Cardiothoracic Anesthesia, Respiration and Airway

Difficult separation from cardiopulmonary bypass and ΔPCO_2

André Denault MD FRCPC,
Sylvain Bélisle MD FRCPC,
Denis Babin MSc,
Jean-François Hardy MD FRCPC

Purpose: Venous-arterial and regional differences of the partial pressure in CO_2 (ΔPCO_2), may be used as index to evaluate the adequacy of the cardiac output to the oxygen consumption. To determine the incidence of elevated ΔPCO_2 and its relationship with difficult separation from bypass (DSB) in patients undergoing cardiac surgery, we conducted a prospective observational cohort study.

Methods: Data were collected from 58 consecutive patients undergoing various cardiac operations requiring cardiopulmonary bypass (CPB). During the procedure, arterial and venous blood gases and lactate were sampled. Blood was drawn after induction of anesthesia, during bypass and at the closure of the chest wall. Difficult separation from bypass was defined as a systolic arterial pressure < 80 mmHg, and diastolic pulmonary artery pressure > 15 mmHg during progressive separation from CPB with inotropic or mechanical support of cardiac function, or hemodynamic instability resulting in reintroduction of extra-corporeal circulation or insertion of an intra-aortic balloon pump.

Results: In our study, 65% of the samples were associated with elevated ΔPCO_2 (> 6 mmHg). Variables associated with difficult weaning were LVEF, duration of bypass and aortic cross-clamping, pre-bypass ΔPCO_2 and in-bypass lactate values ($P < 0.05$). Multivariable analysis identified the pre-bypass ΔPCO_2 and the duration of bypass as predictors of DSB.

Conclusion: Elevated ΔPCO_2 is frequently observed during cardiac surgery and values obtained before bypass were associated with DSB. The ΔPCO_2 gradients could be used as marker of the adequacy of tissue perfusion during cardiac surgery.

Objectif : Les différences veino-artérielles et régionales de pression partielle de CO_2 (PCO_2) peuvent servir d'index à l'évaluation de l'adéquation du débit cardiaque à la consommation d'oxygène. L'observation prospective d'une cohorte a été réalisée dans le but de déterminer l'incidence d'une PCO_2 élevée et sa relation avec le sevrage difficile de la CEC chez des patients qui subissent une intervention cardiaque.

Méthode : On a recueilli les données provenant de 58 patients consécutifs subissant des interventions cardiaques diverses qui nécessitent une circulation extracorporelle (CEC). Pendant l'intervention, on a testé les gaz du sang veineux et artériel et le lactate. Le sang a été prélevé après l'induction de l'anesthésie, pendant la CEC et à la fermeture du thorax. Un sevrage difficile de la CEC a été défini par une pression artérielle systolique < 80 mmHg et une pression artérielle diastolique pulmonaire > 15 mmHg pendant le sevrage progressif de la CEC avec le soutien inotropique ou mécanique de la fonction cardiaque, ou par l'instabilité hémodynamique résultant de la réintroduction de la circulation extracorporelle ou de l'insertion d'un ballon intra-aortique.

Résultats : Dans notre étude, 65 % des échantillons ont été associés à une PCO_2 élevée (> 6 mmHg). Les variables associées au sevrage difficile ont été la FEVG, la durée de la CEC et du clampage aortique total, la PCO_2 précédant la CEC et les valeurs de lactate pendant la CEC ($P < 0,05$). Une analyse multifactorielle a permis d'identifier la PCO_2 pré-CEC et la durée de la CEC comme des facteurs prédictifs de sevrage difficile.

Conclusion : Une PCO_2 élevée est souvent observée pendant une intervention cardiaque et les valeurs obtenues avant la CEC sont associées à un sevrage difficile de la CEC. Les gradients de PCO_2 peuvent être utilisés comme index de l'adéquation de la perfusion tissulaire pendant l'intervention cardiaque.

From the Department of Anesthesiology, Research Center, Montreal Heart Institute, 5000 Belanger Street East, Montreal, Quebec, H1T 1C8, Canada.

Address correspondence to: Dr. A. Denault, Phone: 514-376-3330; Fax: 514-376-1355; E-mail: denault@videotron.ca

Accepted for publication November 1, 2000.

