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Optimal Sweep Gas to Blood Flow Ratio (V/Q) for Initiation of Cardiopulmonary Bypass in a Pediatric Patient Population: A Retrospective Analysis

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Abstract: The optimal setting to achieve a suitable $PaCO_2$ value of 35–45 mmHg upon initiating cardiopulmonary bypass (CPB) in the pediatric population is undefined in the literature. Sweep gas is set upon initiating and modified throughout CPB to reduce potential complications related to compensatory metabolic acidosis or metabolic alkalosis and associated cerebral blood flow fluctuations. This study retrospectively examined 1,077 CPB cases for which $PaCO_2$ values were no less than 30 mmHg and no greater than 50 mmHg on the pre-CPB blood gas result. Through an observation of the results, we attempted to determine the optimal sweep gas setting upon initiating CPB to obtain a physiologic $PaCO_2$ value of 35–45 mmHg. The probability of achieving an optimal $PaCO_2$ value was modeled as a function of the average sweep gas to blood flow ratio during the period before the first blood gas on CPB. The median sweep gas to blood flow ratio (V/Q) was .64 (.51; .76), with a median first $PaCO_2$ value on CPB of 42 mmHg (38.8; 45). A .6 V/Q had an odds ratio (OR) of 1.57 of obtaining a $PaCO_2$ value between 35 and 45 mmHg on the first CPB blood gas when compared with a .4 V/Q (Figure 1). A .9 V/Q had a 1.76 OR when compared with a .4 and a 1.12 OR when compared with .6. Using a .6 V/Q ratio achieved a $PaCO_2$ value within normal physiologic limits with no significant advantage to a higher V/Q ratio overall. However, younger or smaller patients required a higher V/Q to achieve similar probabilities of being within limits and similar $PaCO_2$ values when compared with the older or larger patients. **Keywords:** cardiopulmonary bypass, sweep gas, ventilation, sweep gas to blood flow ratio, pediatric. *J Extra Corpor Technol. 2020;52:112–7*

Unless otherwise clinically indicated, the partial pressure of carbon dioxide ($PaCO_2$) in arterial blood should be maintained within normal physiological limits (35–45 mmHg) during cardiopulmonary bypass (CPB) to reduce the risk of complications related to compensatory metabolic acidosis or metabolic alkalosis. There are a variety of reasons to keep the $PaCO_2$ within the normal physiologic range, including the maintenance of cerebral circulation, the avoidance of hypocapnic lactic acidosis, prevention of ventricular fibrillation, and preventing a leftward shift of the oxyhemoglobin dissociation curve (1,2). In addition, a high $PaCO_2$ value can cause the body to react in a manner similar to hypoxic acidosis, resulting in lactate production and a depletion of the bicarbonate buffer system (3). Increased CO_2 has been shown by Darby and colleagues to decrease ventricular isometric systolic tension (3). Based on these data and normally accepted physiological parameters, a normothermic target $PaCO_2$ value of 35–45 mmHg on CPB is essential to providing adequate patient care.

Carbon dioxide plays a key role in maintaining a normal physiologic pH (7.35–7.45) but remains only a piece of the proverbial puzzle. If the $PaCO_2$ value is within the normal physiologic range of 35–45 mmHg, then the causes for a pH value outside of the 7.35–7.45 range would be of a metabolic or ionic source. Commonly, metabolic acidosis is caused by hypoperfusion and can result in numerous sequelae (4). A reduction in arterial pH results in a marked decrease in ventricular isometric systolic tension that

