LIPPINCOTT WILLIAMS & WILKINS

Critical Care Medicine
OFFICIAL JOURNAL OF THE SOCIETY OF CRITICAL CARE MEDICINE

 Volume 24(10), October 1996, pp 1701-1705

Noninvasive determination of cardiac output using single breath CO sub 2 analysis [Laboratory Investigation]

Arnold, John H. MD; Stenz, Rudiger I. MD; Thompson, John E. RRT; Arnold, Lucy W. MD

From the Departments of Anesthesia (Drs. J.H. Arnold and Stenz), Cardiology (Dr. L.W. Arnold), and Respiratory Care (Mr. Thompson), Children's Hospital, and the Departments of Anesthesia and Pediatrics, Harvard Medical School, Boston, MA.

Supported, in part, by grant HL-02395 from the National Institutes of Health (Dr. L.W. Arnold) and by a grant from Novametrix, Inc.

Address request for reprints to: John H. Arnold, MD, Multidisciplinary Intensive Care Unit, Farley 5, Children's Hospital, 300 Longwood Avenue, Boston, MA 02115.

Abstract

Objective: To examine the utility of single breath CO_2 analysis as a noninvasive measure of cardiac output.

Setting: An animal laboratory in a university-affiliated medical center.

Design: A prospective, animal cohort study comparing 21 parameters derived from single breath CO_2 analysis with cardiac output determined by an ultrasonic flow probe.

Subjects: Six healthy adult sheep.

Methods: The single breath CO_2 analysis station consists of a mainstream capnometer, a variable orifice pneumotachometer, a signal processor, and computer software with capability for both on- and off-line data analysis. Twenty-one derived components of the CO_2 expirogram were evaluated as predictors of cardiac output. Cardiac output was manipulated by successive injections of a hydraulic constrictor placed around the inferior vena cava.

Measurements and Main Results: Thirty-four measurements of cardiac output were available for comparison with derived variables from the CO_2 expirogam. Stepwise linear regression identified two variables that were most predictive of cardiac output: a) the angle between the slope lines for phases II and III of the CO_2 expirogram divided by the volume of CO_2 per breath (angle/mL CO_2); and b) the slope of phase II. The multivariate equation was highly statistically significant and explained 94% of the variance (adjusted r^2 = .94, $p < .0001$). The bias and precision of the calculated cardiac output were .00 and .23, respectively. The mean percent difference for the cardiac output estimate derived from the single breath CO_2 analysis station was 0.36%.

Conclusions: Our data indicate that analysis of the CO_2 expirogram can yield accurate information about the cardiovascular system. Specifically, two variables derived from a plot of

expired CO_2 concentration vs. expired volume predict changes in cardiac output in healthy adult sheep with an adjusted coefficient of determination of .94. Prospective application of this technology in the setting of lung injury and rapidly changing physiology will be essential in determining the clinical usefulness of the technique.

(Crit Care Med 1996; 24:1701-1705)

Key Words: carbon dioxide; cardiac output; respiratory deadspace; gas exchange; mechanical ventilation; respiration disorders; ventilation-perfusion ratio; lungs; critical illness

Analysis of the CO_2 concentration in expired gas provides information about the respiratory deadspace and the efficiency of gas exchange [1,2]. As originally described by Aitken and Clarke-Kennedy [1], Fowler [3], and later by Fletcher [4], quantitative analysis of the expired CO_2 waveform allows the calculation of a number of variables relevant to the monitoring of respiratory efficiency and the relationship between ventilation and pulmonary perfusion. Fletcher and Jonson [5] have completely reviewed the topic and Fletcher et al. [6] have also described the application of single-breath CO_2 analysis in pediatric patients with cyanotic heart disease. In a surfactant-depleted animal model [7], the slope of phase III of the CO_2 expirogram was shown to correlate with the functional residual capacity, and the phase III slope has also been shown to distinguish normal adults from those animals with adult respiratory distress syndrome [8]. Ream and colleagues [9] recently correlated changes in the phase III slope with presumed morphometric increases in the alveolated airway cross-sectional area, suggesting that single breath CO_2 analysis may provide important insight regarding lung growth.

We [10] have recently developed a single breath CO_2 analysis station and described its validation in a lung model and in saline-lavaged animals. We hypothesized that changes in cardiac output would alter pulmonary perfusion and produce measurable changes in the expired CO_2 waveform. The present study examines the relationship of several variables derived from analysis of the CO_2 expirogram to cardiac output in an animal model.

MATERIALS AND METHODS

Analysis of the CO sub 2 Expirogram.

