Effect of bronchial artery blood flow on cardiopulmonary bypass-induced lung injury

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Am J Physiol Heart Circ Physiol 286: H693–H700, 2004. First published October 16, 2003; 10.1152/ajpheart.00888.2003.—Cardiovascular surgery requiring cardiopulmonary bypass (CPB) is frequently complicated by postoperative lung injury. Bronchial artery (BA) blood flow has been hypothesized to attenuate this injury. The purpose of the present study was to determine the effect of BA blood flow on CPB-induced lung injury in anesthetized pigs. In eight pigs (BA ligated) the BA was ligated, whereas in six pigs (BA patent) the BA was identified but left intact. Warm (37°C) CPB was then performed in all pigs with complete occlusion of the pulmonary artery and deflated lungs to maximize lung injury. BA ligation significantly exacerbated nearly all aspects of pulmonary function beginning at 5 min post-CPB. At 25 min, BA-ligated pigs had a lower arterial PO2 at a fraction of inspired oxygen of 1.0 (52 ± 5 vs. 312 ± 58 mmHg) and greater peak tracheal pressure (39 ± 6 vs. 15 ± 4 mmHg), pulmonary vascular resistance (11 ± 1 vs. 6 ± 1 mmHg·l−1·min−1), plasma TNF-α (1.2 ± 0.60 vs. 0.59 ± 0.092 ng/ml), extravascular lung water (11.7 ± 1.2 vs. 7.7 ± 0.5 ml/g blood-free dry weight), and pulmonary vascular protein permeability, as assessed by a decreased reflection coefficient for albumin (σr; 0.53 ± 0.1 vs. 0.82 ± 0.05). There was a negative correlation (R = 0.95, P < 0.001) between σr and the 25-min plasma TNF-α concentration. These results suggest that a severe decrease in BA blood flow during and after CPB causes increased pulmonary vascular permeability, edema formation, cytokine production, and severe arterial hypoxemia secondary to intrapulmonary shunt.

POSTOPERATIVE LUNG DYSFUNCTION frequently develops in patients after cardiopulmonary bypass (CPB) (29, 32). The severity of pulmonary dysfunction varies from mild alterations in gas exchange to the acute respiratory distress syndrome (32). Although the mechanisms behind CPB-induced lung injury are likely complex, the observation that maintenance of a finite pulmonary artery (PA) blood flow during CPB attenuates CPB-induced lung injury (13) suggests that PA ischemia-reperfusion (I/R) plays a significant role in CPB-related lung dysfunction. Bronchial artery (BA) blood flow continues during CPB and may influence the effect of pulmonary I/R on the subsequent lung dysfunction (24, 26). The bronchial circulation originates from the descending aorta and intercostal arteries (6, 42). It supplies the airways, pleura, lymph nodes, nerves, and pulmonary vascular vasa vasorum (10) before draining into the pulmonary circulation through bronchopulmonary anastomoses (3). BA perfusion during CPB has been considered by some investigators to be problematic, possibly contributing to pulmonary vascular congestion (49) and systemic hypotension (25). Others have hypothesized BA blood flow to be a possible ameliorating factor in CPB-induced lung injury (24, 46, 54).

We previously demonstrated that BA perfusion prevented the increased pulmonary vascular permeability and edema caused by I/R of the pulmonary circulation in isolated sheep lungs (40). Similar results were reported in intact dog models of pulmonary I/R injury (18) and lung transplantation (34).

On the basis of these observations, we hypothesized that occluding BA blood flow would exacerbate the lung dysfunction observed after CPB. To test this hypothesis, we exposed pigs to 2 h of CPB with or without BA ligation. To examine the potential effects of the bronchial circulation on lung fluid balance, we measured arterial oxygenation, pulmonary hemodynamics, plasma cytokine concentrations, extravascular lung water (EVLW), and pulmonary vascular permeability during the first 25 min after separation from CPB.

