Assisted Venous Drainage, Venous Air, and Gaseous Microemboli Transmission into the Arterial Line: An In-Vitro Study

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ABSTRACT

The objective of this study was to examine the interaction of cardiopulmonary bypass venous air with assisted venous drainage, focusing on its production of gaseous microemboli in the arterial line.

An in-vitro recirculating cardiopulmonary bypass circuit containing fresh whole bovine blood was monitored with a pulsed-doppler microbubble detector. Air of specific amounts was injected into the venous line and gaseous microemboli counts were obtained distal to the arterial filter. Data was recorded for unassisted drainage, vacuum-assisted drainage, and centrifugal pump-assisted drainage.

Centrifugal pump-assisted drainage produced over 300 microbubbles in one minute distal to the arterial filter when venous air was introduced into the circuit. Of these, 220 were greater than 80 μm in size. Vacuum-assisted drainage produced no microbubbles when the same amount of venous air was introduced into the circuit. However, vacuum-assisted drainage did produce some microbubbles in the arterial line when a stopcock was left open on the venous line for 30 seconds. Unassisted drainage produced no microbubbles at all levels of venous air entrainment.

Air becomes entrained in the venous line from a variety of sources. In a typical gravity-drained situation, the air remains whole and is dissipated in the venous reservoir by buoyancy and filtration. In an assisted-drainage situation, the air is subjected to additional forces. The air is subjected to a greater degree of negative pressure and, with centrifugal pump assisted drainage, is subjected to kinetic energy imparted by the cones or vanes of the pump. The kinetic energy from the centrifugal pump appears to break the air into small bubbles which become suspended in the blood, passing through the reservoir, oxygenator, and arterial filter. In a clinical setting, these bubbles would be passed into a patient’s arterial system.

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INTRODUCTION

Organ dysfunction and neuropsychological deficits are postoperative complications of cardiopulmonary bypass (CPB). Possible causes of these complications include gaseous microemboli (GME). One study reported that GME greater than 50 microns in radius are clinically relevant (1). Another study reported that GME greater than 100 microns should be treated as macro-emboli, due to a strong correlation with postoperative complications (2). In a review of GME, it was reported that GME with diameters greater than 35-40 microns have been causally linked with CPB morbidity, while those with diameters less than 40 microns have not been directly linked with CPB morbidity (3). Two other studies conclude that neuropsychological deficits are related to the number of microemboli delivered (4,5).

Gaseous microemboli can be created in the CPB circuit via oxygenators, temperature gradients, cavitation, vortexing, low reservoir levels, and cardiotomy suction (2,3,6). In addition, Hill has reported that small amounts of venous air will pass up the arterial line as gaseous microemboli (2). These GME were detected prior to the arterial line filter.

This study examines the interaction of CPB venous air with assisted venous drainage, focusing on its contribution to GME in the arterial line. The arterial line filter is typically considered the last line of defense to minimize air transmission, so GME counts and sizes are measured at the outlet of the arterial line filter.

Air may enter the venous line in a variety of ways, including loose purse-string sutures, holes in the vena cava or venous system, and atrial-septal defect or patent foramen ovale with left atriotomy or ventriculotomy. The autopsy findings of a patent foramen ovale in the general population range from 25 to 50% (7). A trans-atrial approach to the mitral valve also creates potential for venous air entrainment.

Assisted venous drainage (AVD) is used to increase the venous return to the pump-oxygenator. According to a recent survey, three methods of AVD were reported to be in use: (1) placement of a centrifugal pump in the venous line, with shunt; (2) application of vacuum to a sealed venous hardshell reservoir; and (3) placement of a roller pump in the venous line, with shunt (Nelson DA, Perflist Survey, perflistr@aol.com; Jan 28, 1998).