The hardware and software utilized in the analysis of the CO_2 expirogram have been previously described [10]. The system consists of a mainstream capnometer, a variable orifice pneumotach, a signal processor, and computer software with capability for both on- and off-line data analysis. The CO_2 signal is provided by a mainstream, non-dispersive, infrared capnometer (Capnogard Registered Trademark 1265, Novametrix Medical Systems, Wallingford, CT) complete with an analog output module. The pneumotachometer is a disposable, variable orifice, differential pressure device (Accutach, Glen Medical Products, Carlsbad, CA). The signal processing hardware represents a modification of an available respiratory mechanics computer (Ventrak Registered Trademark Respiratory Mechanics Monitor, Novametrix Medical Systems). The CO_2 expirogram can be divided into three distinct phases and the details of our waveform analysis have been previously described [10]. The derived components of the CO_2 expirogram that were evaluated in this study included the following 21 parameters: minute CO_2 production, mixed expired CO_2 tension, volume of CO_2 per breath, physiologic deadspace to tidal volume ratio, alveolar deadspace to alveolar tidal

volume ratio, airway deadspace to tidal volume ratio, airway deadspace, alveolar deadspace, alveolar tidal volume, slope of phase II, slope of phase III, slope of phase II divided by the mixed expired CO_2 tension, slope of phase III divided by the mixed expired CO_2 tension, volume of phase I, volume of phase II, volume of phase III, angle between the slope lines for phases II and III, angle between the slope lines for phases II and III divided by the mixed expired CO_2 tension, angle between the slope lines for phases II and III divided by the volume of CO_2 per breath, angle between the slope lines for phases II and III divided by the tidal volume, and efficiency, which was originally defined by Fletcher and co-workers [11].

Animal Preparation.

This protocol was approved by the Animal Care and Use Committee of Children's Hospital and the animals were handled according to the Guidelines for the Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Council (DHHS publication No. [NIH] 85-23, 1985). Adult sheep had anesthesia induced with intramuscular ketamine (20 to 30 mg/kg) and were intubated orally with a 7.5-mm ID endotracheal tube (Mallinckrodt, Glenn Falls, NY). After the establishment of adequate intravenous access, maintenance anesthesia was provided with halothane (0.5% to 1.0% inspired) and muscle relaxation was achieved with pancuronium (0.2 mg/kg/hr). Controlled ventilation was provided by a pistondriven ventilator (Harvard Apparatus, South Natick, MA) at standardized ventilatory settings (FIO_2 = 0.5, tidal volume 10 to 15 mL/kg, with rate adjusted to achieve a $PaCO_2$ between 35 and 45 torr [4.7 and 6.0 kPa]).

Using sterile surgical technique, a left thoracotomy was performed at the 5th to 6th intercostal space. The left internal mammary artery was cannulated after careful dissection and a hydraulic constrictor (Hazen Everett, Teaneck, NJ) was placed around the inferior vena cava at the atrial-caval junction. The arterial pressure waveform and electrocardiogram were displayed continuously throughout the protocol. A previously calibrated, 14-mm ultrasonic flow transducer (T108, Transonic Systems, Ithaca, NY) was placed around the main pulmonary artery, and blood flow was continuously measured. Cardiac output was manipulated by successive injections of the hydraulic constrictor with normal saline. Incremental injections of 0.2 mL of saline into the constrictor were made until the animal manifested systemic hypotension or metabolic acidosis (usually 4 to 6 injections totaling 0.8 to 1.2 mL). Expired tidal volumes were measured continuously and the delivered tidal volume was adjusted to maintain a constant expired tidal volume of 10 mL/kg.

The protocol included co-calibration of the CO_2 analysis station and the blood gas analyzer to a standard calibration gas (10% CO_2). This calibration procedure was repeated at the beginning of each testing sequence. Fifteen minutes after each injection of the hydraulic constrictor, arterial blood gas tensions were measured, using a standard laboratory blood gas analyzer (Ciba Corning, 278 Blood Gas System, Ciba Corning Diagnostics, Medfield, MA), and a 5-min recording of the single breath CO_2 expirogram was saved on a computer disk for subsequent off-line analysis.

Data Analysis.

Derived components from the CO_2 expirogram were evaluated as predictors of cardiac output using stepwise multiple linear regression analysis. Before creation of the multivariate model, a set of bivariate analyses was performed to determine which of the potential predictor

variables was associated with the criterion measure, cardiac output. In each of these analyses, the relationship was examined using linear regression with the effects of the subjects removed by including dummy variables to represent the individual sheep. The results from these analyses were used to select the subset of potential predictors for the multivariate analysis. The effect of the subject was also accounted for in the multivariate model. The Durbin-Watson statistic was computed on the residuals for the model to test for autocorrelation. The analysis included a test of the assumption of slope homogeneity for each predictor variable as well as a test of the assumption of homogeneity of variance for each predictor variable. The residuals were tested for normality and excessive skewness. The results of all such analyses indicated that the data met the underlying assumptions required for the multivariate analysis used in deriving a predictive equation for the criterion measure. Statistical significance was assumed when p was < .05.

