Increase of Alveolar Pressure Reduces Systemic-to-Pulmonary Bronchial Blood Flow in Humans

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We studied the effects of positive alveolar pressure (P_{A}) on systemic to pulmonary bronchial blood flow, {\dot Q}_{br}^{int}, in humans. The {\dot Q}_{br}^{int} was measured during total cardiopulmonary bypass as the volume of blood accumulating in the left heart. This blood was vented by gravity from the left heart via a cannula introduced in the right upper pulmonary vein and advanced to the lowest portion of the left heart. In group A (n = 10) the {\dot Q}_{br}^{int} was measured for 25 to 95 min with constant P_{A} (4.0±0.2 cm H_{2}O, mean ± SE). In group B (n = 10) {\dot Q}_{br}^{int} was measured for 20 min with P_{A} = 4.1±0.2 cm H_{2}O and for a further 20 min with P_{A} = 14.1±0.4 cm H_{2}O. The {\dot Q}_{br}^{int} ranged between 0.32 and 2.76 percent of cardiac output (pump flow) and remained constant with time (group A). The increase of P_{A} from 4.1±0.2 to 14.1±0.4 cm H_{2}O reduced {\dot Q}_{br}^{int} by ~40 percent (p<0.01, group B). We conclude that positive P_{A} reduces {\dot Q}_{br}^{int} during total cardiopulmonary bypass. Therefore, we advise using low P_{A} during assisted ventilation to preserve bronchial blood flow. (Chest 1989; 96:1081-85)

Studies in dogs and sheep have shown that bronchial blood flow to the lung is reduced by PEEP, a technique frequently used during mechanical ventilation in patients with respiratory failure. A reduction of bronchial blood flow may be deleterious for the survival of the lung parenchyma, particularly in some circumstances; eg, in the presence of lung injury, when pulmonary circulation may be compromised and bronchial blood flow increases, or in the presence of pulmonary embolism, when bronchial blood flow is the major source of blood to the lung parenchyma. However, it is not known whether a relationship between alveolar pressure and bronchial blood flow, similar to that observed in dogs and sheep, exists in humans. The present study was undertaken to investigate the effects of positive alveolar pressure (P_{A}) on bronchial blood flow in humans.

Material and Methods

Twenty patients (17 men and three women) were studied while undergoing coronary artery bypass surgery for coronary artery disease. None had lung disease, heart failure, pulmonary hypertension (mean pulmonary artery pressure <20 mm Hg at preoperative cardiac catheterization), or congenital cardiac malformations. All provided written informed consent to both the surgical and experimental procedures. The study had been approved by the local ethics committee. The patients' ages were 60.6±5.4 years (mean ± SD; range, 49 to 68 years). Total cardiopulmonary bypass was achieved using a standard technique. Blood flowed from a two-stage venous cannula (William Harvey extracorporeal cannula, 34 to 46 F Bard) introduced into the inferior vena cava and advanced into the right atrium, to an O_{2}-heat exchanger (Oxy 41, Sorin), to the cardiopulmonary bypass pump (HL10, Gambro) and then, through the aortic cannula (21 to 24 F), back into the aorta. Proximal to the aortic cannula the aorta was clamped as was the pulmonary artery. Through the right superior pulmonary vein a cannula (18 F) was placed in the lowest portion of the left heart. This usually was the left atrium, since the surgeon habitually lifted the cardiac apex to reach the inferoposterior surface of the heart. A second small cannula (8 F), open to atmospheric pressure, was placed, again through the right superior pulmonary vein into the left atrium, so that left atrial pressure was atmospheric. The larger left atrial cannula was connected to a calibrated cylinder placed ~50 cm below the level of the left atrium. The cylinder was connected through a stopcock to a roller pump by which the blood was propelled into the cardiectomy reservoir (Fig 1). The patients were cooled systemically and the heart was arrested with cardioplegic solution (~700 ml). During total cardiopulmonary bypass, the patients were not ventilated. The lungs were kept inflated by a constant flow of air ranging between 4 and 8 L/min. The P_{A} was set by adjusting an expiratory PEEP valve. Alveolar and systemic blood pressures, pump flow (cardiac output), and esophageal and rectal temperatures were continuously monitored.

