Microemboli in our Bypass Circuits: A Contemporary Audit

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Abstract: Cardiopulmonary bypass (CPB) may introduce microemboli into the patient's arterial circulation. These may arise from the CPB circuit. Most relevant studies have been performed in vitro; there are relatively few clinical studies. We used the Emboli Detection and Classification quantifier (EDAC) (Luna Innovations, Roanoke, VA) in a prospective clinical audit of emboli in a contemporary CPB circuit. Following ethics approval, standard clinical CPB circuits in patients undergoing CPB were instrumented with three EDAC system probes placed on the venous line, outlet of the hard-shell venous reservoir (HSVR), and distal to the arterial line filter. This was synchronized with the perfusion data management system and emboli number and volume were recorded at 30-second intervals. Recorded observations and combined data from both the EDAC and data management system were analyzed. We report data from the first 12 patients (24.5 hours of CPB) of a larger series currently being performed. The mean total emboli count per minute was significantly greater downstream of the HSVR than in the venous line and significantly less downstream of the arterial line filter than either of the above. The total count downstream of both the HSVR and the arterial line filter was greater when the vent pump was on vs. off. Despite the significant increase in emboli count downstream of the reservoir during vent operation there was a significant reduction in the total volume of emboli in this position compared with the venous line. This was further reduced by the arterial line filter. Nevertheless, the total embolic volume was greater downstream of the HSVR and the arterial filter with the vent on vs. off. The two overwhelming sources of emboli emanating from our CPB circuit were the use of the left ventricular vent and air entrained from the venous line. Such audit enables refinement of CPB management and potential component redesign which may make CPB safer and improve patient outcome. **Keywords:** cardiopulmonary bypass, emboli, left heart vent. *JECT. 2009;41:P31–P37*

The incidence and implications of microemboli in cardiopulmonary bypass (CPB) have been investigated for several decades. As early as 1976, Clark et al., using a transmission oscillator ultrasonic spectrometer in an animal model of CPB, noted a significantly higher number of emboli at the onset of CPB and with the use of cardiotomy suction, as well as reductions of emboli by the arterial line filter (1). In the intervening period there have been numerous clinical studies on emboli detected in the cerebral circulation during CPB (2–11), and a number of these studies have positively correlated emboli numbers with post-operative neurocognitive deficit. Most of these studies were conducted in the era of bubble oxygenators and lack relevance to current CPB apparatus and practice. The vast majority of studies of emboli behavior within the bypass circuit over the past 15 years have been conducted using in-vitro models of CPB (12–22). Such work has drawn attention to avoidable sources of emboli from the CPB circuit such as device design problems (23) and entrained venous air under both gravity and vacuum assisted conditions (13,15–17), and has resulted in the practice of de-airing the venous line prior to going on CPB, and in a heightened awareness of the need to rectify purse string suture leaks if air appears in the venous line.

Overall, it is fair to claim that much of this work has had a significant and lasting impact on perfusion practice, but contemporary audits of embolism during clinical cardiopulmonary bypass are rare. To our knowledge, very few have been published since our incidental observations during the lidocaine trial (9), which is now almost 10 years old. Exceptions include one early study that identified emboli from the CPB circuit resulting from perfusionist interventions (24) and the more recent comprehensive audit of emboli during CPB by Groom and colleagues (25). This is unfortunate because the undeniable lesson we learned was that "When you look you may be surprised what you find, but if you don't look you won't find it". This begs the question of why we have not continued this work ourselves; a question largely answered by the disincentive of not having a bubble counter we can rely on for accurate results.