The bias and precision were evaluated using the mean and standard deviation of the differences between the measures. The differences between the methods of deadspace measurement (bias) were plotted against the average of the two methods. The bias measures systematic error between the methods and the precision quantifies the random error or variability [12]. The limits of agreement were defined as the mean difference +/- 2 SD and describe the range that includes 95% of the differences between the measures. The percent difference was calculated from the following formula: percent difference (%) = 100 times (difference between the methods)/mean cardiac output measurement.

RESULTS

Six adult sheep (mean weight 49.8 kg, range 44 to 50) were anesthetized and instrumented as described. Baseline arterial blood gases and CO_2 expirograms were obtained 30 mins after completing the surgical preparation. Incremental injections of the constrictor were performed.

A total of 34 separate measurements of cardiac output were available for comparison with derived variables from the CO_2 expirogam. Bivariate linear regression analysis demonstrated that 20 of the 21 potential predictors derived from the CO_2 expirogram were significantly associated with the cardiac output measured by ultrasonic flow probe Table 1. Stepwise linear regression was used to create a multivariate predictive equation of cardiac output. Only two predictors were included in this equation because additional variables did not lead to a statistically significant increase in predictive power. The predictors were: a) the angle between the slope lines for phases II and III divided by the volume of CO_2 per breath (angle/mL CO_2); and b) the slope of phase II. The multivariate equation was highly statistically significant and explained 94% of the variance (adjusted r^2 = .94, p < .0001). The relationships between each predictor and cardiac output measured by ultrasonic flow probe are presented in Figure 1. Table 2 presents the slope and its standard error for each of the substantive variables in the equation. The sign of the slopes indicate that the volume of CO_2 per breath (angle/mL CO_2) was negatively related to cardiac output while the relationship for the slope of phase II was positive. Each of the variables was highly statistically significant in the regression equation and the standard error of the estimate was .25.

Variable	Partial Correlation[a]	*t* Statistic	*p* Value
Angle/mL CO_2	–.96	–16.78	.0000
Angle/P_{ECO_2}	–.96	–16.78	.0000
P_{ECO_2}	.95	15.54	.0000
V_{ECO_2}	.95	16.28	.0000
Angle	–.90	–10.47	.0000
Slope phase II	.89	10.14	.0000
Angle/V_T	–.85	–8.37	.0000
$\dot{V}CO_2$	.83	7.82	.0000
V_D/V_T phys	–.75	–5.93	.0000
Volume phase III	.70	5.13	.0000
Slope phase II/P_{ECO_2}	.70	5.09	.0000
Volume phase I	–.68	–4.81	.0001
V_D/V_T alv	–.67	–4.73	.0001
V_T alv	.66	4.60	.0001
V_D/V_T air	–.64	–4.32	.0002
V_D air	–.59	–3.84	.0007
Volume phase II	–.56	–3.53	.0015
V_D alv	–.56	–3.52	.0016
Efficiency	.49	2.89	.0075
Slope phase III/P_{ECO_2}	–.48	–2.83	.0088
Slope phase III	–.31	–1.69	.1021

Angle/mL CO_2, angle between the slope lines for phases II and III divided by the volume of CO_2 per breath; angle/P_{ECO_2}, angle between the slope lines for phases II and III divided by the mixed expired CO_2 tension; P_{ECO_2}, mixed expired CO_2 tension; V_{ECO_2}, volume of CO_2 per breath; angle, angle between the slope lines for phases II and III; angle/V_T, angle between the slope lines for phases II and III divided by the tidal volume; $\dot{V}CO_2$, minute CO_2 production; V_D/V_T phys, physiologic deadspace/tidal volume ratio; slope Phase II/P_{ECO_2}, slope of phase II divided by the mixed expired CO_2 tension; V_D/V_T alv, alveolar deadspace/alveolar tidal volume ratio; V_T alv, alveolar tidal volume; V_D/V_T air, airway deadspace/tidal volume ratio; V_D air, airway deadspace; V_D alv, alveolar deadspace; slope Phase III/P_{ECO_2}, slope of phase III divided by the mixed expired CO_2 tension.

[a]The partial correlation coefficient is the standard Pearson Product Moment correlation computed after the effects of the other variables have been removed.

