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# The Effect of $PaCO_2$ on Cerebral Perfusion: An Experimental Swine Model

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**Abstract:** Adequate cerebral perfusion is of particular concern to the clinician and is a major factor in postoperative morbidity. Cerebral circulation has the ability to autoregulate blood flow in order to maintain nutrient delivery and prevent high intravascular pressures. The focus of this study was to characterize the impact of gradually changing arterial $CO_2$ levels on cerebral perfusion. A total of eight porcine subjects were placed into either a normothermic group (NG, $N = 4$, rectal temperature = 35.4 ± 1.2° C) or a hypothermic group (HG, $N = 4$, 30.6 ± 0.6° C). After initiation of cardiopulmonary bypass, the $PaCO_2$ values sequentially varied between 24 and 56 mmHg. Arterial, venous, and internal jugular blood gas data were collected at 4 mmHg increments, and relative cerebral blood flow was calculated as CBF = 1 $(C_{arterial}O_2–C_{jugular}O_2)^{-1}$ Physiological parameters were similar in both groups across all test conditions: mean arterial pressure—NG 81.6 ± 11.9 mmHg versus HG 73.4 ± 7.0 mmHg, $p$ = NS, and systemic oxygen consumption—HG 110.6 ± 30.0 mL $min^{-1}$ versus NG 136.4 ± 37.9 mL $min^{-1}$, $p$ = NS. No significant differences were found in CBF in the NG (21.8 ± 4.4 mL $min^{-1}$ 100 gL at $PaCO_2$ = 56 mmHg versus 20.5 ± 5.0 mL $min^{-1}$ 100 $g^{-1}$ at $PaCO_2$ = 24 mmHg) or the HG (24.3 ± 9.5 mL $min^{-1}$ 100 $g^{-1}$ at $PaCO_2$ = 56 mmHg versus 25.6 ± 12.0 mL $min^{-1}$ 100 $g^{-1}$ at PaCO*2* = 24 mmHg). In conclusion, the alteration of $PaCO_2$ under both hypothermic and normothermic conditions resulted in no significant differences in 1 $(C_{arterial}O_2 - C_{jugular}O_2)^{-1}$ in this model. **Keywords:** $PaCO_2$, cerebral perfusion, jugular desturation. *JECT. 2001;33:185–192*

Neurological complications are associated with the conduct of cardiopulmonary bypass (CPB), with methods of perfusion, surgical technique, and anesthetic management all implicated as possible causes (1,2). Although over-all mortality associated with CPB has continued to decline, death resulting from neurological injury has increased (3). Although the specific etiologies of cognitive dysfunction and stroke remain unknown, cerebral hypoperfusion is known to influence postoperative outcome (4).

Cerebral circulation, as with other vascular beds, is able to regulate blood flow to maintain nutrient delivery and prevent high intravascular pressures. However, the mechanisms that couple cerebral blood flow (CBF) to metabolism are not fully understood. Currently, the most widely accepted hypothesis is that metabolic products of neural activity are vasoactive or lead to the release of vasoactive substances. Local resistance of blood vessels, and, therefore flow, is proportional to the local concentrations of these metabolites (5). Various metabolites have been proposed to have the potential to alter CBF, including adenosine, carbon dioxide/H+ concentration, oxygen, potassium, calcium, and prostaglandins (5–11).

Although pH management strategies have received much investigative attention, the importance of tight regulation of arterial $PCO_2$ during bypass, regardless of the strategy employed, remains controversial. The focus of this study was to characterize the impact of gradually changing arterial $CO_2$ levels on cerebral perfusion in a swine model.

## METHODS

All animals used received humane care in compliance with the Guide for the Care and Use of Laboratory Animals published by the National Institutes of Health (NIH Publication No. 85-23, revised 1985). A total of eight mixed gender porcine subjects, approximately 45 kg , were

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**Table 1.** Hemodynamic and blood gas ranges during the experimental period.

| Parameter | Hypothermic | Normothermic |
|---|---|---|
| MAP | 70–80 mmHg | 70–80 mmHg |
| $PaO_2$ | 150–250 mmHg | 125–200 mmHg |
| $PvO_2$ | 30–45 mmHg | 30–45 mmHg |
| $SaO_2$ | 95–100% | 95–100% |
| $SvO_2$ | 70–80% | 70–80% |
| $PaCO_2$ | Varied | Varied |
| $PvCO_2$ | Varied | Varied |

used for this investigation. Animals were identified as either normothermic (NG, $N = 4$) or hypothermic (HG, $N = 4$).

All subjects were placed on CPB. During each experiment, the animal was maintained within normal physiologic ranges of all hemodynamic parameters, and the arterial and jugular venous blood gases were monitored continuously with an in-line blood gas monitor (Terumo Sarns, CDI 500, Ann Arbor, MI). In addition, venous blood gases were monitored using additional in-line monitors (Terumo Sarns, CDI 400, Ann Arbor MI; Terumo Sarns, CDI 100, Ann Arbor, MI). Mean arterial blood pressure and blood gas status were controlled according to predetermined standards (Table 1). Mixed venous saturation, electrocardiogram, and hemodynamics were measured continuously.

