Pediatr Cardiol (2013) 34:75–80
DOI 10.1007/s00246-012-0389-2

ORIGINAL ARTICLE

Cerebral Oximetry Monitoring During Preoperative Phlebotomy to Limit Allogeneic Blood Use in Patients Undergoing Cardiac Surgery

Elisabeth Dewhirst · Peter Winch · Aymen Naguib · Mark Galantowicz · Joseph D. Tobias

Received: 17 February 2012 / Accepted: 9 May 2012 / Published online: 1 June 2012

Abstract Preoperative phlebotomy can minimize the need for allogenic blood products. Frequently, removed blood is replaced with intravenous fluids to maintain euvolemia (acute normovolemic hemodilution [ANH]). During cardiopulmonary bypass (CPB), ANH may present problems when the circuit prime causes further hemodilution and unacceptably low hemoglobin. This investigation aimed to demonstrate that minimum volume replacement after preoperative phlebotomy can be used safely when guided by cerebral oxygenation (rSO_2) measured by near-infrared spectroscopy (NIRS). This prospective study included patients undergoing surgery for congenital heart disease. After preoperative phlebotomy, fluid replacement was guided by mean arterial pressure (MAP), heart rate, and rSO_2, which were measured at baseline, immediately after phlebotomy, and 15 and 30 min after phlebotomy. This study enrolled 38 patients ages 3 months to 50 years. Preoperative phlebotomy removed 9.3 ± 2.9 mL/kg of blood, and 5.6 ± 5.1 mL/kg of crystalloid was administered intraoperatively. Within 30 min after phlebotomy, 23 patients had a MAP decrease of 20 % or more from baseline. This fall in MAP coincided with a decrease in rSO_2 of 20 or more at 2 of 114 measured points. Initially, rSO_2 decreased from 74 ± 9 to 68 ± 10 but thereafter remained constant. On five occasions, rSO_2 decreased 20 or more from baseline, but no patient's NIRS value was less than 45. A decrease in rSO_2 occurred more commonly in younger patients and those who had a larger volume of blood removed. Preoperative phlebotomy without significant volume replacement can be performed safely before CPB. Volume replacement may be more appropriately guided by rSO_2 than by hemodynamic variables.

Keywords Acute normovolemic hemodilution · Cardiopulmonary bypass · Cerebral oxygenation · Congenital heart disease · Euvolemia · Preoperative phlebotomy

E. Dewhirst (✉) · P. Winch · A. Naguib · J. D. Tobias
Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital and Ohio State University, 700 Children's Drive, Columbus, OH 43205, USA
e-mail: elisabeth.dewhirst@Nationwidechildrens.org

M. Galantowicz
Department of Cardiothoracic Surgery, Nationwide Children's Hospital and Ohio State University, Columbus, OH 43205, USA

J. D. Tobias
Department of Pediatrics, Nationwide Children's Hospital and Ohio State University, Columbus, OH 43205, USA

Recent investigations have demonstrated numerous potential risks associated with the administration of allogeneic blood products including systemic infections, wound infections, immunosuppression, autoimmune reactions, prolongation of hospitalization, and increased costs. Given these considerations, various techniques have been developed to limit the need for allogeneic blood products [10, 17, 18].

In acute normovolemic hemodilution (ANH), a quantity of the patient's whole blood is removed before surgical incision and reinfused postoperatively.

In current clinical practice, the volume of blood removed generally is replaced by a 3:1 ratio of crystalloid or a 1:1 ratio of colloid to maintain euvolemia [17]. Although replacement of the blood with crystalloid or colloid maintains normovolemia, hemodilution occurs, with a significant decrease in the hematocrit. The volume replacement and hemodilution may be problematic for patients to be placed subsequently on cardiopulmonary

bypass (CPB) because there will be a secondary hemodilution and a subsequent decrease in the hemoglobin and hematocrit values related to the prime volume of the CPB circuit. Given the data regarding optimal hemoglobin values during CPB, the resultant hemoglobin may be sufficiently low to necessitate the administration of allogeneic blood during CPB, thereby negating the purpose of the technique [6, 16, 21].

