Residual air in the venous cannula increases cerebral embolization at the onset of cardiopulmonary bypass

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Abstract

Objective: When the right atrium (RA) cannula is connected to the venous return line of the cardiopulmonary bypass (CPB) circuit, air is often introduced. Air in the venous cannula may increase cerebral air embolization at initiation of CPB despite the arterial line filter. We measured the volume of air present in the venous cannula after cannulation of the RA. Transcranial Doppler quantified emboli as high-intensity transient-signals (HITS) in both middle-cerebral arteries (MCA) at the beginning of CPB.

Methods: After RA cannulation, the air column in the venous line was measured and the total volume calculated using the known lumen diameter. CPB onset was defined as the instant when the CPB machine started moving the patient’s blood from the RA into the venous reservoir. Starting from CPB onset, HITS were counted: (a) until completion of the first minute on CPB (1-min count) and (b) until aortic cross clamping (pre-clamping count).

Results: We studied 135 patients during coronary artery bypass surgery operated on by 10 cardiac surgeons. HITS during onset of CPB were detected in 95% of patients. Median counts were 10 HITS (25th, 75th percentiles: 3, 26) at 1-min and 21 HITS (8, 51) during pre-clamping. A significant correlation was found between the volume of air in the venous cannula and the HITS counts ($r = 0.524, p < 0.0001$). Absence of retained air was associated with lower HITS counts [3 HITS (1, 11)] compared with any amount of air [13 HITS (4, 29), $p = 0.002$]. The volume of air in the venous cannula, the MCA mean blood flow velocity and the pre-clamping time were the only independent predictors of the pre-clamping HITS counts ($p < 0.001$).

Conclusion: Air in the venous cannula can result in HITS in the MCA. Minimizing the volume of air introduced into the venous cannula after cannulation of the RA can decrease cerebral air embolization at the beginning of CPB.

Keywords: Cerebral embolization; Cardiopulmonary bypass; Transcranial Doppler

1. Introduction

Systemic microembolization is considered a potential mechanism of injury to the brain [1] and other organs such as the kidney [2] during cardiopulmonary bypass (CPB). The composition of the majority of these emboli is gaseous [3], but a smaller fraction is solid particles derived from lipid, clots, thrombi, and atherosclerotic plaques [3,4]. Emboli can be detected in the cerebral circulation as high-intensity transient signals (HITS) using transcranial Doppler (TCD) [5]. Previous studies [1,6—9] have reported that between 6 and 9% of the total number of emboli detected during coronary artery bypass (CABG) surgery occur during the onset of CPB. These embolic signals are assumed to represent air bubbles delivered into the systemic circulation as a result of air retained in the components of the extracorporeal circuit [7,8,10]. Taylor et al. [11], however, have shown that air inadvertently introduced into the venous cannula due to non-occlusive purse strings or caval snares may result in HITS during CPB. During cannulation of the right atrium (RA), air often remains in the venous cannula when the cannula is connected to the venous return line of the CPB circuit. Air is not completely eliminated by the arterial line filter [12,13], and so the presence of air in the venous cannula increases the risk of cerebral air embolization during initiation of CPB. Although the role of cerebral air embolization in causing neurological damage is still debatable [14,15], it seems good practice to minimize the risk of air being introduced into the cerebral circulation. In this investigation, we measured the volume of air retained in the venous cannula after cannulation of the RA and TCD was used to quantify HITS in the cerebral circulation on initiation of CPB. We hypothesized that the volume of air retained in the venous cannula before CPB would be correlated with the counts of HITS in the middle cerebral arteries (MCA) during initiation of CPB.
2. Materials and methods

After IRB approval, patients undergoing CABG surgery under CPB participating in a clinical trial assessing the neuroprotective effects of hypothermia during CPB [16] were studied. Patients were randomized to two different nasopharyngeal temperatures (34 °C or 37 °C) under CPB. Cannulation of the ascending aorta was achieved by using a short (20—22 Fr Medtronic, Minneapolis, MN, USA) or long-tip cannula (size: 24 Fr, Sarns Flex, Ann Arbor, MI, USA) according to the surgeon’s preference. The RA was cannulated through the atrial appendage using a two-stage venous cannula (32/40 or 36/46 Fr; Medtronic®, Minneapolis, MN, USA). The venous cannula was attached by a connector to a 0.5 in. diameter polyvinyl chloride (PVC) tubing (length: 238 cm) connected to the venous inlet of the reservoir. Surgeons were free to practice their individual technique of cannulation and were not aware of the TCD signals at the time of surgery.