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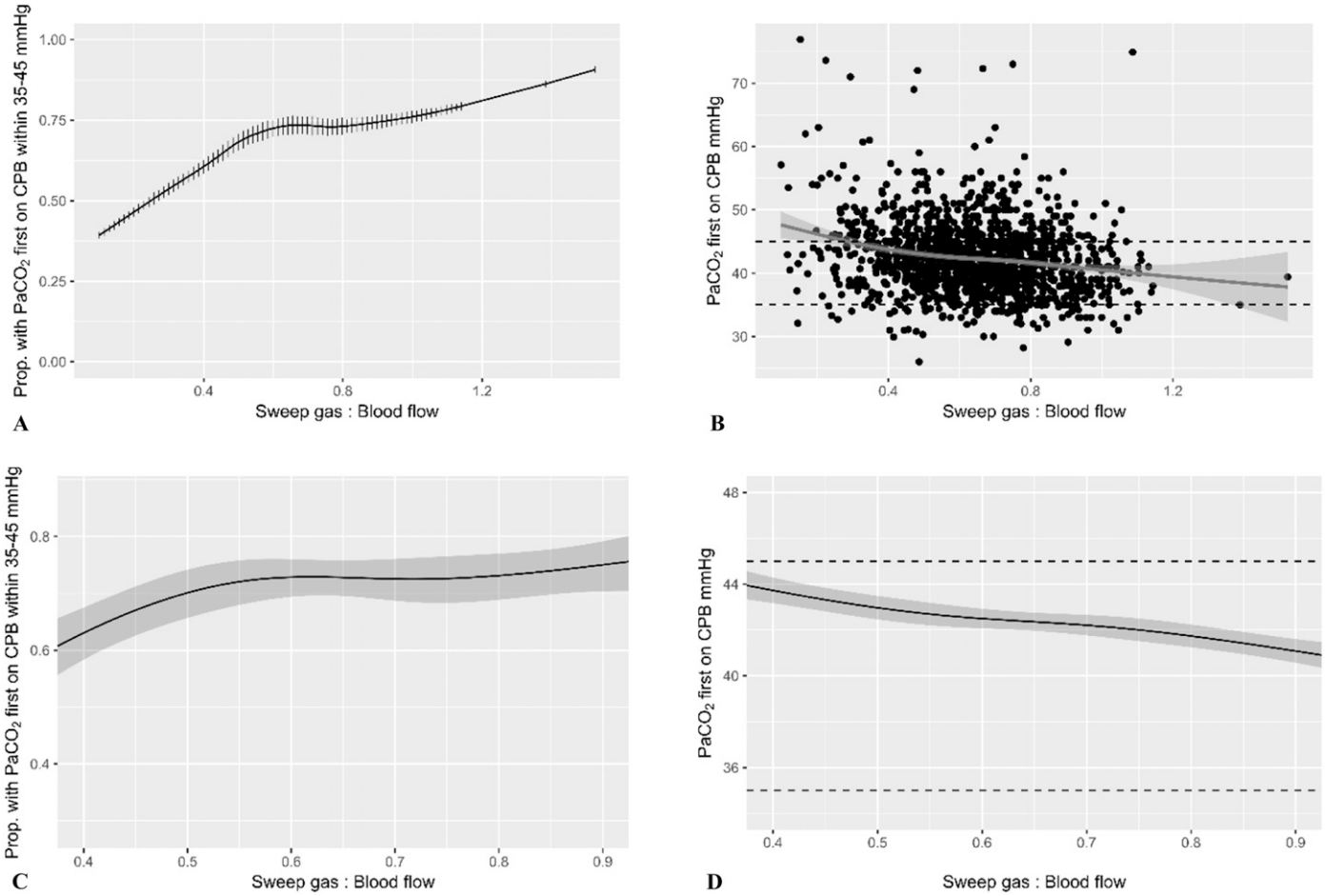

Figure 1. Bivariate associations between $PaCO_2$ and the V/Q ratio. (A) Spike histogram with loess curve showing the proportion of patients with a first $PaCO_2$ value on CPB between 35 and 45 mmHg according to the V/Q ratio. (B) Scatterplot and loess curve (gray line) for $PaCO_2$ on CPB according to the V/Q ratio. Dashed lines indicate the target range of 35–45 mmHg. (C) Model-based estimate of the predicted probability and 95% CI for $PaCO_2$ on CPB between 35 and 45 mmHg according to the V/Q ratio obtained from logistic regression. (D) Model-based estimate of the predicted $PaCO_2$ on CPB according to the V/Q ratio obtained from ordinal regression. Prop, proportion.

almost immediately improves with a pH correction (3). Metabolic alkalosis may be implicated in circulatory disturbances due to the influence alkalosis has on ionic concentrations of various solutes, including calcium (5). Metabolic acidosis and alkalosis should be avoided and treated when necessary, while ensuring they are not compensatory because of suboptimal $PaCO_2$ management, to reduce potential complications associated with each.