At our institution, ANH is routinely performed in all cardiac surgical cases provided the preoperative hematocrit is acceptable. Rather than use an arbitrary ratio for volume replacement during phlebotomy, our goal is to administer the minimum necessary volume as guided by hemodynamic parameters and end-organ perfusion. Hemodynamic stability is assessed using changes in heart rate (HR), mean arterial pressure (MAP), and electrocardiogram (ECG), whereas end-organ perfusion is assessed using cerebral oxygenation (rSO_2) measured by near-infrared spectroscopy (NIRS).

Monitors of NIRS, available since 1993, use near-infrared technology for noninvasive and continuous measurement of cerebral tissue oxygenation [19]. Changes in cerebral blood flow and oxygen delivery have been shown to track with changes in NIRS values [4, 13, 19]. Recent evidence also suggests that cerebral oxygenation monitoring using NIRS may effectively identify periods of cerebral hypoperfusion, which may lead to postoperative neurocognitive deficits [4, 12–15]. These data suggest the utility of this noninvasive monitor as a means of following end-organ perfusion, thereby making it a frequently used supplemental monitoring device for pediatric patients during CPB and surgery for congenital heart disease.

The current study prospectively evaluated changes in hemodynamic parameters (HR and MAP) as well as rSO_2 during phlebotomy in the operating room before surgery for congenital heart disease.

Methods

This study was approved by the institutional review board of Nationwide Children's Hospital's. Over a 6-month period, data were collected prospectively from a consecutive series of patients undergoing cardiac surgery with presurgical phlebotomy planned for blood avoidance.

After placement of routine monitors according to the standards of the American Society of Anesthesiologists, anesthesia was induced with a standard intravenous or inhalation technique, and the trachea was intubated after the administration of a nondepolarizing neuromuscular blocking agent. Maintenance anesthesia comprised 1 minimum alveolar concentration (MAC) of sevoflurane or isoflurane in 100 % oxygen and fentanyl. The NIRS monitor (Foresight; CAS Medical Systems, Branford, CT, USA) with an age- and size-appropriate probe was placed on the forehead before the onset of phlebotomy. Baseline rSO_2 and hemodynamic values (HR and MAP) were recorded.

Phlebotomy was performed through a large-bore peripheral intravenous cannula or the arterial line. Depending on the patient's weight, the blood was collected into a standard citrate-phosphate-dextrose (CPD) blood bank bag or a syringe with citrate added as the anticoagulant. The blood was labeled and kept in the operating room at room temperature. The volume of blood to be removed was calculated based on the patient's weight, the starting hemoglobin value, and a target hematocrit of 22–25 % on CPB. Because no definitive lower limit of hematocrit has been identified by the literature, our target value was based on demonstrated safety within this limit [7, 22].

The hemodynamic values (MAP and HR) and rSO_2 were recorded at baseline (before phlebotomy), immediately after completion of the phlebotomy, and again 15 and 30 min after completion of phlebotomy. As blood was removed, fluid replacement with crystalloid was guided by changes in the hemodynamic parameters and end-organ perfusion as judged by rSO_2. A MAP reduction of 20 % or more from baseline or an HR increase of 20 % or more from baseline was remedied by volume resuscitation using crystalloid, cessation of phlebotomy, or phenylephrine bolus. Arterial blood gas values and plasma lactate concentrations were measured at baseline and after phlebotomy.

Statistical analysis included analysis of variance to compare hemodynamic and rSO_2 values at the times after phlebotomy with pre-phlebotomy values. A nonpaired *t* test and a Fisher's exact test were used to compare demographic data, fentanyl dosing, total amount of blood removed, mean crystalloid replacement, partial pressure of carbon dioxide ($PaCO_2$) values, MAP values, final hemoglobin value, and use of dexmedetomidine between patients who had a decline in rSO_2 values of 20 or more and those who did not. The data are presented as the mean ± standard deviation, with *p* values lower than 0.05 considered significant.

