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Ventilation, Thermal Noise, and Errors in Cardiac Output Measurements after Cardiopulmonary Bypass

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Background: **The authors observed transient increases in the amplitude of respiratory variations in pulmonary artery blood temperature in many patients after cardiopulmonary bypass (CPB). This increased "thermal noise" may significantly influence measurements of thermodilution cardiac outputs (TDCO) performed during this time.**

Methods: **The authors recorded the peak-to-peak amplitude of respiratory variations in pulmonary artery blood temperature in 15 patients during the first 35 min after CPB. Possible relationships between the amplitude of these variations and the magnitude of temperature differences between commonly monitored body temperature sites (nasopharyngeal, rectal, bladder, and pulmonary artery) were also examined. In ten additional patients, the authors investigated the influence of these increased respiratory variations on TDCO measurements by correlating the maximum variation in three successive TDCO measurements with the peak-to-peak amplitude of the respiratory variations in pulmonary artery blood temperature. Potential error in TDCO measurements caused by these increased respiratory variations in pulmonary artery blood temperature were also examined using model calculations of the effects of respiratory variations in pulmonary artery blood temperature on measured TDCO thermal areas.**

Results: **In the first 15 patients, the mean amplitude of respiratory variations in pulmonary artery blood temperature after CPB (mean ± SEM) were: (1) within 5 min after CPB, 0.037 ± 0.004° C; (2) 10 min after #1, 0.025 ± 0.003° C; (3) 20 min after #1, 0.019 ± 0.003° C; and (4) 30 min after #1, 0.012 ± 0.002° C. There were no significant correlations between the magnitude of the respiratory variation in pulmonary artery blood temperature and the observed temperature differences between body sites. Four patients had pulmonary artery blood temperature variations in excess of the maximum amplitude previously reported in man (0.05° C). In the next ten patients, the maximum variation between three successive TDCO measurements taken at specified times in the respiratory cycle (end inspiration, end exhalation, and 3 s after end exhalation) was significantly correlated with the amplitude of respiratory variations in pulmonary artery blood temperature ($r = 0.83$, $P < 0.001$). Four patients with increased respiratory variations in pulmonary artery blood temperature had variations in TDCO measurements exceeding 2 l/min. Subsequent model calculations demonstrated that the magnitude of potential error in TDCO measurements is dependent on both the amplitude of the respiratory variations in pulmonary artery blood temperature and the baseline cardiac output. On the basis of these thermal area calculations, potential errors of 15–50% could be caused by respiratory variations in pulmonary artery blood temperature > 0.05° C.**

Conclusions: **The authors concluded that respiratory variations in pulmonary artery blood temperature are transiently increased in many patients after CPB, and that this increased "thermal noise" may cause significant errors in TDCO measurements. (Key words: Lungs: ventilation. Measurement techniques: thermodilution cardiac output. Temperature: blood; cardiopulmonary bypass.)**

THERMODILUTION cardiac output measurements (TDCO) taken at specific times during the respiratory cycle (*e.g.*, measurements at end expiration *versus* measurements at end inspiration) are known to vary by 5–20%.[1–3] Some of this measurement variation results from true changes in cardiac output resulting from the cyclical mechanical effects of respiration on ventricular preload and afterload.[1,3] Although less frequently discussed, measurement errors caused by small cyclical variations in pulmonary artery blood temperature with respiration may be another factor in these TDCO variations.[2,4–7] Respiratory variations in pulmonary artery blood temperature result from differences in the blood temperature in the inferior and superior vena cava, coupled with changes in the proportion of venous return coming from each cava during the respiratory cycle.[8–12] With respect to TDCO measurements, these respiratory variations in pulmonary artery blood temper-

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ature represent "thermal noise." This noise interferes with measurement of the temperature changes caused by injection of the thermal indicator (*e.g.*, 10 ml of room temperature normal saline) used to measure TDCOs. Under normal circumstances, the peak-to-peak amplitude of this respiratory variation in humans is only 0.01–0.02° C.[7] The potential error caused by this magnitude of thermal noise in humans is relatively small. However, respiratory-induced temperature variations up to 0.05° C have been previously reported.[6] The potential error caused by respiratory variations in pulmonary artery blood temperature of this magnitude in humans has not been systematically studied.

We observed transient increases in the magnitude of respiratory variations in pulmonary artery blood temperature in many patients after cardiopulmonary bypass (CPB). The magnitude of these variations in pulmonary artery blood temperature frequently exceeded the upper limit previously reported in humans (0.05° C).[6] This increased "thermal noise" appeared to cause large variations in TDCO measurements. The purposes of this study were to: (1) quantitate the amplitude and time course of these respiratory variations in pulmonary artery blood temperature in patients after CPB; (2) determine whether differences between nasopharyngeal temperature, "core" temperature (rectal or bladder temperature), and mean pulmonary artery blood temperature could identify patients with increased respiratory variations in pulmonary artery blood temperature; and (3) evaluate the influence of these increased respiratory variations in pulmonary artery blood temperature on TDCO measurements.

