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An In Vitro Study of the Effectiveness of Carbon Dioxide Flushing of Arterial Line Filters

Roland Ryan Beckman, BS; Carl Gisner, BS; Ed Evans, BBA, MA, CP

College of Health Sciences, Midwestern University, Glendale, Arizona

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Abstract: Gaseous microemboli (GMEs) have been connected to neurologic impairment and other ischemic complications after surgery. The components of the extracorporeal circuit (ECC) have a large influence on GME production. This in vitro study investigates the use of carbon dioxide flushing of the 38-µm Medtronic Affinity CB351 and 38-µm Medtronic Affinity 351 arterial line filters (ALFs) to decrease GMEs and time for air to clear the ALF. An adult circuit was implemented with a silicone oxygenator for vacuum-assisted gas removal and to reduce air before ALF. The 48 filters were separated into four equal groups: flushed coated and non-coated and non-flushed coated and non-coated. Carbon dioxide flushing was performed at 6 L/min for 3 minutes. ALFs were retrograde primed at 200 mL/min. An Emboli Detection and Classification Quantifier (EDAC) was used to gather data. The average total emboli and time to clear (seconds) for flush coated were 20.25 ± 16.78 and 142.17 ± 174.80 seconds, respectively, flushed non-coated were 30.5 ± 34.65 and 124.17 ± 131.40 seconds, non-flushed coated were 162.08 ± 79.90 and 390.42 ± 84.36 seconds, and non-flushed non-coated were 163.67 ± 212.67 and 305.92 ± 179.36 seconds. Flushed filters had an average total emboli count of 25.375 ± 27.14 and an average time to clear of 133.167 ± 151.51 seconds. Non-flushed filters had an average total emboli count of 162.875 ± 157.11 and an average time to clear of 348.167 ± 143.70 seconds. Coated and non-coated filters for total emboli and time to clear had p values of .86 and .24, respectively. Flushed and non-flushed filters had total emboli and time to clear p values of <.001 and <.001, respectively. No significant difference was found between coated and non-coated filters involving total embolic count and time to clear. A significant difference was found in total embolic count and time to clear between flushed and non-flushed filters. This study shows that fewer emboli and faster embolic clearance time correlate with carbon dioxide flushing of the ALF. **Keywords:** arterial line filter, cardiopulmonary bypass, emboli. *JECT. 2009;41:161–165*

Cardiopulmonary bypass (CPB) allows for the repair and replacement of many aspects of the heart. Bypass also has many other uses, such as an aid during transplants or assist device administration to name a few. However, complications have been known to arise with this process. Neurocognitive dysfunction is an area of major concern after CPB. This dysfunction can occur because of microemboli, which can include air and solid particles. Gaseous microemboli (GME)-induced neurologic impairment and other ischemic conditions can be observed after surgery. The extracorporeal circuit (ECC) components have been designated as a large GME producer. Butler (1) distinguished the sources of GMEs into five categories: suction of blood and air, cavitation, mechanical blows to the circuit, GME release when the blood is warmed, and injection of GMEs into the circuit. One component of interest in the reduction of GME is the arterial line filter (ALF).

The ALF has a strategic location in the ECC set-up. In theory, the placement of this filter distal to the oxygenator acts as a safety device to reduce the pumping of microemboli to the patient. A study completed by Pugsley et al. (2) involved the use of the ALF during CPB surgeries. They concluded that the neuropsychologic deficits after CPB have a connection to the amount of microemboli pumped to the patient. The results from the patients involved with the implementation of the ALF (40 µm) suggested the amount of microemboli might be decreased by the filter's presence. The combination of the filter and carbon dioxide flushing before the priming of the circuit may further reduce the presence and time to clear of microemboli from the circuit components. Massimino et al. (3) have studied carbon dioxide flushing and suggested there was no significant difference when comparing one flushed and one