In both experimental groups, the $PaCO_2$ was increased from 40 mmHg to 56 mmHg. After reaching 56 mmHg, $PaCO_2$ levels were decreased to 24 mmHg. Following samples at 24 mmHg, the $PaCO_2$ levels were returned to 40 mmHg. Data were collected at each 4mmHg change in $PaCO_2$ from the in-line monitors, anesthesia monitors, and the computer-assisted perfusion system. In addition, laboratory analyses of arterial, venous, and jugular blood gases were performed at $PaCO_2 = 24$ mmHg, 40 mmHg, and 56 mmHg. The results were used to calibrate the blood gas monitors and to verify the integrity of the final data.

### Anesthetic Management

The selected animals were anesthetized with a mixture of intramuscular ketamine (20 mg/kg) and xylazine (2 mg/kg). Each animal was intubated with an endotracheal tube (6.5 F) and ventilated with a tidal volume equivalent to 20–30 mL $kg^{-1}$ body weight at a rate of 15–20 breaths per minute. Electrocardiogram leads were placed, and the heart rate was continuously monitored. The femoral artery and vein were cannulated with 14-gauge needles for hemodynamic monitoring and medication infusion. Subjects were intermittently dosed with pentothal (100 mcg/kg body weight) and pavulon (50 mcg/kg body weight). The antiarrhythmic agent bretylium (3 mg/kg) was administered before opening the chest through a midline sternotomy.

**Table 2.** In-line monitor accuracy—CDI versus laboratory analysis basis.

| Location | pH | $PCO_2$ | $PO_2$ |
|---|---|---|---|
| Arterial sensor (CDI 500) | 0.02 ± 0.04 | –0.4 ± 2.8 | 8.0 ± 34.0 |
| Jugular sensor (CDI 500) | 0.02 ± 0.01 | –0.4 ± 2.2 | –2.0 ± 3.0 |
| Venous sensor (CDI 400 & 100) | 0.04 ± 0.05 | –0.3 ± 2.4 | 2.4 ± 6.0 |
| CLIA '88 Standard | ±0.04 | ±5.0 | ±10% |

### Surgical Management

A midline sternotomy was performed, and the great vessels were dissected free in preparation for cannulation. A purse string suture was placed in the aorta to secure a 7.0-mm arterial cannula (Texas Medical Products, Houston, TX). A second purse string suture was placed in the right atrial appendage, into which a dual stage 34/46 F cannulae (Research Medical Inc., Medvale, UT) was placed. A third cannula (Research Medical Inc., Midvale, UT) (16 F) was placed retrograde into the right internal jugular vein and secured with a purse string suture. Before cannulation, each animal received a bolus dose of 400 IU/kg of bovine lung heparin and adequate anticoagulation (> 480 sec) was assured using celite-based ACT analysis.

### Perfusion Management

A standard CPB circuit was utilized and consisted of a hollow fiber membrane oxygenator (Cobe Cardiovascular, Arada, CO), a hard shell cardiotomy reservoir (Cobe Cardiovascular, Arada, CO), a soft shell venous reservoir (Cobe Cardiovascular, Arada, CO), a 40-micron arterial line filter (Cobe Cardiovascular, Arada, CO), polyvinyl chloride tubing, and a centrifugal pump (Medronic,

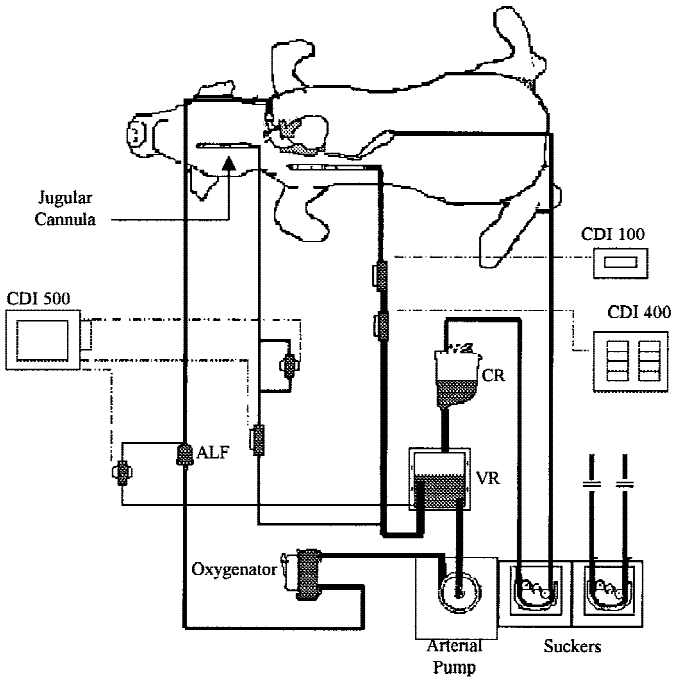


**Figure 1.** Cardiopulmonary bypass circuit. ALF = arterial line filter; CR = cardiotomy reservoir; VR = venous reservoir.

Brooklyn Park, MN) (Figure 1). A CDI 500 shunt sensor was inserted into the arterial filter purge line. A second shunt sensor was placed into a bypass line of the jugular line. In addition, a CDI 400 flow through sensor and a CDI 100 Hct/Sat probe were inserted into the venous line (Table 2).