Systemic to pulmonary bronchial blood flow, {\dot Q}_{br}^{int}, was measured as the volume of blood returning to the left heart. This blood flowed by gravity into the calibrated cylinder, where it was collected during the entire study for at least 3 min every 5 min. The mean {\dot Q}_{br}^{int} was calculated every 5 min. During the first 10 min of cardiopulmonary bypass, {\dot Q}_{br}^{int} was collected, but these measurements were always discarded because cardioplegic solution might be mixed with bronchial blood. Since during the surgical procedure the cardiac output (pump flow) was changed, depending on systemic blood pressure, {\dot Q}_{br}^{int} is reported both as absolute flow and as a percentage of cardiac output.

Study Protocol

In group A (n = 10; mean age, 61.8±5.0 [SD] years) the {\dot Q}_{br}^{int}
was measured as described. Measurements were discontinued during rewarming of the patients, when esophageal temperature increased by more than 2°C from the lowest esophageal temperature recorded during cardiopulmonary bypass. In group A, the PA was kept constant at 4.0 ± 0.2 cm H₂O throughout the study.

In group B (n = 10, mean age 59.4 ± 6.0 (SD) years) the Q̇byp was measured for 20 min with PA = 4.1 ± 0.2 cm H₂O. Then PA was increased in a step-by-step fashion during 2 min to 14.1 ± 0.4 cm H₂O. While PA was constant (range 13 to 16 cm H₂O), the Q̇byp was measured for a further 20 min. In three patients the duration of the cardiopulmonary bypass allowed us to reduce PA to 4.0 ± 0.3 cm H₂O and to measure the Q̇byp for an additional 10 min.

Statistical Analysis

Data are reported as mean ± SE except as noted. In group B we tested the difference between the Q̇byp measurements made during the last 5 min of collection with PA = 4.1 ± 0.2 cm H₂O and the four Q̇byp measurements obtained with PA = 14.1 ± 0.4 cm H₂O. To do so we used the paired t test with the Bonferroni correction because multiple comparisons were made. Therefore, we accepted as significant p<0.01.

Table 1—Group A: Hemodynamic Measurements and Temperatures, Mean (± SE)*

<table>
<thead>
<tr>
<th>Time, min</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>20</th>
<th>25</th>
<th>30</th>
<th>35</th>
<th>40</th>
<th>45</th>
<th>50</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>8</td>
<td>6</td>
<td>6</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Q̇byp ml/min</td>
<td>38 (4)</td>
<td>39 (5)</td>
<td>40 (4)</td>
<td>42 (5)</td>
<td>41 (5)</td>
<td>35 (5)</td>
<td>35 (5)</td>
<td>34 (5)</td>
<td>37 (5)</td>
<td>36 (6)</td>
</tr>
<tr>
<td>Psa, mm Hg</td>
<td>64.1 (3.0)</td>
<td>59.1 (3.6)</td>
<td>60.4 (3.8)</td>
<td>69.6 (3.5)</td>
<td>73.8 (3.6)</td>
<td>71.9 (5.1)</td>
<td>75.3 (4.1)</td>
<td>72.0 (6.1)</td>
<td>77.8 (8.5)</td>
<td>64.8 (2.8)</td>
</tr>
<tr>
<td>CO, L/min</td>
<td>2.7 (0.2)</td>
<td>2.7 (0.2)</td>
<td>2.8 (0.2)</td>
<td>2.8 (0.2)</td>
<td>2.7 (0.2)</td>
<td>2.6 (0.2)</td>
<td>2.3 (0.2)</td>
<td>2.3 (0.2)</td>
<td>2.3 (0.2)</td>
<td>2.3 (0.2)</td>
</tr>
<tr>
<td>Tes, °C</td>
<td>26.7 (0.5)</td>
<td>26.7 (0.4)</td>
<td>26.8 (0.7)</td>
<td>26.8 (0.3)</td>
<td>27.0 (0.4)</td>
<td>26.8 (0.2)</td>
<td>26.7 (0.3)</td>
<td>26.6 (0.4)</td>
<td>26.9 (0.5)</td>
<td>27.8 (0.6)</td>
</tr>
<tr>
<td>T rectum, °C</td>
<td>29.9 (0.6)</td>
<td>29.8 (0.6)</td>
<td>29.3 (0.5)</td>
<td>29.3 (0.4)</td>
<td>28.8 (0.4)</td>
<td>28.9 (0.5)</td>
<td>28.6 (0.5)</td>
<td>28.3 (0.5)</td>
<td>28.2 (0.5)</td>
<td>28.8 (0.4)</td>
</tr>
</tbody>
</table>

*Q̇byp = mean systemic to pulmonary bronchial blood flow; Psa = mean systemic blood pressure; CO = cardiac output (pump flow); Tes, T rectum = esophageal and rectal temperatures.