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Address correspondence to: Roland Ryan Beckman, 185 Estancia Dr. #161, San Jose, CA 95134, E-mail: rrbeckman@hotmail.com; and Carl Gisner, 3412 E. Lavery Lane, Phoenix, AZ 85032, E-mail: Carl.Gisner@gmail.com.
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non-flushed filter of seven different models. However, Hargrove et al. (4) showed that flushing the circuit with carbon dioxide at 6 L/min for 4 minutes was optimal for reducing the residual air in the circuit. This may lead to a more efficient priming of the ECC. Carbon dioxide flooding of the surgical field has also been shown to be beneficial for patients during cardiac surgery as described by Martens et al. (5). This statement was connected with the idea that cerebral embolization of a more soluble gas (carbon dioxide) leads to minor and more reversible lesions. Therefore, the carbon dioxide flushing of the ALF increases the displacement of the lesser soluble gases present in the filter and other circuit compartments.

The focus of this research was to establish the influence carbon dioxide flushing has on the amount of microemboli and the time for those emboli to clear the filter. Coated and non-coated filters of the same model were used to determine whether coating influenced carbon dioxide flushing. The filter apparatus involved inlet and outlet 3/8 × 3/8 × 3/8-in wye ports, a bypass line between the ports, and a purge line connected at the superior aspect of the filter and at the venous reservoir. The Emboli Detection and Classification Quantifier (EDAC) was used for the detection of the microemboli. Past articles suggested the EDAC offers outstanding sensitivity and specificity compared with other detection devices (6,7). The EDAC connectors had three locations throughout the circuit. Carbon dioxide flushing has the potential to be a valuable tool that can reduce negative patient outcomes.

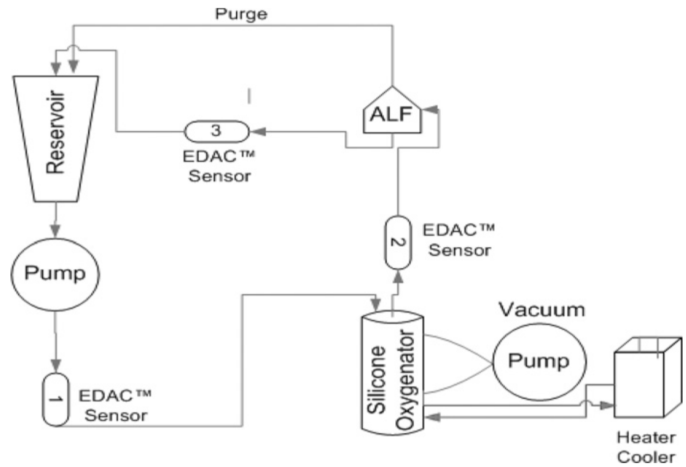

Figure 1. Complete circuit setup with EDAC and a Medtronic oxygenator.

MATERIALS AND METHODS

A Medtronic Affinity CVR reservoir (Medtronic, Minneapolis, MN) was used for the first half of the trials for each group, and a Terumo Capiox 25SX (Terumo Medical, Ann Arbor, MI) reservoir was used for the second half of the trials. The filter tubing assembly was replaced after the first 24 trials, except for the purge line. Twenty-four 38-μm Medtronic Affinity CB351 Carmeda BioActive Surface ALFs and 24 38-μ Medtronic Affinity 351 (Medtronic) filters were used. A standard arterial-venous (A-V) loop setup was used with the addition of a Medtronic Silicone Oxygenator, as shown in Figure 1. Vacuum was applied to the oxygenator, and recirculation ports were capped off. A Cincinnati Sub-Zero heater/cooler (Cincinnati Sub-Zero Products, Cincinnati, OH) was used to keep the Normosol R at 37°C. EDAC (Luna Innovations, Blacksburg, VA) monitor connectors were attached pre-oxygenator, post-oxygenator, and post-ALF.

