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Gaseous Microemboli in a Pediatric Bypass Circuit with an Unprimed Venous Line: An In Vitro Study

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Abstract: Miniaturizing cardiopulmonary bypass (CPB) circuits to reduce hemodilution and allogenic blood product administration is common in cardiac surgery. One major concern associated with smaller CPB circuits is a possible increase in gaseous microemboli (GME) sent to the cerebral vasculature, which is exacerbated by vacuum-assisted venous drainage (VAVD). The use of VAVD has increased with smaller venous line diameter and venous cannulae. This study examines the effects of CPB initiation with an unprimed venous line and VAVD in a pediatric circuit. A CPB circuit was set up with reservoir, oxygenator, and arterial filter with a bag reservoir to simulate the patient. All trials were done in vitro, and GME were measured using the EDAC Quantifier by Luna Innovations. EDAC sensors were placed proximal and distal to the oxygenator and distal to the arterial filter. Group 1 was the control group with no VAVD and a primed venous line. Groups 2, 3, and 4 used an unprimed venous line and VAVD of −40, −20, and −10 mmHg, respectively. Total microemboli counts and total embolic load in micrometers were measured at each sensor. Groups 2 (12,379.00 ± 3180.37) and 3 (8296.67 ± 2818.76) had significantly more microemboli than group 1 (923.33 ± 796.08, $p < .05$) at the pre-oxygenator sensor. Group 2 (57.33 ± 25.01, $p < .05$) had significantly more microemboli than group 1 (5.33 ± 3.21) at the post-oxygenator sensor. No other findings were statistically significant. The results suggest that, if an oxygenator and arterial filter with sufficient air handling capabilities are used, this method to reduce prime volume may not increase GME in the arterial line distal to the arterial filter. **Keywords:** vacuum-assisted venous drainage gravity venous drainage, gaseous microemboli, emboli detection and classification. *JECT. 2009;41:166–171*

Vacuum-assisted venous drainage (VAVD) is often used to increase venous return when a small venous cannula is used, femoral cannulation is needed, or during minimally invasive cardiac surgery. An additional use is to augment the initiation of cardiopulmonary bypass (CPB) with an unprimed venous line. This technique may help reduce hemodilution, thereby reducing blood product use. Both Berryessa et al. (1) and Darling et al. (2) described this technique along with circuit miniaturization to significantly reduce priming volume and transfusion requirements in the pediatric population.

When using VAVD with a low prime circuit, the possibility of an increase in gaseous microemboli in the CPB circuit must be considered. Norman et al. (3) showed that low prime circuits may not remove gaseous emboli as well as conventional circuits. Willcox et al. (4) evaluated the ability of the adult CPB circuit to handle gaseous emboli in the presence of VAVD. They found that suction applied to the venous reservoir significantly decreased the oxygenator's air handling ability, resulting in increased gaseous microemboli distal to the oxygenator. Jones et al. (5) and LaPietra et al. (6) studied varying amounts of suction and found that, as more suction was applied to the venous reservoir, significantly more microemboli were found on the patient side of the CPB circuit. Furthermore, Stock et al. (7) found that an increase in the volume of air in the venous line before initiation of CPB resulted in significantly more gaseous microemboli distal to the arterial filter during the first few minutes of bypass in a setting where VAVD was not used. Rodriguez et al. (8) also showed that increased volumes of air in the venous cannula before initiation of CPB are significantly associated with an increase in transcranial Doppler (TCD) high-intensity transient signals (HITSs) in the left and right middle cerebral arteries at the onset of CPB.

New equipment and technology has been developed to decrease microemboli and improve air handling ability, such as oxygenators and arterial line filters designed to handle air more efficiently. Several studies have shown that various oxygenators, reservoirs, and filters handle air differently (9–13). The recent addition of bubble detectors

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that can be placed on more than one site in the CPB circuit is also a new technology enabling perfusionists to modify their technique to decrease gaseous emboli proximal to the patient. TCD is one technology that has helped change perfusion, anesthesiology, and surgical technique by localizing the cause of microemboli and changing practice accordingly. Taylor et al. (14) showed trends of increased emboli during perfusionist interventions on TCD. A subsequent study from the same center also showed a significant increase in emboli on TCD during perfusionist interventions, such as drug boluses and blood sampling (15).