MATERIALS AND METHODS

TEST CIRCUIT

An in-vitro recirculating CPB circuit was assembled on a Sarns 7000 Modular Pump System (Figure 1). A 2.5 m² membrane oxygenator with integral sealed-hardshell reservoir, 40 μm arterial filter, and 1/2 in roller-pump boot were connected with PVC tubing (3/8 in x 3/32 in). The arterial filter was fitted with a purge line to a filtered port on the reservoir. The arterial line (3/8 in x 3/32 in x 6 ft) was connected from the arterial filter outlet to the 3/8 in filtered port of a 4.5 L hardshell reservoir. This reservoir served as the “patient” in our in-vitro study. The “patient” reservoir was attached to an IV pole, with the outlet of the reservoir 30 in above the floor. The venous line (1/2 in x 3/32 in x 5 ft) was connected to the inlet of the CPB reservoir. In order to simulate cannulation of a peripheral venous site (femoral, jugular, axillary, etc.), the venous line was reduced to 1/4 in x 3/32 in x 18 in tubing at the outlet of the patient reservoir. The internal diameter of 1/4 in tubing is equal to 19 French. This simulates a patient cannulated with a 19F catheter.

The venous line was further modified by placing one 3/8 in x 1/2 in x 1/2 in connector 8 in. from the CPB reservoir and another 3/8 in x 1/2 in x 1/2 in connector 22 in from the CPB reservoir. A centrifugal pump was attached to these connectors with 3/8 in x 3/32 in x 12 in. PVC tubing. The centrifugal pump was powered with a Biomedicus 540 Console. See Figure 1 for further illustration.

Negative pressures in the venous line were measured in two locations. For the centrifugal pump trials, the pressure was measured on a Siemens D-8000 Micromanometer.
Flows were measured primarily by the display of the roller pump console. In addition, two DP38 flowprobes were placed in the venous line to measure flow. One probe (Q1, Figure 1) was placed 8 in distal to the outlet of the centrifugal pump. The other probe (Q2, Figure 1) was placed midway in the “shunt” portion of the venous line.

A vacuum source was attached to the vent port of the CPB reservoir only during the vacuum-assist trials.

Temperature of the perfusate was measured at the inlet of the arterial line filter (P1, Figure 1) and the outlet of the centrifugal pump. Arterial pressure was measured from a stopcock on the luer fitting of the Y-drainage; V-AVD = vacuum assisted venous drainage;

<table>
<thead>
<tr>
<th>Table 1: CPB conditions</th>
<th>un-AVD</th>
<th>BP-AVD</th>
<th>V-AVD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial Flow</td>
<td>2.14 L/min</td>
<td>4.30 L/min</td>
<td>4.30 L/min</td>
</tr>
<tr>
<td>Arterial Pressure (P3)</td>
<td>+30 mmHg</td>
<td>+60 mmHg</td>
<td>+60 mmHg</td>
</tr>
<tr>
<td>CPB Reservoir volume</td>
<td>1500 ml</td>
<td>1500 ml</td>
<td>1500 ml</td>
</tr>
<tr>
<td>Patient Reservoir volume</td>
<td>900 ml</td>
<td>900 ml</td>
<td>900 ml</td>
</tr>
<tr>
<td>Venous pump RPMs</td>
<td>0</td>
<td>1660</td>
<td>0</td>
</tr>
<tr>
<td>Venous Pressure (P1, P2)</td>
<td>+9 mmHg</td>
<td>-50 mmHg</td>
<td>-50 mmHg</td>
</tr>
</tbody>
</table>
Table 2: Bubble counts by size, full-duration venous air, mean and standard deviation

<table>
<thead>
<tr>
<th>Size</th>
<th>N</th>
<th>un-AVD</th>
<th>BP-AVD</th>
<th>V-AVD</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 µm-80 µm</td>
<td>5</td>
<td>0 ± 0</td>
<td>83 ± 31</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>80 µm-120 µm</td>
<td>5</td>
<td>0 ± 0</td>
<td>177 ± 18</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>120 µm-160 µm</td>
<td>5</td>
<td>0 ± 0</td>
<td>42 ± 26</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>160 µm-200 µm</td>
<td>5</td>
<td>0 ± 0</td>
<td>1 ± 1</td>
<td>0 ± 0</td>
</tr>
</tbody>
</table>

un-AVD = un-assisted venous drainage; BP-AVD = biopump assisted venous drainage; V-AVD = vacuum assisted venous drainage

Table 3: Bubble counts by size, half-duration venous air, mean and standard deviation