The circuit was primed with 1200 mL of plasmalyte-A (a balanced electrolyte solution), 50 mL of 8.4% sodium bicarbonate (1 mEq $mL^{-1}$), and 2500 IU $L^{-1}$ of bovine lung heparin.

The CPB procedure was conducted by maintaining a mean arterial blood pressure with the use of flow and/or vasoactive substances (neosynephrine, 80 μg $mL^{-1}$ or sodium nitroprusside 200 μg $mL^{-1}$). Arterial, venous, and rectal temperatures were measured throughout the entire procedure. After separation from CPB, the effects of heparin were reversed with protamine sulfate, administered at a rate of 1 mg of protamine per 100 IU of total heparin administered.

### Termination

The experimental period consisted of a CPB duration of approximately 170 min. During this time, hemotologic and hemodynamic parameters were maintained according to the above protocol.

At termination of each experiment, the animal was euthanized by the concurrent administration of barbiturate (1 mg $kg^{-1}$) and potassium chloride (20 mEq) directly into the aortic root. The ventilator was turned off, and the endotracheal tube was removed. If any electrical activity ensued, or spontaneous breathing occurred, the animal was given an additional dose of the euthanizing drugs.

### Data Collection

The following data were recorded: partial pressure of oxygen in the jugular vein ($P_{jv}O_2$), partial pressure of carbon dioxide in the jugular vein ($P_{jv}CO_2$), arterial hemoglobin-oxygen saturation ($S_aO_2$), arterial partial pressure of oxygen ($P_aO_2$), arterial partial pressure of carbon dioxide ($P_aCO_2$), venous hemoglobin–oxygen saturation ($S_vO_2$), venous partial pressure of oxygen ($P_vO_2$), venous partial pressure of carbon dioxide ($P_vCO_2$), mean arterial pressure (MAP), pump flow, temperature (arterial, venous, and rectal). In addition, $S_vO_2$ and $S_{jv}O_2$ were calculated as:

$$\%\ SO_2 = \frac{(PO_2')^3 + 150\ PO_2'}{(PO_2')^3 + 150\ PO_2' + 23400}$$

where $PO_2' = PO_2 \chi\ 10^{[0.48(pH-7.40)-0.0013([HCO_3-]-25)]}$

At each data collection point, calculated $S_vO_2$ values were compared to measured $S_vO_2$ values to verify the validity of the equation for calculating $S_{jv}O_2$.

The preceding parameters were recorded for all animals following the described sampling sequence. From these measurements, arterial, venous, and jugular venous oxygen content ($CaO_2$, $C_vO_2$, and $C_{jv}O_2$), oxygen delivery ($DO_2$), systemic oxygen consumption ($VO_2$), the difference in oxygen content between arterial blood and jugular venous blood ($A\text{-}_{jv}O_2$), and relative cerebral blood flow ($A\text{-}_{jv}O_2^{-1}$) were calculated as:

$$\begin{aligned} C\times O_2(mL/dL) &= (\%S\times O_2\times[Hb]\times 1.36) + (0.003\times P\times O_2) \\ DO_2(mL/min) &= CaO_2\times \text{flow rate}\times 10 \\ VO_2(mL/min) &= (CaO_2 - CvO_2)\times \text{flow rate}\times 10 \\ A\text{–}JvO_2(mL/dL) &= CaO_2 - CjvO_2 \\ A\text{–}jvO_2^{-1}(mL/min/100\ g) &= 1/(A\text{–}jvO_2) \end{aligned}$$

### Statistical Analysis

Parametric data were analyzed using one-way analyses of variance (ANOVA). When significant f ratios were reached, additional multiple comparison tests were performed and included Fisher's least significance difference. Statistical significance were accepted at the $p < .05$ level.

## RESULTS

Mean CPB time for both groups was 170 ± 23 min. Measured temperatures and $VO_2$ differed significantly between the hypothermic and normothermic group at each sample point. Otherwise, no significant differences were seen between groups or sample times for $DO_2$, $VO_2$, MAP, or $1/(A_{jv}O_2)$ (Figures 2, 3a, 3b).

The values obtained from the CDI monitors were compared to the values obtained from laboratory analyses at $PaCO_2$ = 24, 40, and 56 mmHg. The mean differences (bias) between the CDI and laboratory analysis for pH, $PCO_2$, $PO_2$, and saturation for each sample location were calculated. Each of the monitors fell within the standards for laboratory analyzers set forth by the Clinical Laboratory Improvement Act of 1988 (Table 2).

The equation used to calculate $S_{jv}O_2$ was verified by performing concurrent calculation and measurement of $S_vO_2$ (Figure 4). The mean difference between calculated and measured $S_vO_2$ values was 0.7 ± 3.3%.

## DISCUSSION

Adequate cerebral perfusion continues to be a challenge to clinicians seeking to prevent postoperative neurological morbidity. Cerebral dysfunction does not represent discrete negative outcomes; rather, it is a continuum ranging from stroke, occurring in 2–5% of coronary artery bypass grafting (CABG) patients, to more cryptic cognitive deficits, occurring in 30–80% of the patients (12–23). These events place a significant burden on the health- care delivery system, because the cost of perioperative (both cardiac and noncardiac) stroke is estimated to be $6 billion (US) per year, representing over 25% of the resources spent for stroke treatment (24).

