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Blood Temperature Management and Gaseous Microemboli Creation: An In-Vitro Analysis

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Abstract: Gaseous microemboli have been associated with post operative neurological deficits in patients undergoing cardiopulmonary bypass. Creating an optimal perfusion system that minimizes microemboli production and has enhanced abilities to sequester entrained air during the bypass procedure has been an important focus. This study examines the air-handling capabilities of a cardiopulmonary bypass circuit and correlates blood temperatures with microemboli loads proximal and distal to the arterial line filter within the circuit. Utilizing a Capiox RX25R oxygenator, Capiox 37 micron arterial filter, vacuum assisted venous return, and emboli detectors, 30 mL of air were injected into the venous line of a bypass circuit at eight different temperatures. Emboli were counted distal to the arterial line filter by the EDAQ® Quantifier (Emboli Detection and Classification). The average number of emboli detected distal to the arterial filter progressively increased as the perfusate temperature was dropped. At 37.0°C an average of 1.4 emboli was observed distal to the arterial filter within 90 seconds of the air injection. At 23.0°C an average of 49.8 emboli was detected. Air introduced into the venous side of the bypass circuit resulted in showers of microemboli being sent past the arterial line filter. In addition, as the bovine blood was cooled, the air handling capability of the circuit was diminished. **Keywords:** Emboli Detection and Classification Quantifier, gaseous microemboli, microemboli, venous air, temperature management. *JECT. 2010;42:219–222*

Neurological deficits after cardiopulmonary bypass (CPB) still represent the most severe and debilitating complication. A relationship has been demonstrated between the number of intravascular microemboli detected during CPB and the incidence of postoperative brain injury (1–4).

A large focus has been directed toward the generation of gaseous microemboli (GME) throughout the bypass circuit. Previous correlational studies have focused on the relationship of GME creation with a number of factors including bubble oxygenators, excessive heating gradients, drug administration, flow rate, type of perfusate, unfiltered arterial lines, and vacuum assisted venous drainage and venting (VAVD) (5–10).

The current study examines the effectiveness of bypass circuits to remove GME at various temperature conditions. Bovine blood was used in a circuit that incorporated VAVR and standard length tubing (not miniaturized). The circuit's ability to sequester entrained air was tested and analyzed at eight different blood temperatures between 23 and 37°C.

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The senior author has stated that 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.

MATERIALS AND METHODS

Circuit Design

A model of an adult CPB circuit was used for all experiments (Figure 1). The arterial pump was set up using a standard, adult A-V loop that was just under-occlusive according to the manufacturers instructions. A Capiox RX25R filtered venous reservoir and oxygenator (Terumo, Somerset, NJ), and a 37-micron Capiox arterial filter were used. A second Capiox cardiotomy reservoir was attached to the mast farthest from the arterial pump head that represented the patient. Between the arterial filter and the simulated patient, an I-4500 silicone polymer membrane oxygenator (Medtronic, Minneapolis, MN) was placed in the arterial line to assist in de-airing of the circuit. A venous line containing a venous air injection site, created by placing a luer

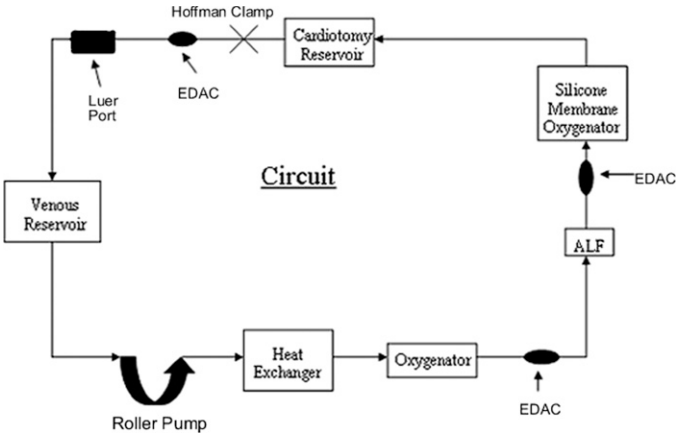

Figure 1. CPB circuit model used.

