JECT. 2002;34:34–39
The Journal of The American Society of Extra-Corporeal Technology

How Effective Are Cardiopulmonary Bypass Circuits at Removing Gaseous Microemboli?

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Presented at Perfusion Innovations in Cardiac Surgery Outcomes 2000—The Key West Meeting, May 2000, Key West, Florida

Abstract: An association has been demonstrated between intravascular microemboli and organ injury during cardiopulmonary bypass (CPB). Air may be inadvertently introduced into the venous line during CPB resulting in the formation of gaseous microemboli (GME). We studied the ability of CPB circuits, from five different manufacturers, to remove GME originating from the introduction of air into the venous line. Using an *in vitro* model of adult CPB, 60 ml of air was introduced into the venous line and the progression of GME through the circuit components was monitored at 5 locations. In all circuits GME were detected in the arterial line following the introduction of air into the venous line. There was a wide variation between manufacturers in the ability of the circuit to remove GME. Air introduced into the venous line during CPB results in the formation of GME that are able to pass through all the circuit components including the arterial filter. The quantity of GME detected in the arterial line is influenced by the design of the circuit components and varies between manufacturers. Air in the venous line should be avoided and if present it must be dealt with promptly. **Keywords:** cardiopulmonary bypass, emboli, manufacturer. *JECT. 2002;34:34–39*

Brain injury is a recognized complication of cardiac surgery. Hypoperfusion, emboli, and the inflammatory response have all been implicated in the etiology of the injury (1). A relationship between the number of intravascular microemboli detected during cardiopulmonary bypass (CPB) and the incidence of postoperative brain injury has been demonstrated (2, 3).

Air or gaseous microemboli (GME) are known to occur throughout CPB (4). The incidence of GME increases with the use of bubble oxygenators (5), excessive heating gradients (6), unfiltered arterial lines (7), low venous reservoir levels (8), and following the administration of drugs to the CPB circuit (9).

We have previously reported the effects of pump flow rate, type of perfusate, and vacuum assisted venous drainage (VAVD) on the ability of the CPB circuit components to remove a quantity of entrained venous air (10). The behavior of GME within the CPB circuit results from a complex interaction between partial pressure, volume, solubility, temperature, buoyancy, velocity, perfusate, and flow effects. Some of these factors are under the influence of the surgical team but many are inherent to the design of the circuit components. Inspection of oxygenators or venous reservoirs produced by different manufacturers reveals a large variation in appearance and design.

The present study compares the ability of CPB components made by five manufacturers to remove GME arising from a fixed quantity of entrained venous air.

MATERIALS AND METHODS

Using a previously described technique (10), an *in vitro* model of adult CPB was constructed from new, sterile components (hard-shell venous reservoir, membrane oxygenator, and arterial filter) from five manufacturers: AVECOR, Baxter, COBE, Medtronic, and TERUMO. Components for each circuit were manufacturer specific except for during COBE experiments when a GISH venous reservoir was used because a COBE hard shell reservoir was not available. The circuit components are detailed in Table 1.

An 8-L polycarbonate carboy served as the patient. All circuits were flushed with CO_2, de-aired, and primed with fresh, anticoagulated bovine blood (Sierra Medical, Santa

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Received December 15, 2001; accepted January 15, 2002.

Table 1. CPB circuit components for each manufacturer.

	Hard Shell Venous Reservoir	Oxygenator	Arterial Filter
AVECOR Cardiovascular, Inc. Minneapolis, MN	Affinity integrated CVR [Model 341]	Affinity Membrane Oxygenator [Model 341]	Affinity Arterial Filter (38 μm) [Model 352]
Baxter Healthcare Corp. Irvine, CA	Bentley BMR-4500S GOLD Venous Reservoir [Model BMR4500SG]	Bentley Spiraloxy Hollow Fibre membrane [Model SPRLOXY]	Bentley AF-1040D Duraflo II (40 μm) [Model 60117301]
COBE Cardiovascular, Inc. Arvada, CO	GISH Biomedical Venous Reservoir [Model CAPVRF45]	COBE Optima Hollow Fibre Membrane [Model 050-255-000]	COBE Sentry Arterial Filter Loop (43 μm) [Model 020-251-301]
Medtronic, Inc. Minneapolis, MN	Maxima Filtered Venous Reservoir [Model 1315]	Maxima Forté Hollow Fibre Membrane [Model MAX-FTE]	Medtronic Arterial Filter (40 μm) [Model M40]
TERUMO Medical Corp. Somerset, NJ	CAPIOX SX18 [Model CX(SX18R]	Membrane Reservoir Oxygenator with Integral Venous	CAPIOX Arterial Filter (32 μm) [Model CX(AF01]