Table 1. Bivariate relationships of potential predictors of cardiac output

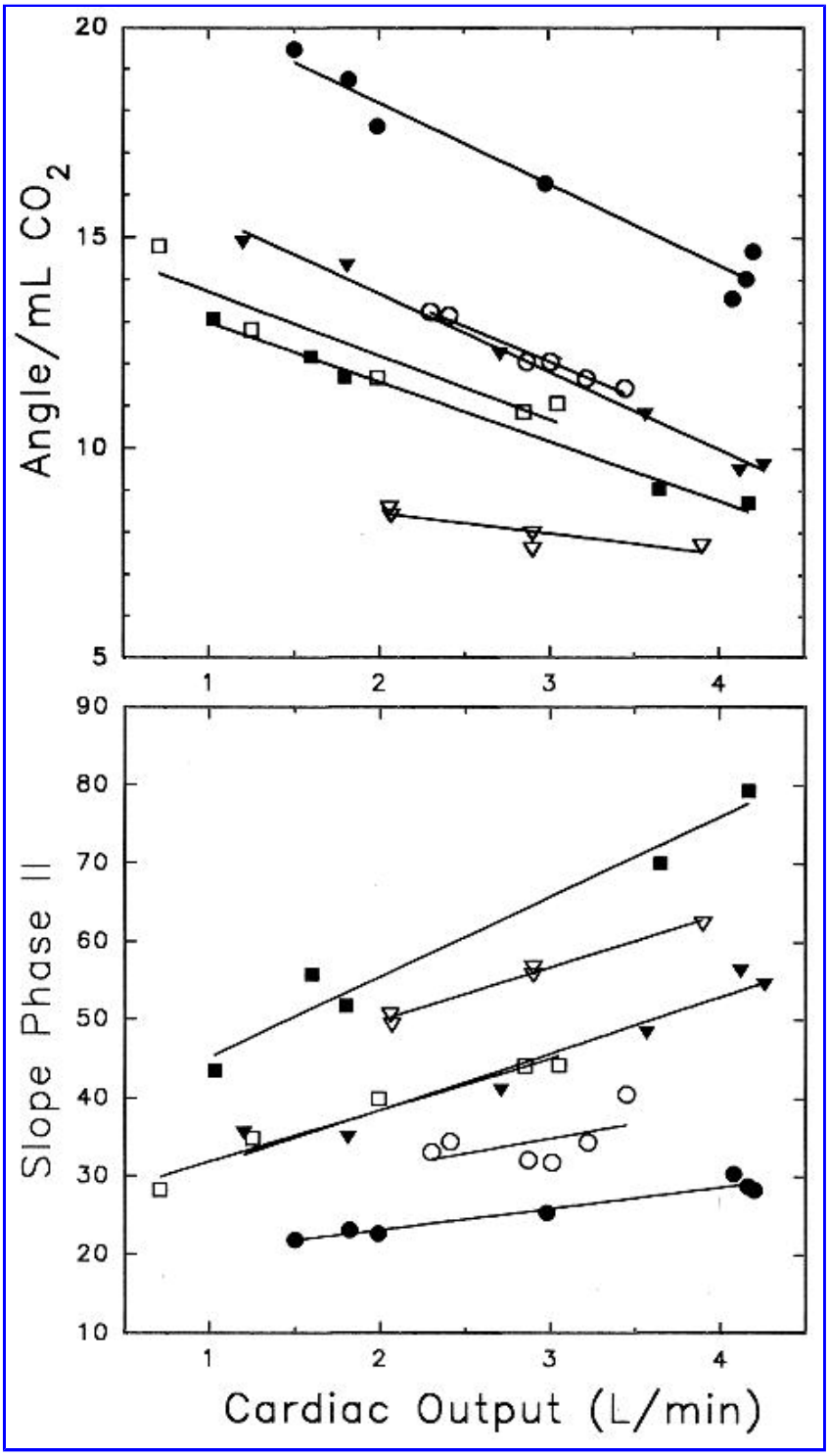

Figure 1. Top: Angle between the slope lines for phases II and III divided by the volume of CO_2 per breath plotted against cardiac output measured by ultrasonic flow probe (r^2 = .92, p < .0001). Individual animals are plotted using different symbols and the individual regression lines are shown. Bottom: Slope of phase II plotted against cardiac output measured by ultrasonic flow probe (r^2 = .79, p < .0001). Individual animals are plotted, using different symbols, and the individual regression lines are shown.

Variable	Slope	Standard Error	*t* Statistic	*p* Value
Angle/mL CO_2	–.408	.047	–8.69	.0000
Slope Phase II	.044	.011	4.09	.0004

Angle/mL CO_2, angle between the slope lines for phases II and III divided by the volume of CO_2 per breath.

Table 2. Coefficients obtained from stepwise regression analysis

The cardiac output measured by ultrasonic flow probe ranged between 0.71 and 4.20 L/min (mean 2.69) and there were no clear systematic errors evident when predicted values were plotted against measured values Figure 2. The bias and precision of the calculated cardiac output were .00 and .23, respectively Figure 3. The limits of agreement were -.45 and .45. The mean percent difference for the cardiac output estimate derived from the single breath CO_2 analysis station was 0.36%. Typical changes in the CO_2 expirogram produced by manipulation of the cardiac output are depicted in Figure 4.