Results

The cohort for the study included 38 patients undergoing surgery for congenital heart disease. The patients ranged in age from 3 months to 50 years (mean, 14.3 ± 13.4 years) and in weight from 4.9 to 120 kg (mean, 45.2 ± 33.7 kg). The spectrum of surgical procedures is outlined in Table 1. The total number of procedures listed in Table 1 is greater than 38 because some patients had more than one

Table 1 Surgical procedures performed in the study cohort

Surgical procedure	No. of patients
Aortic root or valve replacement & repair	10
Pulmonary valve replacement	9
Atrial or ventricular septal defect repair	7
Tricuspid valve replacement	1
Subaortic stenosis/membrane repair	4
Comprehensive stage 2 procedure	3
Fontan operation	2
Anomalous pulmonary venous return repair	2
Glenn procedure	1
Left superior vena cava ligation	1
Transposition of the great vessels	1
Mitral valve repair	1

procedure. The amount of blood removed varied from 3.9 to 15.5 mL/kg (mean, 9.3 ± 2.9 mL/kg), with total crystalloid replacement varying from 0.4 to 19.4 mL/kg (mean, 5.6 ± 5.1 mL/kg), giving a 0.6:1 ratio of crystalloid replaced to blood removed.

For 30 of the 38 patients, less than 1 mL/kg of crystalloid (0.4 ± 0.32 mL/kg) was administered for each milliliter of blood removed. The hemoglobin value decreased from 13 ± 1.9 to 12.4 ± 1.8 g/dL after phlebotomy. After the initiation of CPB, all the patients had an initial hemoglobin of 8.5 gm/dL or more. Allogeneic blood transfusion was avoided for 28 of the 38 patients (74 %), including 5 (71 %) of the 7 patients younger than 1 year of age.

The intraoperative dosing of fentanyl during phlebotomy varied from 1.69 to 10.2 μg/kg (mean, 5.0 ± 2.8 μg/kg). Three patients received sufentanil, and an equivalent opioid dosing was calculated using a 1:10 ratio for sufentanil:fentanyl. Of the 38 patients, 25 received dexmedetomidine, which was started after anesthetic induction and endotracheal intubation. Dexmedetomidine was administered as a loading dose of 1 μg/kg over 10 min followed by an infusion at 0.5 μg/kg/h.

The hemodynamic parameters (HR and MAP) at baseline, immediately after phlebotomy, and 15 and 30 min after phlebotomy are listed in Table 2. Immediately after phlebotomy, MAP decreased from 69 ± 12 to 60 ± 13 mmHg (decrease of 9 mmHg or 11.4 % from baseline; $p = 0.0025$). The mean MAP values then remained essentially unchanged 15 and 30 min after phlebotomy. There was a MAP decrease of 20 % or more from baseline in 12 patients immediately after phlebotomy, in 14 patients 15 min after phlebotomy, and in 16 patients 30 min after phlebotomy. Overall, 23 of the 38 patients at some point after phlebotomy had a MAP decrease of 20 % or more from baseline. Considering all the data points after phlebotomy, MAP decreased 20 % or more from baseline at 42 of the 114 measured points (38 patients with 3 MAP data points after phlebotomy = 142). At only 2 of these 42 points had the rSO_2 decreased by 20 or more from baseline.

No clinically significant changes in HR were seen in the majority of the study cohort (Table 2). Three patients had an HR increase of more than 20 % from baseline within 30 min after phlebotomy. Despite this increase in HR, none of these patients had a decline in rSO_2 value of more than 20 from baseline.

Lactate and pH values before and 30 min after phlebotomy were recorded for 37 patients and are outlined in Table 3. The increase in lactate was 2 mmol/L or more in 1 of the 38 patients (2.17 mmol/L). This patient did not have an rSO_2 decrease of more than 20 from baseline. The decrease in pH was 0.05 or more in 19 of the 38 patients, with the largest decrease being 0.12.

The rSO_2 data at baseline, at completion of phlebotomy, and 15 and 30 min after phlebotomy are listed in Table 4. After phlebotomy, rSO_2 decreased from 74 ± 9 to 68 ± 10 (8 % decrease from baseline; $p = 0.0197$). Thereafter, the rSO_2 remained constant at 15 and 30 min, respectively. On five occasions involving four different patients, rSO_2 decreased by more than 20 from baseline. Two of these five instances coincided with the patient experiencing a MAP decrease greater than 20 % from baseline. In the four patients who had an rSO_2 decrease of more than 20 from baseline, the absolute lowest rSO_2 values were 68, 65, 60, and 52. No patient had an rSO_2 lower than 45. The lowest reading was 48, which was 15 below the baseline rSO_2.