Materials and Methods

Study A

After approval by our Institutional Review Board, we collected data from 15 patients undergoing cardiac surgical procedures. Data collected in this initial study were obtained to examine the amplitude of respiratory variations in pulmonary artery blood temperature after CPB, and to relate the amplitude of these variations to the difference in temperatures between different body sites. Data consisted of strip-chart recordings of the respiratory variations in pulmonary artery blood temperature (Abbott Oximetrix 3 cardiac output computer, Abbott pulmonary artery catheter #P7110EP8H; Mountain View, CA), along with simultaneous recordings of mean pulmonary artery blood temperature, nasopharyngeal temperature, and rectal/bladder temperature (one or the other, as determined by surgeon's preference for "core temperature" monitoring; n = 7 for rectal, n = 8 for bladder). At our institution, patients are typically cooled to a core temperature of 28° C shortly after the onset of CPB, and then rewarmed to a core temperature of 36–38° C before separation from CPB. Ventilator settings established by the attending anesthesiologist (rate of 6–10 breaths/min, and tidal volumes of 10–15 ml/kg) were also recorded. These data were collected at the following times: P1, within 5 min after discontinuation of CPB; P2, 10 min after sample P1; P3, 20 min after sample P1; and P4, 30 min after sample P1. The peak-to-peak amplitude of the respiratory variation in pulmonary artery blood temperature was calculated from the strip-chart recordings. The amplitudes of pulmonary artery blood temperature variation at all four sampling points were analyzed using repeated-measures ANOVA, followed by specific comparison of values at P2, P3, and P4 with values at P1 using a paired *t* test with Bonferroni correction. The amplitudes of pulmonary artery blood temperature variation at sample time P1 were correlated with the differences between mean pulmonary artery blood temperature, nasopharyngeal temperature, and rectal/bladder temperature using Pearson's product moment correlation. For all statistical analyses, a P value < 0.05 was considered significant. Values are reported as mean ± SEM.

Study B

Data collected in study B were obtained to examine the possible role of increased respiratory variations in pulmonary artery blood temperature in causing the increased variability in TDCO measurements that we observed in patients after CPB. With approval of our Institutional Review Board, the following data were collected in ten patients: (1) strip-chart recordings of the respiratory variations in pulmonary artery blood temperature and (2) three TDCO measurements taken at specified times in the ventilatory cycle. The peak-to-peak amplitude of the respiratory variation in pulmonary artery blood temperature (denoted as $\Delta PABT_{max-min}$) was determined from the strip-chart recordings. The TDCO measurements were taken while the patient's lungs were mechanically ventilated, and were initiated at the following times in the ventilatory cycle (one measurement at each time): end inspiration, end exhalation (*i.e.*, return of ventilator bellows to its initial position), and 3 s after end exhalation. For each set of three TDCO measurements, the maximum variation of

the measurements was calculated as the difference between the maximum TDCO measurement and the minimum TDCO measurement (denoted as $\Delta TDCO_{max-min}$). $\Delta PABT_{max-min}$ and $\Delta TDCO_{max-min}$ were measured in each patient at the following sample times: P1, within 5 min after discontinuation of CPB; and P4, 30–35 min after CPB. Using the data from all patients, $\Delta TDCO_{max-min}$ was correlated with $\Delta PABT_{max-min}$ using Pearson's product moment correlation.

Theoretical Calculations

To further investigate the influence of respiratory variations in pulmonary artery blood temperature on TDCO measurements, we performed model calculations based on changes in "thermal areas." The potential errors in TDCO measurements resulting from respiratory variations in pulmonary artery blood temperature are caused by the superimposition of these temperature fluctuations on the temperature change caused by injection of the thermal indicator used to measure the TDCO. Injection of thermal indicator causes a transient decrease in pulmonary artery blood temperature. This change in pulmonary artery blood temperature, when plotted as a function of time, produces a thermodilution (TD) curve (fig. 1, top, panel A). The derived TDCO measurement is inversely proportional to the area under this TD curve, as determined by the modified Stewart-Hamilton equation[6]:

$$TDCO = \frac{(\text{mean blood temperature} - \text{indicator temperature})}{\text{TD curve area}} \times \text{computation constant.}$$

The computation constant takes into account the indicator volume, the specific gravity of the indicator and blood, the specific heat of the indicator and blood, and a measure of heat gain by the indicator as it passes through the catheter. The "zero" reference level used for calculation of this TD curve area is the value of the pulmonary artery blood temperature measured at the start of the TDCO measurement. This TDCO calculation assumes that the "background" pulmonary artery blood temperature is stable throughout the measurement period (*i.e.*, that any change in blood temperature is caused by the injected thermal indicator). Similar to the situation previously described with peripheral intravenous volume infusions,[12] any change in "background" pulmonary artery blood temperature will be superimposed on the temperature change caused by the thermal indicator. The resultant error in TDCO measurements is caused by the effect of this superimposed temperature change on the calculated area of the TD curve.