2.1. Extracorporeal circuit

The characteristics of our extracorporeal circuit and standard CPB protocol have been described in detail elsewhere [17]. The circuit was flushed with medical grade filtered CO₂, primed with 1400 ml of Ringers lactate (5000 IU heparin), and the solution was continuously re-circulated using a scale and the total volume calculated using the known lumen diameter of the tubing line according to the following formula: air volume = \( \pi r^2 L \), where \( \pi \) (pi) is 3.1416, \( r \) = radius, and \( L \) = length of air column in centimeters.

2.2. Measurement of air in the venous cannula

After the venous cannula and its connections were secured, the venous line was inspected for the presence of air. The surgeon held the venous line from the connector in order to maintain the end of the tubing above the level of the heart. This maneuver facilitated the displacement of the air column to the upper wall of the venous line close to the venous cannula. Subsequently, the air column was measured using a scale and the total volume calculated using the known lumen diameter of the tubing line according to the following formula:

### 2.3. Transcranial Doppler

After induction of anesthesia, 2 MHz pulsed-wave Doppler probes (sample volume: 10 ml) were secured on the temporal area bilaterally for monitoring HITS and flow velocities in the right and left MCA. All Doppler signals were reviewed off-line by an experienced ultrasonographer (RAR). The recording Doppler parameters, equipment, criteria for differentiating between HITS and non-embolic signals as well as the degree of inter-observer agreement are described in detail elsewhere [17]. A 9-dB intensity threshold was used during Doppler signal recording. The onset of CPB was defined as the instant when the CPB machine started moving the patient’s blood from the RA into the venous reservoir and this time was marked on the TCD record. Starting from the onset of CPB, HITS were counted: (a) until the completion of the first minute of CPB (1-min count) and (b) until the application of the aortic cross clamp (pre-clamping count). Interventions or manipulation of the aorta were kept at minimum during this period.

2.4. Statistical analysis

HITS counts are presented as medians (25th, 75th percentiles) and their range. Spearman rank correlation was used to investigate the association between HITS counts and air volume or between HITS counts and the time from the onset of CPB to aortic cross clamping. A linear regression analysis was used to determine the best fitting curve. The counts of HITS, air volumes, and time to aortic clamping were stratified by surgeon, type of aortic cannula, and body temperature. Their differences were assessed by non-parametric Mann—Whitney or Kruskal—Wallis tests. The critical value of statistical significance was \( p < 0.05 \). A multivariate linear regression analysis was performed using the count of HITS as dependent variable and incorporating significant univariate descriptors. The nasopharyngeal temperature was kept in the regression model as the design variable. Analyses were performed using SPSS software (version 13.0).

3. Results

One hundred and thirty-five consecutive patients who underwent CABG surgery under CPB by 10 cardiac surgeons were studied. Table 1 shows demographics, CPB characteristics, and number of patients according to participating surgeons and body temperature. The median volume of air observed in the venous cannula before CPB was 1.14 ml (0.51, 2.40 ml) and the median time between the onset of CPB and the application of the aortic cross clamp was 4 min (2, 8 min). HITS in the MCA in the first minute after initiation of CPB were detected in 95% of our patients. The median