Fe Springs, CA) corrected to a hematocrit of 24 ± 1% using isotonic saline. The venous reservoir level was maintained at 800 ± 25 mL via a variably occlusive Hoffman Clamp placed on the venous line between the air introduction port and the venous reservoir. For all experiments a 1-m height differential was maintained between the level of perfusate in the venous reservoir and the level in the carboy. Arterial line pressure, measured at the top of the arterial filter, was maintained at 200 ± 10 mm Hg using a Hoffman clamp placed on the arterial line proximal to the cannula. Flow generation was provided by an occlusive roller pump (model 5000, Sarns, Ann Arbor, MI), and the heat exchanger of the oxygenator was connected to an external heater-cooler unit (Sarns, Ann Arbor, MI) with all circuits studied at 37°C. The oxygenators were ventilated with 95% air and 5% CO_2 to achieve a perfusate pO_2 of 200 ± 50 mm Hg.

Five synchronous Embolus Detection and Classification (EDAC) systems were used to monitor the progression of venous entrained air through the circuit components. The EDAC system relies upon new technology, based on SONAR, designed specifically for embolus quantification. It has been developed jointly by Orincon Corporation and Embolus Inc., funded by the National Institutes of Health and National Medical Technology Testbed. The EDAC system was validated using previously detailed techniques (10, 11). The 5 detectors were mounted on modified Bentley Oxysat Optical Transmission Cells (Baxter Healthcare Corporation, Irvine, CA) cut into the circuit tubing in the venous line, postvenous reservoir, postroller pump, postoxygenator, and postarterial filter. The 5 systems were configured to record embolic activity for 2 min following the introduction of 60 mL of air into the venous line.

In continuity with our previous work, all circuits were studied using gravity siphon venous drainage (GSVD) and vacuum assisted venous drainage at –40 mm Hg (VAVD –40) and –65 mm Hg (VAVD –65). The vacuum was maintained and regulated using a Bentley Vacuum pack (Baxter Healthcare Corporation, Irvine, CA). A 24 French, curved tip, single lumen aortic cannula was used for all cases and venous drainage was via a 2-stage, 34/46 French cannula for GSVD experiments and a 29/29 French venous cannula for VAVD experiments. The sequence of circuit and experimental conditions was determined by a randomization schedule. Eight trials were performed for each circuit under each experimental condition.

Statistics

Data are expressed as the mean and standard deviation of 8 trials. For statistical analysis a two-way ANOVA was performed with multiple comparisons. Significance was expressed at an alpha level of 0.05.

RESULTS

For all experiments and all circuits the introduction of

60 mL of air into the venous line resulted in the detection of GME in the arterial line after the arterial filter. Table 2 and Fig. 1 detail the average GME counts in the arterial line following the introduction of 60 mL of air into the venous line. The number of GME counted in the arterial line varied significantly between manufacturers.

The ability of the circuit to remove GME was primarily dependent upon the design of the circuit components. The number of GME present in the arterial inflow line was a reflection of the combined ability of the venous reservoir, oxygenator, and arterial filter to remove air. Figure 2 individually details the progression of GME through all circuit components for each manufacturer.

The study design did not allow for direct comparison of like components from different manufacturers because the performance of an individual component is influenced by the number of emboli that it receives from the preceding component in the circuit. If the venous reservoir does not remove any emboli or creates additional emboli, then the subsequent components have to be even more efficient at removing GME. In contrast, if the reservoir removes the majority of the emboli, it is difficult to comment on the air handling ability of the subsequent components.