Results

**Group A**

Q̇byp was measured for an average period of 53.5 ± 6.2 min (range, 25 to 95 min). The Q̇byp remained constant with time (Table 1, Fig 2) and ranged between 0.32 and 2.76 percent of cardiac output (Fig 2). Mean systemic blood pressure, cardiac output (pump flow), and esophageal and rectal temperatures were constant (Table 1).

**Group B**

During the first 20 min of the study, PA was 4.1 ± 0.2 cm H₂O. Mean Q̇byp ranged as absolute flow between 44 ± 6 and 42 ± 4 ml/min (Table 2) and as percent of cardiac output between 1.54 ± 0.22 and 1.69 ± 0.22 (Fig 3 and 4). When PA was elevated to 14.1 ± 0.4 cm H₂O, the Q̇byp fell in every patient but one (Fig 3). The mean Q̇byp was 31 ± 4 (1.13 ± 0.16) and 27 ± 5 (0.96 ± 0.19) ml/min (percentage of cardiac output) in the first 5 min and between the 15th and 20th minute of PA elevation, respectively (p<0.01 compared with PA = 4.1 cm H₂O; Table 2, Fig 4). Hemodynamic measurements and esophageal and rectal tempera-
tures were constant (Table 2). In the three (patients 12, 13, and 15, Fig 3) in whom it was possible to reduce PA to ~4 cm H2O, the mean Qbr(p) was 1.28 ± 0.12 (PA = 4.1 ± 0.0 cm H2O), 0.74 ± 0.09 (PA = 14.2 ± 0.1 cm H2O), and 1.22 ± 0.09 (PA = 4.0 ± 0.1 cm H2O) percent of cardiac output.

**DISCUSSION**

In this study systemic-to-pulmonary bronchial blood flow, Qbr(p), was measured in humans during total cardiopulmonary bypass. The Qbr(p), both as absolute flow and as a percentage of cardiac output, remained constant as long as alveolar pressure (PA) was constant; the increase in PA reduced Qbr(p) in a significant manner.

To measure Qbr(p), we used a technique similar to that previously described by Baile et al. Unlike those authors, we clamped the pulmonary artery to prevent blood leakage through the pulmonary valve and blood flow from the right heart to the pulmonary circulation. Theoretically this could happen secondary to increased alveolar and right heart pressures, the latter due to incomplete blood drainage from the right atrium. The Qbr(p) measurements did not prolong the surgery or interfere with the surgical procedure. Qbr(p) was stable over a wide range of time from 25 to 95 min (Fig 2) and was in the same range of that reported by Baile et al on humans without lung diseases during total cardiopulmonary bypass and by other authors on different animal species. Even though none of the patients who participated in our study had clinical lung disease, the relatively wide Qbr(p) range reported (Fig 2 and 3) might be due to subclinical lung impairment. Indeed, only 4/20 patients were nonsmokers (patients 2, 3, 11, and 17; Fig 2 and 3), and nonsmokers tended to have lower flows.

The Qbr(p) was not measured during the first 10 min

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**Table 2—Group B: Hemodynamic Measurements and Temperatures, Mean (± SE)*

<table>
<thead>
<tr>
<th>Time, min</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>20</th>
<th>5</th>
<th>15</th>
<th>20</th>
</tr>
</thead>
</table>
| PA
| 4.1 ± 0.2 cm H2O | | | | | | | |
| No. | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Qbr(p), mL/min | 44 (6) | 43 (5) | 44 (4) | 42 (4) | 31* (4) | 28* (4) | 27* (4) |
| Psa, mm Hg | 62 (3.3) | 62 (4.5) | 63 (4.1) | 65 (3.8) | 66 (3.2) | 62 (2.9) | 66 (3.3) |
| CO, L/min | 2.9 (0.1) | 2.7 (0.1) | 2.7 (0.1) | 2.6 (0.1) | 2.7 (0.1) | 2.7 (0.1) | 2.7 (0.1) |
| Tc, °C | 27.0 (0.1) | 26.9 (0.2) | 26.9 (0.2) | 27.0 (0.3) | 27.1 (0.3) | 27.3 (0.3) | 27.6 (0.4) |
| Trectum, °C | 29.1 (0.3) | 28.8 (0.3) | 28.7 (0.3) | 28.7 (0.3) | 28.7 (0.3) | 28.8 (0.3) | 29.1 (0.3) |

*Qbr(p) = mean systemic to pulmonary bronchial blood flow; Psa = mean systemic blood pressure; CO = cardiac output (pump flow); Tc, T rectum = esophageal and rectal temperatures.