### Table 1

Demographics, characteristics of CPB and distribution of patients per surgeon

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>68 ± 6</td>
</tr>
<tr>
<td>Mean cerebral blood flow velocity <em>a</em> (cm/s)</td>
<td>38 ± 12</td>
</tr>
<tr>
<td>Hematocrit before CPB</td>
<td>0.36 ± 0.04</td>
</tr>
<tr>
<td>Hematocrit during CPB</td>
<td>0.26 ± 0.04</td>
</tr>
<tr>
<td>Short-tip cannula (20—22 Fr)</td>
<td>112 (83)</td>
</tr>
<tr>
<td>Long-tip cannula (24 Fr)</td>
<td>23 (17)</td>
</tr>
<tr>
<td>Nasopharyngeal temperature 37 ºC</td>
<td>67 (50)</td>
</tr>
<tr>
<td>Nasopharyngeal temperature 34 ºC</td>
<td>68 (50)</td>
</tr>
<tr>
<td>Surgeon A</td>
<td>18 (13)</td>
</tr>
<tr>
<td>Surgeon B</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Surgeon C</td>
<td>40 (30)</td>
</tr>
<tr>
<td>Surgeon D</td>
<td>25 (18)</td>
</tr>
<tr>
<td>Surgeon E</td>
<td>31 (23)</td>
</tr>
<tr>
<td>Surgeon F</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Surgeon G</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Surgeon H</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Surgeon I</td>
<td>6 (4)</td>
</tr>
<tr>
<td>Surgeon J</td>
<td>4 (3)</td>
</tr>
</tbody>
</table>

CPB: cardiopulmonary bypass.

*a* It indicates the average velocity from right and left MCA (middle cerebral artery) in all patients measured at the end of the first minute of CPB.
count of HITS per patient from onset of CPB to aortic cross clamping was 21 HITS (8, 51 HITS) (range: 0–221). Sixty-three percent of these HITS occurred within the first minute of CPB [median: 10 HITS (3, 26 HITS) (range: 0–101)].

3.1. HITS counts during the first minute of CPB

There was a significant correlation between the volume of air measured in the venous line and the count of HITS per patient during the first minute of CPB \( (r = 0.524, p < 0.0001) \). In this relationship, larger volumes of air introduced in the venous line were associated with higher counts of HITS. This association is illustrated in Fig. 1 for all patients. In 13% of the patients there was no visible air retained in the venous line. Patients who had no visible air had lower counts of HITS compared with those where air was observed [no retained air, median HITS count: 3 HITS (1, 11 HITS); retained air, median HITS count: 13 HITS (4, 29 HITS), \( p = 0.002 \)]. Significant differences were found among participating surgeons in both the volume of air retained in the venous line \( (p < 0.0001) \) and the count of HITS during the first minute of CPB \( (p = 0.045) \). Fig. 2 shows the volume of retained air and the counts of HITS stratified by surgeon. In addition, the mean blood flow velocity in the MCA measured at the end of the first minute of CPB was significantly associated with the count of HITS \( (r = 0.364, p < 0.001) \). Patients with blood flow velocities equal to or greater than 40 cm/s \( [n = 48 \text{ (range: 40–85 cm/s)}] \) had higher counts of HITS within the first minute of CPB [median count: 25 HITS (8, 38 HITS)] compared with those with lower flow velocities \( [n = 87, \text{median count: 7 HITS (2, 21 HITS)}, p < 0.0001] \). There were no significant differences in the count of HITS due to the differences in nasopharyngeal temperature \( [37 \degree C, \text{median count: 12 HITS}] \).