DETECTION TECHNOLOGY

We must preface the following comments by stating that we are clinicians rather than engineers, so some of the interpretations may be naive. Nevertheless, to summarize, most Doppler emboli counting systems are potentially flawed in the way they process the Doppler shifted ultrasound signal to determine when a counter should be incremented. There is usually some form of comparison between the averaged Doppler signal amplitude and the instantaneous signal amplitude of higher frequencies. When the instantaneous signal exceeds the averaged signal by a threshold amount, the counter is incremented. This works well when emboli are sporadic or appear in small clusters. However, there are many scenarios in perfusion when emboli may appear in large "showers." Doppler systems usually do not provide an accurate count during these sustained showers because the prolonged high frequency signal disturbance is re-interpreted as the average or baseline, and the counter is not incremented. To resolve this problem in our initial work we used a color-flow Doppler system interfaced with a bubble counting device built by our own engineers. "Baseline reinterpretation" was circumvented by including a manually operated controller that allowed progressive increases in sensitivity during emboli showers so that the operator could (approximately) ensure continued matching of the audible signal to counter increments. The system worked well but required a dedicated and practiced operator who did nothing else except run the Doppler. We now have a newer emboli counting device, the *DWL Multiflow* transcranial Doppler (*DWL* GmbH, Sipplingen, Germany), but are disillusioned by its inability to cope with showers of emboli.

In late 2008, we were able to purchase the new Emboli Detection and Classification quantifier (EDAC) (Luna Innovations, Roanoke, VA) with grants from the University of Auckland and the Green Lane Research and Education Fund. The EDAC has provided us with an opportunity to perform an accurate audit of emboli activity during contemporary clinical cardiopulmonary bypass. Although we have performed such an audit before as described, it is likely that patterns and causes of emboli production have changed with the evolution of CPB technology over the last 10 years and such an audit is now due. The major advantage of the EDAC system is 2-fold: It appears to successfully cope with large numbers of emboli (26) and it allows simultaneous monitoring of multiple positions on the CPB circuit.

In this paper we report preliminary observations from our ongoing audit of emboli in the CPB circuit in our current clinical setting.

METHODS

Ethics approval was obtained for a prospective audit of emboli in the CPB circuit in 50 patients undergoing CPB for coronary bypass grafting, valve replacement, or combined procedures. No selection criteria is applied other than the requirement for CPB during surgery and the availability of an operator for the EDAC system. There were no exclusions. At the time of preparing this report, we had studied 13 patients.

PREPARATION OF THE CPB CIRCUIT

The CPB circuit was prepared in the standard fashion with crystalloid prime re-circulated through a 5 μm pre-bypass filter (Pall Corp, Portsmouth, UK). The circuit consisted of: *SMARxT™* (COBE Cardiovascular, Arvada, CO) and silicone replacement tubing, hard shell venous reservoir (HSVR) and Avant 903 or EOS 9 and hollow fiber membrane oxygenator (Sorin Group, Mirandola, Italy), Stockert S3 roller pump (Stockert Instrumente, Munich, Germany), Pall AL6 Arterial line filter (Pall Corp, Portsmouth, UK) with continuous purge, and *MYOtherm* XP cardioplegia delivery system (Medtronic, Minneapolis, MN).

CONDUCT OF CPB

The conduct of CPB followed our normal clinical practice (mild hypothermia - 34–32°C, target hematocrit >.23, flow index 2.0–3.0 L/min/m^2, MAP >50 mmHg) with no alteration arising from the EDAC monitoring. The venous line was de-aired or not prior to going on bypass according to surgeon preference. On bypass, the flow index was 1.8–3.5 L/m^{-2} min^{-1} and the oxygenator sweep gas composition and rate was titrated to clinical need. The HSVR was operated within the manufacturer's recommended guidelines for minimum volume, with a low volume alarm set at that threshold. In accordance with standard practice, cardiotomy suction blood was sequestered for cell salvage at a later stage, diverted straight to the cell saver or added to the venous reservoir as required. Any blood vented from the left ventricle was returned to the venous reservoir. Volume additions to the circuit were made via the dedicated ports on the venous reservoir. Drug additions were made via the sampling manifold to the HSVR in the perfusionists' usual manner.