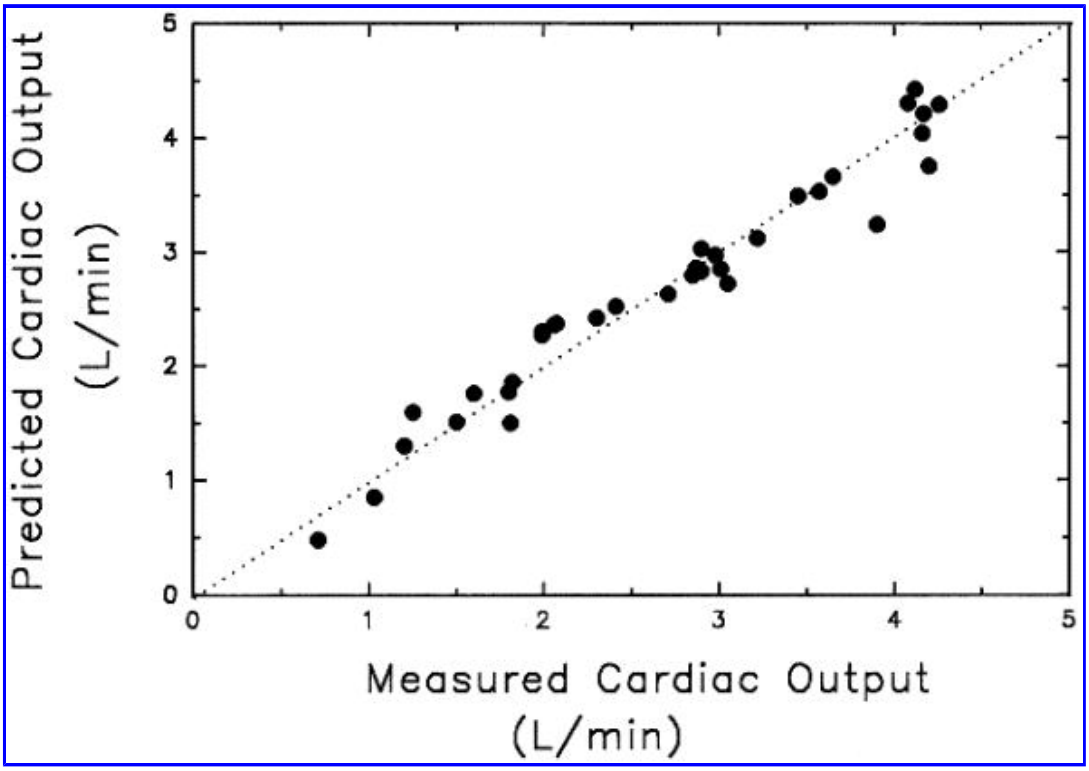

Figure 2. Cardiac output predicted by the multivariate equation plotted against the cardiac output measured by ultrasonic flow probe. Predicted cardiac output = b + ([-.408]X_1 + [.044] X_2), where b is a constant representing the baseline measure of cardiac output, X_1 = angle/mL CO_2, X_2 = slope phase II. Line represents the line of identity, y = x. r^2 = .94, p < .0001.