*p < 0.01 from PA = 4.1 ± 0.2 cm H2O.
of cardiopulmonary bypass. This was necessary because some cardioplegic solution injected into the aortic root might drain into the left atrium via thebesian veins and therefore might be vented mixed with bronchial blood. Flow of cardioplegic solution through the coronary vessels is present for only a short time after the cardioplegic solution injection, when aortic root pressure (proximal to aortic clamp) is greater than left and right atrial pressures. We judged that after a few minutes, aortic root pressure should be returned to zero, as suggested by the visual regression of aortic root distention and that consequently the flow of cardioplegic solution into the left atrium should be negligible.

Different factors may influence the $Q_{br(p)}$ during total cardiopulmonary bypass including the surgical procedure, body temperature, and the hemodynamic status. The surgical procedure was similar in all of the patients and therefore should equally influence groups A and B. Body temperature was unphysiologically low. It is known that a reduction of body temperature reduces $Q_{br(p)}$. Therefore, to avoid the effects of body temperature changes on $Q_{br(p)}$, we continuously monitored esophageal and rectal temperatures and report only those measurements obtained during stable thermal conditions (Tables 1 and 2). Systemic blood pressure and cardiac output influenced $Q_{br(p)}$ as demonstrated by experimental studies. However, in our study changes in the hemodynamic status were negligible during total cardiopulmonary bypass (Tables 1 and 2). Nonetheless, we have taken into account the possible effects of cardiac output (pump flow) changes on $Q_{br(p)}$ by reporting $Q_{br(p)}$ both as absolute flow and as percentage of cardiac output (pump flow).

Our method measures the portion of bronchial blood flow that drains into the pulmonary circulation and does not account for the portion that drains, via bronchial veins, into the azygos vein. It is widely accepted that bronchial blood flow to all the lung parenchyma (intrapulmonary bronchi and lung tissue) drains via the pulmonary circulation into the left atrium, that it is the sole bronchial blood flow significantly reduced by positive PA in animals, and that it is 80 percent of total bronchial blood flow. This partitioning of left and right drainage of bronchial circulation is not affected by the presence or the absence (as in our study) of pulmonary blood flow. The PA was ~4 cm H$_2$O during control conditions (group A and first 20 min in group B). This is the standard PA applied at our Institute during cardiopulmonary bypass to prevent pulmonary atelectasis. The value 14 cm H$_2$O (group B second part of the study) was chosen because it is an end-expiratory pressure frequently reached in patients during mechanical ventilation and is also the mean end-expiratory pressure previously used in animal studies to evaluate the effects of elevated PA on $Q_{br(p)}$. Particularly with elevated PA, some of the bronchial blood flow pooled in the lungs might cause pulmonary vasculature distention and edema. When a technique similar to ours is used on dogs, the possible accumulation or loss of fluids in the lung is measured as lung weight changes and considered in the calculation of bronchial blood flow. Although we were unable to measure lung weight changes, we believe it is unlikely that lung fluids changed during our measurements. In fact, this study was performed while the lungs were in zone 1 (PA>pulmonary vascular pressures), and it has been shown during in vitro experiments that in zone 1, lung weight was constant when PA changes similar to ours were used. Therefore, we think that our measurements of $Q_{br(p)}$ probably represent the entire $Q_{br(p)}$.

The effects of positive PA on bronchial blood flow to the lung in humans during assisted ventilation remain unknown. Our study shows that positive PA reduces bronchial blood flow to the lung during total cardiopulmonary bypass. The study of the mechanisms responsible for the bronchial blood flow reduction due to increased alveolar pressure is beyond the purpose of the present work. However, a reduction of bronchial blood flow driving pressure as well as an active or passive increase of bronchovascular resistance may be suggested. Our study strengthens previous observations obtained in experimental animals and allows us to suggest a reduction of bronchial blood flow to the lung during assisted ventilation with positive PA in humans. A bronchial blood flow reduction may be clinically relevant in case of pulmonary embolism when bronchial blood flow is the major source of blood to the lung parenchyma. It may also have some importance in ARDS, when pulmonary blood flow to injured lung regions decreases and bronchial blood flow increases. In both cases a reduction of bronchial blood flow by positive PA may be deleterious for the healing of the lung parenchyma. Hence, we suggest that the lowest PA, and therefore PEEP, for adequate systemic blood oxygenation should be used during assisted ventilation to preserve bronchial blood flow.

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