<table>
<thead>
<tr>
<th>Size</th>
<th>N</th>
<th>un-AVD</th>
<th>BP-AVD</th>
<th>V-AVD</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 µm-80 µm</td>
<td>5</td>
<td>0 ± 0</td>
<td>145 ± 37</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>80 µm-120 µm</td>
<td>5</td>
<td>0 ± 0</td>
<td>105 ± 44</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>120 µm-160 µm</td>
<td>5</td>
<td>0 ± 0</td>
<td>3 ± 5</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>160 µm-200 µm</td>
<td>5</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
</tr>
</tbody>
</table>

un-AVD = un-assisted venous drainage; BP-AVD = biopump assisted venous drainage; V-AVD = vacuum assisted venous drainage

Table 4: Total bubble count, mean and standard deviation

<table>
<thead>
<tr>
<th>Type</th>
<th>N</th>
<th>un-AVD</th>
<th>BP-AVD</th>
<th>V-AVD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full-Duration</td>
<td>5</td>
<td>0</td>
<td>302 ± 14</td>
<td>0</td>
</tr>
<tr>
<td>Half-Duration</td>
<td>5</td>
<td>0</td>
<td>253 ± 11</td>
<td>0</td>
</tr>
</tbody>
</table>

un-AVD = un-assisted venous drainage; BP-AVD = biopump assisted venous drainage; V-AVD = vacuum assisted venous drainage

closed to air/open to venous line and plunger pushed in, delivering 30 ml; and (3) repeat step 1. This was performed 10 times in 30 seconds. After the last air injection, the bubble counter was activated, and GME activity was monitored for one minute. Once the data was collected and recorded, the system was allowed to return to a bubble-free condition. After verification that no bubbles were present in the system, another full-duration air injection was performed. This process was repeated 5 times to record 5 trials of V-AV data.

For the BP-AVD group the venous biopump was turned on and unclamped, while the venous shunt was clamped. All venous flow was routed through the biopump. The biopump was oriented with the outlet pointing towards the floor. To achieve steady-state in this group, the rpm's of the biopump were adjusted so that the pressure (P1) in the venous line was approximately negative 50 mmHg. The arterial flow was adjusted to achieve a constant 1500 ml in the CPB reservoir (Table 1). The bubble detector was turned on and verified that there was no bubble activity in the circuit. The full-duration dose of air was injected into the system and GME activity was monitored for one minute after the air injection. Once the data was collected and recorded, the system was allowed to return to a bubble-free condition. After verification that no bubbles were present, another full-duration air injection was performed. This process was repeated 5 times to record 5 trials of BP-AV data.

For the V-AV group the biopump was clamped and turned off, while the venous shunt was unclamped. The vacuum source was connected to the vent port of the sealed CPB reservoir. The vacuum was adjusted so that the pressure (P2) in the venous line was approximately negative 50 mmHg. The arterial flow was adjusted to achieve a constant 1500 ml in the CPB reservoir (Table 1). The bubble detector was turned on and verified that there was no bubble activity in the circuit. The full-duration dose of air was injected into the system and GME activity was monitored for one minute after the air injection. Once the data was collected and recorded, the system was allowed to return to a bubble-free condition. After verification that no bubbles were present, another full-duration air injection was performed. This process was repeated 5 times to record 5 trials of V-AV data.

Finally, an open stopcock on the venous line was tested in the un-AV group and the V-AV group. The un-AV system was prepared as described above. The stopcock of the air-injection site was opened for 30 seconds and then closed. GME activity was monitored for one minute after the stopcock was closed. Then the V-AV system was prepared and the stopcock opened to air for 30 seconds. GME activity was again monitored for one minute after the stopcock was closed. As in the other groups, 5 trials of data were taken for the un-AV and V-AV groups. The amount of air entrained in the venous line from the stopcock cannot be quantitatively described.

**STATISTICAL ANALYSIS**

All detected microbubbles greater than 40 µm were summed for each trial and an average total bubble count was calculated for each group tested. Statistical analysis was performed using a non-parametric Kruskal-Wallis test and Wilcoxon 2-sample test. Statistical differences in total bubble counts between all groups were significant at a p-value <.0001 using the Kruskal-Wallis test (chi-squared approximation). Pairwise comparisons of total bubble counts between groups were statistically significant at p-value <.05 using the Wilcoxon 2-sample test. Due to the number of samples taken, statistical significance between size classifications could not be performed.