Table 5 compares the physiologic data of the four patients who had an rSO_2 decrease of 20 or more from

Table 2 Hemodynamic changes before and after phlebotomy

Hemodynamic parameter	Before phlebotomy	At completion of phlebotomy	15 Min after phlebotomy	30 Min after phlebotomy
HR (bpm)	95 ± 33	94 ± 36[a]	89 ± 30[a]	87 ± 31[a]
MAP (mmHg)	69 ± 12	60 ± 13[b]	60 ± 14[b]	61 ± 14[b]

HR heart rate, *bpm* beats per minute, *MAP* mean arterial pressure, *NS* not significant

[a] p = NS vs baseline

[b] $p < 0.05$ vs before phlebotomy

Table 3 Lactate and pH changes before and after phlebotomy

Variable	Before phlebotomy	After phlebotomy
pH	7.37 ± 0.06	7.34 ± 0.04[a]
Lactate (mmol/L)	0.9 ± 0.47	1.87 ± 0.88[a]

[a] $p < 0.05$ vs baseline

Table 4 Near-infrared spectroscopy (NIRS) cerebral oximetry (rSO_2) during phlebotomy

	Immediately before phlebotomy	Immediately after phlebotomy	15 Min after phlebotomy	30 Min after phlebotomy
(rSO_2)	74 ± 9	68 ± 10[a]	70 ± 9[b]	68 ± 8[a]

NS not significant

[a] $p < 0.05$ vs baseline

[b] p = NS vs baseline

baseline with the data of the patients who had a minimal change in rSO_2 (<10 from baseline). Three of these patients had a biventricular anatomy, whereas only one had a univentricular anatomy.

Discussion

Our data illustrate that phlebotomy before the incision in patients undergoing cardiac surgery and CPB can be performed safely and effectively without the need for equivalent volume replacement. In our cohort of patients, 0.6 mL/kg of replacement crystalloid was administered for each 1 mL/kg of blood removed, a minimal volume as reflected by the small hemoglobin decrease immediately after phlebotomy. Despite this practice, we noted no clinically significant decreases in rSO_2 measured by NIRS monitoring. Although rSO_2 had decreased by more than 20 from the baseline value on five occasions, no value was less than 45.

The potential utility of rSO_2 monitoring is demonstrated by the fact that only 2 of 43 MAP data points falling 20 % or more below baseline coincided with a low NIRS value. Likewise, HR was not correlated with NIRS value. Although HR changes may be a relatively sensitive indicator of volume status in the awake state, the administration of anesthetic agents with negative chronotropic effects such as sevoflurane, fentanyl, and dexmedetomidine blunt this response [8, 11]. These data suggest that hemodynamic parameters are of limited value in judging the need for volume replacement during preoperative phlebotomy.

In our cohort of patients, we noted some factors that may be predictive of which patients may have a greater decrease in rSO_2. The patients who had an rSO_2 decrease of 20 or more from baseline were more likely to be younger, weigh less, receive a larger dose of fentanyl, and have a greater volume of blood removed at preoperative phlebotomy. Although we noted no impact of the $PaCO_2$, based on previous work demonstrating the deleterious effects of hypocarbia on rSO_2, especially with low hemoglobin or low MAP, it is our standard clinical practice to ensure that normocarbia is maintained during preoperative phlebotomy [20].

We also noted that patients who experienced an rSO_2 decrease less than 10 from baseline were more likely to have received a dexmedetomidine infusion. Dexmedetomidine has been shown to decrease both cerebral blood flow (CBF) and the cerebral metabolic rate of oxygen ($CMRO_2$) [5]. The two variables remain coupled such that the CBF:$CMRO_2$ ratio remains relatively constant. This may be one explanation for the findings in the current study

Table 5 Patients with and without cerebral oximetry (rSO_2) changes after phlebotomy

