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Carbon Dioxide Elimination during Total Cardiopulmonary Bypass in Infants and Children

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The authors measured the rate of carbon dioxide elimination ($\dot{V}CO_2$) in 25 pediatric patients (age 2 days to 9 yr) during total cardiopulmonary bypass at average venous blood temperatures ranging from 19.5 to 35.9° C. A multiplexed mass spectrometer was connected to the gas inlet and exhaust ports of the bubble oxygenator, and the gas-phase Fick principle was used to determine $\dot{V}CO_2$. A curvilinear relationship was found between log $\dot{V}CO_2$ and venous blood temperature, and a quadratic regression equation ($r^2 = 0.74$) was fit to the data. Q_{10} (the ratio of $\dot{V}CO_2$ before and after a 10° C temperature change) was estimated to be 2.7 or 3.0, depending on the analytic method used. Venous blood temperature as a predictor variable explained a greater proportion of the variability of log $\dot{V}CO_2$ than did nasopharyngeal or rectal temperatures. Analysis of covariance revealed that total circulatory arrest during bypass (utilized in 10 patients for 34 ± 4 min, mean ± SEM) affected the relationship of venous blood temperature with log $\dot{V}CO_2$, by increasing the y-intercept ($P = .008$) but not the slope. These data, with associated 95% prediction intervals, define the expected CO_2 elimination rates at various temperatures during standard bypass conditions in our patients. Real-time measurement of $\dot{V}CO_2$ using mass spectrometry can be a useful routine monitor during CPB that may help to assess patient metabolic function, adequacy of perfusion, and oxygenator performance. (Key words: Carbon dioxide: elimination. Cardiopulmonary bypass. Hypothermia. Measurement techniques: mass spectroscopy. Metabolism. Monitoring: carbon dioxide.)

AN IMPORTANT GOAL in the conduct of cardiopulmonary bypass (CPB) is to match body metabolic requirement with the amount of oxygen supplied directly to the tissues. When perfusion is successful, aerobic metabolism should proceed at the normal rate for a given temperature.

Clinical indices commonly used to detect global oxygen supply/demand mismatch during CPB include metabolic acid/base status, and oxygen tension (P_vO_2) or saturation (S_vO_2) of mixed venous blood.[1,2] The ease and frequency of use of these indices for monitoring adequacy of perfusion has increased with recent technological advances. While very low P_vO_2 or S_vO_2 values usually reflect inadequate tissue oxygenation, the utility of mixed venous oxygenation monitoring is limited, because increases in P_vO_2 or S_vO_2 may reflect arterial-to-venous shunting of blood rather than improved tissue perfusion.[3] The latter point is most extreme in vascular beds that are completely without blood flow, and which neither contribute the metabolic acid and CO_2 that they produce nor extract oxygen from the blood; such beds will not affect arterial blood pH or venous blood oxygenation.

In theory, the steady-state carbon dioxide elimination rate ($\dot{V}CO_2$) from the pump oxygenator during total CPB reflects global aerobic metabolic activity, tissue perfusion, and oxygenator function. Of these factors, the metabolic rate dependence may be predominant. Importantly, when non-perfused vascular beds are present, a diminution in measured $\dot{V}CO_2$ (compared with normal rates) should occur, permitting detection of inadequate perfusion even when arterial blood *p*H, lactate, and P_vO_2 are normal.

As part of an investigation into the use of gas-phase measurement of $\dot{V}CO_2$ during clinical CPB, we sought to define the normal temperature dependence of $\dot{V}CO_2$ in pediatric patients using the technology of multiplexed mass spectrometry.

Materials and Methods

After obtaining approval from our Institutional Review Board, we studied 25 pediatric patients undergoing repair of congenital heart defects using CPB. Table 1 shows the demographic data for the patient population as a whole, and divides patients into groups who did or did not undergo total circulatory arrest ("TCA group" and "No-TCA group," respectively).