Effect of Venous Drainage

VAVD was not a consistent determinant in the number of GME detected in the arterial line. In the circuits manufactured by AVECOR, Baxter, and COBE there was no statistically significant difference between GSVD and either VAVD at −40 mm Hg or at −65 mm Hg. In TERUMO experiments there was a significant difference in arterial line GME counts between GSVD and VAVD at −65 mm Hg ($p = 0.047$), but this did not reach significance when comparing GSVD to VAVD at −40 mm Hg ($p = 0.06$). In Medtronic experiments there was no significant increase in GME counts between GSVD and VAVD at −40 mm Hg ($p = 0.281$) or VAVD at −65 mm Hg ($p = 0.163$), but there was a difference between VAVD at −40 mm Hg and VAVD at −65 mm Hg ($p = 0.036$).

Table 2. The average number of GME detected coming OUT of the arterial filter over a two-minute period following the introduction of sixty milliliters of air into the venous line.

Manufacturer	GSVD	VAVD (−40 mm Hg)	VAVD (−65 mm Hg)
AVECOR	1624 ± 601	1398 ± 564	1573 ± 477
Baxter	3 ± 4	7 ± 7	63 ± 88
COBE	2376 ± 914	1972 ± 876	2043 ± 853
Medtronic	1428 ± 571	1154 ± 1116	1783 ± 347
TERUMO	8 ± 7	141 ± 184	610 ± 601

GSVD: gravity siphon venous drainage, VAVD: vacuum assisted venous drainage.

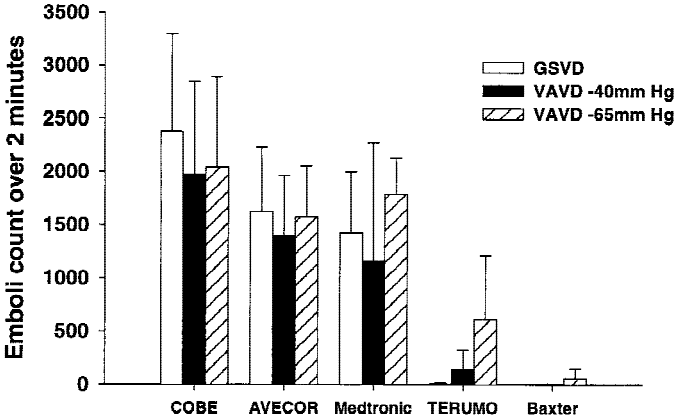

Figure 1. Following the introduction of 60mL of air into the venous line there was a wide variation in arterial line GME counts between manufacturers, which was independent of the method of venous drainage used. (GSVD: gravity siphon venous drainage, VAVD −40: vacuum assisted venous drainage at −40 mm Hg pressure, VAVD −65; vacuum assisted venous drainage at −65 mm Hg pressure.)

In 3 circuits (AVECOR, COBE, and Medtronic) the use of VAVD at −40 mm Hg was associated with a reduction in the number of emboli delivered to the patient when compared to GSVD.

DISCUSSION

Following the introduction of air into the venous line, GME activity was detected throughout all CPB circuits. The number of GME delivered to the patient was primarily dependent upon the design of the circuit components as opposed to the method of venous drainage. However, regardless of circuit design or experimental conditions, entrained venous air always resulted in the detection of GME in the arterial line after the arterial filter. This observation is in agreement with the findings of previous studies (10, 12, 13).

The generation of GME by CPB circuit components has been well documented. The clinical progression from bubble oxygenators to membrane oxygenators was in part due to the increased quantities of GME (14) and microembolic ischemia (15) associated with the use of bubble oxygenators. Mitchell and co-workers have demonstrated that some types of hard shell venous reservoirs, particularly at low levels, are a source of GME production (8, 16). Such research has enabled the identification of a variety of practices, as detailed in Table 3, to be associated with the production of GME. By identifying the source of GME, designs and techniques may be developed to reduce overall microembolic activity and improve patient outcome. However, even if a CPB circuit generates no GME, the risk of inadvertent air embolism is always present. Circuit

