JECT. 2016;48:5–10
The Journal of ExtraCorporeal Technology

Original Articles

Arterial Limb Microemboli during Cardiopulmonary Bypass: Observations from a Congenital Cardiac Surgery Practice

Gregory S. Matte, BS, CCP, LP, FPP;* Kevin R. Connor, BS, CPP, LP;* Hua Liu, MS;* James A. DiNardo, MD, FAAP;† David Faraoni, MD, PhD, FCCP;† Frank Pigula, MD‡

**Department of Cardiac Surgery, Boston Children's Hospital, Boston, Massachusetts; †Department of Anesthesiology, Perioperative and Pain Medicine, Harvard Medical School, Boston, Massachusetts; and ‡Department of Cardiac Surgery, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts*

Abstract: Gaseous microemboli (GME) are known to be delivered to the arterial circulation of patients during cardiopulmonary bypass (CPB). An increased number of GME delivered during adult CPB has been associated with brain injury and postoperative cognitive dysfunction. The GME load in children exposed to CPB and its consequences are not well characterized. We sought to establish a baseline of arterial limb emboli counts during the conduct of CPB for our population of patients requiring surgery for congenital heart disease. We used the emboli detection and counting (EDAC) device to measure GME activity in 103 consecutive patients for which an EDAC machine was available. Emboli counts for GME <40 μ and >40 μ were quantified and indexed to CPB time (minutes) and body surface area (BSA) to account for the variation in patient size and CPB times. Patients of all sizes had a similar embolic burden when indexed to bypass time and BSA. Furthermore, patients of all sizes saw a three-fold increase in the <40 μ embolic burden and a five-fold increase in the >40 μ embolic burden when regular air was noted in the venous line. The use of kinetic venous-assisted drainage did not significantly increase arterial limb GME. Efforts for early identification and mitigation of venous line air are warranted to minimize GME transmission to congenital cardiac surgery patients during CPB.
Keywords: cardiopulmonary bypass, congenital heart disease, air embolism, gaseous microemboli, adverse events, EDAC. *JECT. 2016;48:5–10*

Although massive air embolism into the cerebral circulation can cause stroke and could be associated with major postoperative complications including death, the relationship between gaseous microemboli (GME) and outcomes has been weakly studied (1). In adults, neurocognitive impairment following cardiac surgery with cardiopulmonary bypass (CPB) has been described as confusion, memory loss, lack of concentration, depression, encephalopathy, or delirium and has been correlated with microemboli delivery during bypass (2). It is clear that GME are delivered to all patients through disposable devices currently in use (3–11) and that oxygenator, venous reservoir, venous filter, and arterial line filter (ALF) design all play an important role in GME clearance during CPB (12). Although there have been several in vitro studies investigating GME in pediatric bypass circuits (3–8), in vivo assessment of GME in pediatric patients has been limited to two small series (9,10). While the relationship between GME and outcomes has been defined for adult CPB (2), no comparable relationship has been described in neonates and children with congenital heart disease (CHD) undergoing cardiac surgery (13). The aim of this prospective observational study was to define the embolic burden to CHD patients undergoing CPB at our center using current disposables and techniques.

Received for publication September 21, 2015; accepted January 29, 2016
Address correspondence to: Gregory S. Matte, CCP, LP, FPP, Perfusion Clinical Coordinator, Cardiac Surgery, Boston Children's Hospital, 300 Longwood Avenue, Boston, MA 02115. E-mail: gregory.matte@cardio.chboston.org
The senior author has stated that the authors have reported no material, financial, or other relationship with any healthcare-related business or other entity whose products or services are discussed in this paper.

CPB EQUIPMENT

We had previously used emboli detection and counting (EDAC) machines (Luna Innovations, Inc., Roanoke, VA) with up to three probes for each bypass case: venous

Article available at https://ject.edpsciences.org or https://doi.org/10.1051/ject/201648005

line, post cardiotomy venous reservoir (CVR), and post ALF. Our experience in transitioning to integrated arterial line filtration was consistent with what other investigators had shown in that the Terumo CAPIOX FX series oxygenators (Terumo Cardiovascular Group, Ann Arbor, MI) with integrated arterial line filtration were comparable with the Terumo CAPIOX RX series oxygenators coupled with an external ALF in regard to GME clearance (14). This gave our practice confidence in transitioning to an oxygenator line which saved circuit prime volume and simplified setup by utilizing integrated arterial line filtration.