EDAC MONITORING AND DATA COLLECTION

The 3 EDAC system probes were placed according to manufacturer instructions on the venous line (channel 1), the outlet of the venous reservoir (channel 2), and on the arterial line distal to the arterial line filter (channel 3). A 3 channel record was created on the EDAC Quantifier hard disk for each patient. An EDAC operator's check list was completed and the EDAC Quantifier clock was precisely synchronized with the Stockert Data management System (DMS) clock for each procedure. Commencement of CPB and the EDAC counter was synchronized to the nearest

half minute. The perfusionist was blind to the EDAC display and the EDAC operator noted perfusion and surgical interventions on an observation chart within 30 seconds EDAC time epochs. The EDAC operator avoided feedback to the perfusionist; however, as provided in the study protocol, if any situation arose in which the operator had concerns for patient safety because of a potentially remediable and significant emboli event, they informed the perfusionist of their concerns. The EDAC quantifier recorded 30 second emboli data for each channel, which was stored in the EDAC record, and recording was stopped at first termination of CPB. Patient demographic and automated online perfusion and procedural data was collected in the Stockert DMS patient file (in keeping with normal practice). The method of setting pump occlusion and whether the venous was line de-aired prior to commencing CPB was noted.

EVALUATION OF THE DATA

At the end of each case, the EDAC file was saved and later exported and time-aligned in an Excel spreadsheet (Microsoft, Redmond, WA) with the exported DMS data. Collection of the data in the above manner allowed correlation of the volume, size, and number of emboli detected in each circuit position every 30 seconds, with events that were anticipated to influence emboli numbers in the circuit. Moreover, by aligning the 30-second counts with automated perfusion data and the EDAC operator observation sheet entries, the detection of unanticipated factors that may contribute to the presence of "unexplained" emboli was facilitated. Based on our previous experience, we thought it likely that sources of arterial line emboli would be identified by careful observation in real time and by examination of the data.

PRELIMINARY RESULTS

Data from 13 procedures have been collected to date; 12 of which have been analyzed (one DMS record had missing data due to a serial port error). The 12 procedures include emboli data in 30-second epochs from a total of 24.5 hours of bypass time. From the outset of the audit, there appeared to be an obvious (unexpected) association between the use of vent suction (left ventricular or aortic) to the HSVR and emboli counts downstream from the HSVR. The decision was made to make a preliminary review of the data to verify this observation with a view to establishing any clinical or practice implications.

EMBOLI COUNTS

The mean total (all sizes) emboli count per minute (Table 1) was significantly greater downstream of the HSVR

than in the venous line and significantly less (Analysis of Variance) than both other sites downstream of the arterial line filter (ALF).

This clearly implied that emboli were either being created in the HSVR or entering it from sources other than the venous line. Observations by the EDAC operator consistently identified use of the left ventricular vent suction as being associated with the appearance of more emboli downstream of the HSVR. To further investigate this observation, data for all cases were segregated into periods when the vent pump was off (vent = 0) or when the vent pump was running (vent >0) (Table 2).

Not surprisingly, there was no difference in the emboli count (averaged per minute) in the venous line when the vent pump was running compared with when the vent pump was off. The mean emboli count per minute was significantly greater downstream from the HSVR compared with the venous line in both conditions; however, in keeping with the empirical real time observations, the emboli count was significantly greater downstream of the HSVR with the vent running compared with when the vent was off. Similarly, the mean count (per minute) downstream of the ALF was significantly greater with the vent on (running) compared to off, though it is clear that the combination of filter and the membrane oxygenator is effective in removing many of those leaving the HSVR.

SIZE DIFFERENTIAL

Although emboli >1000 microns were detected on occasion in the venous line, relatively few >120 microns were detected distal to the ALF (Table 3).

Table 1. Mean total emboli count rate throughout CPB circuit.

	V Line	D/second HSVR	D/second ALF	*p*
Mean count/ minute (SD)	2759 (3353)	5447 (3594)	1574 (1535)	<.0001

Table 2. Mean total emboli count rate throughout CPB circuit with vent off or running.