A literature search revealed a single study attempting to identify an optimal sweep gas setting and was conducted in 30 adult patients undergoing a coronary artery bypass graft procedure on CPB (6). The study attempted to determine a superior approach between the three body surface area (BSA) methods used, all of which were significantly below a 1:1 gas to blood flow ratio (6). Beyond the referenced study, none has tested an optimal sweep gas setting outside the confines of manufacturer instructions for use (IFU). The IFU provided with a commonly used CPB oxygenator disposable states a 1:1 sweep gas to blood flow ratio (V/Q) is the appropriate setting (7). The current study hypothesizes a V/Q of 1 to be excessive in most instances and may result in hypocapnia, and examines CPB cases to determine a V/Q ratio that achieves a normal physiologic $PaCO_2$ value for the initiation of normothermic CPB.

METHODS

This study was found to be exempt from review by the Institutional Review Board as a retrospective observational study. Patients were identified for inclusion via the Department of Cardiovascular Perfusion's VISION database (Spectrum Medical, Fort Mill, SC). Patients who underwent surgical repair of congenital heart disease from January 1, 2015 through June 30, 2018 were examined. Patients for whom the pre-CPB $PaCO_2$ value was less than

30 mmHg or greater than 50 mmHg were excluded. Patients with incomplete information in the VISION database were excluded. Patient demographics, cardiac output, pre-CPB $PaCO_2$ and pH values, $PaCO_2$ and pH results from the first blood gas on bypass, and average cardiac output and sweep gas flow before the first blood gas were gathered for comparison.

Conduct of Perfusion

Extracorporeal circuits comprised Terumo Capiox FX series oxygenators (Terumo Cardiovascular Group, Ann Arbor, MI). Circuits were primed with PlasmaLyte-A (Baxter, Deerfield, IL) modified with 20 mEq sodium bicarbonate and 200 mg calcium chloride per liter, 25% albumin, washed packed red blood cells, fresh frozen plasma, tranexamic acid (100 mg/kg up to 1,000 mg), methylprednisolone (30 mg/kg up to 500 mg), antibiotics, and heparin based on circuit size, patient requirements, and departmental guidelines. CPB was established with a V/Q determined by the primary perfusionist. A Sechrist 3500CP-G Low Flow air–oxygen blender (Sechrist Industries, Inc., Anaheim, CA) was used to adjust the sweep rate, and an inline flow meter (Spectrum Medical) electronically captured the measured sweep rate. Target cardiac index was determined by institutional guidelines and measured with a clamp-on flow probe (Spectrum Medical) distal to all shunts in the CPB circuit. An arterial blood gas sample was obtained within the first 5 minutes of bypass as a matter of routine.

Data Collection

Patient demographics, $PaCO_2$, and pH values generated by the Radiometer ABL90 FLEX (Radiometer, Westlake, OH); cardiac index; and sweep gas flow were collected during the normal clinical routine for patients undergoing congenital cardiac surgery with CPB. These data were electronically transmitted to the VISION database. A blood sample size of .5 mL was drawn from the patient before CPB and from the CPB circuit once CPB was established. The sample was immediately administered to the bedside ABL90 blood analyzer, and results were electronically transmitted to the medical record and VISION database. Values provided by the ABL90 which may have been inaccurate because of analyzer error as determined by the analyzer or inaccurate because of sample acquisition error as determined by the clinician were discarded and not reported as a matter of routine.

Statistical

Patient and bypass characteristics were described using medians (25th; 75th percentile) and numbers (%) for continuous and categorical variables, respectively. Spike histograms and scatterplots were used to visualize the bivariate association between the V/Q ratio and the first $PaCO_2$ value on CPB. Logistic regression was used to obtain odds ratios (ORs) with 95% confidence intervals (CIs) and predicted probabilities for the first $PaCO_2$ value on CPB within 35–45 mmHg according to the V/Q ratio. Restricted cubic spline terms with knots placed at the 5th, 35th, 65th, and 95th percentiles were included to model the nonlinear association.

Multivariable logistic regression was used to examine whether the probability of the first $PaCO_2$ value within 35–45 mmHg on CPB according to the V/Q ratio differed by patient age (years), weight (kg), BSA, or patient $PaCO_2$ (mmHg) before bypass. Separate models were fit for each covariate and restricted cubic spline terms used to model nonlinear associations. Predicted probabilities were plotted for selected values of age (e.g., 1 month, 1 year, 6 years, and 12 years) and at the 10th, 25th, 75th, and 90th percentiles of weight, BSA, and $PaCO_2$ before bypass.