METHODS

Preparation

All animals received care in compliance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals. Pigs (35–50 kg) were fasted for 12 h before surgery. They were anesthetized with ketamine (30 mg/kg im and then 3–6 mg iv every 10–20 min) and inhaled halothane. After intubation, they were mechanically ventilated (Harvard Ventilator) with 100% oxygen at an initial rate of 10 breaths/min, a tidal volume of 12 ml/kg, and no positive end-expiratory pressure. Esophageal and rectal temperature probes were inserted, and the left internal jugular vein was cannulated for insertion of a PA catheter. The right carotid artery was cannulated for measurement of blood pressure and to obtain arterial blood gas samples. A left thoracotomy was performed, the azygous vein was divided, and the bronchoesophageal artery was identified by the origin from the medial or anteromedial region of the aorta (15). In eight animals, the bronchoesophageal artery was then ligated and transected, whereas in six animals it was identified and left patent. The order of experiments was randomized over time to control for changes...
in the surgical team. Correct identification and successful ligation of the bronchoesophageal artery were confirmed at the end of each experiment after excision of the heart, lungs, and descending aorta. The thoracotomy was closed, and a midline sternotomy was performed. The left atrium (LA) was then cannulated for continuous LA pressure monitoring. The femoral arteries were cannulated, heparin (300 U/kg) was administered, and the right atrium was cannulated for initiation of CPB using the right atrium and femoral arteries.

The bypass circuit consisted of a membrane oxygenator (Cobe Optima XP, Cobe Cardiovascular; Arvada, CO), a 40-μm arterial filter (Millipore; Billerica, MA), and a roller pump system (Sarns 5000, Sarns 3M; Ann Arbor, MI). The pump was primed with 800 ml of homologous pig blood, 200 ml of lactated Ringer solution, and 50 meq of NaHCO₃. The PA trunk was cross-clamped, and a PA vent was placed to prevent antegrade flow to the lungs. Ventilation was stopped and the endotracheal tube was disconnected from the ventilator. Warm CPB (37°C) was continued for 2 h with a blood flow of 70–80 ml/kg and a targeted mean systemic arterial blood pressure (MAP) of 50–60 mmHg. At termination of CPB, atelectasis was reversed with a single hyperinflation, mechanical ventilation was resumed, and the pigs were weaned from CPB. Throughout the experiment, pH was maintained at 7.35–7.45 by administration of NaHCO₃ and by adjusting the ventilator rate. Intravenous fluids and α-agonists were used to treat systemic hypotension (MAP < 50 mmHg). Atropine and epinephrine were utilized to reverse bradycardia. The pigs were killed by rapid exsanguination from the femoral artery cannulas 30 min after being disconnected from CPB. This period of post-CPB observation was chosen because we have previously found that the nadir in arterial oxygenation occurred during this time period (43).

Interval Measurements

**Hemodynamic measurements.** Vascular and airway pressures (Spacelabs Medical, Instrumentarium; Issaquah, WA) and arterial blood gases (model 248 pH/blood gas analyzer, Ciba Corning Diagnostics; Medfield, MA) and blood samples for cell counts were obtained at baseline before CPB and at 10-min intervals (starting at 5 min) after separation from CPB. Cardiac output (CO) was measured by thermodilution using a 5-ml injection of cold saline (mean of three measurements). The pulmonary vascular resistance (PVR) was calculated as

\[
PVR = \frac{P_{PA} - P_{LA}}{CO}
\]

where \(P_{PA}\) is PA pressure and \(P_{LA}\) is LA pressure.

**Blood cell counts.** Hematocrit (Hct) and white blood cell and platelet counts were measured (Coulter Counter, Beckman Coulter; Fullerton, CA) at the time intervals noted above. Neutrophil counts were determined by manual evaluation of blood smears stained with Wright stain.

**Plasma cytokine concentrations.** Plasma concentrations of TNF-α and IL-6 were measured at the above intervals by solid-phase enzyme-linked immunosorbent assay (R&D Systems; Minneapolis, MN).

**Reflection Coefficient for Albumin**

After exsanguination, the PA and LA were cannulated, and the pulmonary vasculature was flushed with 200 ml of a mixture of autologous blood and 3% Dextran 70 (Hct = 20%) as previously described (39). The PA and LA cannulas were connected to a pressurized stirred reservoir filled with the blood-dextran mixture, and static intravascular pressure (referred to the level of the middle of the lung) was increased to 35 mmHg for 15 min. Intravascular blood was then pumped retrograde and collected in serial 12-ml samples. The reflection coefficient for albumin (\(\sigma_{abl}\)) was estimated by the filtered volumes method modified for a nonflowing system (4).