VENO-ARTERIAL ΔPCO_2 difference (ΔPCO_2) is an index that may be used to evaluate the adequacy of the cardiac output (CO)¹ and to identify the critical oxygen delivery point below which the oxygen consumption-delivery (VO_2/DO_2) relationship becomes dependant.^{2,3}

The role and importance of ΔPCO_2 in cardiac surgery has been studied only in the postoperative period.^{1,4-7} We report our pre-bypass observations on the relationship between ΔPCO_2 and the risk of difficult separation from bypass (DSB).

Methods

This prospective observational study was approved by our research and ethics committee. Data were collected from 58 consecutive patients undergoing various cardiac surgical procedures requiring CPB. The anesthetic management was selected according to the anesthesiologist's preference.

Patient's age, sex, height, weight and pre-operative left ventricular ejection fraction (LVEF) were recorded. Standard monitoring for cardiac surgery was used. The CPB circuit was primed with Ringer's lactate. Arterial and venous blood gases were drawn after induction of anesthesia and every 20 min during cardiopulmonary bypass (CPB). During CPB, the CO was maintained at 2.4 L·m⁻² or according to the mean arterial pressure. A bubble oxygenator, or a membrane in high-risk patients, was used according to the surgeon's choice. Vesical temperature was maintained between 32-34°C during CPB. Hypothermia (21°C) was required in two aortic procedures. After collecting arterial and mixed venous blood gases from the distal port of the pulmonary artery catheter, samples were analyzed at 37°C using α -stat management. (STAT-9, Nova biomedical, Waltham, MA). The manufacturer's precision for PCO₂ is 2.4% (0.6 to 1.6 mmHg for values between 23.5 to 42.6 mmHg). In addition, lactate was obtained from the same sample. During the pre- and in-bypass periods, the maximal values of ΔPCO_2 and lactate were recorded. During CPB, the CO was noted at the time of the blood gas withdrawal. CO determination before and after CPB was obtained by the thermodilution method. The durations of CPB, clamping time, duration of stay in the ICU and in the hospital were recorded and the patients were followed-up until discharge from hospital.

The normal value in humans for ΔPCO_2 is 4 to 6 mmHg.⁸ Clinicians were not blinded to ΔPCO_2 and lactate measurements, but the values were not used to guide the selection of vasoactive medication during separation from bypass. In addition, the anesthesiologists were unaware of the potential relationship

between DSB and those indices at the time of the study. Delayed separation from bypass was defined as a systolic arterial pressure < 80 mmHg, and diastolic pulmonary artery pressure > 15 mmHg during separation from CPB without inotropic or mechanical support of cardiac function⁹ or hemodynamic instability resulting in the reintroduction of CPB or the insertion of an intraaortic balloon pump (IABP). In patients with DSB, a low peripheral arterial blood pressure was confirmed by central aortic pressure measurement. Patients requiring large amounts of vasopressors (nor-epinephrine or epinephrine >4 $\mu\text{g}\cdot\text{min}^{-1}$), inotropes (dobutamine >10 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ or the use of amrinone and milrinone) and/or IABP after CPB were included in the group DSB.

Statistical analysis

The number of patients to be included was based on a difference in 2 mmHg using an α of 0.05 and a β of 0.20. Based on these assumptions, 15 patients per group were necessary. Pre- and in-bypass variables were related with the presence or absence of DSB by using chi-square and Fisher's exact test. Continuous variables were entered in a logistic regression analysis to determine independent predictors of DSB. Univariate analysis were used for preliminary selection (alpha level of 0.25) of factors with $P < 0.1$ to be included in a stepwise hierarchical regression. The final model included all factors significant at the 0.05 alpha level. Age, gender, weight, and height were included in the model to attenuate potential sampling biases. Results are expressed as mean $\pm$ standard deviation.

Results

A total of 58 patients were included in this study: six died. Demographic data are presented in Table I: DSB was observed in 15 patients (26%): four died and five required installation of an IABP. Sixty-five percent of the samples were associated with elevated ΔPCO_2 .

Univariate variables associated with DSB were LVEF, duration of bypass and clamping, pre-bypass PCO₂ and lactate concentration during CPB ($P < 0.05$). The multivariable analysis identified pre-bypass ΔPCO_2 and duration of bypass as predictors of a DSB (Table II).