Anesthetic Management

Premedication was given to 20 of the 25 patients, consisting of intramuscular morphine (n = 20), scopolamine (n = 19), and/or pentobarbital (n = 11). Prior to CPB, the only anesthetic or adjuvant drugs given: halothane (n = 24), fentanyl (n = 22), isoflurane (n = 1), thiopental (n = 6), N_2O (n = 12), pancuronium (n

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TABLE 1. Patient Characteristics and Bypass Data

Variable	All Patients	No-TCA Group (n = 15)	TCA Group (n = 10)	P*
Age (months)	30.9 ± 5.5	47.0 ± 6.1‡	6.7 ± 1.6§	<0.0001
Weight (kg)	12 ± 1.2	14.4 ± 1.2	5.8 ± 0.9	<0.0001
Body surface area (m^2)	0.48 ± 0.04	0.62 ± 0.04	0.29 ± 0.03	<0.0001
Sex (M/F)	16/9	9/6	7/3	0.61
Total CPB duration (min)	120 ± 7	131 ± 10.3	105 ± 9.0	0.092
CPB rewarming duration (min)	48 ± 4	52 ± 4	41 ± 7	0.15
Lowest temperatures: (°C)				
Venous blood	19.5 ± 0.6	19.2 ± 0.4	20.0 ± 1.2	0.47
Nasopharyngeal	20.5 ± 0.5	20.4 ± 0.4	20.6 ± 1.2	0.86
Rectal	25.7 ± 0.4	26.6 ± 0.4	24.1 ± 0.8	0.004
[Hemoglobin]† (g/dl)	8.0 ± 0.2	7.7 ± 0.3	8.4 ± 0.3	0.11
Base excess† (mEq/l)	−2.5 ± 0.5	−3.3 ± 0.4	−1.4 ± 1.1	0.075
$NaHCO_3$ dose† (mmol/kg)	0.94 ± 0.2	0.92 ± 0.2	0.98 ± 0.4	0.90
Cardiac diagnosis:				
Tetralogy of Fallot	9	8	1	0.034
A-V Canal	4	2	2	0.53
VSD	3	1	2	0.35
Transposition great vessels	3	2	1	0.80
ASD	2	1	1	0.65
Other	4	2	2	0.53

Values are mean ± standard error. TCA = total circulatory arrest.
* "TCA group" *vs.* "No-TCA group."
† During cardiopulmonary bypass. The HCO_3 dose administered during CPB excludes the bicarbonate given as part of the pump priming solution. Nine of 25 patients received no HCO_3 during CPB (range 0–4.3 mmol/kg body weight).
‡ Range 2 days–14.5 months.
§ Range 16 months–9 yr 2 months.

= 24), and vecuronium (n = 1). When used, N_2O was discontinued at least 10 min prior to CPB. During CPB, the only anesthetic or adjuvant drugs used were fentanyl, scopolamine, and pancuronium; no patient received volatile agents or N_2O during CPB. The temperature of the operating room was approximately 13–18° C during the pre-CPB and CPB periods. In an attempt to improve the uniformity of cooling and rewarming,[4] all patients received phentolamine 0.75 $mg \cdot kg^{-1}$ as follows: 0.5 $mg \cdot kg^{-1}$ with initiation of CPB, and 0.25 $mg \cdot kg^{-1}$ with the beginning of rewarming.

Perfusion Management

The CPB priming solution contained whole blood 500 ml and heparin 3000 u in all patients. Additionally, the priming volume of crystalloid (lactated Ringer's or plasmalyte), $NaHCO_3$ dose, and bubble oxygenator model were based upon the patient's weight as follows: 1) patients <10 kg: crystalloid 250 ml, $NaHCO_3$ 20 mmol, with BIO-2 oxygenator (American Bentley, Irvine, CA); 2) patients 10–15 kg: crystalloid 500 ml, $NaHCO_3$ 25 mmol, with BEN-5 oxygenator (American Bentley); and 3) patients 15–29 kg: crystalloid 750 ml, $NaHCO_3$ 25 mmol, also with BEN-5 oxygenator. After initiation of CPB using a Sarns non-pulsatile non-occlusive roller-head bypass pump, the patient was cooled to an average minimum venous blood temperature (T_v) of 19.5 ± 0.6° C, using the integral heat exchanger of the oxygenator.