3.2. HITS counts during pre-clamping

There was a significant correlation between the volume of air introduced into the venous cannula and the pre-clamping count of HITS \( (r = 0.507, p < 0.0001) \). Several factors were associated with differences in the count of HITS during this measurement. These included surgeon \( (p < 0.0001) \), duration between the onset of CPB and aortic cross clamping \( (r = 0.451, p < 0.001) \), MCA mean flow velocity \( (r = 0.342, p < 0.0001) \), and length of the tip of the aortic cannula \( (p = 0.01) \). Differences in nasopharyngeal temperature at initiation of CPB did not influence the pre-clamping count of HITS \( [37 \degree C, \text{median count: 20 HITS (9, 51 HITS)}], 34 \degree C, \text{median count: 22 HITS (8, 50 HITS)}, p = 0.963] \). Although higher counts of HITS during this period were observed in patients whose aorta was cannulated with a short-tip cannula relative to the long-tip cannula \( [\text{short cannula, median HITS count: 28 HITS (8, 55 HITS), long cannula, median HITS count: 12 HITS (4, 30 HITS), } p = 0.01] \), surgeons who cannulated the aorta with the short-tip cannula had longer durations of the pre-clamping period than those who used the long-tip cannula \( (p = 0.003) \). The median pre-clamping duration in patients with a short-tip cannula was 5 min (2, 8 min); while in those with a long-tip cannula was only 2 min (2, 4 min).

3.3. Multivariate linear regression analysis

Due to the fact that several variables including the volume of air in the venous cannula, MCA blood flow velocities,
length of the aortic cannula, and the duration of the pre-clamping period became significant during the univariate analysis, their relationship as independent predictors on the pre-clamping count of HITS was investigated using a multivariate regression analysis. Table 2 summarizes these results.

The volume of air in the venous cannula, the MCA mean blood flow velocity at the end of the first minute of CPB, and the duration between CPB onset and the time of aortic cross clamping were the only independent predictors of the pre-clamping count of HITS ($p < 0.0001$). The length of the tip of the aortic cannula did not have any significant effect on the pre-clamping counts of HITS ($p = 0.37$).

### 4. Discussion

Although modern techniques of CPB and better circuit designs have minimized the fatal cases of massive air embolism described in earlier studies [18], recent investigations [12, 13, 17] suggest that systemic air microembolism derived from extracorporeal sources still represents a common problem during conventional CPB. Several clinical studies [1, 6, 8, 9] have documented large amounts of cerebral microemboli during initiation of CPB. This was assumed to be the result of air retained within the CPB circuit [3, 8, 10, 12], but the precise mechanisms contributing to this phenomenon were not clearly identified.

In the present study, the onset of CPB was associated with varying numbers of HITS in the cerebral circulation in 95% of patients undergoing CABG surgery. The counts of HITS in the MCA during initiation of CPB were correlated with the volume of air introduced into the venous cannula at the time of connecting the RA cannula to the venous return line of the CPB circuit (see Fig. 1). These findings suggest that individual techniques of de-airing the venous cannula and its connections have a significant impact on the counts of HITS in the MCA at the onset of CPB (see Fig. 2). The present results are in agreement with a previous in vitro study [12], which demonstrated that air introduced into the venous line always resulted in increased embolic activity distal to the arterial filter. Moreover, we found that careful de-airing of the venous cannula and its connections decreased the number of HITS delivered to the brain during initiation of CPB. Patients with no visible air in the venous line had lower counts of HITS at the beginning of CPB compared with those where air was seen. The fact that a few HITS occurred in the absence of visible air in the venous line suggests that other sources might contribute to the incidence of cerebral emboli during the onset of CPB. One of the most likely sources is the presence of residual air entrapped in the extracorporeal circuit due to failure to completely de-air the arterial line filter (ALF), tubing connectors, or ports before CPB [3, 10].

Several factors present during the onset of CPB may influence the speed of air bubbles traveling from the venous return line into the systemic circulation. These include the speed of venous return [7, 12], low volume level in the reservoir [3, 10, 17], short time for achieving full flow CPB (3, 10) and the physical characteristics of the venous reservoir [12, 17]. The internal design of the extracorporeal components may also influence the ability of the circuit to remove air bubbles [12, 17]. Once air has been introduced into the venous line, venous reservoirs with a long central conduit that extends the venous inlet to the bottom of the reservoir in close approximation to the outflow may facilitate the delivery of air bubbles into the systemic circulation particularly under conditions of low reservoir volume such as those occurring at the onset of CPB [17]. In this type of circuit, air bubbles are less likely to float to the top of the reservoir and may be siphoned directly into the outflow. In addition, a sudden increase in the pump flow rate for achieving full-flow CPB shortens the circulating time of blood between the aortic cannula and the carotid arteries, and increases the speed of air bubbles [3, 7, 13, 17] increasing the likelihood that they will reach the brain before being reabsorbed. While pericardial suction and venting have been considered potential sources for the introduction of air to the venous circuit, we assume that the contribution of pericardial suction and aortic venting on the count of HITS at the beginning of CPB was minimal. In our investigation, pericardial suction was collected into a separate cardiotomy reservoir. Due to the low volume of suction collected prior to and at the onset of CPB, our perfusionists rarely returned the cardiotomy volume into the systemic circulation prior to aortic cross clamping. In addition, active venting was usually deferred until after the first dose of cardioplegia was delivered.