Gravity siphon drainage (GSD) was used in all patients with a body surface area (BSA) of <1.2 m^2 and an anticipated maximum pump flow under 3.0 L/min/m^2 (3.6 L/min). A centrifugal head in the venous line provided kinetic venous-assisted drainage (KVAD) as needed for patients with a BSA ≥1.2 m^2 and/or an anticipated maximum pump flow rate greater than ≥3.6 L/min. This limit was chosen for our practice based on the desire to eliminate ½″ venous tubing from our circuits and the occasional need to use peripheral cannulation with venous cannulae flow-rated less than cannulae placed centrally. Negative pressure in the venous limb of the circuit with KVAD is limited to –40 mmHg in our practice and is measured via a pressure dome connected 8″ proximal to centrifugal head inflow and 3.5–4.5′ distal the venous cannula(e) connection. Terumo CAPIOX FX oxygenators with integrated 32-μ ALFs and 47-μ venous reservoir filters are used in all patients. Table 1 lists the selection of primary circuit components used in our clinical practice based on an anticipated maximum index pump flow rate of 3.0 L/min/m^2 during bypass. Circuit components are upsized as needed when maximum anticipated pump flow rates on bypass exceed the 3.0 index standard (i.e., aortopulmonary collaterals, significant aortic insufficiency, and single ventricle physiology) (15).

Two EDAC machines were available for up to four operating rooms per day. We aimed to collect emboli data on 100 consecutive congenital cardiac surgery patients for which an EDAC machine was available. For the duration of this observational study, the perfusionist applied an EDAC probe to the arterial limb of the bypass circuit for data collection. The EDAC probe was located distal to the Terumo CAPIOX FX oxygenator and therefore was post oxygenator and post ALF. It is well known that the CVR, membrane oxygenator, and ALF significantly attenuate GME transmission during bypass (3,4,15). Since the aim of our study was to quantify GME transmission to the patient, we used only a single probe in the bypass circuit arterial limb.

Table 1. Circuit components based on maximum anticipated bypass flow rate.

Maximum Anticipated Pump Flow Rate (L/min)	Circuit Prime Volume (mL)	Oxygenator with Integrated 32 micron ALF	Primary Tubing Pack Components
Up to 1.2	215	Terumo CAPIOX FX05 for up to 1.5 L/min	3/16 arterial 3/16 boot 1/4 venous
1.2–1.5	230		3/16 arterial 1/4 boot 1/4 venous
1.5–1.8	460	Terumo CAPIOX FX15–30 for up to 5 L/min with assisted drainage	1/4 arterial 1/4 boot 1/4 venous
1.8–2.1	560		1/4 arterial 1/4 boot 3/8 venous
2.1–3.15	595		1/4 arterial 3/8 boot 3/8 venous
3.15–3.6	700		3/8 arterial 3/8 boot 3/8 venous
3.6–4.4	775		3/8 arterial 3/8 boot 3/8 venous centrifugal venous assist head
4.4–5	800		3/8 arterial 1/2 boot step up 3/8 venous centrifugal venous assist head
5.0–7.0	980	Terumo CAPIOX FX25 for up to 7 L/min	3/8 arterial 1/2 boot step up 3/8 venous centrifugal venous assist head

Adapted from Perfusion for Congenital Heart Surgery: Notes on Cardiopulmonary Bypass for a Complex Patient Population (15), with permission of John Wiley & Sons (ISBN 978–1-118–90079–6).

