Can J Anesth/J Can Anesth (2025) 72:319–333
https://doi.org/10.1007/s12630-024-02903-1

REPORTS OF ORIGINAL INVESTIGATIONS

A clinical comparison of the effects of six disposable cardiopulmonary bypass circuits on bleeding and coagulation: a quality assurance project

Une comparaison clinique des effets de six circuits de circulation extracorporelle à usage unique sur les saignements et la coagulation : un projet d'assurance qualité

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Received: 11 March 2024 / Revised: 1 July 2024 / Accepted: 2 July 2024 / Published online: 18 February 2025

Abstract

Purpose *Cardiac surgery requiring cardiopulmonary bypass (CPB) is frequently complicated by excessive bleeding because of coagulopathy. Contact of blood with the CPB circuit is a major contributor. While several Health Canada-approved disposable circuits are available for purchase, there is no existing direct comparative data. Our objective was to conduct a quality assurance project to provide clinical data on the bleeding and coagulation*

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12630-024-02903-1.

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effects of six disposable CPB circuits in a cohort of cardiac surgery patients.

Methods *We compared the effects of six different circuits on bleeding and coagulation in 872 consecutive patients who underwent various types of cardiac surgery over 12 months at Toronto General Hospital (Toronto, ON, Canada). Generalized estimating equations accounting for clustering by surgeon were used to assess the impact of each circuit group on the following: 1) at least moderate bleeding as defined by the Universal Definition of Perioperative Bleeding Score after separation from bypass through the first postoperative day; 2) total allogeneic blood product transfusion within seven days of surgery; and 3) hemostatic therapy administration within seven days of surgery. Changes in coagulation tests before and after bypass were recorded.*

Results *We included 872 patients. There were no major differences between the six types of circuit in prebypass compared with postbypass coagulation tests. Nevertheless, when accounting for surgeon, patient, and procedural characteristics, significant differences between circuit types emerged for all primary and secondary outcomes.*

Conclusion *The findings of this quality assurance project suggest that current Health Canada-approved CPB circuits may have differential effects on coagulation and bleeding. This should be further verified in randomized controlled trials.*

Résumé

Objectif *La chirurgie cardiaque nécessitant une circulation extracorporelle (CEC) est souvent compliquée par des saignements excessifs en raison de la coagulopathie. Le contact du sang avec le circuit de CEC en est un contributeur majeur. Bien que plusieurs circuits jetables approuvés par Santé Canada soient disponibles à l'achat, il n'existe aucune donnée comparative directe. Notre objectif était de réaliser un projet d'assurance qualité afin de fournir des données cliniques sur les effets hémorragiques et coagulants de six circuits jetables de CEC dans une cohorte de chirurgie cardiaque.*

Méthode *Nous avons comparé les effets de six circuits différents sur l'hémorragie et la coagulation chez 872 personnes traitées consécutivement ayant bénéficié de divers types de chirurgie cardiaque pendant 12 mois à l'Hôpital général de Toronto (Toronto, ON, Canada). Des équations d'estimation généralisées tenant compte du regroupement par les chirurgiens et chirurgiennes ont été utilisées pour évaluer l'impact de chaque groupe de circuits sur les éléments suivants : 1) saignement au moins modéré tel que défini par la définition universelle du score de saignement périopératoire après sevrage de la CEC jusqu'au premier jour postopératoire; 2) transfusion totale de produits sanguins allogéniques dans les sept jours suivant l'intervention chirurgicale; et 3) administration d'un traitement hémostatique dans les sept jours suivant la chirurgie. Les changements dans les tests de coagulation avant et après la CEC ont été enregistrés.*

Résultats *Nous avons inclus 872 personnes. Il n'y avait pas de différences majeures entre les six types de circuit dans les tests de coagulation pré-CEC par rapport aux tests de coagulation post-CEC. Néanmoins, si l'on tient compte des caractéristiques des chirurgiennes et chirurgiens, des personnes traitées et de l'intervention, des différences significatives entre les types de circuits sont apparues pour tous les critères d'évaluation primaires et secondaires.*

Conclusion *Les résultats de ce projet d'assurance de la qualité suggèrent que les circuits actuels de CEC approuvés par Santé Canada pourraient avoir des effets différentiels sur la coagulation et les saignements. Cela devrait être examiné plus en profondeur dans des études randomisées contrôlées.*

Keywords cardiopulmonary bypass · extracorporeal circulation · heart-lung machine · patient outcome assessment · standards

Since the introduction of cardiopulmonary bypass (CPB) in cardiac surgery, technological advances have enhanced outcomes and greatly increased safety.[1] Cardiopulmonary bypass involves a disposable extracorporeal circuit, comprising a reservoir, pump, oxygenator, and tubing. It facilitates blood drainage, oxygenation, heart bypass, and a bloodless surgical field. Manufacturing improvements include integrated membrane oxygenators with heat exchangers and filters, causing less red blood cell (RBC) damage than older direct-contact oxygenators; centrifugal pumps causing less RBC damage than older roller pumps; and surface-coated circuitry (e.g., heparin or phosphorylcholine) causing less inflammation and coagulation activation than uncoated circuits.[1]

Despite advancements, CPB circuits lead to significant physiologic derangements. Repeated circulation of blood through the CPB circuit during surgery triggers acute phase reactions, leading to inflammatory responses and coagulation cascade activation.[2] Consequently, coagulopathy causing excessive bleeding remains a major complication in a substantial proportion of patients undergoing cardiac surgery with CPB, necessitating blood product transfusions and increasing morbidity and mortality.[3] Although various Health Canada-approved CPB circuit disposables are available, comparative data examining their impact on coagulation and bleeding are

lacking, hindering evidence-based purchasing decisions. The comparative impact of CPB circuit disposables on transfusion rates is also poorly studied.