Our study demonstrated that the majority of HITS (63%) detected between the beginning of CPB and aortic cross clamping occurred within the first minute of CPB. The volume of air introduced in the venous cannula, the MCA mean blood flow velocities at the end of the first minute of CPB, and the duration of the period between the onset of CPB and application of the aortic cross clamp were independent predictors of the pre-clamping count of HITS. Our finding that higher flow velocities in the MCA were associated with higher counts of HITS supports the assumption that increases in cerebral perfusion in the presence of systemic embolization result in a greater incidence of cerebral emboli [9]. The results of experimental studies suggest that increased cerebral blood flow is the most likely mechanism for the
higher counts of cerebral emboli found in the brains of hypercarbic animals after systemic embolization under CPB when compared with those under hypocarbia [19].

In the present study, nasopharyngeal temperature and the length of the tip of the aortic cannula were not independent predictors of the pre-clamping count of HITS. Previous investigators [17,20] have reported that the long-tip aortic cannula delivers fewer emboli to the cerebral vasculature during CPB compared to the short-tip cannula. Despite the different count of HITS during the pre-clamping period between the two types of aortic cannulae, this relationship was obscured by the stronger association between the HITS counts and the pre-clamping times and the small sample size in the group with the long-tip cannula.

The clinical relevance of cerebral air embolization on neurologic and cognitive outcome is debatable [14,15]. Studies that have documented large quantities of gaseous microemboli during CPB have reported varying incidences of postoperative clinical effects, ranging from non-neurological sequelae [8] or mild cognitive dysfunction [14] to seizures, coma, and death [21]. Although experimental studies have shown that cerebral blood flow or metabolism remains unaffected after air embolization has occurred during hypothermic CPB [22], cerebral air embolization is a concern due to the potentially damaging effect of air bubbles on the cerebral vascular endothelium [23] and the resultant disruption of the blood–brain barrier [21,22]. In addition, experimental studies indicate that air bubbles in blood may promote complement activation [24], leukocyte aggregation [3,22], increased platelet adherence [25], and fibrin deposition in the microvasculature [24] that may predispose to solid emboli.

It has proven difficult to establish a dose–response relationship between the count of HITS during CPB and quantitative measures of cognitive outcome. While some previous studies have found correlation between HITS counts and behavioral outcomes [1,14,26,27], another study failed to find a correlation [15]. Part of the problem relates to the limitation of current Doppler systems in differentiating embolus size and composition [28]. This may be important as previous studies indicate that the composition and size of emboli may have a major impact on the severity of brain injury [29].

In summary, we investigated the effect of different volumes of air retained in the venous cannula on cerebral embolization during the onset of CPB. We found that larger volumes of air introduced into the venous cannula before CPB increase the incidence of cerebral microemboli during the beginning of CPB. Differences in individual techniques of de-airing the venous cannula and its connections have a significant impact on both the volume of air retained in the venous cannula and cerebral embolization during initiation of CPB. Although the clinical relevance of cerebral air embolization in causing neurological damage is unclear, best surgical practice should attempt to reduce the amount of air delivered to the cerebral circulation during CPB. Cerebral embolization, which frequently occurs during the onset of CPB, can be minimized by carefully de-airing the venous cannula when the RA cannula is connected to the venous return line of the CPB circuit.

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References