The effect of respiratory variations in pulmonary artery blood temperature on the measured TD curve area will depend on: amplitude and frequency of the respiratory variations, timing of injection of thermal indicator, and duration of the TD curve. The amplitude of the respiratory variations will determine how much the TD curve is distorted. The timing of injection of thermal indicator will influence the location of the zero reference level used for the TD curve area calculation. Depending on the location of the zero reference level, respiratory variations in background pulmonary artery blood temperature may either increase (fig. 1, top) or decrease (fig. 1, bottom) the area under the TD curve. Maximum error will occur when the TD curve zero reference level is taken at the peak or nadir of the respiratory variation in pulmonary artery blood temperature. When the zero reference level is at the peak (fig. 1, top), the subsequent respiratory change in background pulmonary artery blood temperature will decrease the measured TD curve area by an amount approximately equal to the negative thermal area caused by the respiratory variation in pulmonary artery blood temperature (sum of the shaded areas denoted 1 and 2 in fig. 1, top, panel B). This decrease in the measured TD curve area will cause an increase in the calculated cardiac output. When the zero reference level is at the nadir (fig. 1, bottom), the subsequent respiratory change in background pulmonary artery blood temperature will increase the measured TD curve area by an amount approximately equal to the positive thermal area caused by the respiratory variation in baseline pulmonary artery blood temperature (sum of the shaded areas denoted 3 and 4 in fig. 1, bottom, panel B). This increase in the measured TD curve area will cause a decrease in the calculated cardiac output. Note that, because the respiratory variations in pulmonary artery blood temperature are cyclical and approximately symmetrical, the maximum potential area change caused by these respiratory variations (*i.e.*, the sum of both the positive and negative area changes in fig. 1)

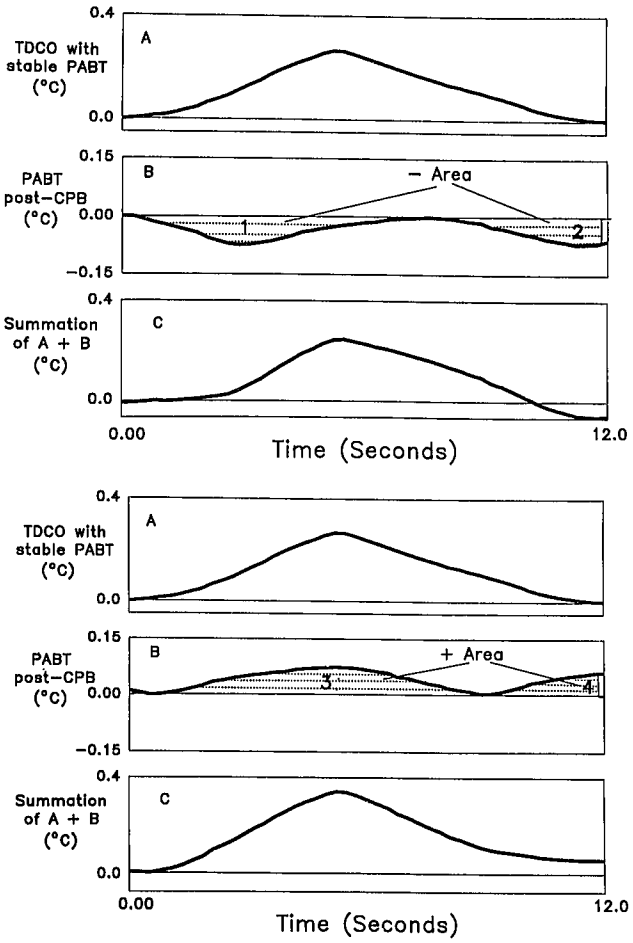

Fig. 1. (*Top*) Thermodilution cardiac output (TDCO) curve with stable baseline (*panel A*). Effect of respiratory variation in pulmonary artery blood temperature (PABT) on baseline curve (*panel B*). Addition of curves in panels A and B (*panel C*). Note, in this example, that the zero reference level for changes in PABT is at the peak of the respiratory temperature variations. Addition of curves A and B thus causes a decrease in the area of the resultant TDCO curve (*panel C*). See text for further explanation. (*Bottom*) TDCO curve with stable baseline (*panel A*). Effect of respiratory variation in PABT on baseline curve (*panel B*). Addition of curves in panels A and B (*panel C*). Note, in this example, that the zero reference level for changes in PABT is at the nadir of the respiratory temperature variations. Addition of curves A and B thus causes an increase in the area of the resultant TDCO curve (*panel C*). See text for further explanation.

is equal to the amplitude of the respiratory variation multiplied by the duration of the TD curve.