Our objective was to conduct a quality assurance project to compare the severity of bleeding, allogeneic blood product and hemostatic product administration, and changes in coagulation tests between six CPB circuit disposables from four manufacturers in a cohort of consecutive cardiac surgical patients at our institution. Our hypothesis was that there would be no clinically significant differences among circuit groups, given that manufacturers must meet the same technical and regulatory standards for marketing approval.[4]

Materials and methods

This quality assurance project received approval from the University Health Network Quality Improvement Review Committee (QIRC [Toronto, ON, Canada]; QI ID#: 21-0209), waiving the need for patient consent. From July 2021 to July 2022, six different CPB circuit disposables from four manufacturers that had marketing approval by Health Canada were trialled sequentially in 6–8-week blocks at Toronto General Hospital (Toronto, ON, Canada). These manufacturers were Medtronic Canada (Brampton, ON, Canada), LivaNova Inc., (London, UK), Terumo Medical Canada Inc., (Vaughn, ON, Canada), and Getinge Canada Ltd., (Mississauga, ON, Canada). For the duration of each block, the circuit being assessed was used in all cases until a minimum of 100 patients were included and all purchased circuits were used. Patients undergoing emergency surgery or ventricular assist device insertion were not included in the analyses. Other than choice of the circuit, clinical practice was not modified. We applied the Revised Standards for Quality Improvement Reporting Excellence (SQUIRE 2.0) guidelines to the writing of this manuscript.[5]

Circuits

Manufacturers were asked to assemble their optimal pump pack configurations, which were then purchased by the institution as per usual processes. Six configurations by four different manufacturers were used with the Quantum heart-lung machine (Spectrum Medical Ltd., Cheltenham, UK): Medtronic Fusion™ Balance™ (Medtronic, Minneapolis, MN, USA) (circuit 1), Medtronic Fusion™ Cortiva™ (circuit 2), LivaNova Inspire™ (LivaNova PLC, London, UK) (circuit 3), Terumo CAPIOX® FX25 (Terumo, Tokyo, Japan) (circuit 4), Getinge VHK7100 + Quadriox-i (Getinge AB, Gothenburg, Sweden) (circuit 5), and Medtronic Affinity NT™ Cortiva™ (circuit 6). Table 1 summarizes the characteristics of the six disposable circuits. The conduct of CPB was performed as per standard institutional practice. Priming was established using standard Plasma-Lyte A (Baxter Corporation, Mississauga, ON, Canada) crystalloid solution, 5,000 IU of heparin, and 100 mL of 25% mannitol. Retrograde autologous prime was attempted when possible. Blood cardioplegia was delivered using the Quest MPS 2 microplegia device (Quest Medical Inc., Allen, TX, USA) for all patients.

Coagulation management and assessment

To achieve adequate anticoagulation for CPB, unfractionated heparin was administered to reach and maintain an activated clotting time (ACT), measured by the Hemochron® Signature Elite system (Werfen, Bedford, MA, USA), of at least 480 sec. After termination of CPB, heparin was reversed with protamine (at a dose of 0.7 mg/100 IU of heparin, with additional doses as necessary to achieve an ACT within 10% of baseline). Coagulation management and transfusion practice were according to a standardized, validated algorithm.[6] Point-of-care whole-blood based assays were conducted before heparinization for CPB and before termination of CPB (once the patient's temperature reached 36 °C after rewarming). The assays included arterial blood gases measured using the RAPIDPoint® 500 system (Siemens, Erlangen, Germany); platelet function using the Plateletworks system (Helena Laboratories, Beaumont, TX, USA), which estimates the number of functioning platelets by obtaining the number of platelets that fail to aggregate in the presence of collagen relative to the total number of platelets; and rotational thromboelastometry using the Rotem® *delta* system (Werfen).

Outcomes, sample size, and statistical analyses

The primary outcome of interest was the proportion of patients in each circuit group experiencing at least moderate bleeding, based on a modified Universal Definition of Perioperative Bleeding (UDPB) score.[7] Patients were classified as having had moderate or severe bleeding if they had a score of ≥ 2, excluding the delay in sternal closure and chest tube drainage variables, measured from separation from bypass to the end of postoperative day 1. Secondary outcomes included allogeneic blood products administered up to postoperative day 7 and hemostatic products administered up to postoperative day 7. Changes in coagulation test parameters from before to after bypass were measured. Safety data collected included major morbidity and mortality within seven days of index surgery. Major morbidity was defined as stroke

Table 1 Cardiopulmonary bypass circuit disposables characteristics

	Circuit 1 Medtronic Fusion™ Balance™	Circuit 2 Medtronic Fusion™ Cortiva™	Circuit 3 LivaNova Inspire™	Circuit 4 Terumo CAPIOX® FX25	Circuit 5 Getinge VHK7100 + Quadriox-i	Circuit 6 Medtronic Affinity NT™ Cortiva™
*Bioactive surfaces of components**	Heparin-free hydrophilic polymer	Heparin covalently bonded	Bonded phosphoryl-choline molecule	Amphiphilic polymer with hydrophobic and hydrophilic properties	Covalently bonded heparin and albumin	Heparin covalently bonded
Oxygenator						
Surface area	2.5 m^2	2.5 m^2	1.75 m^2	2.5 m^2	1.8 m^2	2.5 m^2
Prime volume	260 mL	260 mL	351 mL	260 mL	335 mL	260 mL
Coating	Heparin	As above	As above	As above	As above	As above
Integrated arterial filter	25 μm	25 μm	38 μm	25 μm	32 μm	25 μm
Reservoir						
Cardiotomy filter	30 μm	30 μm	41 μm	Depth filter	40 μm	30 μm
Venous screen	105 μm	105 μm	41/120 μm	47 μm	68 μm	200 μm
Minimum volume	200 mL	200 mL	150 mL	150 mL	150 mL	200 mL
Coating	As above	As above	As above	As above	As above	Uncoated

*This table provides representative data for oxygenator and reservoir types combined with each circuit. Circuits implemented during this quality assurance project may have differed in what reservoir or oxygenator was used in combination with the specified circuit.

(deficit > 24 hr with radiological confirmation), reoperation for bleeding, cardiac arrest requiring cardiopulmonary resuscitation, atrial fibrillation (requiring medication, cardioversion, or resulting in angina, heart failure or symptomatic hypotension), hepatic dysfunction (aminotransferases > 150 $IU{\cdot}L^{-1}$), sepsis (requiring a positive blood culture with presence of both infection and a systemic inflammatory response), limb ischemia (inadequate blood supply to limbs with radiologic confirmation), or respiratory failure (requiring reintubation or intensive care unit admission).

The selected sample size of a minimum of 100 patients for each CPB circuit was based on practical limitations of circuit procurement and the need to complete the recruitment phase of the quality improvement project within one year, and provided sufficient power to detect a 35% reduction in patients experiencing moderate to severe bleeding ($\beta \geq 0.80$, $\alpha = 0.05$).

Data are presented as medians and interquartile ranges [IQRs] or frequencies and percentages as appropriate. The associations between outcomes of interest and type of circuit were assessed using generalized estimating equations accounting for clustering within surgeons, with logit link functions for the primary and secondary outcomes (defined as the proportion of patients experiencing the outcome between groups). Adjustment variables were selected based on clinical judgement and *a priori* specified (age, sex, body mass index [BMI], urgency, previous cardiac surgery, presence of preoperative left ventricular impairment, baseline creatinine, baseline hemoglobin, total time on bypass, and total time of circulatory arrest).