Although neurological complications have always been common and costly problems associated with CPB, improvements in perfusion technology, surgical technique,

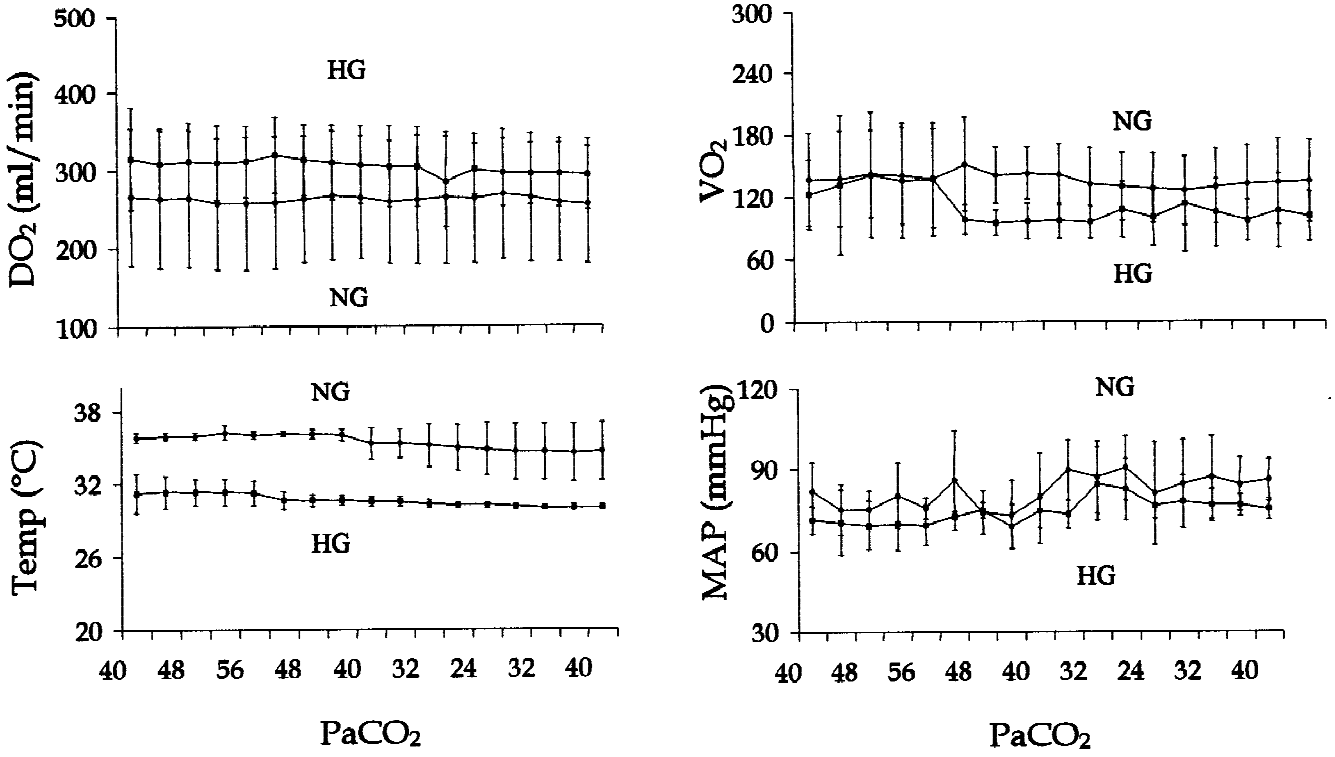


**Figure 2.** Oxygen delivery ($DO_2$, mL/min), oxygen consumption ($VO_2$, mL/min), rectal temperature, and mean arterial pressure (MAP) during the experimental period. HG = hypothermic group; NG = normothermic group.

and anesthetic management have focused attention in this area. The significant improvements in myocardial protection and cardiac outcome have resulted in an increasing percentage of morbidity and mortality associated with central nervous system (CNS) injury (1,2). Although overall mortality associated with CPB has declined, the portion of deaths resulting from neurological injury has increased (3). The problem will likely increase parallel to the demographic shift toward more elderly patients (25), because increasing age is well known to increase risk for postoperative cognitive decline and stroke (19,21,26–31). In addition to microembolic events, cerebral hypoperfusion has been demonstrated to be involved in cognitive dysfunction and stroke (4). Although the relative contribution of each is unknown, it is unlikely that the two are mutually exclusive.