Variable	Patients with an rSO_2 decrease ≥20 from baseline after phlebotomy	Patients with stable rSO_2 (no value <10 from baseline) after phlebotomy
No. of patients	4	16
Age (years)	2.9 ± 4.7	15.2 ± 2.9[a]
Patients <1 year old	3/4	2/16[a]
Weight (kg)	13.1 ± 12.1	50.3 ± 17[a]
Single-ventricle anatomy	1/4	4/16[b]
Fentanyl dose (μg/kg)	7.2 ± 3.5	5.3 ± 2.8[a]
Received dexmedetomidine	0/4	12/16[a]
Blood volume removed (mL/kg)	13.1 ± 1.6	8.1 ± 2.6[a]
Crystalloid replacement (mL/kg)	6.4 ± 6.6	5.4 ± 4.6[b]
Mean MAP when rSO_2 decreased ≥20 % from baseline (mmHg)	54 ± 15	61 ± 12[b]
No. of patients with ≥20 % decrease in MAP	3/4	7/16[b]
Mean HR when rSO_2 decreased ≥ 20 % from baseline (bpm)	126 ± 48	88 ± 33[b]
No. of patients with ≥20 % increase in HR	0/4	2/16[b]
Mean pH after phlebotomy	7.27 ± 0.05	7.34 ± 0.03[a]
Mean lactate after phlebotomy	1.05 ± 0.4	1.4 ± 1.1[b]
$PaCO_2$ after phlebotomy (mmHg)[c]	48 ± 8	45 ± 7[b]

NS not significant

[a] $p < 0.05$

[b] p = NS

[c] Given the timing of the blood draw, these values do not necessarily coincide with the low rSO_2 value

because NIRS reflects a venous-weighted hemoglobin saturation, indicating the oxygen supply and demand balance. Chi et al. noted that rats infused with dexmedetomidine bled acutely but experienced no further decrease in either CBF or $CMRO_2$ after hemorrhage compared with those given saline infusion [3]. In contrast, previous animal studies had shown that dexmedetomidine caused an earlier decompensation during hypovolemia [1, 2].

Various studies have tried to identify the specific rSO_2 value that predicts an adverse neurologic outcome. Kurth et al. [9] exposed 60 neonatal piglets to increasing degrees of cerebral hypoxemia and found increased lactate, major electroencephalography (EEG) changes, and decreased adenosine triphosphate (ATP) in 50 % of the animals at rSO_2 values of 44, 37, and 33, respectively. A prospective evaluation of 101 adult patients during cardiac surgery measured postoperative performance on the mini-mental state examination (MMSE) and the antisaccadic eye movement (ASEM) test [23]. When rSO_2 values were lower than 35, the incidences of impairments on the MMSE and ASEM were significantly higher (respectively, 44 vs 12 % and 33 vs 9 %). This observation also was noted when the rSO_2 was lower than 40 for more than 10 min.

In summary, our data suggest that preoperative phlebotomy is possible without significant volume replacement. Furthermore, given the limited value of HR monitoring and the frequent decrease in MAP values without associated changes in rSO_2, it appears that monitoring end-organ tissue oxygenation may be a more effective means of determining the safe limits of phlebotomy and the need for volume replacement.

Although our cohort size was somewhat limited, we noted that rSO_2 measured by NIRS was well preserved with our current practice. Likewise, we saw no clinically significant changes in pH or lactate values suggesting end-organ hypoperfusion. The practice allows for preoperative phlebotomy with an acceptable hemoglobin value after the dilution of CPB. The ability of an individual patient to tolerate such phlebotomy will vary because we noted less tolerance in younger patients, especially when greater volumes of blood were removed. The tolerance for phlebotomy is likely to be greater in the anesthetized state, with a reduction in oxygen consumption related to anesthesia as well as an increased PaO_2 and oxygen saturation due to the administration of supplemental oxygen.