SAS Studio (SAS Institute Inc., Cary, NC, USA) was used for the statistical analyses. We considered *P* values ≤ 0.05 significant; no adjustments were made for multiple comparisons as this was an exploratory quality assurance project.

Results

The total number of evaluable patients was 872, ranging from 120 to 186 patients for each circuit (Table 2). The median [IQR] age was 63 [54–71] yr and 68% ($n = 593$) of patients were male. The groups' demographics, comorbidities, and baseline laboratory values are shown in Table 2. Over 40% of patients underwent complex surgery, and the median CPB duration was consistent across the groups at approximately 100 min. There were no clinically important differences in baseline anticoagulant or antiplatelet use (Electronic Supplementary Material [ESM] eTable 1).

Fluid management across groups is shown in Table 3, with few clinically significant differences across groups. Pump balances were similar between groups. Circuit 6 had the lowest proportion of patients infused cell salvaged red cells, as well as the lowest median volume infused. The estimated intraprocedural blood loss was not significantly different between groups (Table 3).

There were clinically significant changes from prebypass to postbypass in conventional (Table 3) and point-of-care hemostatic assays that reflected coagulation impairment (Table 4; Figure), with EXTEM clotting time (CT) increasing the most in the circuit 2 group, FIBTEM A10 decreasing the most in the circuit 6 group, and the functional platelet count decreasing the most in the circuit 1 and 3 groups (Table 4). There was marked variability in the extent of impairment within each group.

There were no differences in safety clinical outcomes between circuit groups, aside from a higher incidence of stroke in the circuit 3 group (Table 5); however, there were very few events per group overall.

Primary outcome: bleeding

At least moderate bleeding as measured by a modified UDPB score occurred in 453 (52%) of 864 patients eligible for inclusion in the adjusted analysis, ranging from 44% to 59% among the groups. When clustering by surgeon and when procedural and patient factors were taken into account, circuits 2, 4, 5, and 6 had a lower incidence of at least moderate bleeding relative to circuit 1 (Table 6).

Secondary outcomes

For the outcome of any allogeneic blood transfusion within seven days of surgery, there was no difference in unadjusted analyses. Nevertheless, patients in the circuit 2 and 6 groups received fewer allogeneic blood transfusions after adjustment (Table 6). For the outcome of any hemostatic therapy within seven days of surgery, there was no difference in unadjusted analyses. In adjusted analyses, patients in the circuit 5 and 6 groups had a lower odds of receiving any hemostatic therapy (Table 6). These results are associated with a lower proportion of patients in the circuit 6 group receiving platelet, fibrinogen concentrate, and prothrombin complex concentrate (ESM eTable 2). Patients in the circuit 6 group also received a lower total number of administrations of these products overall (ESM eTable 3). Overall, circuit 6 was associated with the highest transfusion avoidance.

Discussion

In this clinical comparison of six CPB disposable circuits in patients undergoing multiple types of cardiac surgery,

Table 2 Patient and procedural characteristics

Variable	Cardiopulmonary bypass circuit type					
	Circuit 1 Medtronic Fusion™ Balance™ *N* = 186	Circuit 2 Medtronic Fusion™ Cortiva™ *N* = 134	Circuit 3 LivaNova Inspire™ *N* = 130	Circuit 4 Terumo CAPIOX® FX25 *N* = 172	Circuit 5 Getinge VHK7100 + Quadriox-i *N* = 130	Circuit 6 Medtronic Affinity NT™ Cortiva™ *N* = 120
Demographic characteristics						
Age (yr), median [IQR] (*N* = 872)	62 [51–71]	65 [56–73]	64 [58–71]	64 [57–71]	63 [52–70]	65 [53–72]
Sex (male), *n*/total *N* (%) (*N* = 870)	121/186 (65%)	90/134 (67%)	95/130 (73%)	113/171 (66%)	89/129 (69%)	85/120 (71%)
BMI ($kg \cdot m^{-2}$), median [IQR] (*N* = 872)	27 [24–32]	27 [24–30]	28 [25–31]	28 [24–31]	27 [24–32]	27 [24–31]
BSA (m^2), median [IQR] (*N* = 872)	1.9 [1.8–2.1]	1.9 [1.8–2.1]	2.0 [1.8–2.2]	2.0 [1.8–2.1]	1.9 [1.8–2.1]	2.0 [1.8–2.1]
Comorbidities, *n*/total *N* (%)						
Dyslipidemia (*N* = 867)	85/184 (46%)	91/131 (70%)	78/130 (60%)	77/172 (45%)	73/130 (56%)	66/120 (55%)
Hypertension (*N* = 870)	125/185 (68%)	99/133 (74%)	89/130 (68%)	112/172 (65%)	87/130 (67%)	77/120 (64%)
Atrial fibrillation (*N* = 864)	35/186 (19%)	26/133 (20%)	22/126 (17%)	38/172 (22%)	24/129 (19%)	15/118 (13%)
Chronic lung disease (*N* = 868)	19/186 (10%)	16/133 (12%)	17/129 (13%)	18/172 (10%)	19/129 (15%)	14/119 (12%)
History of CVA or TIA (*N* = 867)	16/185 (9%)	13/133 (8%)	13/129 (10%)	14/172 (8%)	13/129 (10%)	13/119 (11%)
Neurologic dysfunction (*N* = 864)	16/184 (9%)	24/133 (18%)	5/128 (4%)	26/172 (15%)	25/128 (10%)	5/119 (4%)
Dialysis dependent (*N* = 864)	5/184 (3%)	2/134 (1%)	0/126 (0%)	5/172 (3%)	2/129 (2%)	1/119 (1%)
History of DVT or PE (*N* = 866)	10/185 (5%)	4/134 (3%)	8/128 (6%)	8/171 (5%)	4/129 (3%)	4/119 (3%)
Diabetes mellitus (*N* = 866)						
Type I	2/184 (1%)	2/134 (1%)	1/128 (1%)	3/172 (2%)	0/129 (0%)	0/119 (0%)
Type II	39/184 (21%)	17/134 (13%)	25/128 (20%)	28/172 (16%)	20/129 (16%)	27/119 (23%)
Type II on insulin	5/184 (3%)	17/134 (13%)	8/128 (6%)	8/172 (5%)	8/129 (6%)	9/119 (8%)
Pulmonary hypertension, *n*/total *N* (%) (*N* = 855)						
Moderate (PAP, 31–55 mm Hg)	13/181 (7%)	4/132 (3%)	4/123 (3%)	15/172 (9%)	1/128 (1%)	2/119 (2%)
Severe (PAP > 55 mm Hg)	3/181 (2%)	4/132 (3%)	3/123 (2%)	3/172 (2%)	5/128 (4%)	1/119 (1%)
Left ventricular function, *n*/total *N* (%) (*N* = 812)						
LVEF > 50%	139/180 (77%)	105/131 (80%)	97/124 (78%)	130/158 (82%)	90/123 (73%)	76/96 (80%)
LVEF 31–50%	34/180 (19%)	24/131 (18%)	23/124 (19%)	22/158 (14%)	27/123 (22%)	16/96 (17%)
LVEF 21–30%	5/180 (3%)	1/131 (1%)	4/124 (3%)	5/158 (3%)	3/123 (2%)	3/96 (3%)
LVEF < 21%	2/180 (1%)	1/131 (1%)	0/124 (0%)	1/158 (1%)	3/123 (2%)	1/96 (1%)
CCS class 4 angina, *n*/total *N* (%) (N = 855)	49/184 (27%)	9/133 (7%)	8/127 (6%)	12/163 (7%)	8 (6%)	2/119 (2%)