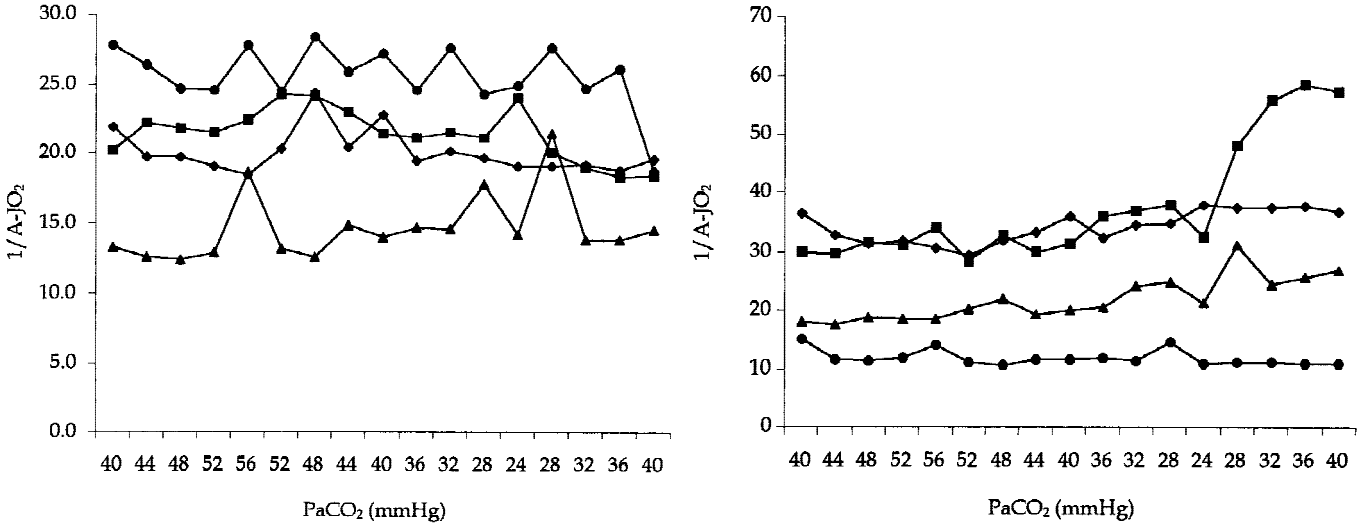


**Figure 3a.** $1/A\text{-}JO_2$ versus arterial $PCO_2$ in the normothermic group. Figure 3b. $1/A\text{-}JO_2$ versus arterial $PCO_2$ in the hypothermic group.

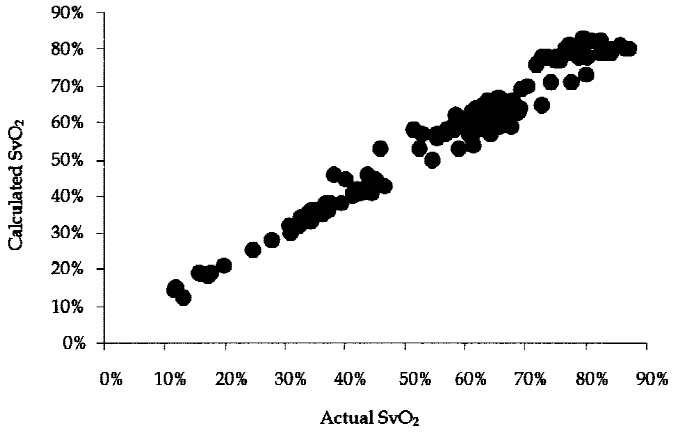


**Figure 4.** Actual versus calculated venous oxygen–hemoglobin saturation.

### Influence of Blood Gas Control

Acid-base management during hypothermic CPB is a long-debated topic, and changes in cerebral blood flow during CPB are intimately related to the $PaCO_2$ maintained during bypass (32,33). The specific strategy (alpha-stat versus pH-stat) employed will not alter cerebral metabolism, but it does affect cerebral blood flow and neurologic outcome (34). Neurological dysfunction has been reported in patients receiving pH-stat management, probably resulting from cerebral hyperemia (34). In a randomized study by Patel and associates, patients receiving alpha-stat management had less disruption of cerebral autoregulation during CPB, accompanied by a reduced incidence of postoperative cerebral dysfunction (35). More recent studies have shown less decline in cognitive performance when alpha stat management is employed, especially with prolonged CPB times (34,36). These data support the theory that alpha-stat management produces stable cerebral autoregulation and enzymatic activity.

### $PaCO_2$ and Cerebral Embolization

Temperature and pH management also influence microembolic phenomena, and modifications in these parameters have increasingly been shown to reduce the incidence of postoperative neuropsychologic dysfunction (37). These findings are significant, because more than one-third of embolic events originate from unknown sources. In a study of 196 patients undergoing routine CABG, over 30% of embolic signals, detected by ultrasound, were not associated with any specific act by the surgeon, perfusionist, or anesthesiologist (38). At least some of these events may be related to the blood gas management performed. For example, the $PaCO_2$ maintained during CPB has been shown to influence the incidence of cerebral emboli. At both normothermia and hypothermia, a decrease in $PaCO_2$ of approximately 25 mmHg reduced the number of measured emboli by 45–60% in a series of swine studies conducted at the Mayo Clinic (39,40).

### $PaCO_2$ and Cerebral Blood Flow

Cerebral oxygen metabolism is intimately related to cerebral perfusion, and several measures are available to reflect this balance. Increasing $C_{a\text{-}jv}O_2$ is associated with cognitive decline independent of age (40,41). During low perfusion states, the brain can compensate for reduced CBF by increasing oxygen extraction from arterial hemoglobin, which is reflected in $S_{jv}O_2$. Such a decrease of $S_{jv}O_2$ indicates a mismatch between oxygen supply and demand. Decreased $S_{jv}O_2$ is associated with reduced cerebral perfusion pressure and increased postoperative cerebral dysfunction (39,42). Furthermore, calculations of relative changes in cerebral blood flow can be made from $C_{a\text{-}jv}O_2$ if the cerebral metabolic rate for oxygen remains unchanged, which can be assumed during stable thermic CPB (7,8). Under such conditions, CBF can be calculated by:

$$CBF = 1 / C_{a\text{-}jv}O_2$$

The cerebral blood flow (CBF) response to metabolic coupling is thought to be curvilinear, but for $PaCO_2$ values between 20 and 80 mmHg the response is almost linear, increasing 1.8 mL/100 g/min/mmHg $PaCO_2$ (7,8). The mechanism of carbon dioxide reactivity seems to be a direct action of H+ on the vascular smooth muscle on the brain side of the blood–brain barrier (5). The response to arterial $PCO_2$ is dependent on the diffusion of carbon dioxide across the blood–brain barrier and the exclusion of $HCO_{3-}$. The result is a decrease in periarteriolar cerebrospinal fluid pH and subsequent dilatation. Although this pH response is not unique to the cerebral vascular bed, the high solubility of $CO_2$ and the exclusion of $H^+$ and $HCO_{3-}$ by the blood–brain barrier make the cerebral vasculature very sensitive to pH (5).

In this study, however, gradually changing $PaCO_2$ levels did not seem to affect cerebral perfusion. In both the hypothermic group and the normothermic group, factors that would affect the validity of the measurement technique were held constant across experimental conditions.

At first glance, these data suggest that slowly drifting $PaCO_2$ does not affect cerebral blood flow, and, therefore, may not be of concern. Indeed, the $A_{\text{-}jv}O_2$, a validated reflection of cerebral blood flow, did not change in response to altered $PaCO_2$. The in-line monitors used for a portion of the data collection performed as assessed by monitor laboratory bias. The physiological variables, including mean arterial pressure and body temperature, were well controlled and should not have influenced the final results. However, the conclusion that $PaCO_2$ does not affect cerebral blood flow would be erroneous based upon this study alone. The reactivity of cerebral circula-

tion to arterial $PCO_2$ is influenced by factors that could not be controlled in this model, including the initial metabolic state of the tissue and the resting caliber of the vessels. In addition, any metabolic or pharmacological process that alters the blood-brain barrier will alter the $PCO_2$ response by allowing $HCO_{3-}$ to cross into the cerebrospinal fluid and alter pH. None of these influences was accounted for in this study.

Furthermore, discretion must be used when translating the results of animal trials into the human response. For example, cerebral $CO_2$ reactivity is much greater in gray matter than white matter, probably because gray matter has a greater vascular density (5). The human brain has a larger portion of gray matter, thus it is reasonable to assume that the $PCO_2$ response in swine is somewhat muted.

## CONCLUSION

Cerebral perfusion, measured by $A_{-jv}O_2$, did not vary significantly in response to steady changes in $PaCO_2$ in this swine model. Future refinements in this model should account for the factors that are known to alter cerebrovascular $CO_2$ reactivity. Further investigation into the impact of $PCO_2$ management during CPB is needed to establish its relative importance to patient outcome and to define optimal blood gas management strategies.

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**Appendix A.** Arterial, jugular, and venous pH changes with changing arterial $PCO_2$.

| | Normothermic pH | | | Hypothermic pH | | |
|---|---|---|---|---|---|---|
| $PaCO_2$ | Arterial | Jugular | Venous | Arterial | Jugular | Venous |
| 40 mmMg | 7.48 ± 0.02 | 7.40 ± 0.03 | 7.43 ± 0.05 | 7.50 ± 0.06 | 7.41 ± 0.06 | 7.46 ± 0.05 |
| 44 mmHg | 7.45 ± 0.03 | 7.41 ± 0.02 | 7.44 ± 0.06 | 7.47 ± 0.05 | 7.41 ± 0.05 | 7.44 ± 0.05 |
| 48 mmHg | 7.43 ± 0.02 | 7.41 ± 0.03 | 7.43 ± 0.06 | 7.45 ± 0.07 | 7.41 ± 0.05 | 7.42 ± 0.05 |
| 52 mmHg | 7.40 ± 0.05 | 7.38 ± 0.03 | 7.40 ± 0.08 | 7.42 ± 0.07 | 7.39 ± 0.04 | 7.41 ± 0.04 |
| 56 mmHg | 7.36 ± 0.07 | 7.36 ± 0.05 | 7.37 ± 0.09 | 7.39 ± .07 | 7.39 ± 0.04 | 7.37 ± 0.04 |
| 52 mmHg | 7.40 ± 0.05 | 7.36 ± 0.03 | 7.37 ± 0.07 | 7.40 ± 0.04 | 7.38 ± 0.03 | 7.39 ± 0.05 |
| 48 mmHg | 7.41 ± 0.06 | 7.36 ± 0.04 | 7.37 ± 0.07 | 7.42 ± 0.05 | 7.38 ± 0.04 | 7.38 ± 0.05 |
| 44 mmHg | 7.45 ± 0.04 | 7.37 ± 0.04 | 7.39 ± 0.09 | 7.44 ± 0.05 | 7.39 ± 0.03 | 7.39 ± 0.03 |
| 40 mmHg | 7.49 ± 0.06 | 7.38 ± 0.04 | 7.41 ± 0.08 | 7.46 ± 0.04 | 7.40 ± 0.04 | 7.43 ± 0.06 |
| 36 mmHg | 7.50 ± 0.05 | 7.39 ± 0.03 | 7.45 ± 0.05 | 7.50 ± 0.06 | 7.41 ± 0.06 | 7.45 ± 0.04 |
| 32 mmHg | 7.54 ± 0.06 | 7.41 ± 0.04 | 7.47 ± 0.06 | 7.54 ± 0.05 | 7.44 ± 0.07 | 7.48 ± 0.06 |
| 28 mmHg | 7.58 ± 0.06 | 7.43 ± 0.04 | 7.51 ± 0.07 | 7.59 ± 0.05 | 7.45 ± 0.10 | 7.52 ± 0.05 |
| 24 mmHg | 7.61 ± 0.06 | 7.45 ± 0.04 | 7.54 ± 0.07 | 7.63 ± 0.04 | 7.48 ± 0.06 | 7.59 ± 0.11 |
| 28 mmHg | 7.58 ± 0.06 | 7.48 ± 0.03 | 7.57 ± 0.07 | 7.59 ± 0.04 | 7.50 ± 0.06 | 7.57 ± 0.05 |
| 32 mmHg | 7.55 ± 0.06 | 7.48 ± 0.03 | 7.55 ± 0.07 | 7.56 ± 0.05 | 7.49 ± 0.06 | 7.56 ± 0.06 |
| 36 mmHg | 7.51 ± 0.06 | 7.47 ± 0.03 | 7.53 ± 0.06 | 7.52 ± 0.05 | 7.48 ± 0.05 | 7.53 ± 0.07 |
| 40 mmHg | 7.49 ± 0.07 | 7.46 ± 0.04 | 7.50 ± 0.07 | 7.48 ± 0.05 | 7.46 ± 0.04 | 7.51 ± 0.04 |
| Average | 7.48 ± 0.05 | 7.41 ± 0.03 | 7.45 ± 0.07 | 7.49 ± 0.05 | 7.43 ± 0.05 | 7.46 ± 0.05 |