This study also showed significantly decreased cognitive test scores in the patient group with >10 perfusionist interventions, suggesting that cerebral microembolization from the bypass circuit may be the cause of neurocognitive deficits after CPB. Ascione et al. (16) used TCD and S100 protein levels with fluorescein angiography and color fundus photography to assess ophthalmic function as a marker for cerebrovascular damage that may not be seen on an MRI. They found that patients that were randomized to CPB for a standard coronary artery bypass graft (CABG) vs. off-pump coronary artery bypass (OPCAB) patients had significantly more HITSs measured by the TCD and significantly higher levels of S100 proteins 1 hour after surgery than OPCAB patients. Furthermore, CPB patients were significantly more likely to have retinal microvascular damage. Although this study did not measure neurocognitive outcomes in patients or long-term outcomes, it did show retinal microvascular damage caused by an increase in embolic load delivered to the patient, and it suggested that microemboli are hazardous to the patient (17). However, neurocognitive scores are not the only outcome that can be affected by increased gaseous microemboli (GME) in the circuit. Increased amounts of air increase exposure to foreign surface area, which can cause increased inflammation and platelet dysfunction.

Studies have shown that VAVD, as opposed to gravity venous drainage (GVD), on bypass greatly increases arterial GME when air is entrained into the venous line. Although the literature suggests that starting CPB with an unprimed venous line and VAVD, which is similar to entraining air in the venous line, may increase gaseous emboli, there are no data that prove this. This study measures microemboli using the Emboli detection and classification (EDAC) quantifier (Luna Innovations, Roanoke, VA). This system uses ultrasound technology to measure the size of GME in blood. The amplitude of backscattered ultrasound echoes is used to accurately estimate the size of GME, regardless of how many emboli pass through the detector (18). This system is incorporated into the CPB circuit with specialized connectors made for this device for various tubing sizes. The connector must be coated in ultrasonic gel before the sensor is connected. The sensors are connected to the data console where the perfusionist can control when GME detection begins and is recorded.

MATERIALS AND METHODS

Circuit Design

A CPB circuit was designed to test for arterial GME as a result of initiating bypass using a vacuum with an unprimed venous line (Figure 1). The test circuit included a "patient" reservoir (Avecor RV-500-1 Venous Blood Reservoir; Medtronic, Minneapolis, MN), roller pump console (Terumo System 1; Terumo Medical, Somerset, NJ), membrane oxygenator and venous reservoir with X coating (Baby RX; Terumo Medical), arterial filter (D736; Sorin, Arvada, CO), 1/4″ venous line, and 3/16″ arterial line. A purge line was attached to the top of the arterial filter and allowed to bleed to the top of the venous reservoir. SMART tubing (SMART; Sorin) was used for all components.

Negative pressure was measured at the venous reservoir with a Baxter vacuum regulator (Baxter, Deerfield, IL), and arterial pressure was measured distal to the oxygenator. A Hoffman clamp was adjusted on the arterial line to simulate a normal pressure drop across the arterial cannula of ~100 mmHg, for an arterial line pressure of 200 mmHg. Arterial temperature was also measured and maintained at 37°C using a heater-cooler device (Hemotherm; Cincinnati Sub Zero, Cincinnati, OH). FiO_2 was set at room air.

A circuit primed with 600 mL of heparinized blood with a hematocrit of 19% was used for all trials. A control trial (group 1) was conducted with a primed venous line and no VAVD. Groups 2, 3, and 4 all used an unprimed venous line and VAVD at –40, –20, and –10 mmHg, respectively. The venous line was deprimed before beginning all trials using VAVD. Simulated CPB was initiated by unclamping the venous line and applying vacuum to the venous reservoir,

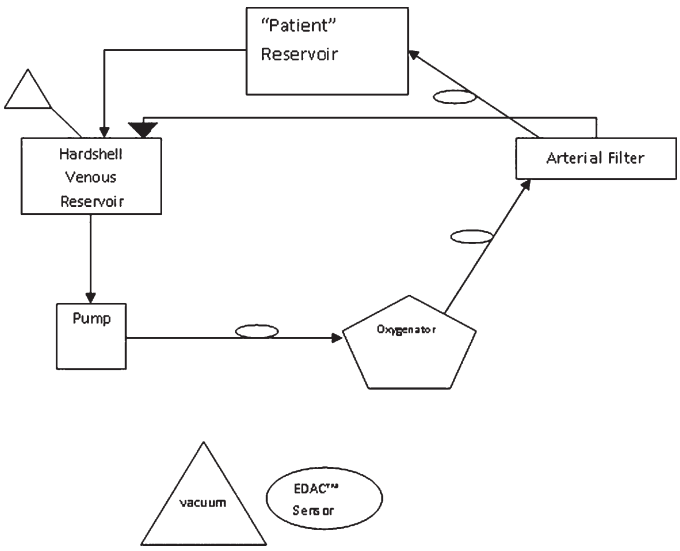

Figure 1. Emboli detection and classication.

ensuring adequate venous drainage before beginning forward flow. Vacuum was removed after the venous line was fully primed and forward flow was initiated. The level in the venous reservoir was maintained above the minimum operating level at all times. Flows were maintained at 300 mL/min to simulate the initiation of CPB at half flow for this size circuit.