Table 2 continued

Variable	Cardiopulmonary bypass circuit type					
	Circuit 1 Medtronic Fusion™ Balance™ $N = 186$	Circuit 2 Medtronic Fusion™ Cortiva™ $N = 134$	Circuit 3 LivaNova Inspire™ $N = 130$	Circuit 4 Terumo CAPIOX® FX25 $N = 172$	Circuit 5 Getinge VHK7100 + Quadriox-i $N = 130$	Circuit 6 Medtronic Affinity NT™ Cortiva™ $N = 120$
Myocardial infarction, *n*/total *N* (%) ($N = 866$)						
Within 7 day	1/184 (1%)	6/134 (4%)	4/129 (3%)	5/172 (3%)	4/129 (3%)	4/118 (3%)
7–29 days	9/184 (5%)	11/134 (8%)	12/129 (9%)	6/172 (3%)	9/129 (7%)	9/118 (8%)
30–90 days	1/184 (1%)	0/134 (0%)	0/129 (0%)	4/172 (2%)	2/129 (2%)	0/118 (0%)
> 90 days ago	8/184 (4%)	10/134 (7%)	6/129 (5%)	11/172 (6%)	14/129 (11%)	10/118 (8%)
Preoperative bloodwork, median [IQR]						
Hemoglobin ($g \cdot L^{-1}$) ($N = 864$)	137 [125–148]	141 [123–150]	139 [124–149]	138 [127–149]	139 [128–151]	141 [125–151]
INR ($N = 796$)	1.1 [1.0–1.1]	1.1 [1.0–1.1]	1.1 [1.0–1.1]	1.1 [1.0–1.1]	1.1 [1.0–1.1]	1.1 [1.0–1.1]
Platelets ($\times 10^9 \cdot L^{-1}$) ($N = 862$)	213 [175–261]	215 [178–272]	214 [175–259]	202 [174–249]	217 [178–251]	224 [189–269]
Fibrinogen ($g \cdot L^{-1}$) ($N = 519$)	3.2 [2.6–3.7]	3.1 [2.6–3.6]	2.9 [2.6–3.2]	3.3 [2.9–3.8]	3.2 [2.6–3.7]	3.4 [2.7–4.0]
ACT (sec) ($N = 865$)	108 [102–114]	113 [105–118]	116 [110–122]	106 [101–112]	110 [103–118]	108 [104–117]
Creatinine ($\mu mol \cdot L^{-1}$) ($N = 868$)	78 [70–95]	81 [72–94]	81 [71–98]	83 [71–97]	85 [72–97]	78 [70–91]
Viscoelastic and functional testing results, median [IQR]						
EXTEM CT (sec) ($N = 853$)	63 [57–70]	65 [59–72]	67 [60–74]	64 [59–69]	66 [60–73]	67 [60–75]
FIBTEM A10 (mm) ($N = 853$)	18 [15–23]	17 [14–22]	17 [14–21]	17 [15–21]	17 [13–20]	17 [14–21]
Functional platelet count ($\times 10^9 \cdot L^{-1}$) ($N = 854$)	137 [111–170]	148 [123–189]	158 [128–188]	139 [109–166]	136 [110–172]	160 [134–196]
Procedure and baseline mechanical support characteristics, *n*/total *N* (%) ($N = 872$)						
Scheduled	172/186 (92%)	109/134 (81%)	95/130 (73%)	154/172 (90%)	118/130 (91%)	98/120 (82%)
Unscheduled—urgent	9/186 (5%)	12/134 (9%)	15/130 (12%)	7/172 (4%)	7/130 (55)	14/120 (12%)
Unscheduled—emergency	5/186 (3%)	13/134 (10%)	20/130 (15%)	11/172 (6%)	5/130 (4%)	8/120 (7%)
Mechanical circulatory support						
Preprocedure IABP ($N = 865$)	2/184 (1%)	2/133 (2%)	2/128 (2%)	1/172 (1%)	0/129 (0%)	0/119 (0%)
Preprocedure VAD or ECMO ($N = 863$)	2/184 (1%)	0/133 (0%)	0/129 (0%)	0/172 (0%)	0/126 (0%)	0/119 (0%)
Redo status, *n*/total *N* (%) ($N = 862$)						
Previous cardiac surgery	44/184 (24%)	24/133 (18%)	26/126 (21%)	17/171 (10%)	25/129 (19%)	22/119 (18%)