As a first approximation, the maximum potential error in TDCO measurements caused by the respiratory variation in pulmonary artery blood temperature can be calculated based on this maximum potential area change. Note that, because the TD curve area term appears in the denominator of the TDCO equation, the effect of a given area change on the calculated TDCO is not simply additive, but will vary depending on the cardiac output. Because a high cardiac output is associated with a small TD curve area, a given change in TD curve area (caused by respiratory temperature variations) will have a relatively greater effect in a patient with a high cardiac output. Conversely, a given change in TD curve area will have a relatively lesser effect in a patient with a low cardiac output (because of the larger TD curve area). To illustrate this effect of changes in cardiac output, hypothetical model calculations of maximum potential errors in TDCOs were calculated for a range of cardiac outputs (3–7 l/min). These model calculations are based on injections of 10 ml of room temperature injectate (22° C) into patients with a mean blood temperature of 36° C. The value of the computation constant for the Abbott oximetric catheter using these parameters is 0.578. By rearranging the above TDCO equation, the respective TD curve areas for TDCO values of 3, 4, 5, 6, and 7 l/min are 2.89, 2.17, 1.73, 1.44, and 1.24° C-s, respectively. As explained above, the maximum potential area change caused by respiratory variations in pulmonary artery blood temperature (*i.e.*, the sum of positive and negative area changes in fig. 1) is equal to the amplitude of the respiratory variation multiplied by the duration of the TD curve (*e.g.*, 0.05° C × 10 s = 0.5° C-s). For model calculations, a value of 10 s was selected for the duration of an average TD curve. The effect of respiratory variations in pulmonary artery blood temperature ranging between 0 and 0.07° C were assessed, such that the resultant maximum potential area change varied between 0.0 and 0.7° C-s. The distribution of this maximum potential area change between positive and negative areas (fig. 1, panel B) was determined by the average value for this distribution in the patient data of study A at time P1. The resultant maximum potential error in TDCO values was calculated by summing the errors caused by adding the positive areas and subtracting the negative areas from the TD curve areas listed above for TDCO values of 3, 4, 5, 6, and 7 l/min (see results).

Results

Study A

The pulmonary artery blood temperature and TD curves from one of the study patients at sample times

P1 and P4 are shown in figure 2. Note the large amplitude of the respiratory variation in pulmonary artery blood temperature at sample time P1, and resultant distortion of the TD curve. The amplitude of the respiratory variation in pulmonary artery blood temperature returns to a more normal range by sample time P4.

The peak-to-peak amplitude of respiratory variation in pulmonary artery blood temperature showed considerable variation between patients (*e.g.*, range at P1 0.008–0.068° C). Four of these 15 patients had respiratory variations in pulmonary artery blood temperature that exceeded the maximum amplitude previously reported in humans (0.05° C).[6] The average amplitude and range of the respiratory variation in pulmonary artery blood temperature for the four measurement periods are shown in table 1. All patients showed maximal variation in pulmonary artery blood temperature at either P1 (11/15) or P2 (4/15), followed by decreasing magnitudes at P3 and P4. Repeated-measures ANOVA showed a significant difference between values at the four sampling points ($P < 0.001$). Values at P1 were significantly higher than values at P2, P3, and P4 by paired *t* tests with Bonferroni correction (table 1).

Although there was a trend toward increased amplitude of respiratory variations in pulmonary artery blood temperature at time P1 with increasing values of the difference between nasopharyngeal and bladder/rectal temperature (fig. 3), this trend did not reach statistical significance (variation amplitude *versus* the temperature difference between the following: nasopharyngeal and rectal temperatures (fig. 3, open circles), $P = 0.08$, $r^2 = 0.50$; nasopharyngeal and bladder temperatures (fig. 3, closed circles), $P = 0.88$; and nasopharyngeal and corresponding bladder or rectal temperatures ($P = 0.14$, $r^2 = 0.16$; fig. 3). There were also no consistent correlations between the amplitude of the respiratory variations in pulmonary artery blood temperature and the temperature differences between: (1) nasopharyngeal and pulmonary artery temperatures ($P = 0.45$) and (2) bladder/rectal and pulmonary artery temperature ($P = 0.18$).

Because ventilator settings were determined by the attending anesthesiologist and not by study protocol, we retrospectively examined relationships between the amplitude of respiratory variation in pulmonary artery blood temperature at time P1 and the following ventilatory parameters: tidal volume, peak inspiratory pressure, and respiratory rate. There were no significant correlations between the amplitude of temperature variation and any of these ventilatory parameters (amplitude *versus* tidal volume, $P = 0.35$, $r = 0.26$; amplitude *versus* peak inspiratory pressure, $P = 0.37$, $r = 0.25$; and amplitude *versus* respiratory rate, $P = 0.71$, $r = 0.1$).