Data Collection

The EDAC quantifier was placed proximal and distal to the oxygenator and on the arterial line distal to the arterial filter. Configuration for all three channels was set as gain offset at 41.0032 dB, slope of 0 dB/μs, limit at 58.75 dB, and a peak threshold of 16 with amplitude formula boundary set at 200. Gaseous emboli were measured for 3 minutes beginning at the initiation of CPB. Between each trial, the blood was circulated with the EDAC turned on. The next trial was initiated once no emboli were seen for 2 minutes in the circulating volume, ensuring no recirculation of emboli. Each trial was repeated three times.

Statistics

Analysis of variance (ANOVA) was used to determine whether a significant difference existed between groups at each EDAC channel. The Tukey honestly significant difference (HSD) post hoc test was used to determine where significant differences occurred between groups. Repeated-measures ANOVA was used to show differences between the three channels. Data are listed as mean ± SD. All statistical analyses were performed using SPSS version 15.0 for Windows (SPSS, Chicago, IL). Differences were considered statistically significant at $p = .05$.

RESULTS

Microemboli measured at each channel are listed in Table 1, with statistical analyses listed in Table 2. Table 3 shows GME counts in 50-μm increments. Post hoc comparisons using the Tukey HSD test indicated that the mean total microemboli between groups 2 (12,379.00 ± 3180.37) and 3 (8296.67 ± 2818.76) were significantly different from group 1 (923.33 ± 796.08, $p < .05$). Group 4 did not differ significantly from groups 1, 2, or 3 (Figure 2). The only significant difference in the post-oxygenator channel was between group 1 (5.33 ± 3.21) and group 2 (57.33 ± 25.01, $p < .05$; Figure 2). There were no statistically significant differences between groups in terms of total number of GME measured distal to the arterial filter.

Repeated-measures ANOVA showed a significant difference in microemboli count and size between channel 1 and channel 3 in all trials, suggesting that the oxygenator and arterial filter absorbed most of the microemboli.

A comparison of size of microemboli also showed significant differences among the three channels [Wilks' $\lambda = .025$, $F(2,8) = 153.9$, $p < .0005$; Figure 3]. Microemboli were significantly larger at the pre-oxygenator sensor compared with the post-oxygenator sensor, as well as at the post-oxygenator site compared with the site distal to the arterial filter.

DISCUSSION

These trials used the new emboli detection and classification technology of Luna Innovations to detect whether gaseous emboli measured in the outflow of an in vitro CPB test circuit increased with initiation of CPB using VAVD and an unprimed venous line compared with the control. Large amounts of gaseous emboli were absorbed by the oxygenator. There was also a trend toward larger amounts of emboli before the oxygenator as suction applied to the reservoir increased. Previous studies have also shown larger amounts of GME with increased suction (5,6).

This study suggests the importance of an arterial filter. Although it was obvious from these data that initiating CPB with VAVD and an unprimed venous line increases the amount of microemboli entering the circuit, it was interesting that no significant differences were found in any groups distal to the arterial filter, although different arterial filters remove GME at different rates. A recent study by Riley (19) showed that some arterial filters are superior to others in terms of removing microemboli. Furthermore, a study by Whitaker et al. (20) found

Table 1. Average amount and size of GME over 3 minutes.

Trial	C1 Count	C1 Size (μm)	C2 Count	C2 Size (μm)	C3 Count	C3 Size (μm)
Group 2	12,379	8.30×10^{-5}	57.33	7.07×10^{-8}	4.67	1.99×10^{-9}
SD	3180.37	1.35×10^{-5}	25.01	3.18×10^{-8}	2.52	1.76×10^{-9}
Group 3	8296.67	6.20×10^{-5}	39.67	7.83×10^{-8}	2.33	6.40×10^{-10}
SD	2818.76	8.00×10^{-6}	17.24	4.86×10^{-8}	2.52	5.72×10^{-10}
Group 4	7432.84	4.67×10^{-5}	31.17	5.03×10^{-8}	2.59	1.12×10^{-9}
SD	2832.33	1.58×10^{-5}	7.09	2.02×10^{-8}	1	5.64×10^{-10}
Group 1 (control)	923.33	4.87×10^{-6}	5.33	3.09×10^{-9}	5.33	2.56×10^{-9}
SD	796.08	3.75×10^{-6}	3.21	2.82×10^{-9}	3.06	2.08×10^{-9}

Group 1, control group; group 2, VAVD at −40 mmHg; group 3, VAVD at −20 mmHg; group 4, VAVD at −10 mmHg.