**RESULTS**

Table 1 shows the CPB conditions and settings for the 3 groups tested. The arterial flow in the un-AV group is lower due to lack of venous assistance through the 19F portion of the
Centrifugal pump-assisted drainage produced over 300 microbubbles in one minute distal to the arterial filter when the full-duration dose of air was introduced into the venous line. Of these, 220 were greater than 80 μm in size. When the half-duration dose of air was introduced into the venous line, centrifugal pump-assisted drainage produced 253 microbubbles in one minute distal to the arterial filter. Of these, 108 were greater than 80 μm in size (Tables 2-4).

Vacuum-assisted drainage produced no microbubbles in one minute distal to the arterial filter when the full-duration and half-duration dose of air was introduced into the venous line (Tables 2-4). Vacuum-assisted drainage produced 41 microbubbles in one minute distal to the arterial filter when a venous line stopcock was left open for 30 seconds. These bubbles were between 40 μm and 80 μm in size (Table 5).

Unassisted drainage produced no detectable microbubbles distal to the arterial filter at all levels of venous air entrainment.

By the non-parametric Kruskal-Wallis test, there were overall significant differences in total bubble count among all groups tested (p<.0001). The following pairwise comparisons were statistically significant by the Wilcoxon test: BP-AV Full vs. BP-AV Half; BP-AV Full vs. un-AV Full; BP-AV Half vs. un-AV Half; BP-AV Full vs. V-AV Full; BP-AV Half vs. V-AV Half; V-AV Stopcock vs. un-AV Stopcock; and V-AV Stopcock vs. V-AV Full (p<.05).

**DISCUSSION**

Assisted venous drainage has increased in use due primarily to minimally invasive cardiac procedures. It has been in limited use previously for femoral venous cannulation situations such as redo cardiac procedures and emergent procedures requiring CPB. The basic idea behind assisted drainage is to increase the venous return through smaller venous canulae by applying a more negative pressure to the venous line than exists by gravity alone. This negative pressure is usually achieved via a vacuum source or by placing a pump in the venous line.

Oftentimes during CPB air becomes entrained in the venous line from a variety of sources. These sources may include loose purse-string sutures around the cannulation site, holes in the vena cava or venous system, or atrial-septal defects or patent foramen ovale with left atriotomy or ventriculotomy. In a typical gravity-drained CPB circuit, the venous air remains whole and should be dissipated within the venous reservoir. The mechanisms of air dissipation in the reservoir include buoyancy and filtration as the air passes through the venous filter. In this study, the venous reservoir had a venous filter made of a 47 μm polyester screen. Other reservoirs have no venous filters or filters which range from 150 μm to 200 μm in pore size (Medtronic, Sorin Biomedical, Cobe, Aovecor; Technical Specifications, Manufacturers’ Brochures). In an assisted drainage CPB circuit, the venous air is subjected to forces that differ from that of gravity drainage. The air is subjected to a greater degree of negative pressure, and with centrifugal pump assisted drainage, the air is subjected to kinetic energy imparted by the cones or vanes of the pump as well.

The effect that assisted drainage has on venous air, specifically that of GME production and transmission into the arterial line of the CPB circuit, has been unstudied. It has been shown that GME are created in the CPB circuit via oxygenators, temperature gradients, cavitation, vortexing, low reservoir levels, and cardiotomy suction (2,3,6). The GME production from these sources have generally been less than 45 μm (not including bubble oxygenators). However, no studies have been performed to show any link between venous air, assisted drainage, and GME in the arterial line leading to the patient.