Table 2 continued

Variable	Cardiopulmonary bypass circuit type					
	Circuit 1 Medtronic Fusion™ Balance™ *N* = 186	Circuit 2 Medtronic Fusion™ Cortiva™ *N* = 134	Circuit 3 LivaNova Inspire™ *N* = 130	Circuit 4 Terumo CAPIOX® FX25 *N* = 172	Circuit 5 Getinge VHK7100 + Quadriox-i *N* = 130	Circuit 6 Medtronic Affinity NT™ Cortiva™ *N* = 120
Procedure type, *n*/total *N* (%) (*N* = 868)						
Aortocoronary bypass	77/186 (20%)	66/134 (17%)	62/130 (16%)	78/168 (20%)	55/130 (14%)	52/120 (13%)
Ascending aorta	26/186 (14%)	21/134 (15%)	22/130 (17%)	20/172 (12%)	21/130 (16%)	16/120 (13%)
Aortic arch	9/186 (5%)	5/134 (4%)	4/130 (3%)	5/172 (3%)	8/130 (6%)	3/120 (3%)
Descending aorta	0/186 (0%)	2/134 (1%)	1/130 (1%)	0/172 (0%)	1/130 (1%)	1/120 (1%)
ASD repair	6/185 (3%)	4/133 (3%)	5/129 (4%)	8/168 (5%)	4/128 (3%)	5/120 (4%)
Aortic valve	65/184 (35%)	47/133 (35%)	43/130 (33%)	53/167 (32%)	49/128 (38%)	43/120 (36%)
Left ventricle aneurysmectomy	0/183 (0%)	1/133 (1%)	2/130 (2%)	0/166 (0%)	0/128 (0%)	4/120 (3%)
Mitral valve	52/184 (28%)	24/133 (18%)	28/130 (22%)	47/168 (28%)	33/128 (26%)	21/120 (18%)
Myectomy	15/186 (8%)	6/133 (5%)	8/130 (6%)	8/166 (5%)	10/128 (8%)	8/120 (7%)
Pulmonary valve	4/185 (2%)	8/133 (6%)	7/130 (5%)	4/167 (2%)	1/128 (1%)	4/120 (3%)
Tricuspid valve	20/185 (11%)	10/133 (8%)	7/129 (5%)	20/167 (12%)	10/128 (8%)	9/120 (8%)
VSD repair	0/185 (0%)	1/133 (1%)	0/130 (0%)	2/167 (1%)	1/128 (1%)	1/119 (1%)
Cardiopulmonary bypass variables						
Total bypass time (min), median [IQR] (*N* = 869)	97 [79–126]	100 [74–146]	98 [77–132]	103 [76–133]	106 [78–151]	98 [73–142]
Cross-clamp time (min), median [IQR] (*N* = 867)	74 [56–99]	76 [55–115]	80 [56–107]	78 [55–105]	80 [55–115]	79 [57–114]
Circulatory arrest, *n*/total *N* (%) (*N* = 872)	12/186 (6%)	10/134 (7%)	6/130 (5%)	8/172 (5%)	10/130 (8%)	5/120 (4%)
Pump prime (mL), median [IQR] (*N* = 865)	778 [505–1,035]	718 [535–1,055]	735 [610–1,055]	735 [605–1,040]	805 [605–1,055]	710 [545–1,035]
Total heparin dose (× 1,000 IU), median [IQR] (*N* = 849)	50 [40–60]	53 [45–65]	55 [45–66]	50 [40–60]	53 [44–65]	50 [40–65]
Total protamine dose (mg), median [IQR] (*N* = 799)	350 [300–428]	350 [300–400]	350 [300–430]	350 [280–400]	350 [300–400]	350 [300–400]
Total tranexamic acid dose (g), median [IQR] (*N* = 833)	2 [2–3]	2 [2–3]	2 [2–3]	2 [2–2]	2 [2–3]	2 [2–2]

ACT = activated clotting time; ASD = atrial septal defect; BSA = body surface area; BMI = body mass index; CCS = Canadian Cardiovascular Society; CT = clotting time; CVA = cerebrovascular accident; DVT = deep venous thrombosis; ECMO = extracorporeal membrane oxygenation; IABP = intra-aortic balloon pump; INR = international normalized ratio; IQR = interquartile range; LVEF = left ventricular ejection fraction; PAP = pulmonary artery pressure; PE = pulmonary embolism; TIA = transient ischemic attack; VAD = ventricular assist device; VSD = ventricular septal defect

Table 3 Fluid management and postcardiopulmonary bypass laboratory values

Variable	Cardiopulmonary bypass circuit type						
	Circuit 1 Medtronic Fusion™ Balance™ *N* = 186	Circuit 2 Medtronic Fusion™ Cortiva™ *N* = 134	Circuit 3 LivaNova Inspire™ *N* = 130	Circuit 4 Terumo CAPIOX® FX25 *N* = 172	Circuit 5 Getinge VHK7100 + Quadriox-i *N* = 130	Circuit 6 Medtronic Affinity NT™ Cortiva™ *N* = 120	*P* value*
Circuit-associated fluid balance							
Intraoperative crystalloids (mL), median [IQR] (*N* = 862)	1,500 [0–2, 100]	1,300 [0, 1, 500]	1,500 [750–1,700]	1,000 [500–1,500]	1,500 [0, 1, 500]	1,352 [750–1,600]	< 0.001
Pump balance in (mL), median [IQR] (*N* = 859)	1,400 [883–1,981]	1,233 [850–1,985]	1,300 [792–1,855]	1,350 [850–2,103]	1,288 [819–1,929]	1,205 [800–1,918]	0.83
Cell salvage infused, *n*/total *N* (%) (*N* = 842)	109/183 (60%)	91/130 (70%)	83/128 (65%)	91/169 (54%)	87/127 (69%)	52/105 (50%)	0.003
Cell salvage volume infused (mL), median [IQR] (*N* = 487)	375 [228–654]	240 [0–448]	326 [0–601]	320 [191–470]	356 [125–480]	193 [118–357]	0.005
Viscoelastic and functional testing results (at rewarming from bypass), median [IQR]							
EXTEM CT (s) (*N* = 844)	78 [71–89]	87 [79–96]	85 [78–95]	80 [73–88]	82 [77–92]	87 [78–97]	< 0.001
FIBTEM A10 (mm) (*N* = 844)	13 [10–16]	17 [14–22]	12 [10–14]	13 [11–15]	12 [10–14]	12 [10–14]	0.003
Functional platelet count ($\times 10^9 \cdot L^{-1}$) (*N* = 853)	102 [75–130]	122 [90–147]	108 [85–137]	139 [109–166]	117 [84–140]	122 [98–150]	< 0.001
Postoperative laboratory values (postprotamine or at admission to ICU), median [IQR]							
Hemoglobin ($g \cdot L^{-1}$) (*N* = 829)	106 [95–116]	105 [94–116]	107 [97–113]	105 [96–116]	106 [94–118]	104 [95–117]	0.88
INR (*N* = 870)	1.4 [1.2–1.5]	1.3 [1.2–1.4]	1.3 [1.2–1.4]	1.3 [1.2–1.4]	1.3 [1.3–1.4]	1.3 [1.2–1.4]	0.03
Platelets ($\times 10^9 \cdot L^{-1}$) (*N* = 761)	170 [140–202]	171 [133–209]	159 [137–191]	163 [133–196]	166 [145–184]	168 [145–207]	0.57
Fibrinogen ($g \cdot L^{-1}$) (*N* = 760)	2.5 [2.1–3.0]	2.4 [2.2–2.8]	2.6 [2.3–3.0]	2.4 [1.9–3.0]	2.1 [1.9–2.6]	2.9 [2.3–3.5]	0.003
Postprotamine ACT (sec) (*N* = 848)	116 [109–126]	118 [111–126]	122 [116–133]	114 [107–123]	118 [112–129]	115 [106–120]	< 0.001
Creatinine ($\mu mol \cdot L^{-1}$) (*N* = 866)	73 [63–91]	74 [64–93]	73 [66–92]	76 [67–92]	74 [66–87]	75 [66–89]	0.59
Procedural bleeding							
Estimated intraprocedural blood loss (mL), median [IQR] (*N* = 859)	600 [500–1,000]	600 [400–800]	600 [400–1,000]	600 [500–1,000]	600 [100–1,000]	600 [300–1,000]	0.22
Universal definition of perioperative bleeding class (class 2 or greater; moderate to massive bleeding), *n*/total *N* (%) (*N* = 872)	108/186 (58%)	72/134 (54%)	76/130 (58%)	86/172 (50%)	66/130 (51%)	52/120 (43%)	0.11