MATERIALS AND METHODS

The Luna Innovations software creates bins of emboli based on their size. These bins run from 0 to 1000 μ in increments as low as 10 μ. All emboli >1000 μ are counted in a single bin. Our embolic data were separated into two bins; <40 μ and >40 μ. The Luna Innovations hardware and software does not have the ability to distinguish gaseous emboli from particulate. We characterized our embolic data as GME given the greater likelihood that emboli detected after the ALF are gaseous as opposed to particulate (16). CPB equipment currently on the market either has integrated arterial line filtration in the 25–40 μ range or it includes external arterial line filtration in the 20–40 μ range (15). The Terumo CAPIOX FX oxygenators have integrated ALFs with a pore size of 32 μ. The 40 μ standard was chosen as a demarcation in line with other published reports using that standard (2,4,7–11) and because the EDAC software cannot bin emboli precisely to the 32 μ pore size that the FX series offers. EDAC data recording was started with the commencement of bypass and stopped at the end of CPB.

CPB was conducted per department standard. Bypass circuits were CO_2 flushed before crystalloid priming with

Plasma-Lyte A 7.4 (Baxter Healthcare, Deerfield, IL) and circulated through a ≤5 μ prebypass filter (Sorin Group USA Inc., Arvada, CO). The circuit prime was adjusted for a dilutional hematocrit once on bypass of 25–30% depending on the patient diagnosis with the aim of a hematocrit of 30–35% for separation from bypass. Reconstituted whole blood (red blood cells with plasma added) was used as needed for patients requiring a blood prime. Sodium bicarbonate and calcium gluconate were added to the prime before it was ventilated. A blood gas sample was analyzed for blood prime circuits to ensure proper pH, blood gas, and electrolyte values. The prime was kept circulating at 30°C–32°C before the arteriovenous loop was divided on the sterile field. No forms of autologous priming of the bypass circuit were used. All patients received 300 U/kg of heparin as a bolus dose with more given as needed for a target activated clotting time (ACT) of ≥480 seconds before instituting and while on bypass. Typical target bypass flow rates while warm were 2.5–3.0 L/min/m^2 with flow decreasing in step with depth of hypothermia and surgeon preference. Patient blood pressure was managed with adjustments to pump flow rate, phenylephrine, and isoflurane as needed during CPB. Alpha-stat blood gas management was used for patients cooled to >30°C whereas pH-stat management was used for patients cooled to ≤30°C. A level sensor servoregulated to the arterial roller head pump was placed on the venous reservoir for all cases and was set at or above the manufacturer recommended minimum operating volume. A Sorin Xtra (Sorin Group USA Inc.) autotransfusion device was used for processing shed blood and residual pump circuit volume for all cases.

No interventions were made on bypass based on real-time EDAC data. Studies were saved for off-line analysis. Twelve studies were excluded from analysis because of significant electrical interference causing false-positive emboli detection. False-positive emboli detection caused by electromagnetic interference was defined as apparent emboli activity on the EDAC monitor during setup without flow through the bypass circuit.

Data Analysis

Emboli counts for GME < 40 μ and >40 μ were quantified and indexed to CPB time (minutes) since there was a wide range of time spent on bypass (interquartile range [IQR]: 92–158 minutes). We divided our population into two groups based on BSA <1.2 m^2 and ≥1.2 m^2 since it is our practice to use KVAD for patients in the larger BSA group. Indexed GME counts were compared relative to patient weight, patient BSA, oxygenator size, use of an aortic cross-clamp, whether maximum pump flow rate exceeded 80% or 90% of the oxygenator's rated flow, type of drainage used (GSD vs. KVAD), target patient temperature on bypass, and whether venous line air was regular. We defined "regular venous line air" as venous air visible to the perfusionist occurring longer than 5 minutes. This time threshold allowed the surgeon to attempt to alleviate the cause of venous line air.

Statistical Analysis

Categorical variables are expressed as number and percentage. We used the Shapiro–Wilk test to assess continuous variables for normality. Data are presented as median and IQR or mean and SD. Groups were compared using the Student *t* test or Wilcoxon rank sum test for continuous variables and the Chi-square test for categorical variables.

A p value <.05 was considered statistically significant for all tests. Statistical analyses were performed using STATA version 14.0 for Mac OS (StataCorp, College Station, TX).