Cumulative probability ordinal regression with a logit link function was used to obtain predicted mean values of $PaCO_2$ on first CPB according to the V/Q ratio. Nonlinear associations were modeled using spline terms as described previously. Mean values were obtained from the fitted cumulative probability models. All analyses were conducted using the R software environment for statistical computing and graphics version 3.6.0 and regression models fit using the rms package (version 5.1.3).

RESULTS

Demographics

A total of 1,366 CPB cases were identified in the VISION database. A total of 29 CPB cases were excluded because of incomplete information, and an additional 260 CPB cases were excluded for $PaCO_2$ values <30 mmHg or >50 mmHg

Table 1. Descriptive characteristics of study participants.

Variable	Overall (n = 1,077)
Age (years)	.75 (.25, 5.00)
Weight (kilograms)	7.92 (4.90, 18.90)
Body surface area (m^2)	.37 (.27, .76)
Cardiac output (L/min)	.90 (.61, 1.87)
pH before CPB	7.37 (7.32, 7.42)
pH on CPB	7.34 (7.30, 7.38)
$PaCO_2$ before CPB	39.00 (36.00, 43.00)
$PaCO_2$ on CPB	42.00 (38.70, 45.00)
Sweep gas flow on CPB	.62 (.37, 1.18)
V/Q ratio	.64 (.51, .76)
Patients with first on CPB $PaCO_2$ between 35 and 45 mmHg, n (%)	781 (72.5)

Values are medians (25th; 75th) percentiles for continuous variables and number (%) for categorical variables. Parameters deemed "on CPB" were taken from the first blood gas on CPB. Cardiac output, sweep, and V/Q ratios were averaged over the time period before the first CPB blood gas.

Table 2. Predicted probabilities of first $PaCO_2$ on CPB within 35–45 mmHg and predicted $PaCO_2$ values relative to the V/Q ratio.

V/Q Ratio	Predicted Probability (95% CI)*	Predicted First $PaCO_2$ on CPB (95% CI)†
.4	.65 (.60; .70)	43.39 (42.82; 43.96)
.5	.71 (.66; .75)	42.92 (42.39; 43.47)
.6	.74 (.71; .78)	42.32 (41.89; 42.76)
.7	.76 (.72; .80)	41.64 (41.18; 42.11)
.8	.76 (.72; .81)	41.09 (40.59; 41.61)
.9	.77 (.72; .81)	40.66 (40.11; 41.22)

V/Q ratios shown in 10 percentile increments for values spanning the 10th to 90th percentiles. Restricted cubic spline terms with knots placed at the 5th, 35th, 65th, and 95th percentiles were used to flexibly model $PaCO_2$ as a function of the V/Q ratio.
*Predicted probabilities obtained from logistic regression.
†Predicted values obtained from ordinal regression.

on the pre-CPB blood gas. The application of exclusion criteria resulted 1,077 CPB cases available for analysis. Demographics, preoperative, and intraoperative characteristics are summarized in Table 1.

Intraoperative Variables

The median initiation V/Q was .64 (.51; .76), with a median first $PaCO_2$ value on CPB of 42 mmHg (38.8; 45) (Table 1). The predicted probabilities of the first $PaCO_2$ value on CPB within 34–45 mmHg are summarized in relation to the V/Q in Table 2. The predicted probability of being within range increases from .65 (.60; .70) to .74 (.71; .78) at a .4 and .6 ratio, respectively. The probability of being within range levels off at a V/Q of .6 with no significant improvement observed at higher V/Q ratios (Table 1; Figure 1). However, the predicted first $PaCO_2$ when modeled as a semi-continuous variable was closer to 40 mmHg at higher V/Q ratios. A .6 V/Q has an OR of 1.58 (1.27; 1.97) of obtaining a $PaCO_2$ value between 35 and 45 mmHg on the first blood gas on CPB when compared with a .4 V/Q (Figure 1). A .9 V/Q has a 1.81 (1.26; 2.62) OR when compared with a .4 and a 1.15 (.82; 1.60) OR when compared with .6. Figure 2 illustrates a higher probability of being within $PaCO_2$ limits at lower V/Q ratios for older and larger patients than for younger and smaller patients. Younger or smaller patients required a higher V/Q to