Clamps were attached proximally to the inlet of the ALF and in the middle of the bypass line. One stopcock was placed on the top of the ALF for purge line attachment and carbon dioxide flow into the filter. Carbon dioxide flowed through the ALF at 6 L/min for 3 minutes. The vent port was open to prevent over-pressurization of the venous reservoir. At the end of 3 minutes, the carbon dioxide flushing was stopped, the stopcock was turned off to the ALF, and the bypass line clamp was placed distal to the ALF outlet. Two liters of Normosol R was added to the reservoir at room temperature for the first 24 trials, and 3 L was used for the last 24 trials to maintain an adequate level in the reservoir. The Normosol R was circulated through the tubing at 6 L/min bypassing the filter until no bubbles were detected. Flow was reduced to 200 mL/min. The distal outlet clamp was moved distal to the outlet wye connector, and the stopcock was turned on to the purge line and ALF to allow for retrograde priming. Once fluid filled the purge line, the proximal clamp to the ALF inlet was moved to a medial position on the bypass line, and the distal clamp on the outlet side was removed. Recording by the EDAC started once the outlet side clamp was removed. Flow was increased to 6 L/min. The ALF was taken out of the holder and rocked diagonally, forward and backward, and tapped softly two times. The ALF was inverted and suspended. The EDAC count was reset once the filter was suspended and undisturbed. The ALF was left inverted for 5 minutes. After 5 minutes, the EDAC count was reset, and simultaneously, the filter was picked up, rocked diagonally, forward and backward, and tapped softly two times. The ALF was reverted and placed correctly back into the holder. The EDAC count was reset when the ALF was correctly placed and not being touched. The ALF was monitored for another 5 minutes. At the end of the 5-minute period, the data collection was stopped, the pump was turned off, clamps were added distally to the outlet and proximally to the inlet connectors of the ALF bypass line, and the stopcock was turned off to the ALF. The filter was de-primed, and a new filter was placed into the filter tubing assembly.

RESULTS

Data were collected from 48 filters: 24 coated and 24 non-coated. The coated and non-coated filters were split into two groups: those being flushed with carbon dioxide and those not being flushed with carbon dioxide. The data collected was statistically analyzed using a two-factor ANOVA. The SE, an estimate of SD, was used on all bar graphs to allow for better visualization. Table 1 shows the statistical analysis of the total emboli recorded between each of the four groups. Flushed coated filters average with SD was 20.25 ± 16.78, flushed non-coated was 30.5 ± 34.65, non-flushed coated was 162.08 ± 79.90, and non-flushed non-coated was 163.67 ± 212.67. Figure 2 is a bar graph that shows the average total emboli of each group. Table 2 shows the statistical analysis of time to clear from each of the four groups. Flushed coated filters had an average time to clear of 142.17 ± 174.80 seconds, flushed non-coated had 124.17 ± 131.40 seconds, non-flushed coated had 390.42 ± 84.36 seconds, and non-flushed non-coated had 305.92 ± 179.36 seconds. Figure 3 depicts the average time to clear in each group. Figure 4 shows the average emboli of all flushed filters compared with the average of all non-flushed filters. Figure 5 shows the average time to clear of all flushed filters compared with the average of all non-flushed filters. Analysis of total emboli had a p value of .86 between coated and non-coated filters and an F to F crit ratio of 0.03:4.06. Analysis of time to clear for coated and non-coated filters had a p value of .235 and an F to F crit ratio of 1.45:4.06. The statistical analysis of flushed filters compared with non-flushed total emboli had a p value of <.001 and an F to F crit ratio of 17.09:4.06, and the time to clear had a p value of <.001 and an F to F crit ratio of 25.47:4.06.

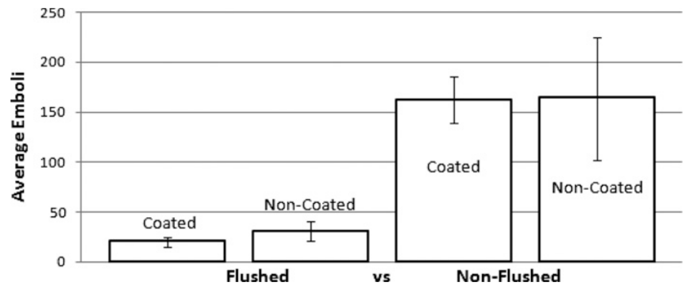

Figure 2. Average total emboli for flushed coated and non-coated and non-flushed coated and non-coated filters.