RESULTS

We included 103 patients (median weight: 9.4 kg; IQR: 5.1–31.3) from October 2014 to April 2015. Of these patients, 79 were included in the group with BSA < 1.2 m^2 and 24 were included in the group with BSA ≥ 1.2 m^2. Demographic and CPB characteristics are described in Table 2.

Figure 1A shows that GME < 40 μ/min/BSA were comparable in patients with a BSA < 1.2 m^2 (1411; range: 380–3566) and patients with a BSA ≥ 1.2 m^2 (1194; range: 86–1937) when no regular air was present in the venous line. Also shown is that the regular air in the venous line significantly increases the embolic burden for all patients in both groups seeing a three-fold increase in GME < 40 μ/min/BSA under those conditions (GME < 40 μ/min/BSA; BSA < 1.2 m^2—no air: 1411 to air: 4416 and BSA ≥ 1.2 m^2—no air: 1194 to air: 3520). Figure 1B shows the embolic load for GME > 40 μ/min/BSA was comparable in patients with a BSA < 1.2 m^2 (18; range: 2–63) and patients with a BSA ≥ 1.2 m^2 (15; range: 2–33) when no regular air was present in the venous line. There was a five-fold increase in the embolic burden for emboli >40 μ/min/BSA with regular air in the venous line (GME > 40 μ/min/BSA; BSA < 1.2 m^2—no air: 18 to air: 87 and BSA ≥ 1.2 m^2—no air: 15 to air: 85). Although KVAD was mainly used in patients with BSA ≥1.2 m^2, no difference in the number of GME < 40 μ/min (Figure 1A) and GME > 40 μ/min (Figure 1B) was observed between the two groups after adjustment for BSA, with p = .707 and .816, respectively. Higher <40 μ/min GME counts were also associated with increased >40 μ/min GME counts (Figure 2).

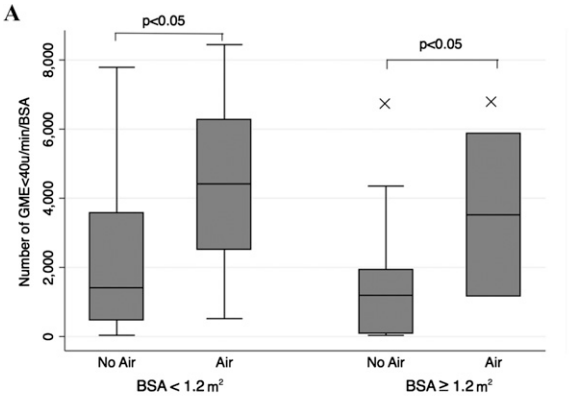
DISCUSSION

A microbubble is defined as an air bubble <1000 μ in diameter (17). Capillaries are generally considered to be 4–9 μ and GME greater than or equal to these dimensions

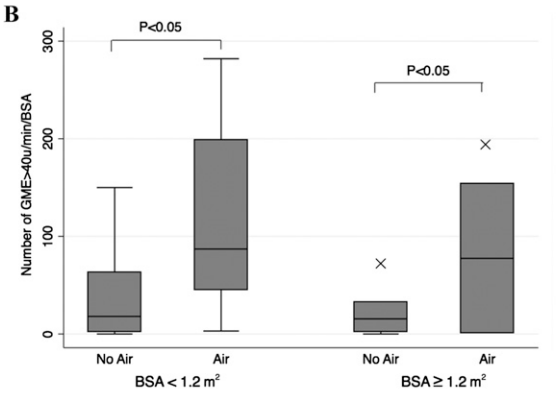
Table 2. Demographic and CPB management.