*Categorical data, Chi square test or Fisher's exact test for cell counts ≤ 5; continuous data, Kruskal–Wallis omnibus test

ACT = activated clotting time; CT = clotting time; ICU = intensive care unit, INR = international normalized ratio; IQR = interquartile range

Table 4 Percent change in viscoelastic and functional platelet testing from baseline to rewarming by circuit group

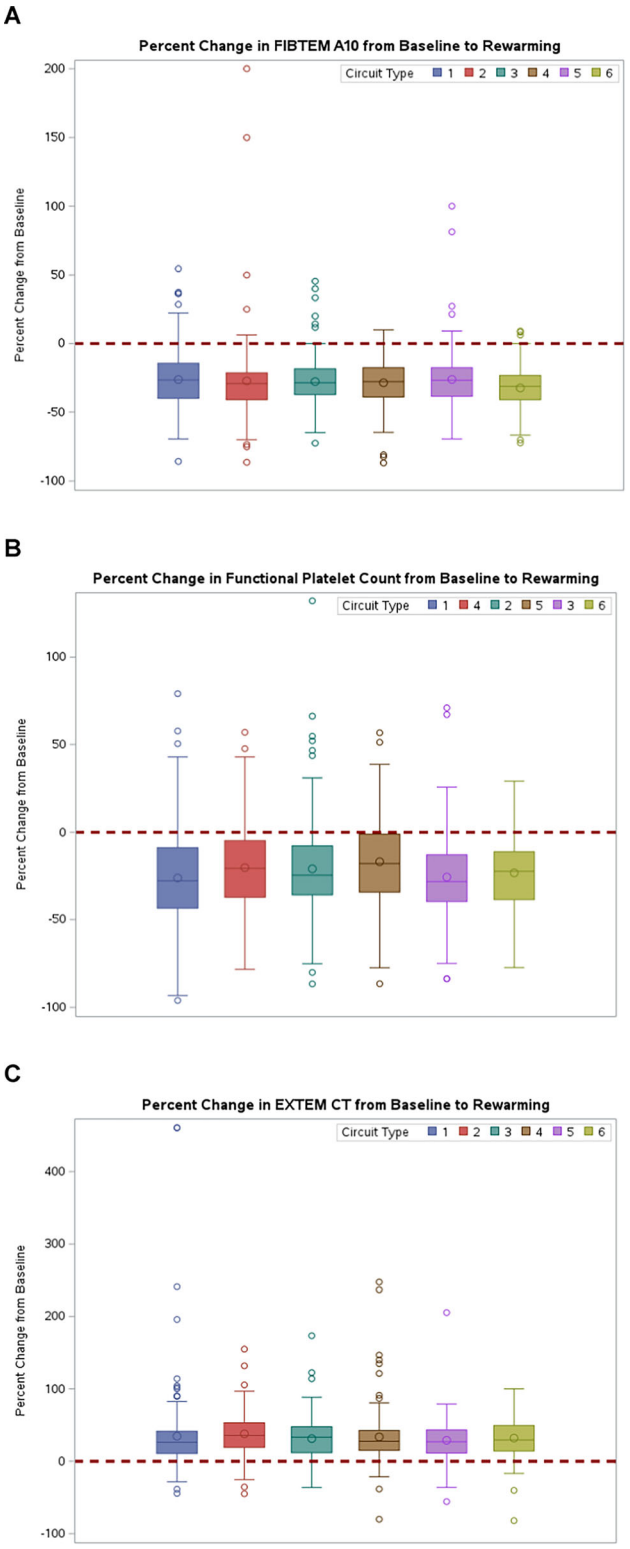
Variable	Cardiopulmonary bypass circuit type						
	Circuit 1 Medtronic Fusion™ Balance™	Circuit 2 Medtronic Fusion™ Cortiva™	Circuit 3 LivaNova Inspire™	Circuit 4 Terumo CAPIOX® FX25	Circuit 5 Getinge VHK7100 + Quadriox-i	Circuit 6 Medtronic Affinity NT™ Cortiva™	*P* value*
Coagulation parameter percent change compared with preoperative baseline, median [IQR]							
EXTEM clotting time (N = 830)	26% [11–41]	35% [19–53]	33% [12–47]	27% [15–42]	27% [11–43]	29% [14–49]	0.04
FIBTEM A10 (N = 830)	− 26% [−40 to − 14]	− 29% [−41 to − 21]	− 29% [−37 to − 18]	− 28% [−39 to − 18]	− 27% [−38 to − 18]	− 31% [−41 to − 23]	0.10
Functional platelet count (N = 840)	− 28% [−44 to − 9]	− 25% [−36 to − 8]	− 28% [−40 to − 13]	− 21% [−37 to − 5]	− 18% [−34 to − 1]	− 22% [−39 to − 11]	0.01

*Kruskal–Wallis omnibus test

we found that all circuits predictably caused clinically important deterioration of coagulation status as measured by conventional and point-of-care coagulation assays. While there were no dramatic differences in measured coagulation parameters between circuit groups, after adjusting for important confounders there was important variability in rates of bleeding and allogeneic blood product and hemostatic product administration between the groups. Specifically, for severity of bleeding as measured by the UDPB, four of the circuits had a decrease in the incidence of moderate to massive bleeding compared with the reference circuit. Additionally, circuit 6 in particular was associated with less allogeneic blood and hemostatic product administration both in terms of the absolute proportion of patients receiving any of these products and the total number of administrations between groups—suggesting it may perform better in terms of transfusion avoidance.