Discussion

In this prospective study we observed elevated ΔPCO_2 in 37 patients, which was more than half of our cohort. In patients with DSB, we observed similar risk factor as previously described such as LVEF, duration of bypass and clamping. However, in those patients with DSB, the ΔPCO_2 before and during bypass was

TABLE I Characteristics of the patients

Variable	Easy		Difficult		P
	Mean $\pm$ SD	95% CI	Mean $\pm$ SD	95% CI	
Sex	F=10 M=32		F=5 M=10		0.507
Procedures					0.016
Revascularisation	32		6		
Non-Revascularisation	10		9		
Valvular surgery	8		5		
IVS repair			1		
Aortic surgery			2		
Complex procedures	1		1		
Foramen ovale closure	1				
Age	60.8 $\pm$ 9.5	57.8 - 63.7	60.3 $\pm$ 14.0	52.6 - 68.1	0.896
Weight	74.9 $\pm$ 16.5	69.8 - 80.1	71.0 $\pm$ 15.9	62.2 - 79.8	0.430
Height	167.1 $\pm$ 12.1	163.3 - 170.9	168.2 $\pm$ 9.5	162.9 - 173.5	0.756
LVEF (%)	57 $\pm$ 13	53 - 61	47 $\pm$ 13	39 - 54	0.013
Bypass time (min)	72 $\pm$ 24	64 - 80	117 $\pm$ 42	93 - 140	0.001
Clamping time (min)	49 $\pm$ 21	42 - 56	64 $\pm$ 29	48 - 80	0.032
ICU stay (days)	4.1 $\pm$ 1.7	3.6 - 4.7	7.2 $\pm$ 3.8	4.7 - 9.8	0.022
Hospital stay (days)	11.3 $\pm$ 11.9	7.5	20.1 $\pm$ 13.3	11.1 - 29	0.040
Mortality (%)	4.8		26.7		0.036
CI pre(L·m ⁻¹ ·m ⁻²)	2.2 $\pm$ 0.5	2.1-2.4	2.1 $\pm$ 0.5	1.9 - 2.4	0.618
CI per(L·m ⁻¹ ·m ⁻²)	2.4 $\pm$ 0.2	2.3-2.4	2.2 $\pm$ 0.3	2.0 - 2.4	0.056
PvO ₂ pre (mmHg)	48.1 $\pm$ 7.7	45.7 - 50.5	52 $\pm$ 16.2	42.7 - 61.4	0.229
PvO ₂ per (mmHg)	47 $\pm$ 6.5	44.9 - 49	76.4 $\pm$ 78.6	32.8 - 120	0.169
(Δ PCO ₂ pre (mmHg)	6.2 $\pm$ 2.6	5.4 - 7.1	8.1 $\pm$ 3.3	6.2 - 10.0	0.039
(Δ PCO ₂ per (mmHg)	7.3 $\pm$ 3.3	6.3 - 8.3	9.5 $\pm$ 4.5	7.0 - 12.0	0.048
Lactate pre (mMol·L ⁻¹)	1.7 $\pm$ 0.6	1.5 - 1.9	2.0 $\pm$ 0.8	1.5 - 2.3	0.108
Lactate per (mMol·L ⁻¹)	3.2 $\pm$ 0.9	2.9 - 3.5	5.0 $\pm$ 2.4	3.7 - 6.3	0.011

Complex procedures = combined valvular and revascularisation

IVS = interventricular septum

LVEF = left ventricular ejection fraction

ICU = intensive care unit

CI = cardiac index

PvO₂ = partial pressure in oxygen of venous blood

Δ PCO₂ pre = delta PCO₂ or veno-arterial PCO₂ difference value before bypass

Δ PCO₂ per = veno-arterial PCO₂ difference value during bypass

Lactate pre = lactate value before bypass

Lactate per = lactate value during bypass

also higher. This is the first study to report such an association. These observations support a relationship with DSB and an unmatched VO₂/DO₂. This mismatch will be associated with an increase in Δ PCO₂.

Ariza studied 10 patients after CPB and found that the Δ PCO₂ was not associated with inadequate tissue perfusion: only two patients had elevated Δ PCO₂ but all their patients were low risk with good LVEF and none required inotropes post operatively.⁴ Lebuffe *et al.* and Ruokonen *et al.*^{1,6} observed an association between low systemic and regional blood flow and increased Δ PCO₂ after cardiac surgery and Cavalieri⁵ observed an association between post-op high Δ PCO₂ and complications. In a randomized study involving 393 patients using goal-oriented hemodynamic thera-

py, Pölönen *et al.*⁷ observed that Δ PCO₂ was higher in the control group and this group had higher morbidity and longer ICU stay.