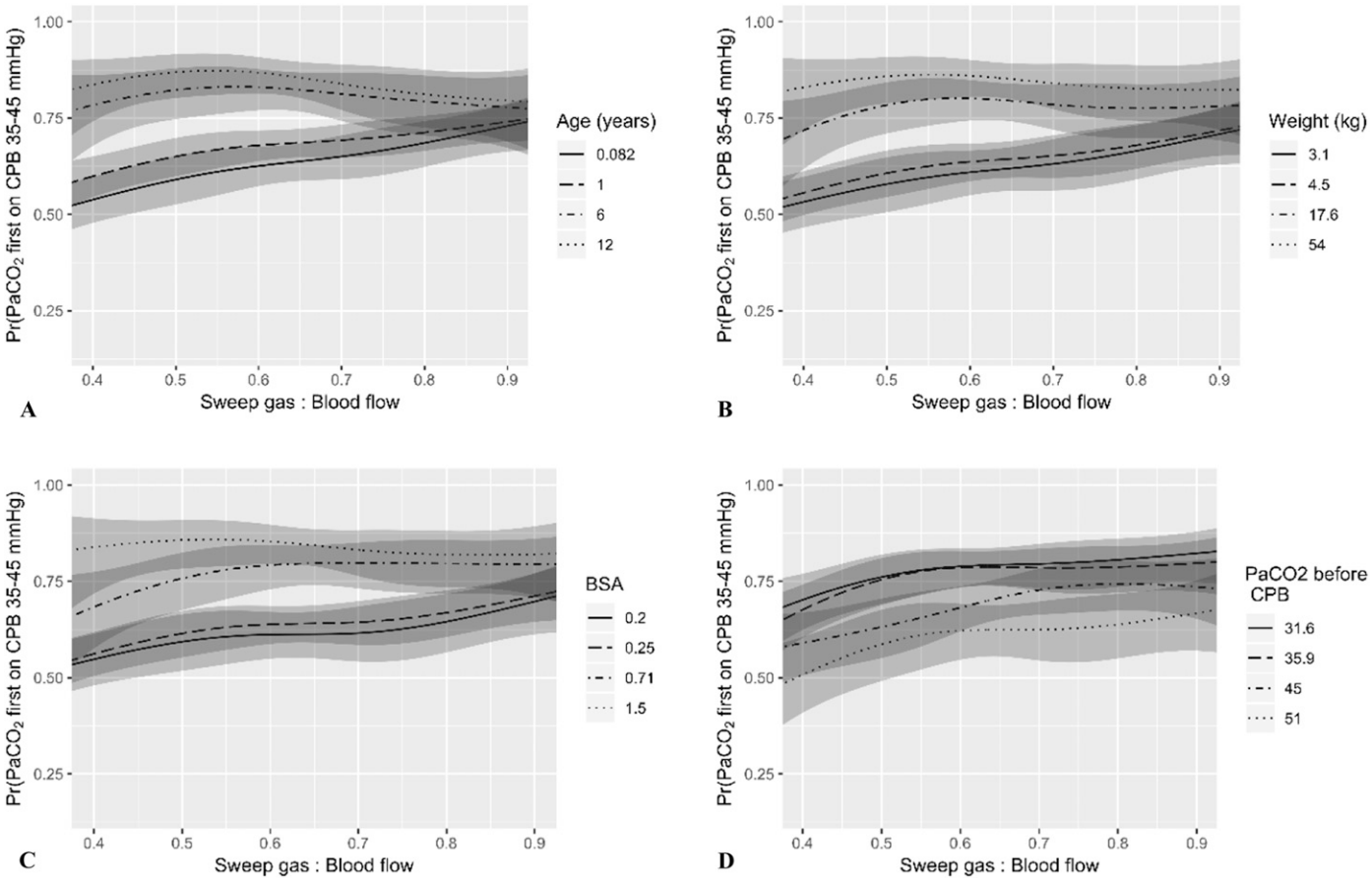

Figure 2. Predicted probability and 95% CI for $PaCO_2$ on CPB between 35 and 45 mmHg according to the V/Q ratio and covariates of interest. (A) Probabilities shown for selected values of age (1 month, 1 year, 6 years, and 12 years). (B) Values for weight shown at the 10th, 25th, 75th, and 90th percentiles. (C) Values for BSA shown at the 10th, 25th, 75th, and 90th percentiles. (D) Values for $PaCO_2$ before bypass shown at the 10th, 25th, 75th, and 90th percentiles. Pr, probability.

achieve similar probabilities of being within limits and similar $PaCO_2$ values when compared with the older or larger patients (Figures 2 and 3). Figure 2D illustrates an increased probability of being within range for all pre-CPB $PaCO_2$ values up to a V/Q ratio of .6. There was a statistically significant difference among groups in the predicted $PaCO_2$ value with the larger ($\chi^2 = 21.3$, d.f. = 6, $p < .01$) and older patients ($\chi^2 = 13.5$, d.f. = 6, $p = .04$) using the FX15 and FX25 oxygenators (Terumo Cardiovascular Group, Ann Arbor, MI), having lower predicted $PaCO_2$ values across all V/Q settings (Figure 3).