Cardiopulmonary bypass-associated coagulopathy is well recognized, with studies showing that the conduct of CPB results in at least a 30–40% drop in coagulation factor and platelet levels and a transient platelet dysfunction.[8] Robust literature comparing disposables from a variety of manufacturers, however, is limited. As such, the findings of this study provide novel and clinically important information that modern CPB disposables may significantly differ in their impact on the coagulation system and bleeding.

Although the cause of CPB-associated coagulopathy is multifactorial, specific components of CPB circuits have been shown to be important contributors. The most studied factor is the effect of circuit coating, with multiple studies comparing the effects of coated biocompatible circuits on various outcomes.[9] Although the results of these studies are not consistent, the totality of evidence suggests that biocompatible circuits reduce bleeding and blood transfusions.[9] Our results are inconsistent with this finding as the reservoir in the circuit with the lowest rates of transfusion did not have a biocompatible coating. This raises many questions. There are several circuit components with manufacturer differences that may have produced these results.[10] First, the cardiotomy reservoir has a large contact area with blood, varying priming volumes, and filters for both venous drainage and cardiotomy suction. Its design specifics may impact damage to cellular and noncellular blood components, driving coagulation system activation while on bypass with resultant dysfunction.[11] Nevertheless, the relative impact of various characteristics of reservoirs on coagulation has not been well studied in clinical settings. Second, the oxygenator also has a high surface area in contact with the blood, and varying priming volumes. As a result, it may also cause damage to blood components,[12] and thereby influence the degree of coagulopathy related to its design specifics.



◀**Figure 1** Percent change in viscoelastic and functional parameters from baseline to rewarming postbypass. Boxplots are shown by circuit type for the change in FIBTEM A10 (A), functional platelet count (B), and EXTEM clotting time (C). Boxes denote interquartile ranges, circles inside boxes denote group means, horizontal line inside boxes denote medians, whiskers denote ranges, and dots denote outliers.

Circuit 1 = Medtronic Fusion™ Balance™; Circuit 2 = Medtronic Fusion™ Cortiva™; Circuit 3 = LivaNova Inspire™; Circuit 4 = Terumo CAPIOX® FX25; Circuit 5 = Getinge VHK7100 + Quadriox-I; Circuit 6 = Medtronic Affinity NT™ Cortiva™; CT = clotting time

Limitations

Although we found a significant difference between the circuits and the measured bleeding and transfusion outcomes, these were not strongly reflected by results from the point-of-care coagulation assays. One reason for this finding may be that the point-of-care coagulation assays are not sensitive enough to detect relatively subtle differences between the CPB disposables in a relatively small study with wide variability in patient- and surgery-related factors. Accurate determination of bleeding in cardiac surgery is difficult, and future studies examining this as a primary endpoint may benefit from the integration of clinical decision support systems and new technologies.[13]

This quality assurance project has important limitations that affect the validity and generalizability of our findings. Most importantly, it was a single-centre, nonrandomized comparison, and although a validated point-of-care-based coagulation management algorithm has been established at the centre for several years, perioperative coagulation management was left to the discretion of the attending anesthesiologists. As such, we cannot exclude the influence of unmeasured confounders on the results, nor can we be sure that the findings are generalizable to other centres and practices. One important unmeasured potential confounder is the use of cardiotomy suction, which can impact coagulation[11] and is routinely used at our hospital, but we did not capture the extent of its use for individual cases; thus, its impact on our findings cannot be determined. Another important confounder is individual surgical technique and the types of cases individual surgeons tend to book. While we accounted for clustering by surgeon in our analysis, residual confounding may still remain. Lastly,

Table 5 Clinical outcomes within 7 days of index surgery

Clinical outcome within 7 days of index surgery	Cardiopulmonary bypass circuit type						
	Circuit 1 Medtronic Fusion™ Balance™	Circuit 2 Medtronic Fusion™ Cortiva™	Circuit 3 LivaNova Inspire™	Circuit 4 Terumo CAPIOX® FX25	Circuit 5 Getinge VHK7100 + Quadriox-i	Circuit 6 Medtronic Affinity NT™ Cortiva™	*P* value*
Stroke	2/79 (1%)	2/69 (1%)	6/53 (5%)	0/87 (0%)	5/49 (4%)	1/51 (1%)	0.003
Any neurologic deficit lasting > 24 hr with radiological confirmation (N = 388)							
Reoperation for bleeding	3/79 (2%)	8/69 (6%)	9/53 (7%)	5/87 (3%)	4/48 (3%)	4/51 (3%)	0.14
(N = 387)							
Cardiac arrest requiring CPR	0/79 (0%)	2/69 (1%)	2/53 (2%)	1/87 (1%)	0/48 (0%)	0/51 (0%)	0.28
(N = 387)							
Atrial fibrillation	60/79 (32%)	55/69 (41%)	39/53 (30%)	73/87 (42%)	31/48 (24%)	39/51 (33%)	0.19
Requiring medication, cardioversion, or resulting in angina, congestive heart failure, or symptomatic hypotension (N = 387)							
Hepatic dysfunction	0/79 (0%)	3/69 (2%)	1/53 (1%)	4/87 (2%)	3/48 (2%)	1/51 (1%)	0.25
Aminotransferases > 150 IU·L^{-1} (N = 387)							
Sepsis	1/79 (1%)	1/69 (1%)	2/53 (2%)	2/87 (1%)	0/48 (0%)	0/51 (0%)	0.75
Requiring a positive blood culture, with presence of both infection and a systemic inflammatory response (N = 387)							
Limb ischemia	0/79 (0%)	0/69 (0%)	1/53 (1%)	1/87 (1%)	1/48 (1%)	1/51 (1%)	0.56
Inadequate blood supply to the limbs (with radiological confirmation) (N = 387)							
Respiratory failure	11/79 (6%)	10/69 (7%)	11/53 (8%)	11/87 (6%)	5/49 (4%)	7/52 (6%)	0.79
Requiring reintubation or ICU readmission (N = 389)							

*Chi square test or Fisher's exact test for cell counts ≤ 5

CPR = cardiopulmonary resuscitation; ICU = intensive care unit

Table 6 Results of adjusted generalized estimating equation analysis for transfusion outcomes