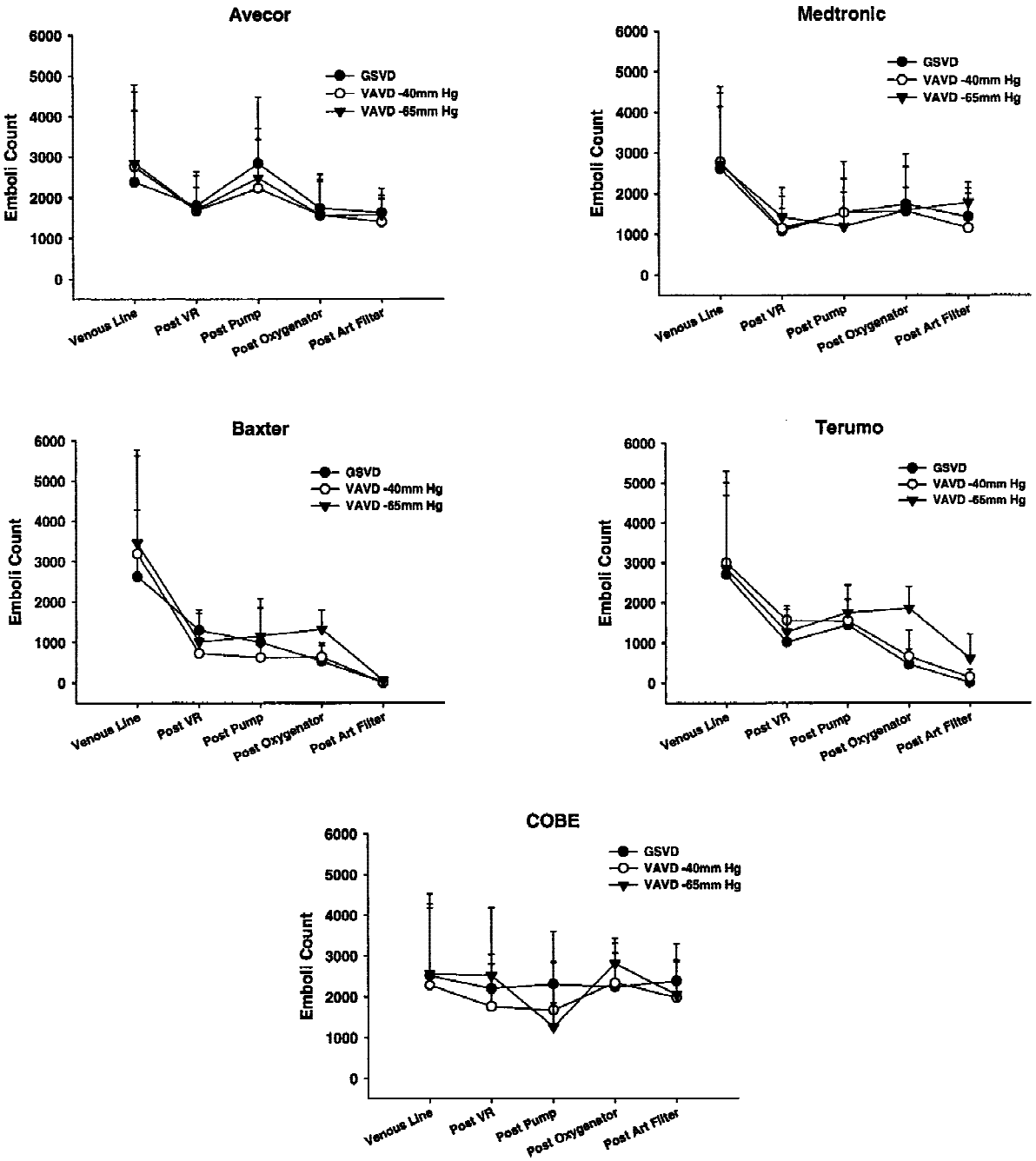

Figure 2. Graphs illustrating the progression of GME for individual manufacturers. The number of GME detected in the arterial line is dependent on the cumulative performance of the individual circuit components. (GSVD: gravity siphon venous drainage, VAVD −40: vacuum assisted venous drainage at −40 mm Hg pressure, VAVD −65: vacuum assisted venous drainage at −65 mm Hg pressure, Post VR: postvenous reservoir: Post Art Filter: postarterial filter.)

components must also be able to remove any circulating GME.

