the second, third, and fourth breath.

The correlation between two-, three-, and four-breath Fick cardiac outputs and dye-dilution cardiac outputs was best using the three-breath maneuver (r^2 = 0.87, 0.94, and 0.90, respectively). Figure 3 shows the concordance plot of three-breath Fick-CO_2 cardiac outputs with simultaneous dye-dilution determinations. All Fick outputs were within 22% of the averaged dye-dilution values.

We found the three-breath technique gave estimates of $PvCO_2$ 2–4 mmHg lower than the equilibrium method. Figure 4 shows the correlation between the three-breath $PvCO_2$ determination and the equilibrium values (r^2 = 0.91) in 12 subjects. The difference between the two estimates of $PvCO_2$ did not vary with weight (r^2 = 0.29). Seven patients in the cardiac output study had rebreathing capnograms with a plateau allowing equilibrium estimates of $PvCO_2$. The mean equilibrium—three-breath $PvCO_2$ difference was 3.93 ± 1.51 mmHg (±SD) in this group.

TABLE 1. Demographic and Cardiac Output Data

Patient	Weight (kg)	Age	Lesion	vCO_2 ($ml\ CO_2/min$)		Hb (g/l)	Oxygen Saturation (%)	Number of Re-breathing Replicates	Calculated Cardiac Output (ml/min) After 'n' Expired Breaths			Mean Dye-dilution Cardiac Output (ml/min) (n = 3)
				(ml/min)	(ml/kg/min)				n = 2	n = 3	n = 4	
A	7.17	8 months	VSD	59	8.2	152	100	3	1130	1030	940	1270
B (Day 1)	12.6	3.5 yr	Tetralogy of Fallot	86	6.8	115	98.8	2	3490	2530	2340	2030
B (Day 2)				96	7.6	103	100	2	2110	2060	1420	2000
C	39.4	14 yr	Arotic aneurysm	190	4.8	110	100	2	6070	5640	5020	7280
D	2.8	5 days	Transposition of great arteries	24	8.6	100	90	3	420	380	350	490
E	34.1	9 yr	VSD	205	6.0	125	100	2	5720	4660	4440	4350
F	43.3	18 yr	Glenn shunt-defect (tetralogy repaired in past)	230	5.3	139	82	5	7750	6430	5820	6340
G	13.4	3.5 yr	AVSD	74	5.5	98	100	2	2110	1920	1690	1680
H	35.4	13 yr	Tetralogy of Fallot	205	5.8	120	100	2	4980	4220	3900	3900
I	10.7	1 month	ASD Type I	94	8.8	135	100	2	2180	2060	1910	1730
J	19.9	5 yr	ASD	123	6.2	103	100	3	3660	3080	2810	2480

Discussion

We describe a rapid, practical method to non-invasively determine cardiac output of small subjects. Previously described non-invasive Fick techniques rely on one of two methods to estimate $PvCO_2$: 1) the equilibrium method of Collier as refined by McEnvoy *et al.*,[8] and 2) exponential methods. In infants, rapid CO_2 recirculation yields a rebreathing capnograph that does not rise to an asymptotic value of $PvCO_2$; despite altering rebreathing bag volumes, a continuous rising P_{CO_2} with persistent ventilatory oscillations is seen.

To estimate cardiac output using the three-breath determination of $PvCO_2$ described, arterial blood samples are not required. Although the blood-gas equilibrium of alveolar CO_2 is a contentious issue,[13] at rest the normal $PETCO_2$-Pa_{CO_2} gradient has been measured to be −2.5 mmHg.[8] We found a similar gradient (−2 to −4 mmHg) between the three-breath estimate of $PvCO_2$ and the equilibrium estimate in our study. The Fick cardiac outputs based on the equilibrium $PvCO_2$-Pa_{CO_2} gradient should, therefore, be expected to be similar to those based on a three-breath $PRBCO_2$-$PETCO_2$ gradient.