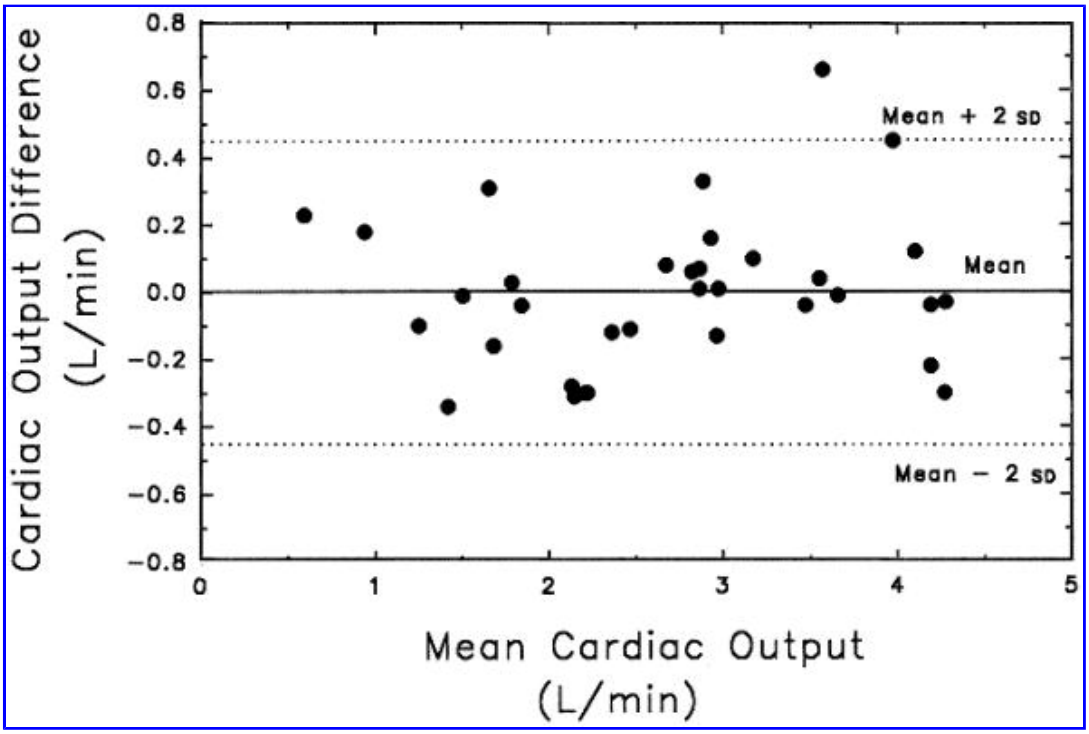

Figure 3. The bias of the predicted cardiac output is plotted against the average cardiac output ([predicted cardiac output--measured cardiac output]/2. The mean difference is .00 and the limits of agreement are -.45 and .45 (mean difference +/- 2 SD).

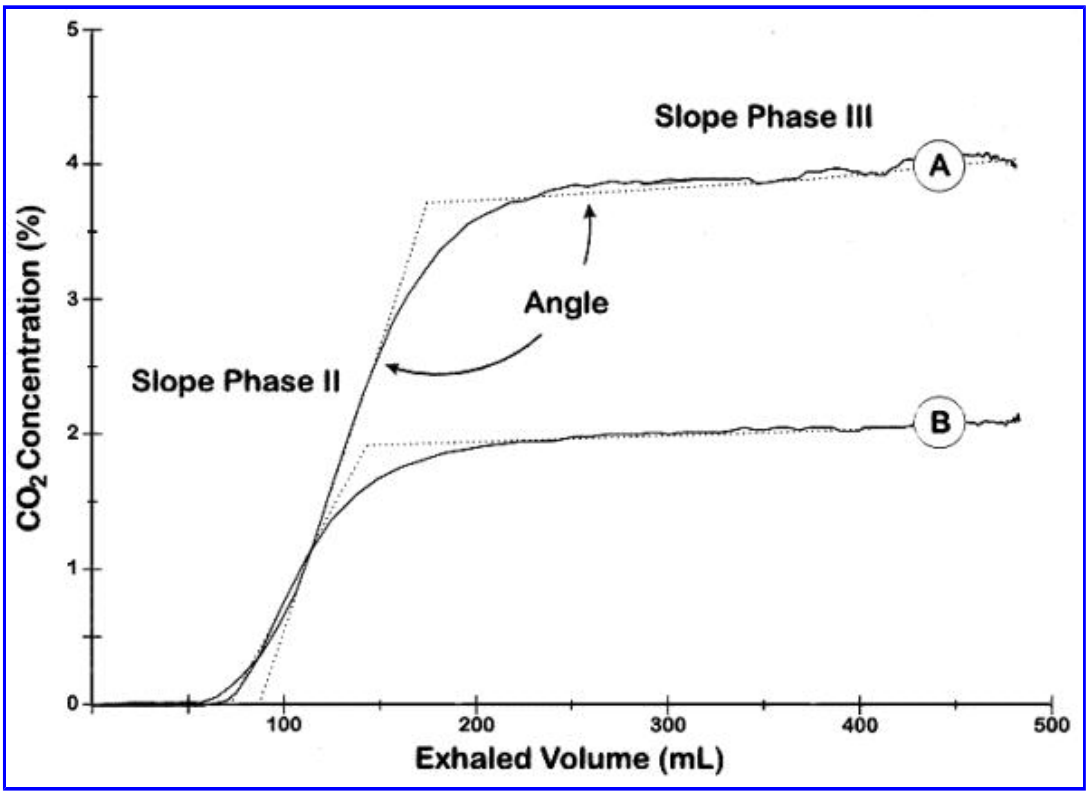

Figure 4. Typical changes observed in the CO_2 expirogram as cardiac output decreases from 2.3 L/min (A) to 0.95 L/min (B). The slope of phase II decreases from 42.3% to 27.0%/L, while the slope of phase III decreases from 1.1% to 0.5 %/L. The angle between the slope

lines for phases II and III increases as a result and when corrected for the volume of CO_2 per breath changes from 11.4 degrees/mL to 22.0 degrees/mL.

DISCUSSION

Our data indicate that analysis of the CO_2 expirogram can yield accurate information about the cardiovascular system. Specifically, two variables derived from a plot of expired CO_2 concentration vs. expired volume predict changes in cardiac output in healthy adult sheep with an adjusted coefficient of determination of .94.