	Total (n = 103)	BSA < 1.2 m^2 (n = 79)	BSA ≥ 1.2 m^2 (n = 24)	p Value
Body weight (kg)	9.4 (5.1–31.3)	6.9 (4.6–13.5)	61.9 (51.5–73.2)	<.001
BSA	.46 (.29–1.10)	.35 (.26–.57)	1.66 (1.48–1.87)	<.001
Oxygenator (%)				
5	55 (53)	55 (70)	0 (0)	<.001
15	39 (38)	24 (30)	15 (63)	
25	9 (9)	0 (0)	9 (37)	
Prime volume (mL/kg)	32 (21–45)	38 (29–49)	14 (13–15)	<.001
Blood prime (%)	71 (69)	70 (89)	1 (4)	<.001
Aortic clamp (%)	88 (86)	66 (86)	22 (92)	.447
Target temperature (°C)	28 (4)	28 (4)	31 (2)	.004
Maximum pump flow ≥ 80% (%)	13 (13)	6 (8)	7 (29)	.005
Maximum pump flow ≥ 90% (%)	3 (3)	1 (1)	2 (8)	.071
KVAD (%)	25 (24)	1 (1)	24 (100)	<.001
CPB duration (minutes)	128 (92–158)	129 (90–155)	122 (94–163)	.873
Emboli < 40 μ/min (n)	828 (186–2025)	755 (186–1755)	2115 (327–3640)	.017
Emboli < 40 μ/min/BSA (n)	1550 (512–4169)	1751 (527–4235)	1219 (174–2124)	.165
Emboli > 40 μ/min (n)	12 (2–38)	8 (2–32)	22 (4–163)	.049
Emboli > 40 μ/min/BSA (n)	20 (2–82)	25 (3–82)	16 (2–95)	.571

Data are expressed in median and interquartile range, mean and SD, or number and percentage.



GME<40μ/min/BSA; BSA<1.2 - No Air: 1411 (range 380-3566), Air: 4416 (range 2520-6282).
GME<40μ/min/BSA; BSA≥1.2 - No Air: 1194 (range 86-1937), Air: 3520 (range 1174-5875).



GME>40μ/min/BSA; BSA<1.2 - No Air: 18 (range 2-63), Air: 87 (range 45-199).
GME>40μ/min/BSA; BSA≥1.2 - No Air: 15 (range 2-33), Air: 85 (range 2-150).

Figure 1. Number of GME (A) <40 μ/min/BSA and (B) >40 μ/min/BSA in children with or without regular air in the venous line. All children with a BSA ≥ 1.2 m^2 were exposed to KVAD, with X: p > .05, compared to children with BSA < 1.2 m^2.

may occlude the microvascular bed producing ischemia and activating an endothelial based inflammatory response (18). Even though most GME > 40 μ are removed from CPB circuits with current venous and ALFs (14), those <40 μ have the ability to coalesce upon exiting the ALF and can later become lodged within capillaries (19). These lodged microbubbles then transform from a sphere to a cylindrical shape in the vessel increasing dissolution time by at least 50% (20). This dissolution time may further increase since GME do not only exist as gas bubbles in whole blood, but they may be encapsulated with proteins, lipids, platelets, and white blood cells (21). Longer dissolution times increase the risk of watershed ischemic injury.

Our study of 103 congenital cardiac surgical patients is the largest to date characterizing arterial limb GME delivery

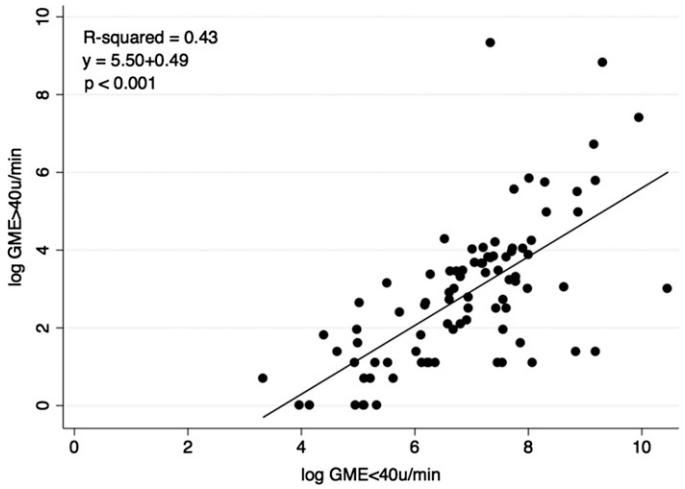


Figure 2. Correlation between GME < 40 μ/min and >40 μ/min after logarithmic transformation.

during CPB in this heterogeneous population. We examined numerous factors and found that the presence of venous line air was associated with a significant increase in GME of all sizes. Furthermore, after adjustment for BSA, the use of KVAD independent of venous air was not associated with increased GME.