port into the venous line, was connected from the "patient" reservoir to the Capiox RX25R filtered venous reservoir. The Capiox CE-601 Level Alarm was placed on the venous reservoir and set to alarm when the level in the venous reservoir reached 500 mL. A Cincinnati Sub-Zero heater cooler (CSZ, Cincinnati, OH) was attached to the heat exchanger and set to 37°C. To confirm arterial blood temperature, a Biomedicus BIO-CAL 370 temperature probe (Medtronic, Minneapolis, MN) was placed on the arterial outlet. Three EDAC® Quantifier (Emboli Detection and Classification) (Luna Innovations, Blacksburg, VA) sensor connectors were inserted: one distal to the oxygenator, one distal to the arterial line filter (ALF), and one proximal to the air injection site according to manufacturer guidelines. Transducers were attached to the connectors according to manufacturer guidelines. VAVR was regulated using the Baxter suction regulator (Baxter, Deerfield, IL) and suction was set to –60 mmHg. After the circuit was fully assembled, the ALF and membrane oxygenator were CO_2 flushed for 5 minutes each at a flow of 5 L/min. Then the system was primed with 3 L of Normosol-R (Hospira, Inc., Lake Forest, IL) at 4.5 L/min making sure all air was removed and each reservoir contained 1 L. Flow was generated by a Cobe roller pump (Cobe CV, Arvada, CO). Arterial line pressure was zeroed at the transducer and monitored using the Medtronic pressure display box. An unspecified amount of prime was removed, and filtered bovine blood, which had been previously heparinized and stored for 2 days at 5°C, was introduced into the circuit until a hematocrit of 22% was achieved. Finally, the venous line was partially occluded with a Hoffman clamp until levels in both reservoirs maintained at approximately 1 L.

Air Entrainment

A venous air injection site was created by placing a luer port into the venous line distal to the EDAC® transducer and cardiotomy reservoir and proximal to the venous reservoir. Thirty milliliters of room air was measured in a syringe and introduced into this luer port as a steady stream over 10 seconds.

Experimental Conditions

Bovine blood, Hct of 22%, was maintained at 37°C, 35°C, 33°C, 31°C, 29°C, 27°C, 25°C, and 23°C. Between each trial the perfusate temperature was stabilized before the next was begun. The venous and cardiotomy reservoir levels were kept at approximately 1 L, but were never allowed to fall below 900 mL. Flow was maintained at 4.5 L/min, and vacuum-assisted venous drainage suction set at –60 mmHg. In all test runs the sampling manifold was closed and the arterial filter purge was left open. The arterial filter purge line was connected to the filtered portion of the reservoir. The oxygenator recirculation line was clamped during all test runs. The FiO2 was set at 80% and the gas flow at 4 L.

Emboli Detection

The EDAC® Quantifier measured embolic activity at three locations within the circuit. Three transducers were attached to connectors inserted into the circuit according to manufacturer's guidelines; transducer #1 was located immediately before the air injection site, transducer #2 was placed immediately before the ALF, and transducer #3 was placed distal to the ALF but before the I-4500 silicone membrane oxygenator. After each test run the EDAC® was also used to ensure all air was removed from the circuit. The EDAC® system consists of a transducer connected to a Pentium (Intel, Santa Clara, CA) personal computer utilizing a Windows based system (Microsoft Corporation, Redmond, WA). As stated in the EDAC® user manual, signal analysis and process enables rejection of motion artifacts, radio frequency, and other causes of false signals. The system is able to measure GME as small as 10 microns, with count rates greater than 1000 emboli per second and flow rates from .2 L/min to 6.0 L/min.

Conduct of Study

An initial EDAC® recording was taken to ensure no air was passing through distal to the ALF or proximal to the air injection site. At 37°C EDAC® recording was started. After 15 seconds had elapsed, 30 mL of air was injected into the venous line luer port over a 10 second interval. Recording was continued for 90 seconds. At this point recording was stopped and the process was repeated until five total test runs were collected. The same procedure was followed for temperatures of 35°C, 33°C, 31°C, 29°C, 27°C, 25°C, and 23°C. After all recordings were collected the circuit was disassembled and data were analyzed.