Briefly, Hct and albumin concentration were determined in duplicate for each sample, and \(\sigma_{abl}\) was estimated iteratively from the relationship

\[
\frac{C}{C_0} = \frac{1 - \text{Hct}_0 - \sigma}{1 - \text{Hct} - \sigma}
\]

where \(C\) represents albumin concentration and \(C_0\) and \(\text{Hct}_0\) represent initial reservoir values for albumin concentration and Hct. The \(\sigma_{abl}\) for each lung was determined from the sample with the greatest change in Hct from \(\text{Hct}_0\).

**Extravascular Lung Water and Blood-Free Dry Lung Weight**

EVLW and blood-free dry lung weight (BFDSLW) were determined after the period of increased intravascular pressure using hemoglobin concentration as the intravascular marker, as previously described (40).

**Statistics**

All time course data were analyzed with a two-factor (group, lung), split-plot ANOVA. When significant variance ratios were obtained, least-significant differences were calculated to allow comparison of individual means. Non-time course data were compared by unpaired Student’s t-test. The mean values of arterial \(P_O_2\) (\(P_{A_O_2}\)), TNF-α, and IL-6 were found to be directly proportional to SDs, indicating non-homogeneity of variance; therefore, these data were transformed to logarithms before statistical analysis. The relationship between plasma cytokine concentrations and \(\sigma_{abl}\) was analyzed by least-squares linear regression. Values presented in the text are means ± SE. Differences were considered significant when \(P \leq 0.05\).

**RESULTS**

Pig body weight averaged 42.4 ± 1.3 kg and was not different between the groups. There were also no differences in baseline or post-CPB hematological parameters between groups. Baseline Hct and total leukocyte, neutrophil, and platelet concentrations averaged 31 ± 2%, 15,700 ± 1,600, 7,200 ± 1,200, and 516,000 ± 32,000 cells/mm³, respectively, falling to 25 ± 2%, 3,910 ± 701, 1,770 ± 587, and 258,000 ± 36,000 cells/mm³, respectively, during the post-CPB period.

**CPB with Patent BA**

Figure 1 shows the effect of warm CPB with a patent PA on gas exchange. The \(P_{A_O_2}\), while pigs were ventilated with 100% \(O_2\), decreased from 541.0 ± 15.1 mmHg before CPB to 181.1 ± 45.4 mmHg at 5 min after CPB but then increased to 311.9 ± 57.7 mmHg at 25 min (\(P < 0.05\)). This was accompanied by an unchanged arterial \(P_{CO_2}\) (\(P_{A CO_2}\)), an increased minute ventilation (\(V_{min}\), an small but significant decrease in \(pH\) from pre-CPB levels.

CPB with a patent BA did not alter peak tracheal pressure (\(P_{Tr}\)) compared with the pre-CPB measurement of 8.2 ± 1.2 mmHg (Fig. 2). Mean \(P_{PA}\) increased from a pre-CPB value of 15.2 ± 1.5 to 34.3 ± 4.9 mmHg at 5 min post-CPB and remained elevated (\(P < 0.05\)). CPB caused a decrease in CO from 4.4 ± 0.5 to 2.7 ± 0.3 l/min by 5 min post-CPB. At 25 min, the mean CO had partially recovered (3.4 ± 0.5 l/min) but was still significantly decreased from baseline. \(P_{LA}\) averaged 9.2 ± 0.8 mmHg before CPB and did not change after CPB (data not shown). Because of trends toward recovery of both \(P_{PA}\) and CO, however, PVR was increased only at the 5-min
time point ($P < 0.05$) after termination of CPB (Fig. 2). Neither right atrial pressure (8.1 ± 1.2 mmHg) nor MAP (74.7 ± 1.1 mmHg) was altered by CPB (data not shown).

EVLW/BFDW averaged 7.74 ± 0.53 in these lungs at the end of the experiment after the period of increased intravascular pressure (Fig. 3). The $\sigma_{\text{inh}}$ of the pulmonary circulation measured at the same time point was 0.82 ± 0.05. As shown in Fig. 4, plasma TNF-α and IL-6 concentrations increased to $1.05 \pm 0.51$ and $1.95 \pm 1.09$ ng/ml, respectively, by 5 min post-CPB and remained elevated compared with baseline levels ($P < 0.002$).