The majority of CPB circuits currently in use with arterial line filtration are designed to prevent GME > 40 μ from being transmitted to the patient. It has been demonstrated that GME up to 40 μ are regularly delivered to CPB patients (7,9,10,22). GME larger than the ALF pore size may still be transmitted due to device imperfections and increased bypass system pressure contorting air emboli and forcing them through pores smaller than their overall size (23). GME delivered post ALF are also known to increase with manipulation of the heart at the surgical field (11,24), commencement of bypass (9,10,24), cross-clamp removal (9,24), venous line air entrainment (10,24,25), higher pump flow rates and circuit pressures (3,7,8), administration of medications to the circuit (24,26), use of a left ventricular vent with return to the CVR (25,26), the use of augmented venous return with higher negative pressures increasing GME counts (7,8,10), lower perfusate temperatures (7,27), and the use of pulsatile perfusion (7,8).

It has been documented that a primary source of post arterial filter GME is venous air entrainment (9,28). Clark et al. (9) demonstrated that increased venous air was associated with more and larger GME delivered post arterial filter and with more GME in the first 2 minutes of bypass and just before and after cross-clamp removal. The high GME count in the first 2 minutes of bypass was related to incomplete de-airing of the venous cannulae, a common source of venous line air. The authors felt that the GME increase before cross-clamp removal was related to de-airing of the right heart with closure of the right atriotomy.

We also examined the use of KVAD vs. GSD. Vacuum-assisted venous drainage (VAVD) exerts additional negative pressure on the venous tubing when GSD is already in use. This increase in negative pressure can be associated with increased venous line air and a subsequent increase in arterial line GME (6–8,10,29). The same effect can be expected with KVAD since it may also increase venous line air. In addition, KVAD has been shown to increase venous line GME by churning the air–blood mixture creating an increased number of smaller air emboli and forming an emulsion, which is not as readily removed within the CVR, oxygenator bundle, and ALF (30). Our study did not allow assessment of VAVD in regard to generation of GME relative to the KVAD and GSD techniques. However, when GME counts were normalized for BSA, the use of KVAD was not associated with an increased embolic load over that seen with GSD. This would imply that the effect of regular air in the venous line dwarfs the effect of KVAD in the generation of GME (Figure 1).

Higher <40 μ/min GME counts were also significantly related to increased >40 μ/min GME counts (Figure 2). An in vivo study of adult cardiac surgical patients concluded that the arterial load of smaller GME was positively correlated with the arterial load of larger GME (24). Our findings are consistent with that study.

Emboli detection devices currently in use significantly underestimate GME volume and numbers (5). Particularly worrisome is that this underestimation may be as high as 97% at circuit flow rates greater than 6 L/min(5). In relation to the size of the GME being counted, the EDAC has been shown to underestimate average bubble diameters at all flows by 38% as well (5). Considering that GME are likely underestimated with current monitoring devices and that increased GME load is associated with adverse neurologic outcomes in adult patients (1,2,17), we believe that GME should be minimized to the greatest extent possible in all patients during CPB.

Our study presents some major limitations. The choice of a GME cutoff of 40 μ can be considered arbitrary; however, this cutoff was based on the threshold defined in the available literature. The primary objective of our study was to describe the GME burden in CHD patients undergoing cardiac surgery; our study was not designed to assess the relationship between the burden of microemboli and clinical outcomes. Further large studies will be needed to assess the relationships between total GME burden, GME size, and outcomes in CHD patients undergoing cardiac surgery.