There are several limitations to our study. This was an observational study. The PaCO₂ is influenced also by CO₂ production and alveolar ventilation.¹⁰ The adequate interpretation of Δ PCO₂ requires a steady state of these two factors. Finally, DSB was the only outcome measured.

In summary, elevated Δ PCO₂ is frequently observed during cardiac surgery. High pre-CPB Δ PCO₂ was an independent predictor for DSB. Further studies are required to confirm this observation, to determine the mechanism of its increase and the benefit of its correction during cardiac surgery.

TABLE II Logistic regression for predicting difficult separation bypass

Variable	Odds ratio	95% CI	Univariate P	Multivariate P
Sex	0.62	0.17 - 2.20	0.474	-
Age	0.99	0.94 - 1.05	0.893	-
Weight	0.98	0.95 - 1.02	0.424	-
Height	1.01	0.96 - 1.06	0.752	-
LVEF (%)	0.94	0.89 - 0.99	0.019	-
Bypass (min)	1.05	1.02 - 1.08	0.001	0.002
Clamping (min)	1.03	1.00 - 1.06	0.040	-
(ΔPCO ₂ pre (mmHg)	1.31	1.01 - 1.71	0.044	0.030
(ΔPCO ₂ per (mmHg)	1.16	0.99 - 1.35	0.074	-
Lactate pre (mMol·L ⁻¹)	2.23	0.83 - 6.02	0.113	-
Lactate per (mMol·L ⁻¹)	2.36	1.28 - 4.34	0.0001	-

LVEF = left ventricular ejection fraction

Bypass = duration of bypass

Clamping = duration of clamping

ΔPCO₂ pre = veno-arterial PCO₂ difference value before bypassΔPCO₂ per = veno arterial during bypass

Lactate pre = lactate value before bypass

Lactate per = lactate value during bypass

- 7 Pölönen P, Ruokonen E, Hippeläinen M, Pöyhönen M, Takala J. A prospective, randomized study of goal-oriented hemodynamic therapy in cardiac surgical patients. *Anesth Analg* 2000; 90: 1052–9.
- 8 Adrogue HJ, Rashad MN, Gorin AB, Yacoub J, Madias NE. Assessing acid-base status in circulatory failure. Differences between arterial and central venous blood. *N Engl J Med* 1989; 320: 1312–6.
- 9 Hardy J-F, Searle N, Roy M, Perrault J. Amrinone, in combination with norepinephrine, is an effective first-line drug for difficult separation from cardiopulmonary bypass. *Can J Anaesth* 1993; 40: 495–501.
- 10 Idris AH, Staples ED, O'Brien DJ, et al. Effect of ventilation on acid-base balance and oxygenation in low blood-flow states. *Crit Care Med* 1994; 22: 1827–34.

Acknowledgment

The authors wish to thank André Couturier for statistical support.

References

- 1 Lebuffe G, Decoene C, Pol A, Prat A, Vallet B. Regional capnometry with air-automated tonometry detects circulatory failure earlier than conventional hemodynamics after cardiac surgery. *Anesth Analg* 1999; 89: 1084–90.
- 2 Zhang H, Vincent J-L. Arteriovenous differences in PCO₂ and pH are good indicators of critical hypoperfusion. *Am Rev Respir Dis* 1993; 148: 867–71.
- 3 Van Der Linden P, Rausin I, Deltell A, et al. Detection of tissue hypoxia by arteriovenous gradient for PCO₂ and pH in anesthetized dogs during progressive hemorrhage. *Anesth Analg* 1995; 80: 269–75.
- 4 Ariza M, Gothard JWW, MacNaughton P, Hooper J, Morgan CJ, Evans TW. Blood lactate and mixed venous-arterial PCO₂ gradient as indices of poor peripheral perfusion following cardiopulmonary bypass surgery. *Intensive Care Med* 1991; 17: 320–4.
- 5 Cavaliere F, Martinelli L, Guarneri S, Varano C, Rossi M, Schiavello R. Arterial-venous PCO₂ gradient in early postoperative hours following myocardial revascularization. *J Cardiovasc Surg* 1996; 37: 499–503.
- 6 Ruokonen E, Soini HO, Parviainen I, Kosonen P, Takala J. Venoarterial CO₂ gradient after cardiac surgery: relation to systemic and regional perfusion and oxygen transport. *Shock* 1997; 8: 335–40.