We have demonstrated a wide variation in the ability of comparable CPB circuit components produced by different manufacturers to remove GME. What needs to be identified is why this difference occurs. Is it due to variations in the internal structure of the components or is it due to differences in the coatings applied to the blood surface of the components or is it a combination of such factors? The amount of time blood spends in a component, particularly in contact with an active coating may influence the quantity of GME that are removed. Similarly, the internal pressure, turbulence, and pressure drop relating to a component will influence both GME production and removal.

If we are to continue to improve patient outcome, then

Table 3. Known causes of gaseous microbemboli (4).

Bubble oxygenation
High gas-to-blood flow ratio (bubble oxygenator)
Low CPB reservoir levels
Excessive cooling and heating gradients (i.e., >10°C)
Drug injections into circuit
Mechanical jarring of circuit
Inadequate debubbling (especially of arterial filter)
Gaseous or vaporous cavitation
Damaged membrane material
Counter-diffusion phenomena
Over occluded roller pump
Excessive cardiotomy/vent suction
Pulsatile flow through microporous membrane oxygenator

we must continue to question current practice while evaluating new or alternative practices. Kincaid et al. (17) studied the ability of arterial filters to remove lipid microemboli from cardiotomy-scavenged blood in a standardized animal model of CPB. They compared the effectiveness of 3 different arterial filters used individually and in combination to blood cell saver devices at reducing the number of cerebral lipid microemboli. While there was some variation in performance between arterial filters, the cell savers were found to be significantly more competent at reducing cerebral lipid microembolization.

The results of the present study have both clinical and research implications. Clinically, air introduced into the venous line either inadvertently or following initiation of CPB with air in the venous line or due to a non-occlusive caval snare or atrial purse string will result in GME being delivered to the patient. Current circuit components are unable to remove all GME arising from the introduction of 60 mL of air into the venous line. The surgical team must be as attentive to air in the venous line as they are to air in the arterial line. The initiation of CPB with air in the venous line should be avoided, and the entrainment of venous air during CPB should be dealt with promptly.

During the present study it was noted that air bubbles were not visible with the naked eye in any part of the blood primed circuit following the introduction of 60 mL of air. This observation supports the routine use of a bubble detector during clinical cases and particularly during operations when entrained air is anticipated such as open-heart procedures or when using high CPB flow rates or during VAVD with high levels of suction (10). The perfusionist must always be alert to the risk of embolization.

The research implications are two-fold: first, it would appear that the design of the circuit component does influence the air handling ability of the circuit. It is apparent that more research is needed to improve overall component performance with regard to air handling. Second, when designing or reviewing scientific studies that use comparative emboli counts as an outcome measure, it is not only important to study the method of embolus detection used but also the similarity in CPB circuit design between study groups. This raises a specific problem with regard to what "the gold standard" should be when comparing new techniques such as off pump coronary artery surgery (OPCAB) with conventional on pump surgery.

CONCLUSION

Air introduced into the venous line during CPB results in the formation of GME. The behavior and propagation of GME through the CPB circuit is influenced by the design of the circuit components. Despite a wide variation in the GME removal rates between the circuits tested, the introduction of 60 mL of air into the venous line always resulted in the detection of GME in the arterial line prior to the arterial cannula. Research should be directed towards improving the air handling performance of the circuit and clinical practice should be directed towards eliminating the introduction of air into the circuit.

ACKNOWLEDGMENTS

We gratefully acknowledge the technical advice and support provided by the staff of Embolus Incorporated and Orincon Corporation, particularly John Sevick. We thank members of the CardioNeuroprotection team and Department of Perfusion at Wake Forest University School of Medicine for their continued support. We are very grateful to Wilson Somerville and Addie Larimore of the editorial team for their help in the preparation of this manuscript. This study was funded by the National Institutes of Health, the National Medical Technology Testbed, and Baxter Healthcare Corporation.

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