DISCUSSION

The CO_2 exchange rate within an oxygenator relies primarily on the sweep gas flow rate. Increasing the sweep gas flow rate or V/Q removes more CO_2, reducing the gas-side partial pressure of CO_2 and increasing the gradient for CO_2 exchange. Arterial $PaCO_2$ is controlled by adjusting the V/Q, and the actual sweep gas setting varies significantly within the congenital cardiac population. Because of the lack of quantitative evidence for sweep gas or V/Q settings, trial and error are commonly used to obtain appropriate CO_2 values.

It has been established that hemoglobin, temperature, pH, and $PaCO_2$ determine 85% of all changes in cerebral oxygenation on CPB (8). The primary causes of diminished cerebral oxygenation are a decrease in hemoglobin due to hemodilution, vasoconstriction due to hypocapnia, and the leftward shift of the oxyhemoglobin dissociation curve in alkalosis and hypothermia (8). Karabulut et al.(6) used 1.35, 1.6, and 2 L/min/m^2 sweep flow rates which, based on their reported pump flow of 2 L/min/m^2, would equate to V/Q ratios of .675, .8, and 1, respectively. Karabulut et al. (6) found a V/Q of 1 caused $PaCO_2$ levels to fall outside normal physiologic limits in an adult population. During rewarming, even with the increase in CO_2 production, the .8 and 1 V/Q groups had $PaCO_2$ values less than physiologic limits with averages of 32 and 28 mmHg, respectively.

The current study hypothesized a V/Q ratio of 1:1 for the onset of CPB would be too high and result in lower than