References

1. Blake DW (2000) Dexmedetomidine and hemodynamic responses to simulated hemorrhage in experimental heart failure. Anesth Analg 91:1112–1117
2. Blake DW, Ludbrook J, Van Leeuwen AF (2000) Dexmedetomidine and haemodynamic responses to acute central hypovolaemia in conscious rabbits. Clin Exp Pharmacol Physiol 27:801–809
3. Chi OZ, Hunter C, Liu X, Weiss HR (2011) The effects of dexmedetomidine on regional cerebral blood flow and oxygen consumption during severe hemorrhagic hypotension in rats. Anesth Analg 113:349–355
4. Cooper JA, Tichauer KM, Boulton M, Elliott J, Diop M, Arango M, Lee TY, St Lawrence K (2011) Continuous monitoring of absolute cerebral blood flow by near-infrared spectroscopy during global and focal temporary vessel occlusion. J Appl Physiol 110:1691–1698
5. Drummond JC, Dao AV, Roth DM, Cheng CR, Atwater BI, Minokadeh A, Pasco LC, Patel PM (2008) Effect of dexmedetomidine on cerebral blood flow velocity, cerebral metabolic rate, and carbon dioxide response in normal humans. Anesthesiology 108:225–232
6. Guzzetta NA (2011) Benefits and risks of red blood cell transfusion in pediatric patients undergoing cardiac surgery. Paediatr Anaesth 21:504–511
7. Habib RH, Zacharias A, Schwann TA, Riordan CJ, Durham SJ, Shah A (2003) Adverse effects of low hematocrit during cardiopulmonary bypass in the adult: should current practice be changed? J Thorac Cardiovasc Surg 125:1438–1450
8. Hogue CW Jr, Talke P, Stein PK, Richardson C, Domitrovich PP, Sessler DI (2002) Autonomic nervous system responses during sedative infusions of dexmedetomidine. Anesthesiology 97: 592–598
9. Kurth CD, Levy WJ, McCann J (2002) Near-infrared spectroscopy cerebral oxygen saturation thresholds for hypoxia-ischemia in piglets. J Cereb Blood Flow Metab 22:335–341
10. Lavoie J (2011) Blood transfusion risks and alternative strategies in pediatric patients. Paediatr Anaesth 21:14–24
11. Marty J, Reves JG (1989) Cardiovascular control mechanisms during anesthesia. Anesth Analg 69:273–275
12. Moritz S, Kasprzak P, Arlt M, Taeger K, Metz C (2007) Accuracy of cerebral monitoring in detecting cerebral ischemia during carotid endarterectomy: a comparison of transcranial Doppler sonography, near-infrared spectroscopy, stump pressure, and somatosensory evoked potentials. Anesthesiology 107:563–569
13. Nollert G, Jonas RA, Reichart B (2000) Optimizing cerebral oxygenation during cardiac surgery: a review of experimental and clinical investigations with near infrared spectrophotometry. Thorac Cardiovasc Surg 48:247–253
14. Orihashi K, Sueda T, Okada K, Imai K (2004) Near-infrared spectroscopy for monitoring cerebral ischemia during selective cerebral perfusion. Eur J Cardiothorac Surg 26:907–911
15. Rigamonti A, Scandroglio M, Minicucci F, Magrin S, Carozzo A, Casati A (2005) A clinical evaluation of near-infrared cerebral oximetry in the awake patient to monitor cerebral perfusion during carotid endarterectomy. J Clin Anesth 17:426–430
16. Sakamoto T, Zurakowski D, Duebener LF, Hatsuoka S, Lidov HG, Holmes GL, Stock UA, Laussen PC, Jonas RA (2002) Combination of alpha-stat strategy and hemodilution exacerbates neurologic injury in a survival piglet model with deep hypothermic circulatory arrest. Ann Thorac Surg 73:180–189
17. Testa L, Tobias JD (1996) Techniques of blood conservation (part 1): isovolemic hemodilution. Am J Anesthesiol 23:20–28
18. Testa L, Tobias JD (1996) Techniques of blood conservation (part 2): autologous transfusion therapy, cell saver devices, and pharmacologic control of erythropoiesis and coagulation. Am J Anesthesiol 23:63–72
19. Tobias JD (2006) Cerebral oxygenation monitoring: near-infrared spectroscopy. Expert Rev Med Devices 3:235–243

20. Tobias JD (2011) Assessment of cerebral oxygenation using near-infrared spectroscopy during isovolemic hemodilution in pediatric patients. J Clin Monit Comput 25:171–174
21. Wypij D, Jonas RA, Bellinger DC et al (2008) The effect of hematocrit during hypothermic cardiopulmonary bypass in infant heart surgery: results from the combined Boston hematocrit trials. J Thor Cardiovasc Surg 135:355–360
22. Wypij D, Jonas RA, Bellinger DC, Del Nido PJ, Mayer JE Jr, Bacha EA, Forbess JM, Pigula F, Laussen PC, Newburger JW (2008) The effect of hematocrit during hypothermic cardiopulmonary bypass in infant heart surgery: results from the combined Boston hematocrit trials. J Thorac Cardiovasc Surg 135:355–360
23. Yao FS, Tseng CC, Ho CY, Levin SK, Illner P (2004) Cerebral oxygen desaturation is associated with early postoperative neuropsychological dysfunction in patients undergoing cardiac surgery. J Cardiothorac Vasc Anesth 18:552–558