**Appendix B.** Arterial, jugular, and venous $PCO_2$ changes during the experimental period.

| Target | Normothermic $PCO_2$ (mmHg) | | | Hypothermic $PCO_2$ (mmHg) | | |
|---|---|---|---|---|---|---|
| $PaCO_2$ | Arterial | Jugular | Venous | Arterial | Jugular | Venous |
| 40 mmMg | 40.0 ± 0.0 | 52.3 ± 7.5 | 48.3 ± 9.4 | 40.0 ± 0.0 | 52.8 ± 5.3 | 50.0 ± 6.5 |
| 44 mmHg | 44.0 ± 0.0 | 52.3 ± 8.0 | 48.8 ± 9.4 | 43.0 ± 2.0 | 52.8 ± 3.9 | 50.3 ± 5.6 |
| 48 mmHg | 48.0 ± 0.0 | 52.8 ± 7.4 | 50.3 ± 10.9 | 48.0 ± 0.0 | 54.0 ± 3.6 | 53.3 ± 3.9 |
| 52 mmHg | 52.0 ± 0.0 | 56.3 ± 6.1 | 54.5 ± 11.2 | 52.0 ± 0.0 | 55.0 ± 2.9 | 56.0 ± 4.2 |
| 56 mmHg | 56.0 ± 0.0 | 57.8 ± 6.6 | 57.5 ± 12.2 | 56.0 ± 0.0 | 58.5 ± 3.7 | 61.5 ± 4.1 |
| 52 mmHg | 52.0 ± 0.0 | 57.5 ± 11.1 | 58.3 ± 11.9 | 52.0 ± 0.0 | 59.0 ± 2.6 | 57.8 ± 4.6 |
| 48 mmHg | 48.0 ± 0.0 | 59.8 ± 9.9 | 56.0 ± 9.6 | 48.0 ± 0.0 | 58.5 ± 2.1 | 57.8 ± 2.1 |
| 44 mmHg | 44.0 ± 0.0 | 57.5 ± 7.9 | 53.0 ± 8.5 | 43.0 ± 2.0 | 56.8 ± 3.2 | 54.8 ± 4.0 |
| 40 mmHg | 40.0 ± 0.0 | 56.3 ± 7.0 | 51.0 ± 8.5 | 40.3 ± 0.5 | 54.8 ± 3.7 | 51.0 ± 0.8 |
| 36 mmHg | 36.0 ± 0.0 | 53.5 ± 7.8 | 45.8 ± 6.6 | 36.0 ± 0.0 | 52.0 ± 4.5 | 47.5 ± 2.6 |
| 32 mmHg | 32.0 ± 0.0 | 51.5 ± 5.8 | 43.3 ± 5.9 | 32.0 ± 0.0 | 48.5 ± 5.4 | 44.8 ± 2.6 |
| 28 mmHg | 28.0 ± 0.0 | 48.5 ± 5.4 | 40.5 ± 6.1 | 28.3 ± 0.5 | 46.3 ± 6.1 | 42.3 ± 1.5 |
| 24 mmHg | 24.0 ± 0.0 | 45.8 ± 5.4 | 38.0 ± 4.5 | 24.0 ± 0.0 | 43.3 ± 6.0 | 36.0 ± 2.2 |
| 28 mmHg | 28.0 ± 0.0 | 41.3 ± 5.4 | 34.5 ± 5.4 | 28.0 ± 0.0 | 40.5 ± 6.5 | 34.8 ± 1.7 |
| 32 mmHg | 32.0 ± 0.0 | 41.3 ± 5.9 | 38.5 ± 9.3 | 32.0 ± 0.0 | 42.0 ± 5.5 | 36.5 ± 1.9 |
| 36 mmHg | 36.0 ± 0.0 | 42.8 ± 5.9 | 38.3 ± 7.3 | 36.0 ± 0.0 | 43.5 ± 4.5 | 40.0 ± 2.4 |
| 40 mmHg | 39.5 ± 0.6 | 45.0 ± 5.4 | 41.3 ± 8.1 | 40.0 ± 0.0 | 45.8 ± 3.0 | 42.3 ± 1.7 |
| Average | 40.0 ± 0.0 | 51.3 ± 7.0 | 46.9 ± 8.5 | 39.9 ± 0.3 | 50.8 ± 4.3 | 48.0 ± 3.1 |