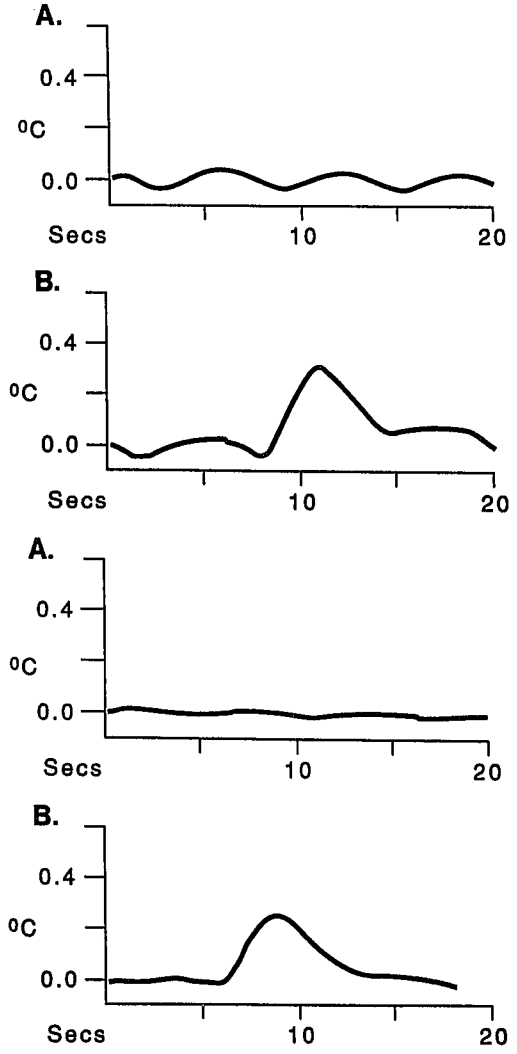

Fig. 2. (*Top*) Graph of pulmonary artery blood temperature (PABT; *panel A*) and thermodilution cardiac output (TDCO) curve (*panel B*) in a patient shortly after cardiopulmonary bypass (CPB; sample time P1). Note the increased magnitude of the respiratory variations in PABT. These large respiratory variations caused significant distortion of the TDCO curve. (*Bottom*) Graph of PABT (*panel A*) and TDCO curve (*panel B*) in the same patient 30 min after CPB (sample time P4). Note that the magnitude of respiratory variations in PABT is significantly reduced compared with the *top*. The TDCO curve is only minimally distorted by this residual respiratory variation in PABT.

Table 1. Respiratory Variation in Pulmonary Artery Blood Temperature after Cardiopulmonary Bypass

	Measurement Period			
	P1	P2	P3	P4
Mean variation ± SEM (° C)	0.037 ± 0.004	0.025 ± 0.003*	0.019 ± 0.003†	0.012 ± 0.002†
Range (° C)	0.008–0.068	0.008–0.043	0.008–0.043	0.004–0.026

* Significantly different from value at P1 by paired *t* test with Bonferroni correction; $P < 0.05$.

† Significantly different from value at P1 by paired *t* test with Bonferroni correction, $P < 0.005$.

Study B

$\Delta TDCO_{max-min}$ was significantly greater at sample time P1 (2.25 ± 0.28 l/min; fig. 4, closed circles) compared with sample time P4 (0.91 ± 0.16 l/min; fig. 4, open circles; $P < 0.01$ by paired *t* test). This significant increase in $\Delta TDCO_{max-min}$ at time P1 *versus* time P4 was accompanied by a significant increase in the magnitude of respiratory variation in pulmonary artery blood temperature ($\Delta PABT_{max-min}$) at sample time P1 (0.052 ± 0.007° C) compared with sample time P4 (0.023 ± 0.003° C, $P < 0.01$ by paired *t* test). Using the data from both sample times P1 and P4 (fig. 4), we found a significant correlation between $\Delta TDCO_{max-min}$ and $\Delta PABT_{max-min}$ ($r = 0.83$, $P < 0.001$). The slope of the regression line between these two variables was 37 $l \cdot min^{-1} \cdot {}^{\circ} C^{-1}$ (least-squares linear regression; $\Delta TDCO_{max-min} = 0.19 + (37.3 \times \Delta PABT_{max-min})$). As explained below, this slope must be considered in the context of the average cardiac output (5.74 l/min) of the patients from whom these data were obtained.

Theoretical Calculations

Calculation of actual positive and negative thermal areas (fig. 1, top, panel B, and bottom, panel B) from the strip-chart recordings of pulmonary artery blood temperatures at sample time P1 from the 15 patients in study A revealed an average ratio of positive area to negative area of 1.43 ± 0.12 to 1 (range 0.82–2.25). Based on this ratio, the positive area for model calculations was set equal to 59% of the maximum potential area change caused by the respiratory variation in pulmonary artery blood temperature (*e.g.*, for a respiratory variation of 0.05° C and TD curve duration of 10 s, the maximum potential area change would be 0.05° C × 10 s = 0.5° C s; the positive area change would be 0.5° C s × 0.59 = 0.295° C s; and the negative area change would be 0.5° C s × (1 − 0.59) = 0.205° C s). The results of our model calculations, based on potential changes in measured "thermal area," are shown in figure 5. The magnitude of potential error in TDCO measurements is seen to increase substantially both

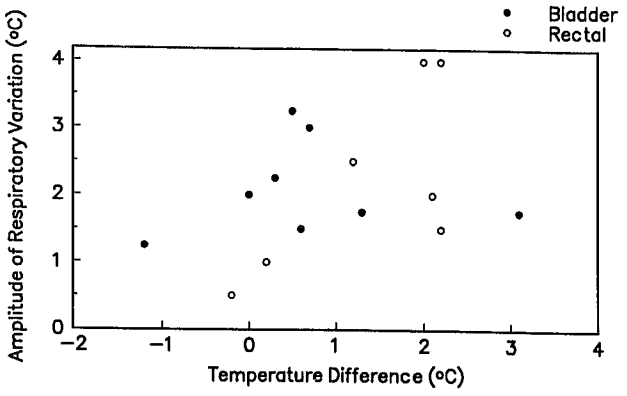

Fig. 3. Peak-to-peak amplitude of the respiratory variation in pulmonary artery blood temperature plotted against the difference between nasopharyngeal temperature and "core" (bladder or rectal) temperature. Data from patients who were monitored with bladder temperature are indicated by closed circles; data from patients who were monitored with rectal temperature are indicated by open circles. All data are from the measurement period P1.