It is clear, from the results of this study, that assisted venous drainage with a Biopump (BP-AV) can create GME in the CPB circuit when certain amounts of venous air are present. The GME that are created are passed through every component of the circuit and ultimately to the patient. The size and number of these GME which pass up the arterial line are remarkably large. Over 300 bubbles were counted distal to the arterial filter in just one minute of time. According to the detector, 220 of the bubbles were greater than 80 μm in size. With the half-duration dose of venous air over 250 bubbles were counted in one minute, 108 of those were greater than 80 μm in size. Since many studies consider GME greater than 50 μm as clinically relevant (1,2,3) and the incidence of neuropsychological deficits appear directly related to the number of microemboli (4,5), these results should cause some concern. Of significance, bubble detectors are limited and may require further investigation to achieve an absolute quantitative analysis. However, these results clearly indicate that GME of potentially clinically significant size can be transmitted to the patient.

The BP-AV and V-AV did an equal job in creating venous assistance. In both of these groups a venous pressure of negative 50 mmHg created identical returns. The difference in the GME count between the Biopump group and the Vacuum group is probably due to the high kinetic energy imparted upon the air by the cones of the Biopump. In both groups the negative pressure was identical. The only differentiating factor was the pump itself. It appears that the pump breaks the air into small bubbles which become suspended in the blood, passing through the reservoir and all other components. The vacuum better preserves the air in larger pieces which are more easily dissipated through buoyancy and filtration. However, when the stopcock

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**Table 5: Total bubble count, size 40 μm to 80 μm, mean and standard deviation**

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>un-AVD</th>
<th>V-AVD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open Stopcock; 30 seconds</td>
<td>5</td>
<td>0 ± 0</td>
<td>41 ± 21</td>
</tr>
</tbody>
</table>

un-AVD = un-assisted venous drainage; V-AVD = vacuum-assisted venous drainage
was opened on the venous line, the vacuum assist did pass some GME distal to the arterial filter.

There were no GME detected distal to the filter in any of the unassisted drainage trials. In a typical gravity-drained system, venous air is usually regarded as insignificant. With the advent of assisted venous drainage this view may need some adjusting. Venous line air will probably always exist despite best efforts of the surgeon, and the question may be how to minimize the impact venous air will have on GME production. Because air passes quickly and often unnoticed through the venous line due to the higher negative pressure, it is difficult to react quickly enough. In the case of Biopump assisted drainage, the best remedy would be to shut the pump off until the air has passed. However, that is difficult to do in a timely fashion and once the air has been exposed to the kinetic energy of the cones or vanes, the damage is done.

Since venous air is at the crux of this study, the amount of air injected, its frequency, or the manner in which it was injected should be representative of a clinical situation. In a clinical situation the amount of venous air and the frequency with which it occurs is variable.

With regards to the amount of air, a 30 ml bolus is not unrealistic. Ten 30 ml bolus in 30 seconds may or may not be on the high side, but 300 ml in 30 seconds is certainly realistic. An open stopcock on the venous line will entrain air, but the amount or frequency is probably a function of the negative pressure within the venous line. In our case it could be observed that air was more quickly "sucked" into the venous line through the stopcock with V-A VD compared to un-A VD. For that reason alone, the total volume of air entrained is greater in the V-AVD group compared with the un-AVD group (open stopcock group only). The manner in which air enters the venous line may or may not be similar to the air injections in this study. For example, in this study, air was injected fairly rapidly through a small luer fitting on the venous line. In a clinical situation the same volume of air may enter the venous line, but through a larger opening with less turbidity. Whether this would make a difference is questionable, considering that the air will be subjected to the force of a high-velocity pump.

The minimum conditions necessary to cause GME beyond the arterial filter would be interesting to know. Other variables such as a smaller pore-size arterial filter may have some effect on outcome. Oxygenator design and reservoir design may also impact the degree of GME transmission. These variables were beyond the scope of this study but are certainly relevant.

CONCLUSION

Biopump assisted venous drainage may present serious problems for the patient in the presence of venous line air. It is clear that gaseous micro-emboli of clinical relevance can be passed through the CPB circuit and into the arterial line leading to the patient. These micro-emboli are passed through the oxygenator and arterial filter. To a lesser degree, vacuum assisted venous drainage may produce gaseous micro-emboli in the presence of large amounts of venous air. Unassisted venous drainage produced no gaseous micro-emboli in the presence of venous air.

ACKNOWLEDGEMENTS

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REFERENCES