**CPB with Ligated BA**

As shown in Fig. 1, ligation of the BA resulted in significantly greater abnormalities of gas exchange after termination of CPB with $\text{Pao}_2$ tensions consistently <100 mmHg ($P < 0.01$) despite ventilation with 100% $\text{O}_2$. There were no significant differences between the two groups with respect to $V_{\text{min}}$, $\text{Paco}_2$, or pH (Fig. 1).

Ligation of the BA resulted in a marked increase in peak $P_{\text{Tr}}$ after termination of CPB that differed at all time points from the BA-patent group (Fig. 2). For example, the peak $P_{\text{Tr}}$ at 25 min post-CPB was 39.2 ± 6.4 mmHg compared with 15.4 ± 3.7 mmHg in the BA-patent group ($P < 0.01$). The time courses of mean $P_{\text{PA}}$ (Fig. 2) and $P_{\text{LA}}$ (data not shown) were similar to the BA-ligated group. The CO, however, was significantly decreased at 25 min in BA-ligated animals (Fig. 2). PVR was significantly increased in this group at 15 and 25 min compared with the pre-CPB level and the corresponding PVR values in BA-patent lungs ($P < 0.05$; Fig. 2). Right atrial pressure was not altered by CPB (7.8 ± 1.2 mmHg) and was similar to the right atrial pressure in BA-patent lungs (data not shown).
shown). MAP decreased significantly from 83.0 ± 6.4 to 54.7 ± 5.9 mmHg at 5 min post-CPB and remained lower than baseline (although not different from the BA-patent lungs) for the rest of the post-CPB period (P < 0.05; data not shown). The BA-ligated animals were similar to BA-patent animals in regard to the ease of CPB termination and the total dosage of fluids and arterial pressors used in the post-CPB period.

EVLW/BFDW was significantly greater in BA-ligated lungs, averaging 11.73 ± 1.27 (P < 0.05; Fig. 3). Pulmonary vascular protein permeability was also increased in these lungs as evidenced by a significant reduction in σ_{alb} to 0.53 ± 0.10 (P < 0.05). As shown in Fig. 4, unlike BA-ligated animals, plasma TNF-α concentrations in the patent BA group did not increase in the post-CPB time period compared with baseline and differed by a significant ANOVA interaction F-ratio (P < 0.02) from BA-ligated animals, confirming a different time course. Although the mean plasma concentrations of IL-6 tended to be lower in the patent BA group after CPB, the differences were not statistically significant (P > 0.05) and were driven by two animals in the BA-ligated group with IL-6 concentrations that were an order of magnitude greater than all other values.

Relationships Among PaO₂, σ_{alb}, and Plasma Cytokine Concentrations

There was no significant correlation between the final PaO₂ and either σ_{alb} (R = 0.65, P = 0.11) or the concentrations of plasma TNF-α (R = 0.36, P = 0.31) or IL-6 (R = 0.42, P = 0.22). There was a significant negative correlation (R = 0.95, P < 0.001) between σ_{alb} and the plasma TNF-α concentration measured at 25 min post-CPB (Fig. 5). This correlation remained significant after removal of the BA-patent animals (R = 0.96, P < 0.02) or the single BA-ligated animal with the highest TNF-α concentration (R = 0.74, P = 0.05). A negative correlation (R = 0.82, P < 0.01) was also found between σ_{alb} and the plasma IL-6 concentration measured at 25 min post-CPB, but this correlation was lost (R = 0.48, P = 0.28) when the animal with the greatest plasma IL-6 concentration (and lowest σ_{alb}) was excluded from the analysis (data not shown). Plasma concentrations of TNF-α and IL-6 were significantly correlated with each other (R = 0.73, P < 0.00001).

DISCUSSION

CPB has long been known to cause acute lung injury in both humans and animal models (32). This injury is characterized by decreased gas exchange and decreased lung compliance associated with increased PVR, permeability, and edema (32). The mechanisms behind these abnormalities are poorly understood but are thought to result from the injurious effects of both cellular and humoral mediators within the pulmonary circulation.
These include toxic products of sequestered neutrophils as well as prostanoids, cytokines, and reactive oxygen species (32).