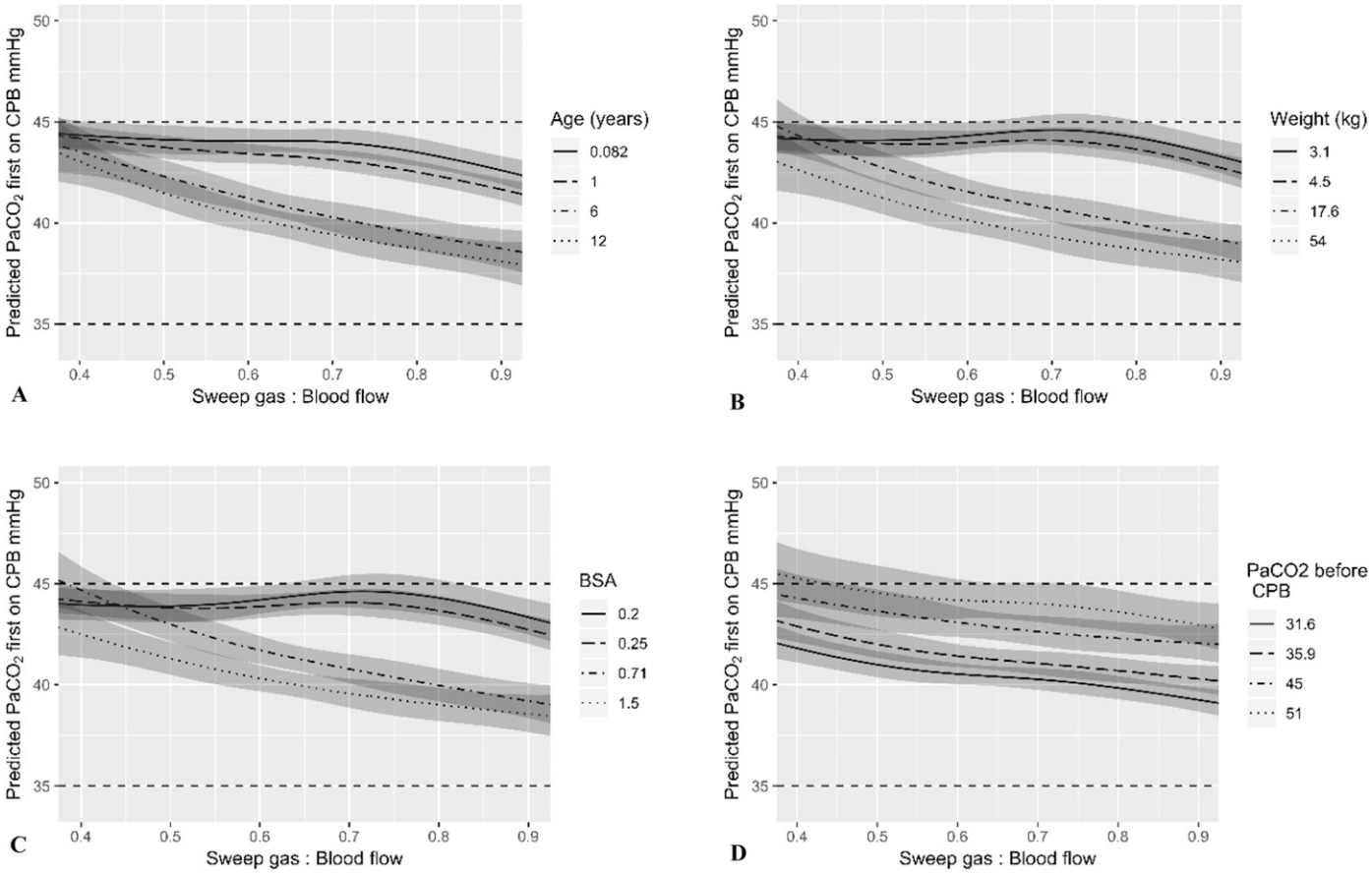

Figure 3. Predicted mean $PaCO_2$ values on CPB according to the V/Q ratio and covariates of interest. (A) Probabilities shown for selected values of age (1 month, 1 year, 6 years, and 12 years). (B) Values for weight shown at the 10th, 25th, 75th, and 90th percentiles. (C) Values for BSA shown at the 10th, 25th, 75th, and 90th percentiles. (D) Values for $PaCO_2$ before bypass shown at the 10th, 25th, 75th, and 90th percentiles.

acceptable $PaCO_2$ values. Although a V/Q ratio closer to one resulted in a lower $PaCO_2$ value on CPB as predicted, it was still within physiologic limits for the period of time before the first blood gas sample. However, we observed little difference in the probability of being within 35–45 mmHg or predicted $PaCO_2$ values for V/Q ratios between .6 and .9 when examining all CPB cases. Patients younger than 1 year and weighing less than 4.5 kg correspond to the use of a Terumo FX05 oxygenator and may require a higher V/Q ratio to obtain appropriate $PaCO_2$ values when compared with their older and larger counterparts. Those patients in the 17.6 and 54 kg groups corresponded to FX15 and FX25, respectively. The older and larger patient probabilities of being within parameter and the predictability of doing so improved up until approximately a V/Q of .6 and then tapered off, indicating there was no improvement or advantage at the higher V/Q settings.

LIMITATIONS

In addition to the single-center retrospective analysis study design, this study was limited by minor variability in the timing of the first blood gas drawn on CPB because of the lack of a set protocol which would have been in place with a prospective study design. These data are only applicable to the V/Q set for the initiation and first few minutes of CPB as only the time period up to the first blood gas was examined. Partial pressure of carbon dioxide values from a prime blood gas sample were not gathered for analysis within this study but "blood prime vs. not blood primed" was analyzed without any significance. This study was also limited by the use of a single oxygenator manufacturer, air–oxygen blender manufacturer, and air flow measurement device and, therefore, may not be easily generalized to other oxygenator or air–oxygen blender manufacturers. Furthermore, evaluating a 1:1 ratio was not feasible as there were too few patients exposed to a V/Q ratio greater than .9.

CONCLUSION

Using a .6 V/Q ratio at the onset of CPB achieved a $PaCO_2$ value within normal physiologic limits. No material advantage was observed for higher V/Q ratios when examined across all CPB cases. However, the smaller congenital patient population using smaller oxygenators may benefit from a higher V/Q to achieve similar probabilities of a $PaCO_2$ value within normal physiologic limits. A V/Q of .6–.9 appears to equally achieve an acceptable $PaCO_2$ value within the larger congenital patient population. Further research with a randomized controlled trial methodology is required to determine the optimal V/Q for subpopulations because, as is usually the case in congenital cardiac patients, one size may not fit all.

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