Mean count/minute	Vent = 0	Vent >0	*p*
V Line	2681 (2343)	2794 (2510)	.67
D/second HSVR (SD)	4095 (3066)	6007 (3757)	<.0001
D/second ALF (SD)	1093 (1169)	1774 (1652)	<.0001

Table 3. Mean arterial line emboli per minute downstream of the arterial line filter by size.

Microns	0–20	20–40	40–60	60–80	80–100	100–120	120–140
All data	946	486	114	20	5	2	1
Vent on	1061	556	126	22	6	2	1
Vent off	668	317	85	16	4	2	1

EMBOLIC VOLUME LOAD

The mean total embolic volume per minute is shown for the three monitoring positions in Table 4. Although emboli numbers were higher downstream of the HSVR compared with the venous line (Table 1), the total volume load is considerably reduced downstream of the HSVR and there is a further reduction downstream of the AFL.

When the vent pump was running (vent >0), the mean embolic volume per minute was significantly greater downstream from both the HSVR and the arterial line filter compared with when the vent pump was off (Table 5). However the arterial line embolic volume load with the vent on was very small; equating to 0.0015 mL of air per hour of CPB.

More subtle associations of emboli in the circuit with previously reported perfusionist interventions such as sampling and drug additions were overwhelmed by the emboli recorded when the vent suction was running. However, when the data is reviewed only in the vent off condition there are some clear associations with both surgical and perfusionist interventions.

Initiation of CPB reliably resulted in large numbers of emboli in the venous line (Table 6: compare with vent = 0 column in Table 2). This resulted in larger numbers than the whole case average (Table 2) transiting both the HSVR and ALF.

These venous line emboli were associated with surgical manipulation of the venous cannulas and the heart, placement of atrial purse-string sutures during CPB, insertion of retrograde and caval cannulas during CPB, and visible air in the venous line. Embolic activity in the venous line occasionally occurred with no sign of visible venous line air or any surgical manipulation but was immediately attenuated by increasing occlusion of the venous line variable clamp to eliminate even negligible "venous tug," and thus reducing the degree of negative pressure in the venous line. Volume addition to the HSVR via the unfiltered quick prime port most frequently resulted in an increase in emboli detected downstream from the reservoir as did rapid bolus injection into the sampling manifold.

DISCUSSION

The EDAC quantifier uses fixed beam ultrasonic imaging with a shorter duration pulse than the pulsed Doppler ultrasound signal. Multiple microbubbles in the measurement beam are counted and classified using SONAR and RADAR based algorithms enabling detection of thousands of emboli per second in flows up to 6 L/min (26). Its only current disadvantage is that carotid artery monitoring is not practicable, but it should be observed that all important observations in our previous work (except the issues pertaining to de-airing of the heart) would have been made whether the ultrasound probe was sited on the carotid artery or the CPB arterial line. Moreover, the facility for carotid monitoring using EDAC may become available in the near future and a separate study to evaluate contemporary non-CPB contributions to emboli exposure will be proposed at that time. Furthermore development of reliable discrimination of solid vs. gaseous emboli using EDAC technology has been demonstrated in prototype and is hoped to be validated in commercially available EDAC devices in the future.

The advanced discrimination of the EDAC quantifier with simultaneous three channel monitoring coupled with real time automated data retrieval from the heart lung machine has facilitated a more accurate examination of emboli behavior during CPB than was previously possible. We were interested to assess the impact of changes in practice such as formal de-airing of the venous line and a new generation of perfusion circuit components in light of our previous audit and in-vitro studies.

Of immediate surprise was the apparent influence of vent suction in the genesis of emboli exiting the HSVR. While there have been casual observations that cardiotomy return is a source of emboli (27), there is only one recent report in which Myers and colleagues showed (in-vitro) that vent return to HSVRs resulted in a dramatic increase in gaseous emboli downstream. Numbers were variably attenuated distally in the circuit depending on the oxygenator filter combination (28). Our preliminary results show an increase in emboli counts downstream from the HSVR during use of vent suction to the HSVR (left ventricular or aortic) and confirm this for the first time in the clinical setting.