Table 2. Determination of significance.

Average Total Emboli (I Group)	Average Total Emboli (J Group)	Mean Difference of Total Emboli Between Two Groups (= I – J)	SE	Significance	95% Confidence Interval	
					Upper Bound	Lower Bound
Pre-oxygenator						
Blood0	Blood–40	11,455.667*	1989.455	.002	–18,145.37	–4,765.97
	Blood–20	–7,373.333*	1989.455	.030	–14,063.03	–683.63
	Blood–10	–5,990.333	1989.455	.084	–12,680.03	699.37
Blood–40	Blood0	11,455.667*	1989.455	.002	4,765.97	18,145.37
	Blood–20	4,082.333	1989.455	.316	–2,607.37	10,772.03
	Blood–10	5,465.333	1989.455	.123	–1,224.37	12,155.03
Blood–20	Blood0	7,373.333*	1989.455	.030	683.63	14,063.03
	Blood–40	–4,082.333	1989.455	.316	–10,772.03	2,607.37
	Blood–10	1,383.000	1989.455	.953	–5,306.70	8,072.70
Blood–10	Blood0	5,990.333	1989.455	.084	–699.37	12,680.03
	Blood–40	–5,465.333	1989.455	.123	–12,155.03	1,224.37
	Blood–20	–1,383.000	1989.455	.953	–8,072.70	5,306.70
Post-oxygenator						
Blood0	Blood–40	–52.000*	12.222	.014	–93.10	–10.90
	Blood–20	–34.333	12.222	.112	–75.43	6.76
	Blood–10	–16.333	12.222	.678	–57.43	24.76
Blood–40	Blood0	52.000*	12.222	.014	10.90	93.10
	Blood–20	17.667	12.222	.617	–23.43	58.76
	Blood–10	35.667	12.222	.096	–5.43	76.76
Blood–20	Blood0	34.333	12.222	.112	–6.76	75.43
	Blood–40	–17.667	12.222	.617	–58.76	23.43
	Blood–10	18.000	12.222	.602	–23.10	59.10
Blood–10	Blood0	16.333	12.222	.678	–24.76	57.43
	Blood–40	–35.667	12.222	.096	–76.76	5.43
	Blood–20	–18.000	12.222	.602	–59.10	23.10
Post-arterial filter						
Blood0	Blood–40	.667	2.000	.997	–6.06	7.39
	Blood–20	3.000	2.000	.587	–3.73	9.73
	Blood–10	3.333	2.000	.496	–3.39	10.06
Blood–40	Blood0	–.667	2.000	.997	–7.39	6.06
	Blood–20	2.333	2.000	.769	–4.39	9.06
	Blood–10	2.667	2.000	.680	–4.06	9.39
Blood–20	Blood0	–3.000	2.000	.587	–9.73	3.73
	Blood–40	–2.333	2.000	.769	–9.06	4.39
	Blood–10	.333	2.000	1.000	–6.39	7.06
Blood–10	Blood0	–3.333	2.000	.496	–10.06	3.39
	Blood–40	–2.667	2.000	.680	–9.39	4.06
	Blood–20	–.333	2.000	1.000	–7.06	6.39

*Denotes statistical significance at $p = .05$.

a significant reduction in microemboli when a leukocyte-depleting filter was used compared with a standard arterial filter.

Initiating bypass with vacuum and an unprimed venous line is a method used to decrease hemodilution, thereby reducing the amount of blood products given to the patient. This would be particularly advantageous in the neonatal population, where even small amounts of fluid can decrease the patient's hematocrit dramatically. Prior research suggests this would result in large amounts of gaseous emboli sent to the patient. Although there is extensive research in VAVD and GME in adult CPB circuits and patients, many of which are referred to in this paper; there are insufficient data in pediatric CPB circuits and patients. Pediatric reservoirs, oxygenators, and filters handle microemboli differently than the adult versions that have been studied. Furthermore, pediatric CPB is conducted differently than adult CPB, especially at the onset of bypass in the neonatal population, where flows are much lower, giving air more time to rise to the top of the reservoir.

The results of this study suggest that, with an oxygenator and arterial filter that have sufficient air handling capabilities, microemboli amounts would not significantly differ between primed venous line initiation and unprimed venous line VAVD initiation; however, the study was very limited. More extensive research is needed on this topic specifically in the pediatric and neonatal settings.