Statistical Analysis

Mean GME counts and sizes recorded postALF were compared at all eight temperatures. The average total embolic load for all eight temperatures was also evaluated

post ALF. A single-factor analysis of variance was run on all results for total embolic load. *T*-tests were used to determine the significance of GME changes in comparison to the normothermic embolic load values.

RESULTS

Throughout this experiment transducer #1, which was located immediately before the air injection site, was continuously monitored and showed no sign of emboli. This confirmed that the silicon membrane oxygenator with vacuum adequately served the purpose of de-airing the circuit. Transducer #2, which was placed immediately before the arterial filter, was intended to give the investigator an idea of how efficient the oxygenator was at sequestering the entrained air. Figure 2 shows the number of GME that made their way through the oxygenator. The data shows that nearly all GME over the size of 40 microns were filtered by the oxygenator, but the number of smaller GME that passed this transducer increased steadily as the temperature was dropped.

For all experiments, the introduction of 30 mL of air into the venous line resulted in the detection of GME at transducer #3, which was placed distal to the arterial filter. Table 1 and Figures 3 and 4 show the mean embolic loads in cubic centimeters along with the total average GME counts for transducer #3.

Figure 4 shows that the majority (87%) of all emboli detected distal to the arterial filter fell into the 0–20 micron diameter range, 12.5% of all emboli detected fell into the 20–40 micron batch, and the remaining .5% was in the 40–60 micron batch. No emboli measuring greater than 60 microns in diameter were detected beyond the arterial filter.

A single-factor analysis of variance was run for the total embolic loads measured at transducer #3. A *p*-value of 3.05^{-21} was derived, confirming that the air handling abilities of the circuit definitely change significantly as the blood temperature changes. Subsequently, two-sample *t*-tests were run for each temperature in relation to the normothermic (37°C) total embolic load results. A significant increase in embolic load appeared when the blood temperature was dropped to 31°C or below.

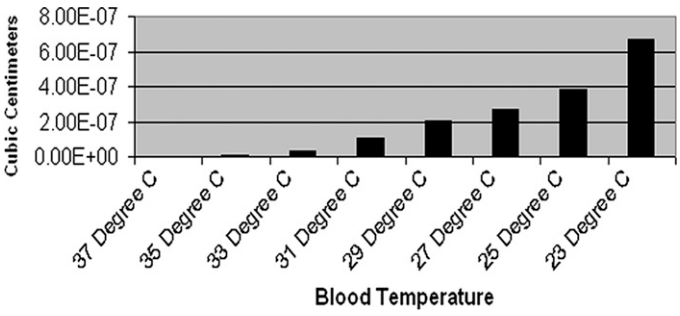

Figure 3. Transducer #3 total embolic load.

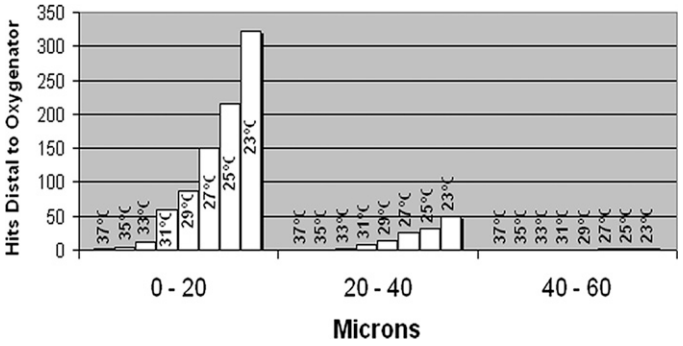

Figure 2. Transducer #2 embolic batches.

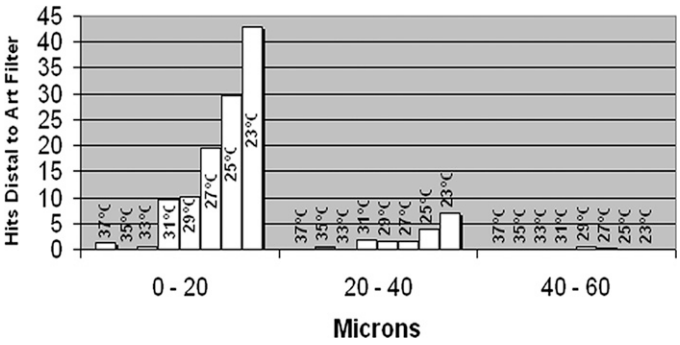

Figure 4. Transducer #3 embolic batches.