Table 4. Mean embolic volume (mL/min).

	D/second V Line	D/second HSVR	D/second ALF	p
mL/minute (SD)	.510765 (1.01)	.000537 (.0011)	.000024 (.000027)	<.0001

Table 5. Mean embolic volume in mL/minute with vent off or running.

Total/minute	Vent = 0	Vent >0	p
D/second HSVR (SD)	.000375 (.00045)	.000604 (.0013)	<.01
D/second ALF (SD)	.0000186 (.000021)	.0000257 (.000028)	<.001

Table 6. First minute of CPB.

	V Line	D/second HSVR	D/second ALF	p
Mean count/ minute (SD)	6971 (7797)	5302 (4951)	1313 (1911)	<.05

Our current practice of sequestering pericardial suction blood (PSB) is based on evidence supporting avoidance of its direct reinfusion (29) and we have previously reported using the Avant 903 and EOS HSVRs' capability to isolate PSB (30). The "clean" vent blood is returned to a port on the HSVR that bypasses the cardiotomy blood filter and is directed into the venous blood flow path. Pericardial suction blood is directed separately through the cardiotomy depth filter where it can be sequestered in the upper portion of the reservoir and subsequently washed in a cell processor, discarded if the volume is small, or added directly to the extracorporeal circulation if required. The vent suction blood variably combines with air that in essence constitutes entrained venous air to the HSVR. Emboli numbers downstream of the HSVR were not necessarily related to the speed of the vent pump. For example, the vent pump could be "idling" at 300 mL per minute with no blood being retrieved in the pump and consequently there was no increase in emboli down stream of the HSVR. Alternatively it could be retrieving vent blood at the same pump speed resulting in a marked genesis of emboli. Judicious use of the vent at minimum flow rates attenuated emboli from the HSVR and indeed servo regulating the vent pump to a low negative pressure would appear to provide an automated approach to attenuating such emboli generation. The question then arises whether other approaches are warranted? Does this increased embolic load resulting from the unfiltered vent suction blood constitute a greater risk to the patient than mixing it with PSB through the cardiotomy depth filter and directly re-infusing both to the patient? Alternately, the HSVR could be redesigned to provide separate depth filtration to the vent blood and a splash free blood flow path?

We identified other sources of emboli within the CPB circuit, the most commonly associated with air entrained in the venous line from the surgical field. Despite almost universal de-airing of the venous line at the cannula connection, commencement of CPB was associated with large numbers of emboli in the venous line that transited the circuit. Furthermore, and not surprisingly, any manipulation of the heart reliably resulted in emboli that transited the CPB circuit to the arterial circulation. Such maneuvers included:

- Repositioning cannulas
- Insertion of caval cannulas during CPB
- Insertion of retroplegia cannulas during CPB

The above causes could be frequently avoided by placement of cannulas prior to commencing CPB and application of a second atrial purse string.

We have reported the following perfusion interventions (apart from use of the vent) to be associated with emboli generation:

- volume addition to the HSVR via the quick prime port
- rapid bolus injection via the sampling manifold
- excessive venous line negative pressure resulting in venous line "tug" or "chatter"

The latter phenomenon was not obvious at first as on most occasions the "tug" on the venous line was minor and there was no visible venous line air or any surgical manipulation. The "unexplained" detection of emboli in the venous line led to this finding. Most often the venous line variable occluder was maximally open at the time, regardless of the size of the patient. This often resulted in transient spikes of negative pressure in the venous line sufficient to entrain air presumably from around the atrial or retroplegia cannula purse string suture. The application of a second purse string suture could attenuate this entrained air.

We could not identify emboli resulting from blood sampling or small volume drug additions by the perfusionist but the effect of these relatively subtle maneuvers was likely overwhelmed by other sources of emboli. The impact of pericardial suction blood through the cardiotomy filter has not been assessed.