The bypass pump was adjusted to deliver blood to the ascending aorta at a flow rate that depended on the venous blood temperature as follows (pump flow units are $l \cdot min^{-1} \cdot m^{-2}$): $T_v \geq 37°$ C, flow = 2.5; T_v 25–37° C, flow = 2.0; T_v 20–25° C, flow = 1.5; and $T_v < 20°$ C, flow = 0.5. The heart was arrested with cold cardioplegic solution (Plegisol, Abbott, Chicago, IL; $[K^+] = 16$ mmol/l). Following a period of active rewarming, total CPB was converted to partial CPB (with ejection of blood by the left ventricle) when T_v averaged 35.9 ± 0.3° C. The CPB rewarming duration was measured from onset of full rewarming until onset of partial CPB.

Total Circulatory Arrest

In 10 of the 25 patients (TCA group), it was elected preoperatively to use hypothermic total circulatory arrest (duration 34 ± 4 min) after a period of active cooling using CPB. These TCA group patients also received surface cooling, with ice surrounding the head and a cooling blanket under the body. Surface cooling began before surgical draping and continued until commencement of rewarming. TCA group patients also received methylprednisolone 30 $mg \cdot kg^{-1}$ in the priming solution, and thiopental 9 mg/kg 3–5 min prior to onset of total circulatory arrest.

Measurement Technique

Measurements of CO_2 elimination were made using a non-invasive technique. Measurements were obtained

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only after the initial cooling period was completed (T_v within 1–2° C of the lowest value), while the lungs were not being ventilated, and only during total CPB. The latter was defined by the lack of discernible ejection of blood by the left ventricle based on the radial arterial pressure waveform.

We used the gas phase Fick principle[5] to measure $\dot{V}CO_2$ in real-time. Oxygenator effluent gas was periodically sampled by a multiplexed mass spectrometer (MGA-1100 and Advantage® system, Perkin-Elmer, Pomona, CA; gas withdrawal rate 240 ml · min^{-1}) by means of a needle placed inside the tubing venting the oxygenator's gas exhaust port. The mass spectrometer detected the ^{12}C carbon fragment to measure the dry-gas CO_2 concentrations, and was calibrated regularly against gas standards (Scott Medical Products, Plumsteadville, PA). Scavenging of the oxygenator effluent gas into a suction line was not performed, in order to minimize room air contamination of the gas sample.

Inflow gas to the oxygenator was adjusted using a calibrated rotameter, and consisted of oxygen from the hospital supply system passing through a O_2/air gas blender set for 100% O_2. At regular intervals during each study, the composition of the oxygenator gas inflow (abbreviated F_i) was measured by diverting the mass spectrometer's sampling path with a stopcock. Occasional data points with inflow concentrations of CO_2 > 0.1% were deleted to simplify data analysis.

At intervals of 5–15 min, we recorded venous blood, nasopharyngeal, and rectal temperatures, gas flow, and fractional concentrations of CO_2 and N_2 in the effluent gas samples (F_eCO_2 and F_eN_2, respectively). Data collection was suspended during circulatory arrest, during long periods of stable hypothermia, when the oxygenator gas inflow was less than 400 ml · min^{-1}, and during the initial rapid cooling phase of CPB. When active rewarming commenced, the frequency of sampling was increased. Contamination of the gas effluent sample with room air was detected by a nitrogen concentration difference across the oxygenator ($F_eN_2 - F_iN_2$) greater than 5% atmospheric, and were not analyzed. Such data occurred most frequently at very low gas inflow rates as the mass spectrometer gas withdrawal rate approached the total oxygenator gas flow rate. Venous blood temperature was measured at the blood inlet of the oxygenator using the integral thermistor.