Cardiopulmonary bypass circuit type	Patients, *n*/total *N* (%)	Univariable analysis *Odds ratio (95% CI)*	Multivariable analysis† (*N* = 829 patients included) *Odds ratio (95% CI)*
Outcome 1: modified UDPB score ≥ 2 (moderate to severe bleeding) on day of surgery*			
Circuit 1: Medtronic Fusion™ Balance™	107/185 (58%)	Reference	
Circuit 2: Medtronic Fusion™ Cortiva™	70/132 (53%)	0.64 (0.72 to 1.04)	0.64 (0.53 to 0.78)
Circuit 3: LivaNova Inspire™	75/128 (59%)	0.99 (0.77 to 1.28)	1.03 (0.65 to 1.63)
Circuit 4: Terumo CAPIOX® FX25	85/171 (50%)	0.74 (0.55 to 0.99)	0.66 (0.46 to 0.93)
Circuit 5: Getinge VHK7100 + Quadriox-i	64/129 (50%)	0.73 (0.56 to 0.96)	0.64 (0.45 to 0.90)
Circuit 6: Medtronic Affinity NT™ Cortiva™	52/119 (44%)	0.60 (0.42 to 0.83)	0.61 (0.49 to 0.77)
Outcome 2: Requirement for any allogeneic blood product transfusion within 7 days of surgery (red cells, platelets, or plasma)			
Circuit 1: Medtronic Fusion™ Balance™	95/185 (51%)	Reference	
Circuit 2: Medtronic Fusion™ Cortiva™	60/132 (45%)	0.81 (0.59 to 1.12)	0.53 (0.30 to 0.92)
Circuit 3: LivaNova Inspire™	63/128 (49%)	0.90 (0.62 to 1.30)	0.79 (0.50 to 1.23)
Circuit 4: Terumo CAPIOX® FX25	80/171 (47%)	0.85 (0.54 to 1.33)	0.78 (0.52 to 1.17)
Circuit 5: Getinge VHK7100 + Quadriox-i	64/129 (50%)	0.94 (0.76 to 1.17)	0.94 (0.56 to 1.57)
Circuit 6: Medtronic Affinity NT™ Cortiva™	44/119 (37%)	0.57 (0.38 to 0.86)	0.52 (0.35 to 0.78)
Outcome 3: Requirement for any hemostatic therapy within 7 days of surgery (fibrinogen concentrate, PCC, or rFVIIa)			
Circuit 1: Medtronic Fusion™ Balance™	27/185 (15%)	Reference	
Circuit 2: Medtronic Fusion™ Cortiva™	14/132 (11%)	0.74 (0.40 to 1.36)	0.54 (0.22 to 1.29)
Circuit 3: LivaNova Inspire™	20/128 (16%)	1.04 (0.68 to 1.60)	0.98 (0.43 to 2.25)
Circuit 4: Terumo CAPIOX® FX25	21/171 (12%)	0.85 (0.47 to 1.54)	0.84 (0.34 to 2.02)
Circuit 5: Getinge VHK7100 + Quadriox-i	12/129 (9%)	0.60 (0.35 to 1.00)	0.31 (0.13 to 0.77)

Table 6 continued

Cardiopulmonary bypass circuit type	Patients, *n*/total *N* (%)	Univariable analysis *Odds ratio (95% CI)*	Multivariable analysis† (*N* = 829 patients included) *Odds ratio (95% CI)*
Circuit 6: Medtronic Affinity NT™ Cortiva™	5/119 (4%)	0.28 (0.13 to 0.61)	0.20 (0.07 to 0.58)

The adjusted generalized estimating equation analysis accounted for correlations of patients within surgeon groups, treated as individual clusters; *N* = 864 patients were eligible for inclusion.

*Bleeding was classified as at least moderate if on the day of surgery patients required any of 1) ≥ 2 units pRBC, 2) ≥ 2 units of frozen plasma, 3) any platelet transfusion, 4) any PCC, 5) any fibrinogen concentrate, 6) any rFVIIa, or 7) any need for chest reopening for bleeding.

†Adjustment variables included age, sex, BMI, urgency status, previous cardiac surgery, presence of left ventricular impairment, baseline creatinine, baseline hemoglobin, total time on bypass, and time of circulatory arrest. Individual surgeons were specified as a cluster in the model wherein outcomes within the cluster were assumed to be correlated.

BMI = body mass index; CI = confidence interval; PCC = prothrombin complex concentrate; pRBC = packed red blood cells; rFVIIa = recombinant activated factor VII; UDPB = universal definition of perioperative bleeding

we did not report on user experience or training requirements, performance optimization, and cost-effectiveness.

Conclusion

The findings from our quality assurance project suggest that current Health Canada-approved CPB circuits may have a differential effect on coagulation and bleeding after cardiac surgery, but limitations preclude us from making definitive conclusions about the relative effects of the tested circuits. Nevertheless, the results are robust enough to conclude that further studies, ideally randomized controlled trials, are warranted.

Author contributions *Sunpreet Takhar*, *Brian Beairsto*, *Cyril Serrick*, *Stuart A. McCluskey*, and *Keyvan Karkouti* contributed to all aspects of this manuscript, including study conception and design; acquisition, analysis, and interpretation of data; and drafting the article. *Selene Martinez-Perez* and *Raphael Derman* contributed to the analysis and interpretation of data and drafting the manuscript. *Margarita Otalora-Esteban* contributed to interpretation of data and drafting the manuscript. *Cielo Bingley* contributed to study design, data acquisition and analysis, and drafting the manuscript. *Justyna Bartoszko* contributed to study design; acquisition, analysis, and interpretation of data; and drafting the article.

Disclosures Justyna Bartoszko is in part supported by a merit award from the Department of Anesthesiology & Pain Medicine, University of Toronto (Toronto, ON, Canada); has received honoraria from Octapharma; and has received research support from Grifols and Canadian Blood Services. Keyvan Karkouti is in part supported by a merit award from the Department of Anesthesiology & Pain Medicine, University of Toronto (Toronto, ON, Canada) and has received research support, honoraria, or consultancy for speaking engagements from Octapharma, Instrumentation Laboratory, and Bayer.

Funding statement Peter Munk Cardiac Centre, Toronto General Hospital Quality Improvement Grant; Department of Anesthesia and Pain Management, Toronto General Hospital-University Health Network (all, Toronto, ON, Canada).

Editorial responsibility This submission was handled by Dr. Philip M. Jones, Deputy Editor-in-Chief, *Canadian Journal of Anesthesia/ Journal canadien d'anesthésie*

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