Second, KVAD was used in patients with a BSA ≥ 1.2 m^2 in our study. Since BSA and the KVAD could both influence the GME count, we elected to adjust for BSA in addition to the duration of CPB. Although the use of KVAD was not associated with any increase in GME count after adjustment for BSA, it is not certain that the use of KVAD in patients with comparable BSA would not increase the GME count. Further studies are needed to assess the effect of KVAD compared with GSD on GME count when used in the same population.

In addition, this study was not designed to assess the burden of GME at different time points during the surgery. The method of indexing GME counts to CPB time could underestimate patient risk to increased GME counts with longer stable bypass periods masking the effect of interventions known to significantly increase GME counts.

Finally, the strong relationship between visible venous line air and increased GME counts offers an opportunity to address a modifiable factor without changing CPB equipment. Many of the other factors known to increase GME delivered to the patient are less easily addressed or modifiable (aortic cross-clamping, use of a left ventricular vent, requisite pump flow rate, etc.). Other authors have documented a decrease in GME transmission with changes to their disposables including the use of smaller pore sizes in both arterial line and venous filters (31). This would

appear to be an obvious next step to reduce arterial limb GME delivery during CPB. Perfusionists continuously monitor venous return and air in the venous line and relay important changes to the surgeon. This intervention requires no change to the disposables in use. Regular venous line air should be readily addressed. The data we present support efforts to mitigate venous line air to minimize GME transmission to congenital cardiac surgery patients requiring CPB.

ACKNOWLEDGMENTS

The authors would like to thank Sharon Boyle, Perry Dekkers, Linda Durham, Katie Faella, Molly Hageman, Robert Howe, William Regan, and Nathalia Toutenel for their assistance with data collection for this project.