Data Analysis and Statistical Tests

$\dot{V}CO_2$ (in ml · min^{-1} · kg^{-1}) was calculated as $\{F_eCO_2\} \times \{\text{gas flow rate}\} \div \{\text{body weight}\}$. For the gas transfer rate calculations, we assumed equality between the effluent and inflow gas flow rates. All $\dot{V}CO_2$ values are expressed at ATPD. Linear models were fit to the log transform of $\dot{V}CO_2$ to ensure homoscedasticity. Q_{10} (the variation in metabolic activity produced by a 10° C change) was determined from the linear regression slope of the log $\dot{V}CO_2$ *versus* T_v relationship, transformed to a linear scale. Q_{10} values were also computed individually by fitting separate simple linear regression functions to each patient's data; the mean of the individual slopes was then calculated.

TABLE 2. Carbon Dioxide Q_{10} Data

Temperature Range (°C)	Q_{10}	95% Confidence Interval* for Q_{10}
<25	5.4	3.2–9.1
25–30	6.5	1.8–23
>30	1.2	0.82–1.7
All data	2.7	2.5–3.0

Q_{10} data are calculated from the slope of the simple linear regression of T_v on log $\dot{V}CO_2$ over the specified range of temperature values, using data pooled from no-TCA and TCA groups (25 patients, multiple determinations per patient). When Q_{10} values were computed by fitting separate simple linear regression functions to each patient's data, the mean Q_{10} was 3.0 ± 0.23. This method yielded a 95% confidence interval of 2.5–3.5.

* The asymmetric confidence intervals with high upper limits result from the exponential transform of confidence limits estimated for data on the logarithmic scale.

Patient descriptive variables (table 1) in the TCA and no-TCA groups were compared with the two-tailed *t* test, χ^2 test (sex), or Fisher's exact test (cardiac diagnoses). The effects of age, weight, total bypass time, total warming time, and use of TCA on the relationship of log $\dot{V}CO_2$ with T_v were assessed by analysis of covariance, adjusted for within- and among-subject variation. To avoid interpretational inaccuracies, single factors were chosen to represent clusters of correlated variables. After important mediating variables were identified, coefficients for the best-fitting polynominal regression model relating log $\dot{V}CO_2$ with T_v were estimated. T_v for each regression model is expressed as a deviation from the group mean value in order to reduce the correlation between the linear and quadratic terms (table 2). Attempts to represent curvature of the data as an exponential function rising to an asymptote by nonlinear regression were unsuccessful. Observations were then pooled across relevant subject categories to establish prediction intervals from the data. The effect of different temperature monitoring sites was examined using analysis of variance and linear modeling. Values are presented as mean ± standard error.

Results

Younger and smaller patients tended to undergo total circulatory arrest (TCA); age, weight, and the use

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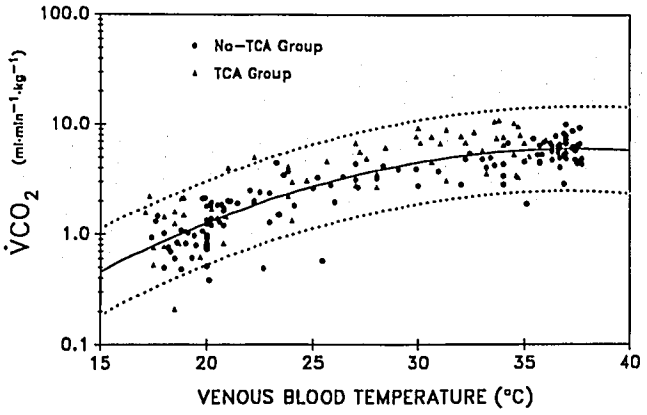

FIG. 1. Data from all 25 patients (198 total determinations). Carbon dioxide elimination rate ($\dot{V}CO_2$, logarithmic scale, per kg body weight) as a function of venous blood temperature. Data were collected using a gas-phase technique. The polynomial regression curve ($r^2 = 0.74$) and 95% prediction intervals are shown (see table 4).

of TCA were significantly associated with one another (table 1). Therefore, the presence or absence of TCA was used to represent age and weight also in further analyses. Total CPB duration and CPB rewarming duration were correlated with each other (r = 0.67, table 1); we chose the former to represent the two variables. Use of TCA is the only variable identified that affects the relationship of $\dot{V}CO_2$ with venous blood temperature (T_v).