**Appendix C.** Arterial, jugular, and venous $PCO_2$ changes with changing arterial $PCO_2$

| Target $PaCO_2$ | Normothermic $PO_2$ | | | Hypothermic $PO_2$ | | |
|---|---|---|---|---|---|---|
| | Arterial | Jugular | Venous | Arterial | Jugular | Venous |
| 40 mmMg | 211.3 ± 43.4 | 27.8 ± 8.3 | 26.3 ± 6.6 | 217.5 ± 29.0 | 31.5 ± 11.0 | 34.0 ± 11.2 |
| 44 mmHg | 198.8 ± 48.3 | 26.0 ± 8.0 | 25.0 ± 7.3 | 197.8 ± 21.2 | 30.0 ± 9.6 | 33.5 ± 14.0 |
| 48 mmHg | 169.8 ± 22.1 | 25.3 ± 8.1 | 24.5 ± 7.9 | 189.0 ± 25.4 | 31.3 ± 9.4 | 31.5 ± 9.7 |
| 52 mmHg | 152.5 ± 22.8 | 26.0 ± 6.3 | 24.5 ± 7.2 | 187.5 ± 18.3 | 31.8 ± 9.2 | 34.5 ± 11.4 |
| 56 mmHg | 144.3 ± 15.2 | 29.0 ± 4.5 | 26.5 ± 5.3 | 197.3 ± 16.0 | 31.8 ± 6.2 | 34.5 ± 10.7 |
| 52 mmHg | 166.8 ± 14.8 | 27.8 ± 6.8 | 23.8 ± 8.9 | 217.5 ± 17.8 | 31.8 ± 8.1 | 38.3 ± 2.2 |
| 48 mmHg | 181.3 ± 16.9 | 29.5 ± 8.5 | 25.5 ± 9.0 | 230.5 ± 12.1 | 33.0 ± 10.1 | 38.8 ± 3.1 |
| 44 mmHg | 191.8 ± 17.0 | 28.8 ± 4.6 | 25.3 ± 8.3 | 228.3 ± 28.2 | 31.5 ± 9.5 | 37.3 ± 4.6 |
| 40 mmHg | 202.8 ± 25.2 | 28.3 ± 5.9 | 25.3 ± 7.6 | 221.3 ± 19.2 | 31.8 ± 10.6 | 37.0 ± 5.6 |
| 36 mmHg | 199.3 ± 28.1 | 26.5 ± 4.9 | 26.5 ± 5.3 | 215.0 ± 18.5 | 31.0 ± 9.9 | 36.0 ± 5.6 |
| 32 mmHg | 193.8 ± 18.2 | 26.8 ± 4.9 | 25.5 ± 4.7 | 209.0 ± 41.8 | 31.5 ± 9.9 | 35.0 ± 9.6 |
| 28 mmHg | 209.0 ± 10.0 | 26.8 ± 2.2 | 25.5 ± 4.8 | 218.8 ± 22.6 | 32.8 ± 5.3 | 32.5 ± 8.9 |
| 24 mmHg | 214.8 ± 19.8 | 25.0 ± 5.2 | 25.0 ± 4.7 | 222.8 ± 17.6 | 28.3 ± 8.6 | 30.8 ± 8.2 |
| 38 mmHg | 192.5 ± 16.1 | 26.0 ± 4.2 | 24.0 ± 5.2 | 203.5 ± 31.9 | 32.3 ± 10.3 | 31.3 ± 6.8 |
| 32 mmHg | 176.0 ± 15.3 | 22.3 ± 4.5 | 23.5 ± 4.7 | 209.8 ± 11.3 | 32.0 ± 10.7 | 32.3 ± 4.1 |
| 36 mmHg | 164.5 ± 21.8 | 22.5 ± 4.9 | 23.8 ± 5.0 | 204.5 ± 10.6 | 31.8 ± 12.0 | 32.0 ± 7.3 |
| 40 mmHg | 152.8 ± 21.5 | 21.5 ± 1.7 | 23.5 ± 4.4 | 184.5 ± 10.4 | 32.0 ± 1.7 | 32.3 ± 6.0 |
| Average | 183.6 ± 22.1 | 26.2 ± 5.5 | 24.9 ± 6.3 | 209.1 ± 20.7 | 31.5 ± 9.0 | 34.2 ± 7.6 |