Research efforts are currently being devoted to finding the various sources of microemboli generation, the effects of microemboli on patient outcomes, and methods of determining the different types of microemboli and

Table 3. Average number of gaseous emboli per channel over 3 minutes.

Trial	0–50 μm	50–100 μm	100–150 μm
Pre-oxygenator			
Group 2	12,245.00	130.67	3.33
SD	3,169.92	20.13	1.53
Group 3	8,174.67	121.00	1.00
SD	2,843.39	27.62	1.00
Group 4	6,863.67	70.30	0.98
SD	2,817.52	20.22	0.00
Group 1	916.67	6.33	0.33
SD	794.52	5.13	0.58
Post-oxygenator			
Group 2	57.33	0.00	0.00
SD	25.01	0.00	0.00
Group 3	39.67	0.00	0.00
SD	17.24	0.00	0.00
Group 4	31.17	0.00	0.00
SD	7.09	0.00	0.00
Group 1	5.33	0.00	0.00
Post-filter			
Group 2	4.67	0.00	0.00
SD	2.52	0.00	0.00
Group 3	2.33	0.00	0.00
SD	2.52	0.00	0.00
Group 4	2.59	0.00	0.00
SD	1.00	0.00	0.00
Group 1	5.33	0.00	0.00
SD	3.06	0.00	0.00

Group 1, control group; group 2, VAVD at –40 mmHg; group 3, VAVD at –20 mmHg; group 4, VAVD at –10 mmHg.

the type that causes more neurocognitive deficits postoperatively. Until clinicians know more about microemboli, precautions must be taken to decrease the embolic load a patient receives. Furthermore, any air entering the CPB circuit is a source of increased exposure to foreign surface area, causing increased inflammation and platelet dysfunction.

Although an increase in embolic load delivered to the patient on CPB can be detrimental, an increase in the use

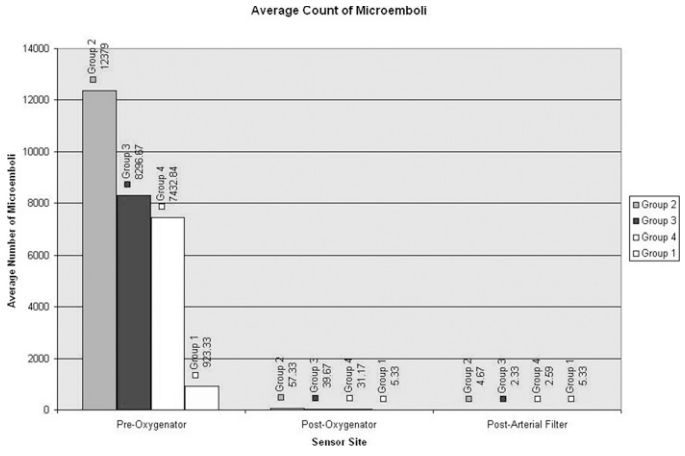

Figure 2. Group 1, control group; group 2, VAVD at –40 mmHg; group 3, VAVD at –20 mmHg; group 4, VAVD at –10 mmHg.

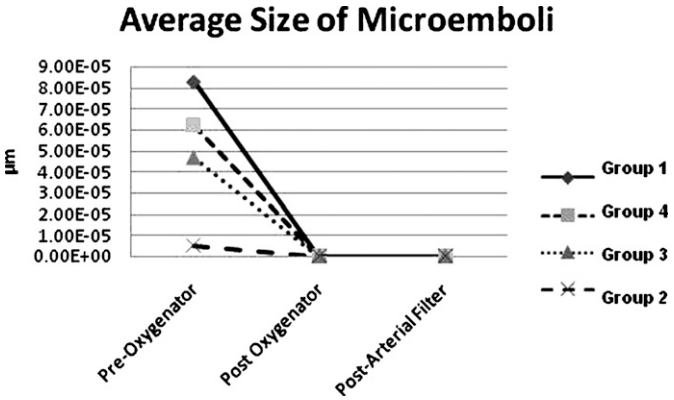

Figure 3. Group 1, control group; group 2, VAVD at –40 mmHg; group 3, VAVD at –20 mmHg; group 4, VAVD at –10 mmHg.

of blood products given to the patient can also be detrimental. Patients that receive more blood products have significantly more complications, longer hospital stays, and an increase in morbidity and mortality (21). This study is a step in examining whether bypass initiation with an unprimed venous line and VAVD increases emboli sent to the patient. If leaving the venous line unprimed is found to be safe, this may help decrease the amount of hemodilution and the amount of blood products transfused perioperatively.

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