Figure 1 shows the curve of log $\dot{V}CO_2$ plotted as a function of T_v for the 198 $\dot{V}CO_2$ observations in all 25 patients. $\dot{V}CO_2$ tends to increase with temperature. The Q_{10} for CO_2 averages 2.7 ± 1.0 when a straight line is fit to the data from all patients over the entire T_v range, and averages 3.0 ± .23 when straight lines are fit individually by patient and then meaned (table 2). No patient exhibited signs suggestive of malignant hyperthermia during the perioperative period.

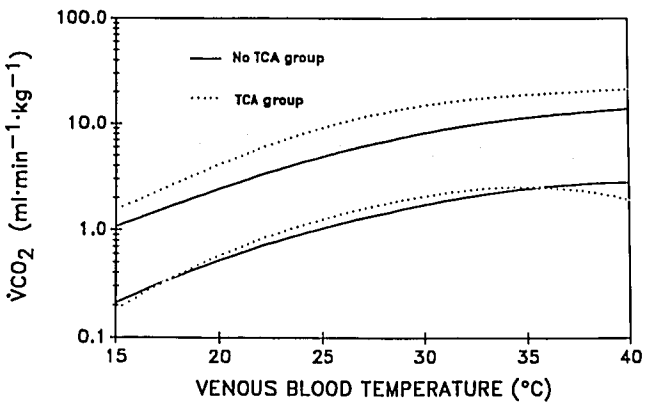

FIG. 2. Ninety-five percent prediction intervals of CO_2 elimination rate ($\dot{V}CO_2$, logarithmic scale) as a function of venous blood temperature from "TCA group" (patients undergoing total circulatory arrest, n = 10), and "no-TCA group" (patients not undergoing TCA, n = 15). Curves are plotted on same axes to demonstrate the substantial overlap between prediction intervals of the two groups.

Figure 1 also demonstrates that curvature exists in the relationship between log $\dot{V}CO_2$ and T_v; this curvature presents as a significant ($P < 0.0001$) lack of fit of the data by a straight line, and is adequately represented as a second order polynomial. The 95% prediction intervals for $\dot{V}CO_2$ are depicted in figure 1. Because of the curvature, it may not be appropriate to represent the Q_{10} for our patients by a single value. When the data are divided into three temperature segments, the calculated Q_{10} values differ for each segment (table 2).

The substantial overlap of the 95% prediction envelopes for the log VCO_2 *versus* T_v data in the no-TCA and TCA groups are depicted in figure 2. For purposes of predicting the value of $\dot{V}CO_2$ that could be expected for a given T_v value, separate polynomial regression models were developed for the pooled data, and for each TCA condition. The estimated $\dot{V}CO_2$ values and 95% prediction intervals for these conditions are presented in table 3, to facilitate clinical use of the data since log scales may be difficult to read. The polynomial coefficients for the associated statistical models are shown in table 4. The only statistically significant difference between the TCA and no-TCA group curves was a small increase in the y-intercept term ($P = 0.008$, table 4) in the TCA group.

Plotting log $\dot{V}CO_2$ *versus* venous blood temperature produced the smallest scatter, in comparison with the other temperature monitoring sites. Thus, use of T_v as a predictor variable explained the largest amount of variability in log $\dot{V}CO_2$ ($r^2 = 0.77$), as compared with nasopharyngeal temperature ($r^2 = 0.69$) or rectal temperature ($r^2 = 0.09$).