REFERENCES

1. Mitchell S, Gorman D. The pathophysiology of cerebral arterial gas embolism. J Extra Corpor Technol. 2002;34:18–23.
2. Pugsley W, Klinger L, Paschalis C, Treasure T, Harrison M, Newman S. The impact of microemboli during cardiopulmonary bypass on neuropsychological functioning. Stroke. 1994;25:1393–9.
3. Liu S, Newland RF, Tully PJ, Tuble SC, Baker RA. In vitro evaluation of gaseous microemboli handling of cardiopulmonary bypass circuits with and without integrated arterial line filters. J Extra Corpor Technol. 2011;43:107–14.
4. Dogal N, Mathis R, Lin J, Qiu F, Kunselman A, Undar A. Evaluation of three hollow-fiber membrane oxygenators without integrated arterial filters for neonatal cardiopulmonary bypass. Perfusion. 2012;27:132–40.
5. De Somer FM, Vetrano MR, Van Beeck JP, Van Nooten GJ. Extracorporeal bubbles: A word of caution. Interact Cardiovasc Thorac Surg. 2010;10:995–1001.
6. Hudacko A, Sievert A, Sistino J. Gaseous microemboli in a pediatric bypass circuit with an unprimed venous line: An in vitro study. J Extra Corpor Technol. 2009;41:166–71.
7. Win KN, Wang S, Undar A. Microemboli generation, detection and characterization during CPB procedures in neonates, infants, and small children. ASAIO J. 2008;54:486–90.
8. Wang S, Baer L, Kunselman AR, Myers JL, Undar A. Delivery of gaseous microemboli with vacuum-assisted venous drainage during pulsatile and nonpulsatile perfusion in a simulated neonatal cardiopulmonary bypass model. ASAIO J. 2008;54:416–22.
9. Clark JB, Qiu F, Guan Y, Woitas KR, Myers JL, Undar A. Microemboli detection and classification during pediatric cardiopulmonary bypass. World J Pediatr Congenit Heart Surg. 2011;2:111–4.
10. Wang S, Woitas K, Clark JB, Myers JL, Undar A. Clinical real-time monitoring of gaseous microemboli in pediatric cardiopulmonary bypass. Artif Organs. 2009;33:1026–30.
11. Lou S, Ji B, Liu J, Yu K, Long C. Generation, detection and prevention of gaseous microemboli during cardiopulmonary bypass procedure. Int J Artif Organs. 2011;34:1039–51.
12. De Somer F. Impact of oxygenator characteristics on its capacity to remove gaseous microemboli. J Extra Corpor Technol. 2007;39:271–3.
13. Naik R, Wagner J, Chowdhury D, et al. The impact of cerebral embolization during infant cardiac surgery on neurodevelopmental outcomes at intermediate follow-up. Perfusion. 2014;29:443–9.
14. Preston TJ, Gomez D, Olshove VF Jr, Phillips A, Galantowicz M. Clinical gaseous microemboli assessment of an oxygenator with integral arterial filter in the pediatric population. J Extra Corpor Technol. 2009;41:226–30.
15. Matte GS. Perfusion for Congenital Heart Surgery: Notes on Cardiopulmonary Bypass for a Complex Patient Population. Oxford, United Kingdom: Wiley-Blackwell; 2015.
16. DeFoe GR, Dame NA, Farrell MS, Ross CS, Langner CW, Likosky DS. Embolic activity during in vitro cardiopulmonary bypass. J Extra Corpor Technol. 2014;46:150–6.
17. Myers GJ. Gaseous Microemboli during Cardiopulmonary Bypass. Milan, Italy: Sorin Group; 2011:21–8.
18. Lipowsky HH, McKay CB, Seki J. Transit time distributions of blood flow in the microcirculation. In: Shih-Jen L, Skalak TC, eds. Microvascular Mechanics: Hemodynamics of Systems and Pulmonary Microcirculation. New York, NY: Springer-Verlag; 1989:13–27.
19. Tabor RF, Chan DYC, Grieser F, Dagastine RR. Anomalous stability of carbon dioxide in pH controlled bubbles coalescence. Angew Chem Int Ed Engl. 2011;50:3454–6.
20. Branger AB, Eckmann DM. Theoretical and experimental intravascular gas embolism absorption dynamics. J Appl Physiol. 1999;87:1287–95.
21. Chung EML. Transcranial Doppler embolus detection: A primer. Ultrasound. 2006;14:202–10.
22. Jabur GNS, Willcox TW, Zahidani SH, Sidhu K, Mitchell SJ. Reduced embolic load during clinical cardiopulmonary bypass using a 20 micron arterial filter. Perfusion. 2014;29:219–25.
23. Pascale F. Removal of gaseous microemboli from extracorporeal circulation. Med Instrum. 1985;19:70–2.
24. Lynch JE, Wells C, Akers T, et al. Monitoring microemboli during cardiopulmonary bypass with the EDAC quantifier. J Extra Corpor Technol. 2010;42:212–8.
25. Willcox TW, Mitchell SJ. Microemboli in our bypass circuits: A contemporary audit. J Extra Corpor Technol. 2009;41:31–7.
26. Myers GJ, Voorhees C, Haynes R, Eke B. Post-arterial filter gaseous microemboli activity of five integrated cardiotomy reservoirs during venting: An in vitro study. J Extra Corpor Technol. 2009;41:20–7.
27. Sleep J, Syhre I, Evans E. Blood temperature management and gaseous microemboli creation: An in-vitro analysis. J Extra Corpor Technol. 2010;42:219–22.
28. Dickinson TA, Riley JB, Crowley JC, Zabetakis PM. In vitro evaluation of the air separation ability of four cardiovascular manufacturer extracorporeal circuit designs. J Extra Corpor Technol. 2006;38:206–13.
29. Wang S, Undar A. Vacuum-assisted venous drainage and gaseous microemboli in cardiopulmonary bypass. J Extra Corpor Technol. 2008;40:249–56.
30. Rider SP, Simon LV, Rice BJ, Poulton CC. Assisted venous drainage, venous air, and gaseous microemboli transmission into the arterial line: An in-vitro study. J Extra Corpor Technol. 1998;30:160–5.
31. Groom RC, Quinn RD, Lennon P, et al. Detection and elimination of microemboli related to cardiopulmonary bypass. Circ Cardiovasc Qual Outcomes. 2009;2:191–8.