Table 1. Transducer 3 embolic count.

	Average Total Load (cubic cm)	Average Total Emboli Count	Average Count 10–20 micron	Average Count 20–40 micron	Average Count 40–60 micron	Average Count 60–80 micron	Average Count 80–100 micron	Average Count Over 100 micron
37°C	3.65E-09 ± 3.61E-10	1.40 ± .29	1.40 ± .29	.00 ± .00	.00 ± .00	.00 ± .00	.00 ± .00	.00 ± .00
35°C	8.91E-09 ± 8.13E-10	.40 ± .12	.00 ± .00	.40 ± .12	.00 ± .00	.00 ± .00	.00 ± .00	.00 ± .00
33°C	3.28E-08 ± 9.33E-11	.40 ± .12	.40 ± .12	.00 ± .00	.00 ± .00	.00 ± .00	.00 ± .00	.00 ± .00
31°C	1.09E-07 ± 3.31E-09	11.40 ± .75	9.60 ± .63	1.80 ± .29	.00 ± .00	.00 ± .00	.00 ± .00	.00 ± .00
29°C	2.02E-07 ± 8.75E-09	12.20 ± .74	10.20 ± .66	1.60 ± .25	.40 ± .12	.00 ± .00	.00 ± .00	.00 ± .00
27°C	2.71E-07 ± 8.23E-09	21.20 ± 1.04	19.40 ± 1.00	1.60 ± .23	.20 ± .08	.00 ± .00	.00 ± .00	.00 ± .00
25°C	3.84E-07 ± 4.47E-09	33.60 ± 1.64	29.60 ± 1.47	4.00 ± .41	.00 ± .00	.00 ± .00	.00 ± .00	.00 ± .00
23°C	6.67E-07 ± 6.61E-09	49.80 ± 1.62	42.80 ± 1.41	7.00 ± .52	.00 ± .00	.00 ± .00	.00 ± .00	.00 ± .00

DISCUSSION

The physical law of gas solubility states that as the temperature of a liquid drops, the partial pressure of a gas in the liquid will decrease causing the solubility of the gas to simultaneously increase. The results of this study seem to contradict the solubility-based hypothesis that GME will decrease in a linear fashion as the blood temperature is dropped. The outcome provides compelling evidence that there are additional factors in play that are counteracting any GME reduction resulting from lower perfusate temperatures. The fact that EDAC® transducer #1 remained clear of GME throughout the experiment leads us to believe the source of the interference doesn't lie solely within the changing physical characteristics of the blood. It is proposed that there is some interaction between the more viscous cold blood and the heat exchanger or membrane oxygenator that enables an increasing amount of GME to surpass the oxygenator and arterial filter in a bypass circuit.

As an interesting side note, there was an attempt to collect data at temperatures below 23°C, but it was evident in transducer #2 that showers of emboli were being spontaneously created throughout the circuit. This occurred even before air was injected into the venous line and persisted indefinitely. The vacuum was removed from our venous reservoir in an attempt to clear the circuit, but the emboli persisted. As the blood was slowly warmed back to approximately 23°C, the emboli dissipated from the circuit. This phenomenon seemed to be inexplicable and it is suggested that it be revisited during further studies, as it may have practical significance for deep hypothermic circulatory arrest (DHCA) cases.

This study provides evidence that the level of hypothermia used during bypass will have an effect on the amount of microemoli being sent to the patient. The statistical analysis suggests that, when taking only embolic load into account, it will be prudent to keep patients at or above 31°C during normal (non-DHCA) CPB cases. The obvious limitation to the results is that only one circuit design was used for this experiment. Also, emboli behavior may be different in an in-vivo model using human blood. The investigators' stance is that further investigation should be done before changes are made in clinical practice. Previous studies have focused solely on the air handling capabilities of different manufactured components (11–12). It is now proposed that future studies examine in-vivo models and focus on correlations between blood temperature and GME creation with the use of different types of circuit components.

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