Discussion

We demonstrated that the rate of CO_2 elimination is readily measured in the gas phase during clinical CPB using a multiplexed mass spectrometer. Using our patient data, this technique may be valuable as a clinical tool for routine patient management. $\dot{V}CO_2$ showed a clear dependence upon venous blood temperature, with the latter explaining 74% of the variability in CO_2 elimination. The difference in CO_2 elimination between the TCA and no-TCA groups manifested as a small but statistically significant increase in y-intercept in the TCA group. This increase in $\dot{V}CO_2$ for a given temperature during rewarming could indicate improved global aerobic metabolic function when TCA is utilized, but further research is needed before the clinical implications of these observations can be determined.

Abbott *et al.*[6] measured $\dot{V}CO_2$ during CPB in four patients using a gas-phase technique incapable of gen-

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erating $\dot{V}CO_2$ data until after CPB was completed. By modifying and simplifying their technique, we were able to obtain results in real-time, and to demonstrate the applicability of $\dot{V}CO_2$ monitoring to patient care and clinical research. In addition to defining the relationship between $\dot{V}CO_2$ and temperature, our research extends the observations of Abbott *et al.* to study patients during conditions more representative of those in common use today in the United States. For example, our patients' oxygenators were ventilated with gas containing no CO_2, whereas the patients of Abbott *et al.* received CO_2 in concentrations of 5–15%. In another study, $\dot{V}CO_2$ was measured in the blood phase in dogs undergoing partial CPB with normothermia by Kawashima *et al.*[7]

The rise in $\dot{V}CO_2$ that we observed with increasing temperature may have several potential causes. Metabolic CO_2 generation increases with temperature (the Arrhenius effect), shivering may occur, and the rightward shift in the oxyhemoglobin dissociation curve may increase the availability of oxygen in peripheral tissues. As regional blood flow is improved, mobilization of CO_2 stores may occur from hypoperfused body tissues. Additionally, gas solubility in fluids and tissue stores is reduced as temperature rises (increasing the partial pressure), and carbonic anhydrase activity may increase. Changes in oxygenator efficiency may also occur as gas flow, blood flow, and inlet blood P_{CO_2} vary. These factors all tend to increase CO_2 efflux across the oxygenator.[5]

A Q_{10} of 2.5–3.0 is consistent with most biological systems. Using a steady-state immersion/perfusion hypothermic method, Kent and Peirce showed in the dog that the Q_{10} for O_2 was 2.8, and similar values have been shown for humans and *in vitro* tissues.[8] The curvature apparent in our data may be an artifact, since the relationship between log $\dot{V}CO_2$ and T_v analyzed separately for each patient demonstrated no significant deviation from a straight line fit, although slopes and intercepts differed (table 2). Further research is needed to help identify the causes of this inter-patient variability in $\dot{V}CO_2$, as indicated by the wide 95% confidence intervals obtained for the data grouped by temperature range (table 3). Etiologies for the observed variability may include: differences in sympathetic and vascular tone affecting the regional distribution of blood flow, the use of different metabolic substrates altering the respiratory quotient, dissimilar rates of cooling and rewarming, unequal degrees of hemodilution, and variations in the degree of neuromuscular blockade and sup-

TABLE 3. Predicted Values of $\dot{V}CO_2$ at Various Venous Temperature Points

	Venous Temperature (°C)	$\dot{V}CO_2$ Estimate ($ml \cdot min^{-1} \cdot kg^{-1}$)	$\dot{V}CO_2$ 95% Prediction Interval
All patients	15	0.45	0.18–1.1
	20	1.3	0.53–3.0
	25	2.7	1.1–6.6
	30	4.5	1.9–11
	35	5.8	2.4–14
	38	6.0	2.5–15
No-TCA group	15	0.48	0.21–1.1
	20	1.1	0.52–2.4
	25	2.2	1.0–4.9
	30	3.8	1.7–8.2
	35	5.3	2.5–11
	38	6.0	2.7–13
TCA group	15	0.53	0.18–1.5
	20	1.5	0.58–4.1
	25	3.4	1.3–9.1
	30	5.6	2.1–15
	35	6.9	2.5–19
	38	6.8	2.3–20