The behavior of gaseous emboli in the circulation is complex. They may coalesce if trapped in close proximity to form larger bubbles or conversely break up in areas of turbulence, and the life span of bubbles in blood may vary from seconds to many minutes depending on size and composition (31). Gas microemboli can be coated with platelets or protein further altering their behavior (32). We can now quantify emboli size and we postulate that the emboli entrained from the surgical field and the open HSVR atmosphere consist of air. The exception may be when carbon dioxide flooding of the surgical field is used (33) which was not used in this series.

The sensitivity of the EDAC quantifier provides an unprecedented ability to measure very small emboli in large numbers. On the face of it, the high number of emboli resulting from the vent in this series may be a cause for concern. However there are other considerations. By far, the majority of emboli we detected are less than 60 microns in size and there is an exponential reduction in emboli greater than 20 microns. Although we show that the number of emboli increased at the HSVR outlet when the vent was in use, we demonstrated a 10,000-fold decrease in the embolic volume downstream of the reservoir and a 25,000 times decrease in the embolic volume distal to the arterial filter compared with the embolic volume entering the CPB circuit. This equated to .001 mL of arterial line emboli per hour of CPB. These results suggest that the Avant 903 and EOS HSVR are very effective at removing entrained air as are the other downstream components (oxygenator and ALF).

The embolic load from the circuit (arterial line emboli) during CPB will be variably distributed to and within the brain. As cerebral blood flow is 20% of cardiac output at

rest it can be expected that the brain might receive 20% of these emboli during CPB. Brain blood flow is further influenced by other factors during CPB such as hypothermia and alpha-stat acid base management both which have been shown to reduce embolic load and to protect the brain (34,35). As we are not able to simultaneously quantify emboli in the cerebral circulation and in the perfusion circuit, we are yet to address the issue of impact of CPB circuit emboli on patient outcome.

The use of ultrasound technologies has resulted in a mass of evidence that cerebral embolism is causally linked to both stroke and neurocognitive deficits following cardiac surgery. Some of this evidence is circumstantial, such as the finding of markedly elevated risk of stroke in the presence of mobile aortic atheroma (an obvious risk factor for embolism) (36), but most relevant studies provide direct evidence of embolism by correlating numbers of Doppler-detected emboli against the occurrence of stroke (37) and neurocognitive deficits (5–7,38–40). More recently, Abu-Omar et al. (2004) (41) showed a significant post-operative reduction in task associated functional MRI activation, with a related increase in activity in specific regions, which were interpreted as compensatory adaptations for damage in other areas. These increases in activity were significantly and directly correlated against Doppler-detected emboli numbers.

Not surprisingly, there is little debate over the importance of embolism per se in brain injury after cardiac surgery. However, there has been much discussion over the relative contributions of bubbles as opposed to solid emboli. Solid emboli, and atheroma in particular, appeal as the most likely cause of stroke and there is substantial circumstantial evidence supporting this view (36). In contrast, the relative importance of bubbles and smaller "solid" emboli (which include blood cell and platelet aggregates, tissue debris, and lipid) in causation of neurocognitive deficits has not been determined. In large part this is due to the fact that it has proven difficult to reliably distinguish between bubbles and particulates using Doppler emboli detection devices, so it has not been possible to test the hypothesis that one may be more important than the other. Such debate over relative pathogenicity is largely irrelevant because the potentially harmful effects of arterial bubbles are well established (31,41). There can be little doubt that if arterial gas embolism can be avoided then it should be, irrespective of whether bubbles are more or less of a problem compared with particulates. We now have a commercially available device capable of reliable discrete detection of emboli simultaneously throughout the CPB circuit. Elucidation of the source of emboli during CPB and an understanding of their size and volume with the ability to precisely relate these data to automated perfusion data provides a platform for accurate review of management of CPB to reduce embolic insult.

CONCLUSION

We have identified the left ventricular vent as an important contributor to emboli in the CPB circuit for the first time in the clinical setting. Consistent with our previous work, we also confirmed air entrained from the venous line as an important source. Such audit enables refinement of CPB management and potential component redesign to make CPB safer and improve patient outcome.

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