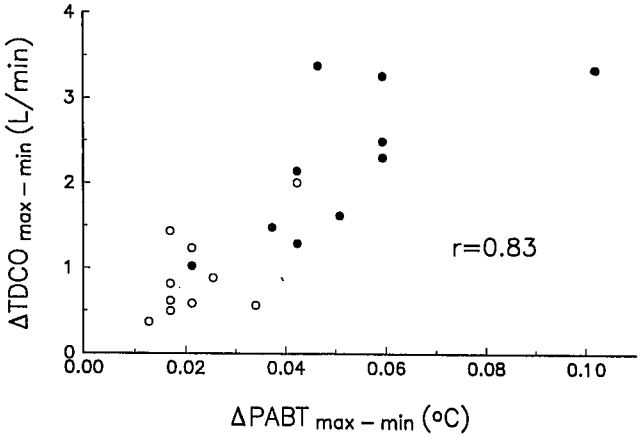

Fig. 4. Variation in thermodilution cardiac output measurements taken at three points in the ventilatory cycle ($\Delta TDCO_{max-min}$) *versus* the peak-to-peak amplitude of respiratory variation in pulmonary artery blood temperature ($\Delta PABT_{max-min}$). See text for explanation.

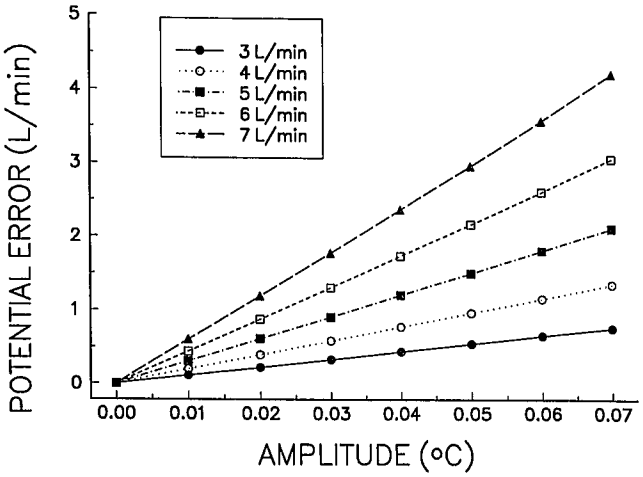

Fig. 5. Theoretical calculations of maximum potential error in thermodilution cardiac output measurements caused by respiratory variations in pulmonary artery blood temperature. Potential error is seen to increase with increases in the amplitude of respiratory temperature variations in pulmonary artery blood temperature, as well as with increases in cardiac output. See text for further explanation.

with increases in the amplitude of respiratory variations in pulmonary artery blood temperature and with increases in cardiac output. In particular, note that the slope of a regression line between maximum potential error and the amplitude of respiratory variations in pulmonary artery blood temperature would be expected to vary as a function of cardiac output. For comparison with the data obtained in study B, we also performed model calculations using a cardiac output of 5.74 l/min (*i.e.*, the average cardiac output of the patients in this latter study). The slope of this model regression line was 40 $l \cdot min^{-1} \cdot ° C^{-1}$, which is very similar to the value of 37 $l \cdot min^{-1} \cdot ° C^{-1}$ obtained from the data in study B (fig. 4).

Discussion

Prior studies have documented significant effects of respiratory variations in pulmonary artery blood temperature on TDCO measurements in dogs.[4,5] Respiratory variations in pulmonary artery blood temperature of up to 0.086° C have been reported in the dog.[5] These large temperature variations introduce significant potential errors in TDCO measurements. The effect of respiratory variations in pulmonary artery blood temperature on TDCO measurements in humans has received little attention. This lack of attention may relate to the fact that respiratory variations in pulmonary artery blood temperature in humans are usually of lesser magnitude than those recorded in the dog. Although we were unable to find any systematic study of respiratory variations in pulmonary artery blood temperature in humans, Ganz suggests a normal range of 0.01–0.02° C in his review of thermodilution measurement techniques.[7] The potential error caused by respiratory variations of this magnitude is quite small.

Our results document that patients subjected to CPB may show a transient increase in the magnitude of respiratory variations in pulmonary artery blood temperature, and that this increased variation can cause significant errors in TDCO measurements. Approximately 30% of patients (4/15 in study A, 4/10 in study B) exhibited variations exceeding the maximum amplitude previously reported in humans (0.05° C).[6] This increased respiratory variation in pulmonary artery blood temperature was usually maximal when measured during the first 5 min after CPB, although, in 4 of 15 patients in study A, respiratory variation was not maximal until the second measurement (approximately 10 min after CPB). Respiratory variation in pulmonary artery blood temperature was significantly decreased by 30 min after CPB. The magnitude of respiratory variation at this final measurement period was within the "normal" range suggested by Ganz (0.01–0.02° C)[7] in 18 of 25 patients.