TABLE 4. Polynomial Regression Coefficients*: $\dot{V}CO_2$ Versus Venous Temperature: Effect of Total Circulatory Arrest (TCA)

Group	Intercept Term (a_0)	Linear Term (a_1)	Quadratic Term (a_2)	r^2
All patients	0.537 ± 0.026 ($P < 0.0001$)†	0.0466 ± 0.002 ($P < 0.0001$)	−0.0022 ± 0.0004 ($P < 0.0001$)	0.74
No-TCA group	0.470 ± 0.031 ($P < 0.0001$)	0.0451 ± 0.0021 ($P < 0.0001$)	−0.00152 ± 0.0005 ($P = 0.0013$)	0.79
TCA group	0.603 ± 0.046 ($P < 0.0001$)	0.0488 ± 0.0042 ($P < 0.0001$)	−0.00248 ± 0.0010 ($P = 0.0061$)	0.69
P value‡	0.008	0.22	0.19	—

All values are mean ± standard error.

* The polynomial coefficients (terms) relate to the equation:

$$\log_{10} \dot{V}CO_2 = a_0 + a_1 \cdot (T_v - T_m) + a_2 \cdot (T_v - T_m)^2,$$

where T_v is the venous blood temperature, and T_m is the mean value of T_v derived from all observations within each group, as follows: 1) All patients T_m = 27.0° C; 2); No-TCA group T_m = 27.4° C; and 3) TCA group T_m = 26.4° C.

† *P* values testing hypothesis that coefficient is equal to zero.

‡ *P* values comparing coefficient of "No-TCA group" *versus* "TCA group."

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pression of shivering. These variables were not controlled prospectively in this study.

The gas-phase method for $\dot{V}CO_2$ determination presents several advantages over the blood phase oxygen uptake ($\dot{V}O_2$) technique, which has been applied to CPB previously.[9] Direct determinations of blood O_2 and CO_2 content by chemical reaction are accurate techniques for $\dot{V}O_2$ and $\dot{V}CO_2$ measurement,[10] but are cumbersome and time-consuming, and require discrete samples. For these reasons, real-time monitoring is difficult so blood oxygen content often is estimated from P_{O_2} measurements through the use of "standard" oxyhemoglobin dissociation curves. However, the marked hypothermia, alkalosis, and changes in 2-,3-diphosphoglycerate usually present during CPB may introduce inaccuracy in such estimates.[11,12] By measuring changes in gas concentration across the pump oxygenator, gas-phase methods such as ours circumvent many of the problems associated with blood-phase $\dot{V}CO_2$ and $\dot{V}O_2$ measurements. Effluent CO_2 analysis is a standard technique for evaluating membrane lung gas exchange.[5]

Limitations

Limitations of our technique involve the non-steady-state nature of clinical CPB, in that temperature gradients always exist among the different body regions. Because of these gradients, the representation of a patient's temperature using a single value is merely an approximation. We chose the venous blood temperature as our standard value because it explained the largest proportion of variability log $\dot{V}CO_2$, and also for theoretical reasons, since T_v should represent the average temperature of those tissues that contribute CO_2 to the blood.

We have noticed that one bubble oxygenator, the Harvey® H-1700 (Bard, Billerica, MA) cannot be utilized for gas-phase $\dot{V}CO_2$ measurements because its design incorporates the obligatory entrainment of room air in variable quantities. Membrane oxygenators present little problem in this regard.

Other Gas-phase Monitoring Techniques

For theoretical reasons, routine gas-phase monitoring of CO_2 elimination (compared with oxygen uptake) is preferred for routine clinical use when using existing clinical operating room mass spectrometers that do not undergo special calibration techniques. Since oxygen uptake measurement involves accurately detecting small differences between large concentrations of gas (*e.g.*, 99–97.5%), small errors in measurement (typically crowded into the high end of a 0–100% scale) are magnified when computing $\dot{V}CO_2$. Determination of $\dot{V}CO_2$, however, is made from a more precise measurement of the effluent CO_2 concentration alone, since CO_2 is usually absent from inlet gas and the mass spectrometer signals obtained typically represent the middle range of a 0–10% full-scale instrument.