A number of investigators have examined the noninvasive determination of cardiac output, using the modified Fick equation in animals [13,14] and in humans [15-18]. Although mixed venous CO_2 tension may be accurately estimated in patients with ventilation-perfusion abnormalities using partial CO_2 rebreathing techniques [19], the accuracy of the estimation is critically dependent on an adequate period of equilibration, which requires at least 20 secs of partial rebreathing. Capek and Roy [13] demonstrated in healthy dogs that measurement of CO_2 elimination during a 30-sec period of partial rebreathing could predict cardiac output measured by thermodilution with an r^2 of .83. Gedeon and colleagues [14] described a similar system of partial CO_2 rebreathing for 8 mins in animals with induced abnormalities of both gas exchange and cardiovascular function. Their technique predicted cardiac output obtained by thermodilution with an r^2 value of .85 and a precision of 15%. However, accurate application of the Fick principle to quantitate cardiac output does require sampling of arterial blood to measure $PaCO_2$ [20,21] and renders the method more invasive than single breath CO_2 analysis.

Even when $PaCO_2$ is measured directly, the coefficient of determination has varied between .49 in adults with obstructive lung disease studied at rest [20] and .87 in critically ill adults who had timed gas collections over 10 to 15 mins [21]. More recently, Neviere and colleagues [22] examined a partial CO sub 2 rebreathing system with 20 secs of equilibration in adult patients with obstructive lung disease and demonstrated an r^2 value of .92 when compared with thermodilution. Fletcher [23] has demonstrated the utility of single breath CO_2 analysis in patients with abnormalities of pulmonary perfusion and we have been intrigued by the near-continuous, noninvasive information that may be derived by careful analysis of the CO_2 expirogram. Our data suggest that single breath CO_2 analysis offers noninvasive estimation of changes in cardiac output with accuracy that is superior to that obtained with application of the modified Fick equation and partial CO_2 rebreathing.

Several investigators have reported the effects of altered cardiac output or pulmonary blood flow on measured deadspace. Gerst and colleagues [24] noted that the measured deadspace increased as pulmonary blood flow decreased during controlled hemorrhage in dogs. Although specific deadspace compartments were not quantified, the authors [24] speculated that an increased alveolar deadspace was an important indicator of significant changes in pulmonary blood flow. Fletcher and colleagues [6] applied the single breath test for CO_2 to children with congenital heart disease. In patients with cyanotic heart disease and pulmonary hypoperfusion, there was a marked increase in the alveolar deadspace without a consistent change in Phase III slope. In subsequent work, Fletcher [25] noted that the alveolar deadspace to tidal volume ratio reliably predicted PaO_2 and presumably the degree of pulmonary perfusion. Our data suggest that although the alveolar deadspace correlates significantly with cardiac output, other components of the CO_2 expirogram are more powerful

predictors of decreased pulmonary blood flow produced by progressive decreases in venous return. The predictive equation for cardiac output which we derived includes the slope of phase II as well as the angle created by the slope lines for phases II and III (normalized for the volume of CO_2 per breath), which is influenced in part by the slope of phase II. We speculate that the slope of phase II, which represents the transition from airway deadspace to alveolar gas, is the most sensitive indicator of pulmonary inefficiency produced by progressive decreases in pulmonary blood flow.

We acknowledge that our data have several limitations. Changes in cardiac output were produced by successive inflation of an occluder around the inferior vena cava. The changes in the CO_2 expirogram that we observed may not be applicable to the settings of increased cardiac output that arise spontaneously or are produced pharmacologically. Furthermore, our findings in animals with normal lung function may not be applicable to patients with derangements of ventilation-perfusion relationships and increased shunt fraction. Placement of the ultrasonic flow probe around the pulmonary artery required a thoracotomy and the animals were studied with an open hemithorax. This circumstance may have altered ventilation-perfusion relationships particularly in the non-dependent lung. Finally, we allowed a 15-min period for equilibration and stabilization of measured parameters in deriving our predictive equation, which is different from the rapidly changing clinical setting in which precise determination of cardiac output is most helpful.

Single breath CO_2 analysis, and specifically two derived parameters (the angle between the slope lines for phases II and III divided by the volume of CO_2 per breath, and the slope of phase II), offer breath-to-breath information about cardiac output continuously and without the need for an arterial blood gas determination. Prospective application of this technology in the setting of lung injury and rapidly changing physiology will be essential in determining the clinical usefulness of the technique.