DISCUSSION

GMEs have a large impact on CPB patient outcomes. The brain is very susceptible to injury because of its sensitivity to ischemic and/or embolic events. Possible neurologic complications include stroke, coma, seizures, and memory impairment (8). Over the past few decades, large steps have been taken to reduce embolic complications. One of these steps was the development and implementation of the membrane oxygenator, which began to replace bubble oxygenators in the mid-1980s (9).

Other steps involved the implementation of safety devices, such as level sensors and bubble detectors, and properly priming and checking the equipment. These steps

Table 1. ANOVA of total emboli count for flushed and non-flushed and coated and non-coated filters.

	Total Emboli Count					
Summary	Flushed	Non-Flushed	Total			
Coated						
Count	12	12	24			
Sum	243	1945	2188			
Average	20.25	162.0833333	91.16666667			
Variance	281.4772727	6384.628788	8435.971014			
Non-coated						
Count	12	12	24			
Sum	366	1964	2330			
Average	30.5	163.6666667	97.08333333			
Variance	1200.818182	45227.87879	26831.12319			
Total						
Count	24	24				
Sum	609	3909				
Average	25.375	162.875				
Variance	736.3315217	24684.89674				
ANOVA						
Source of variation	SS	DF	MS	*F*	*P*	*F* crit
Sample	420.0833333	1	420.0833333	0.031647793	0.859619381	4.061706349
Columns	226875	1	226875	17.0920683	0.00015738	4.061706349
Interaction	225.3333333	1	225.3333333	0.016975924	0.896929516	4.061706349
Within	584042.8333	44	13273.70076			
Total	811563.25	47				

SS, sum of squares; DF, degrees of freedom; MS, mean square.

Table 2. ANOVA of time to clear for flushed and non-flushed and coated and non-coated filters.

	Time to Clear					
Summary	Flushed	Non-Flushed	Total			
Coated						
Count	12	12	24			
Sum	1706	4685	6391			
Average	142.1666667	390.4166667	266.2916667			
Variance	30,555.78788	7116.265152	34,093.95471			
Non-coated						
Count	12	12	24			
Sum	1490	3671	5161			
Average	124.1666667	305.96166667	215.0416667			
Variance	17,266.15152	32,168.62879	32,260.04167			
Total						
Count	24	24				
Sum	3196	8356				
Average	133.1666667	348.1666667				
Variance	22,955.88406	20,651.10145				
ANOVA						
Source of Variation	SS	DF	MS	*F*	*P*	*F* crit
Sample	31,518.75	1	31,518.75	1.447360617	0.235385527	4.061706349
Columns	554,700	1	554,700	25.47216923	8.25438×10^{-6}	4.061706349
Interaction	13,266.75	1	13,266.75	0.609217417	0.439261685	4.061706349
Within	958,175.1667	44	21,776.70833			
Total	1,557,660.667	47				

SS, sum of squares; DF, degrees of freedom; MS, mean square.

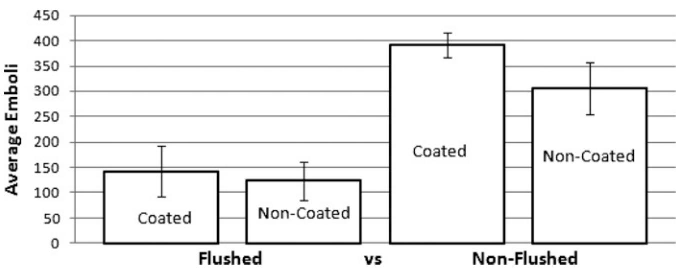

Figure 3. Average time to clear for flushed coated and non-coated and non-flushed coated and non-coated filters.