This transient increased variation in pulmonary artery blood temperature is most likely caused by uneven rewarming of body regions on CPB. This would result in a greater temperature differential between blood in the inferior and superior vena cava, and, hence, greater fluctuation in pulmonary artery blood temperature during the ventilatory cycle when the proportion of venous return form each cava is altered. We investigated whether examination of temperature differences between body sites commonly monitored during CPB (nasopharyngeal temperature as an index of rapidly perfused tissues, and rectal/bladder temperature as an index of slowly perfused tissues), or the differences between these body temperatures and mean pulmonary artery blood temperature, would be able to identify patients with large variations in pulmonary artery blood temperature. Although there was a trend toward increasing variation amplitude with increasing values of the difference between nasopharyngeal and bladder/rectal temperature (fig. 3), this trend did not reach statistical significance. Although expanding our study to include more patients may document a significant

trend, the amount of scatter that is present in the available data indicates that this relationship would still have limited clinical utility for predicting which patients have large respiratory variations.

Our inability to document a clinically useful relationship between variation amplitude and differences in recorded body temperatures may be caused by: (1) a poor correlation between these temperature differences and the temperature differential between blood in the inferior and superior vena cava and (2) patient differences in other factors influencing respiratory variations in pulmonary artery blood temperature, which limited our ability to detect a correlation across patients. With regard to the latter explanation, other factors potentially influencing respiratory variations in pulmonary artery blood temperature include patient differences in pulmonary compliance, thoracic cage/lung geometry, central blood volume, and ventilatory parameters. Of these factors, the only one previously studied is ventilatory parameters. In individual subjects, changes in ventilatory parameters will influence the amplitude of respiratory temperature variations (*e.g.*, in a given patient, a decrease in tidal volume will decrease the variation amplitude).[8-10] However, for our patient group (using ventilatory parameters within the normal range), we were unable to demonstrate any significant relationship across patients for variation amplitude *versus* various ventilatory parameters.

In view of the above findings, the best way to identify patients with increased respiratory variations is to use TDCO computers that display the TDCO curve. By starting a TDCO measurement in the normal fashion, but then not actually injecting any thermal indicator, the computer will display a curve corresponding to background pulmonary artery temperature. This curve of pulmonary artery temperature can then be examined for cyclical variations occurring at the respiratory frequency.

These increased respiratory variations in pulmonary artery blood temperature may cause significant errors in TDCO measurements. Results from study B demonstrated a significant relationship between $\Delta PABT_{max-min}$ (peak-to-peak amplitude of respiratory variation in pulmonary artery blood temperature) and $\Delta TDCO_{max-min}$ (difference between the maximum and minimum value of three consecutive TDCO measurements obtained at defined points during the respiratory cycle; fig. 4). In the immediate post-CPB period, four of ten patients showed variations in consecutive TDCO measurements exceeding 2 l/min. Both the respiratory variations in pulmonary artery blood temperature and the variations in TDCOs decreased significantly over the next 30 min. The residual variation in TDCOs at 30 min is probably caused by a combination of the mechanical effects of ventilation on venous return, as well as a smaller influence of residual respiratory "thermal noise."

Theoretical calculations based on potential changes in TD curve area were carried out to further delineate the possible role of increased respiratory temperature variations in causing the increased variability of TDCO measurements that we observed after CPB. These calculations (fig. 5) predict that increased respiratory variations in pulmonary artery blood temperature can be a significant source of error. These calculations also illustrate the influence of both "signal" amplitude (temperature change caused by injection of thermal indicator) and "noise" amplitude (respiratory temperature variations) on the resultant potential error. An increase in cardiac output (reduced signal amplitude) or an increase in respiratory temperature variations (increase noise amplitude) will decrease the signal-to-noise ratio and increase the potential error. On the basis of these TD curve area calculations, potential errors of 15–50% could be caused by respiratory variations in pulmonary artery blood temperature $> 0.05°$ C.

Note that, for automated TDCO measurements, the distal portion of the TD curve may be exponentially extrapolated from the initial downsloping portion of the TD curve. Our model estimation of "maximum" potential error based on changes in thermal areas does not account for this process. Such exponential extrapolation could decrease the influence of respiratory variations in pulmonary artery blood temperature during the distal portion (*i.e.*, the extrapolated portion of the TD curve), and decrease the influence of these variations on TDCO measurements. More importantly, however, distortion of the initial portion of the TD curve by respiratory variations in pulmonary artery blood temperature could lead to erroneous extrapolation of the distal portion of the TD curve, and increase the associated error. This additional error would be critically dependent on injection timing and the specific algorithm used for curve extrapolation. For these reasons, our model calculations based on changes in actual thermal area (rather than curve extrapolations) should only be considered as an approximation of potential clinical errors associated with respiratory variations in pulmonary artery blood temperature.