As pulmonary dead space increases, the Collier estimate of $PvCO_2$ is not affected, since alveolar, end-tidal, and dead space gas should be in equilibrium. If dead space is increased, a large $PETCO_2$-Pa_{CO_2} gradient and, therefore, an artifactually low cardiac output will result if the $PvCO_2$-$PETCO_2$ gradient is calculated using the

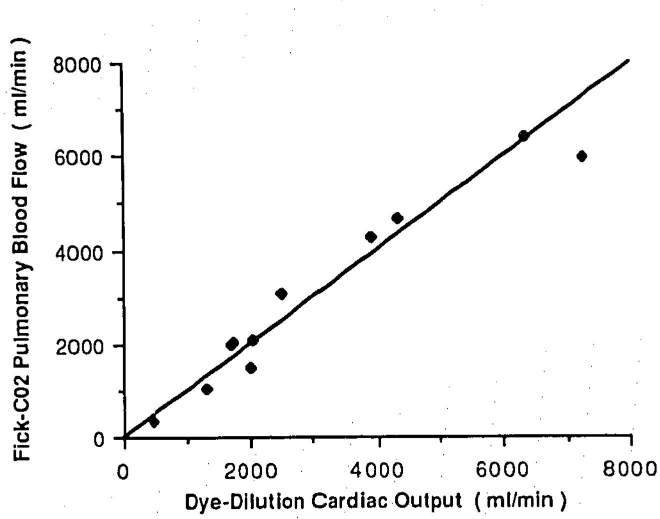

FIG. 3. A concordance plot showing the correlation between non-invasive Fick and dye-dilution determinations of cardiac ouputs (r^2 = 0.94). The line of identity is shown.

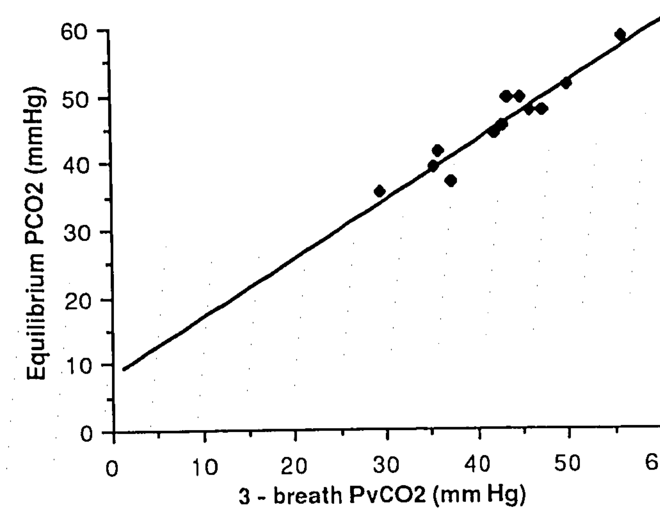

FIG. 4. Least squares regression plot of P_vCO_2 as determined by the equilibrium and three-breath technique (r^2 = 0.91). The regression line is represented by the curve y = 0.886x + 8.039.

equilibrium method.[14] The concordance of our Fick-CO_2 and dye dilution cardiac outputs indicates that the three-breath $P_{RB}CO_2$-$P_{ET}CO_2$ gradient accurately reflects the $P\bar{v}CO_2$-Pa_{CO_2} gradient. We speculate that the same factors that lead to an increased $P_{ET}CO_2$-Pa_{CO_2} gradient also increase the three-breath $P_{RB}CO_2$-$P\bar{v}CO_2$ gradient, and yield accurate pulmonary blood flow determinations.

If this assertion is correct, we would expect that the three-breath technique will estimate the effective pulmonary blood flow (which will ordinarily equal the systemic cardiac output), will be resistant to error resulting from increased dead space (for example, rapid shallow respirations), and will underestimate the actual pulmonary blood flow in states with increased venous admixture (pulmonary hypotension or pulmonary embolism). Our finding that PBF can be rapidly, non-invasively estimated within 22% of dye-dilution methods suggests that this technique will be clinically useful.

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