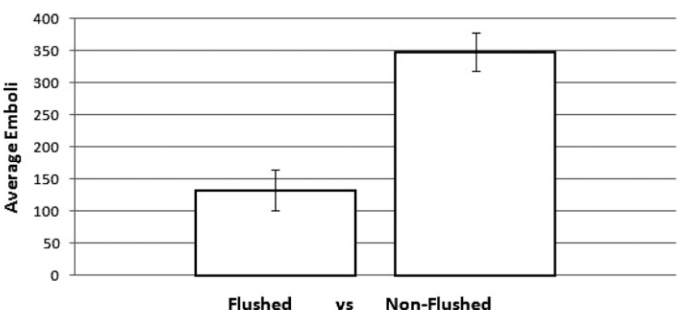

Figure 4. Average emboli for flushed and non-flushed filters.

were focused on problems associated with inattention to the reservoir level, rupture/disconnection of tubing and connectors, over-pressurization of reservoirs, mechanical malfunctions, and inadequate de-airing of the circuit. The placement of the ALF into the ECC reduced emboli being pumped to the patient. The addition of an ALF may be one of the most beneficial components in protecting the patient from gaseous emboli (10).

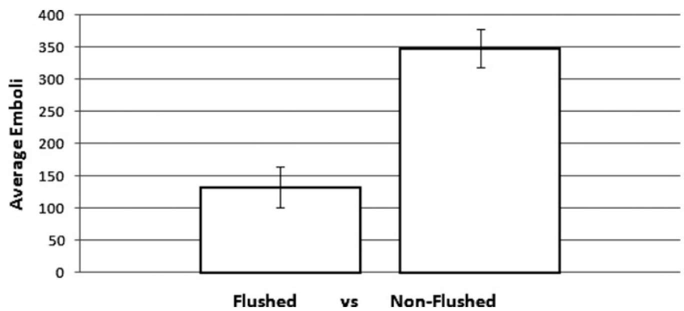

Figure 5. Average time to clear for flushed and non-flushed filters.

The combination of carbon dioxide flushing and the ALF promises to be a valuable tool in the reduction and possibly the elimination of gaseous emboli. Similar to the study of Hargrove et al. (4), flushing of the bypass circuit and its components has the ability to significantly reduce residual air. The study of Massimino et al. (3) suggested little benefit with flushing of filters; however, a limitation could involve the small sample size. This study involved the same brand of ALF in each trial with a larger sample size, which could explain the different outcomes. Another factor could be the use of the Micropure Model 1100 ultrasonic microcontaminant monitoring system in the study of Massimino et al. and the EDAC in this study. Carbon dioxide flushing of the filter has been shown by this study's data to reduce embolic count and time to clear. The total embolic count of flushed filters was significantly lower than non-flushed filters. The time to clear also was significantly less in flushed filters compared with the non-flushed filters. Flushing of the ALF reduces embolic count and time to clear and should be applied during the set-up of the ECC to minimize GMEs transferred to the patient.

An acidic prime may present itself because of the influx of carbon dioxide. In the clinical setting, high pCO_2 values have been seen with carbon dioxide flushing when corrective actions have not been taken. However, corrections can be achieved by using ventilating gases after priming the bypass circuit. Hensley et al. (11) suggested blowing off carbon dioxide with the ventilation gases at ~2–3 L/min.

Limitations of the study include an increase in technique precision, differing types and levels of the reservoir, sample size, and vacuum application. As the trials progressed, the quality of the process improved because of procedural repetition. The first 24 trials, 6 trials for each of the four groups, involved the use of a Medtronic reservoir, whereas the second 24 trials involved a Terumo reservoir. Throughout all the trials, there was a fluctuation of the reservoir level because of prime depletion from ALF changeout. An even larger sample size of filters could add strength to these findings. The BRAT 2 was used to apply the vacuum in the first 24 trials, but it became inactive. The last 24 trials were finished with the vacuum being maintained with a roller pump at an RPM of 150. The results were not affected by these issues, because the trials were not started until there were no emboli seen in channel 2 of the EDAC. The specific aspect of interest, carbon dioxide flushing of the ALF, therefore was not compromised.

Further studies of a similar nature will be able to reinforce the effects of carbon dioxide flushing. More studies with larger sample sizes could provide valuable information. This study only used the Medtronic Affinity filters; therefore, future studies with multiple brands of arterial line filters would create a general result for most brands on the market.

ACKNOWLEDGMENT

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