Strategies that may be used to reduce the error in TDCO measurements caused by this increased respiratory variation in pulmonary artery blood temperature include: use of iced injectate, timing injections of thermal indicator to a specific point in the respiratory cycle, and alteration of ventilation during TDCO measurements. Use of iced injectate, rather than room-temperature injectate, for TDCO measurements should reduce the error caused by respiratory thermal noise *via* improvement in the signal-to-noise ratio (the "signal" being the temperature curve caused by injection of the thermal indicator).[13] For identical cardiac outputs, the area under the TD curve will be approximately twice as large when using iced injectate compared with room-temperature injectate. This increased thermal indicator area would reduce the associated error by approximately 50%. Although most previous studies in humans have indicated no decrease in TDCO measurement accuracy using 10 ml of room temperature injectate *versus* 10 ml of iced injectate (and two of these studies were in hypothermic patients), none of these studies were performed in the immediate post-CPB period.[14-17]

Whether injection of thermal indicator should be performed at a specific point in the respiratory cycle, or at several different points in the respiratory cycle, is controversial.[1-3,18,19] Measurements timed to a specific point in the respiratory cycle show less variation, but may be more subject to systematic bias. For human studies, this bias has been attributed to the effects of mechanical ventilation on true cardiac output.[1,3,18] With respect to errors caused by increased respiratory variations in pulmonary artery blood temperature (as demonstrated in the current study), using injections timed to the respiratory cycle will not eliminate the potential for error, but would potentially reduce the variation between successive measurements, because each measurement would be exposed to a similar error (*i.e.*, a "systematic" error). The maximum amplitude of the potential error would also be reduced, because the error should always be either positive or negative (rather than potentially bidirectional, as may occur with random injections). As the amplitude of respiratory variations in pulmonary artery blood temperature decreases with time after CPB, this systematic error in TDCOs would decrease. Although this results in a more accurate measurement, the resultant reduction in systematic error could produce an artifactual "trend" in the TDCO measurements.

The most effective strategy for reducing the error caused by increased respiratory variations in pulmonary artery blood temperature is to hold ventilation before and during the TDCO measurement. Because the effect of respiration on the fluctuations in pulmonary artery blood temperature does not disappear immediately with cessation of ventilation (*i.e.*, there is a phase lag of up to 5 s for stabilization of pulmonary artery blood temperature when the ventilator is halted at end exhalation), ventilation should be held for at least 5 s before initiation of the TDCO measurement. Although this strategy will eliminate potential errors from respiratory thermal noise, it requires holding ventilation for 15–30 s for each TDCO measurement. This maneuver may be potentially dangerous in an unstable patient immediately after CPB, and introduces the potential for possible serious operator error if the operator is distracted and neglects to resume ventilation in a timely fashion. Although the error in TDCO measurements will not be completely eliminated, potential error can be reduced by altering the ventilatory parameters. In a given patient, decreasing the tidal volume will decrease the amplitude of the respiratory variation in pulmonary artery blood temperature.[8-10] When using TDCO monitors that are capable of displaying the TDCO curves, the extent of reduction in the respiratory variation in pulmonary artery blood temperature with reduction in tidal volume can be assessed by examination of TDCO curves.

A final strategy for reduction of the error caused by the respiratory thermal noise is to use measurement algorithms that adjust for these noise effects. Potential algorithms include those previously described by Johnson and Norman[20,21] and Yelderman.[22]

Linear drift in baseline pulmonary artery blood temperature has recently been documented as another source of error in TDCO measurements in the post-CPB period.[23] Although this source of error is also related to uneven rewarming of body regions on CPB, it should not be confused with the results of the current study. Baseline drift should have minimal effects on the variability of TDCO measurements taken in close proximity to each other, but will affect TDCO measurement accuracy. Although errors caused by respiratory variations in pulmonary artery blood temperature can be eliminated by holding ventilation, errors caused by baseline drift cannot. Both types of error, however, will decrease with time after CPB as temperatures are equalized among body regions.

This study was performed using a commercially available cardiac output measuring system (Abbott Oximetrix 3 cardiac output computer and Abbott

#P711OEP8H pulmonary artery catheters). The accuracy and response time of this system for measuring changes in pulmonary artery temperature was not assessed before each study, because such calibration is not recommended as being necessary for usual clinical applications. The response time of this system for measuring temperature changes could influence the magnitude of detected respiratory variations in pulmonary artery temperature, and, hence, different results may be obtained with systems having significantly different response times. Currently, there are no established standards for thermal measurement characteristics of thermodilution cardiac output measuring systems. However, most manufacturers of pulmonary artery catheters purchase their thermistors from a single source,§ and, thus, most catheters should have similar thermal measurement characteristics.

In summary, patients subjected to CPB may show transient increases in the amplitude of respiratory variations in pulmonary artery blood temperature, and these increased variations may cause significant errors in TDCO measurements. Temperature differences between nasopharyngeal temperature, rectal/bladder temperature, and mean pulmonary artery blood temperature are not reliable indicators of the amplitude of these respiratory variations. When using TDCO monitors that display the TDCO thermal curves, patients with increased respiratory variations can be identified by examinations of displayed temperature curves for increased temperature fluctuations at the respiratory frequency. The magnitude of potential error from increased pulmonary artery blood temperature variations can be reduced by using iced injectate, and by timing injections of thermal indicator to a specific point in the respiratory cycle. However, the only reliable method for prevention of these errors is to hold patient ventilation before and during TDCO measurements.

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