REFERENCES

1. Aitken RS, Clarke-Kennedy AE: On the fluctuation in the composition of the alveolar air during the respiratory cycle in muscular exercise. J Physiol 1928; 65:389-411 Bibliographic Links | [Context Link]

2. Fowler WS: Lung function studies. V. Respiratory dead space in old age and in pulmonary emphysema. J Clin Invest 1950; 29:1439-1444 [Context Link]

3. Fowler WS: Lung function studies. II. The respiratory dead space. Am J Physiol 1948; 154:405-416 [Context Link]

4. Fletcher R: The Single Breath Test For Carbon Dioxide. Lund, Berlings, Arlov, 1986 [Context Link]

5. Fletcher R, Jonson B: Deadspace and the single breath test for carbon dioxide during anaesthesia and artificial ventilation. Effects of tidal volume and frequency of respiration. Br J Anaesth 1984; 56:109-119 [Context Link]

6. Fletcher R, Niklason L, Drefeldt B: Gas exchange during controlled ventilation in children with normal and abnormal pulmonary circulation: A study using the single breath test for carbon dioxide. Anesth Analg 1986; 65:645-652 Bibliographic Links | [Context Link]

7. McRae KM, Neufeld GR: Capnogram reflects the severity of acute lung injury in a surfactant

depletion model. Anesthesiology 1993; 79:A291 Bibliographic Links | [Context Link]

8. Ream R, Schreiner MS, Hanson W, et al: Phase III slope of the CO2 expirogram in patients with ARDS. Anesthesiology 1993; 79:A301 Bibliographic Links | [Context Link]

9. Ream RS, Schreiner MS, Neff JD, et al: Volumetric capnography in children: Influence of growth on the alveolar plateau slope. Anesthesiology 1995; 82:64-73 Ovid Full Text | Bibliographic Links | [Context Link]

10. Arnold JH, Thompson JE, Arnold LW: Single breath CO sub 2 analysis: Description and validation of a method. Crit Care Med 1996; 24:96-102 Ovid Full Text | Bibliographic Links | [Context Link]

11. Fletcher R, Jonson B, Cumming G, et al: The concept of deadspace with special reference to the single breath test for carbon dioxide. Br J Anaesth 1981; 53:77-81 [Context Link]

12. Bland JM, Altman DG: Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986; i:307-310 [Context Link]

13. Capek JM, Roy RJ: Noninvasive measurement of cardiac output using partial CO sub 2 rebreathing. IEEE Trans Biomed Eng 1988; 35:653-661 [Context Link]

14. Gedeon A, Krill P, Kristensen J, et al: Noninvasive cardiac output determined with a new method based on gas exchange measurements and carbon dioxide rebreathing: A study in animals/pigs. J Clin Monit 1992; 8:267-278 Bibliographic Links | [Context Link]

15. Russell AE, Smith SA, West MJ, et al: Automated non-invasive measurement of cardiac output by the carbon dioxide rebreathing method: Comparisons with dye dilution and thermodilution. Br Heart J 1990; 63:195-199 Bibliographic Links | [Context Link]

16. Muiesan G, Sorbini CA, Solinas E, et al: Comparison of CO sub 2-rebreathing and direct Fick methods for determining cardiac output. J Appl Physiol 1968; 24:424-429 Bibliographic Links | [Context Link]

17. Franciosa JA: Evaluation of the CO sub 2 rebreathing cardiac output method in seriously ill patients. Circulation 1977; 55:449-455 Bibliographic Links | [Context Link]

18. Clausen JP, Larsen CA, Trap-Jensen J: Cardiac ouput in middle-aged patients determined with CO sub 2 rebreathing method. J Appl Physiol 1970; 28:337-342 Bibliographic Links | [Context Link]

19. Collier CR: Determination of mixed venous CO sub 2 concentration by rebreathing. J Appl Physiol 1956; 9:25-29 [Context Link]

20. Mahler DA, Matthay RA, Snyder PE, et al: Determination of cardiac output at rest and during exercise by carbon dioxide rebreathing method in obstructive airway disease. Am Rev Respir Dis 1985; 131:73-78 Bibliographic Links | [Context Link]

21. Davis CC, Jones NL, Sealey BJ: Measurements of cardiac output in seriously ill patients using a CO sub 2 rebreathing method. Chest 1978; 73:167-172 Bibliographic Links | [Context Link]

22. Neviere R, Mathieu D, Riou Y, et al: Carbon dioxide rebreathing method of cardiac output measurement during acute respiratory failure in patients with chronic obstructive pulmonary disease. Crit Care Med 1994; 22:81-85 Bibliographic Links | [Context Link]

23. Fletcher R: Gas exchange during anaesthesia and controlled ventilation in children with

congenital heart disease. Pediatr Anaesthesia 1993; 3:5-17 [Context Link]

24. Gerst PH, Rattenborg C, Holaday DA: The effects of hemorrhage on pulmonary circulation and respiratory gas exchange. J Clin Invest 1959; 38:524-538 [Context Link]

25. Fletcher R: Relationship between alveolar deadspace and arterial oxygenation in children with congenital cardiac disease. Br J Anaesth 1989; 62: 168-176 Bibliographic Links [Context Link]

Accession Number: 00003246-199610000-00017