The monitoring of CO_2 tension alone in the oxygenator effluent gas (P_eCO_2) has been recommended,[13] however, this partial pressure will be a function of variables relating to the oxygenator (blood flow, gas flow, and oxygenator efficiency), as well as venous blood PCO_2. The use of infrared capnography to measure P_eCO_2 may be confounded by unrecognized sample dilution with room air. In contrast, our mass spectrometric technique permits identification of nitrogen, N_2O, and other gases, the presence of which would indicate contamination within the gas stream. $\dot{V}CO_2$ is more reflective of patient metabolic function; when $\dot{V}CO_2$ is combined with the P_eCO_2 value, perfusion-related problems can be identified with greater specificity. For example, elevated P_eCO_2 together with normal $\dot{V}CO_2$ would indicate inadequate gas inflow to the oxygenator.

Potential Clinical Implications

There are several reasons why a $\dot{V}CO_2$ measurement may lie outside of the prediction interval defined above. $\dot{V}CO_2$ values *above normal* for a given T_v may indicate hyperactive metabolism (*e.g.*, hyperthyroidism) or subclinical shivering due to inadequate muscle relaxation. This monitor may be valuable for detecting early malignant hyperthermia crisis during rewarming on CPB, when temperature normally rises quickly. In one patient who was potentially malignant hyperthermia susceptible and required surgery with CPB,** we retrospectively compared $\dot{V}CO_2$ data collected during CPB with the results of the present study: all data points fell within the 95% prediction interval. That patient showed no clear signs of malignant hyperthermia before or during CPB.

$\dot{V}CO_2$ values *below normal* for a given T_v may indicate: 1) impaired or non-uniform nutritive regional blood flow, causing a reduction of the total mass of perfused body tissue, and which may benefit from vasodilator therapy; 2) impaired O_2 delivery, such as excessive hemodilution, hypoxemia, or inadequate blood flow rate; 3) oxygenator malfunction or improper operation (*e.g.*, inadequate roller-pump occlusion); 4) reduced metabolic CO_2 production by the patient (*e.g.*, hypothyroidism); and 5) technical monitoring problems, particularly room air contamination of the oxygenator effluent gas.

It should be recognized that the data presented here

** Larach DR, High KM, Larach MG, Hensley FA Jr, Martin DE, Williams DR: Cardiopulmonary bypass interference with dantrolene prophylaxis of malignant hyperthermia. J Cardiothoracic Anesth 1:448–453, 1987.

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are specific for the precise conditions under which we performed CPB. While the data were obtained during routine operations and apparently normal perfusions, small base deficits were present during CPB, and optimization $\dot{V}CO_2$ at any T_v was not necessarily achieved. The influences of various factors upon $\dot{V}CO_2$, such as the pump flow rate, the rates of cooling and rewarming, patients' disease states, and the use of drugs such as vasodilators, vasoconstrictors, anesthetics, and muscle relaxants, deserve further research.

Real-time determination of CO_2 elimination may be a useful continuous monitor of metabolic, circulatory, and oxygenator function during CPB. Detection of a $\dot{V}CO_2$ below the 'normal' range defined herein may provide evidence of tissue non-perfusion, despite lack of abnormalities in arterial blood *p*H and lactate, or in mixed venous oxygenation. We believe this technique is applicable to membrane as well as bubble oxygenation, and to adults in addition to pediatric patients. By using microcomputer technology, we have recently achieved full automation of this monitoring technique, thereby simplifying its clinical application. Further investigation is needed to determine whether interventions designed to increase $\dot{V}CO_2$ during CPB, in real time, can be helpful in optimizing the bypass state. The "normal" ranges of $\dot{V}CO_2$ defined for this patient population can help to guide patient management during CPB, with the goal of improving the safety of total CPB during cardiac surgery, and of partial CPB during extracorporeal membrane oxygenation (ECMO).

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