The observation that a significant component of CPB-induced pulmonary dysfunction occurs from I/R lung injury (13) led to the long-standing hypothesis that BA blood flow could be an important attenuating factor in this injury (24, 46, 54). Despite this, few studies have attempted to directly examine the role of BA perfusion as a potential modulator of CPB-induced lung injury. To test this hypothesis, we chose to examine a pig model of CPB. This preparation takes advantage of the bronchial circulation anatomy of the pig, which originates from a single bronchoesophageal artery in most cases (15). To maximize CPB-induced lung injury, we performed warm CPB (31) with an occluded PA (1) and a completely deflated, nonventilated lung (36, 41, 48, 53). We assessed lung injury over the first 25 min after CPB because our previous experience with this preparation demonstrated that the peak alveolar-arterial oxygen tension difference occurred over this time period (17, 43).

We found that BA ligation markedly exacerbated nearly all aspects of pulmonary function, including systemic arterial hypoxemia, peak Pr, PVR, EVLW, and pulmonary vascular protein permeability. Arterial oxygenation was markedly depressed on 100% O2 in BA-ligated animals throughout the 25-min observation period after CPB, indicating a severe right-to-left intrapulmonary shunt (Fig. 1). This hypoxemia likely contributed to the significant decrease in CO observed in this group (Fig. 2). Relative arterial hypoxemia also occurred in the BA-patent group, but the nadir PaO2 of 181 mmHg indicated an approximate shunt fraction of 23% compared with the estimated shunt fraction in BA-ligated animals of ~50% (assuming normal mixed venous O2 tensions) (35). Moreover, the intrapulmonary shunt fraction rapidly improved in the presence of BA flow but likely remained unchanged in the BA-ligated animals.

The initial difference in estimated shunt fraction between the two groups roughly correlated with the approximately twofold difference in peak Pr that was present at all time points after CPB (Fig. 2). Peak Pr can increase from either decreased static lung compliance, increased airway resistance, or a combination of both. The observation that the estimated shunt fraction and peak Pr increased by about the same percentage in BA-ligated animals suggests that the predominant mechanism for the Pr increase was a decrease in static lung compliance rather than increased airway resistance. Hypoxemia from increased airway resistance would result from ventilation/perfusion mismatch, not intrapulmonary shunt. A decrease in static lung compliance could have occurred from a combination of surfactant dysfunction and pulmonary edema. We confirmed an increase in pulmonary edema in the BA-ligated compared with BA-patent animals (Fig. 3). Although we have no data regarding potential differences in surfactant activity as a function of BA patency, other studies have demonstrated that CPB does interfere with surfactant function (14, 30, 44).

Bronchial blood flow could contribute to edema clearance from the lung via direct absorption of fluid (20) or enhancement of lymphatic function (51). Thus the increase in EVLW observed in the BA-ligated lungs could have resulted from either increased edema formation or decreased edema clearance. To examine the contribution of a pulmonary vascular protein permeability change, we measured σ alb at the end of the 25-min observation period. We found that σ alb was significantly decreased in BA-ligated animals (Fig. 3), indicating increased vascular protein permeability. Interestingly, the σ alb in the BA-patent pigs was identical to our previous measurement of σ alb in unjured control sheep lungs (0.82 ± 0.03) (40) and similar to an estimate of normal σ alb (0.84) in the lungs of intact sheep (37). This suggests that BA perfusion was capable of maintaining normal pulmonary vascular protein permeability in the face of 2 h of warm, nonventilated PA ischemia followed by reperfusion. These results are consistent with those of Eising et al. (11), who found that 2 h of warm CPB in pigs (with intact bronchial circulation) did not increase plasma protein extravasation.

We did not find a significant correlation between σ alb and the final PaO2 (P = 0.11). Other factors likely contributed to the increased shunt fraction separate from increases in pulmonary vascular permeability, such as surfactant dysfunction and resulting atelectasis. Moreover, σ alb measured by the filtered volume technique underestimates the degree of endothelial barrier dysfunction in the presence of a hemorrhagic vascular injury (38), which may have been present to a variable degree in the BA-ligated lungs.

To begin to understand the mechanisms behind the protective effect of BA perfusion in CPB-induced lung injury, we measured plasma concentrations of TNF-α and IL-6. Both cytokines have been shown to increase in plasma after animal and human CPB (52), and both are capable of increasing pulmonary endothelial permeability directly (22, 28) or through a priming effect on activated neutrophils (16, 21). TNF-α is particularly interesting because it was shown to play a critical injurious role in the early reperfusion injury in intact (12) and isolated (22) rat lung models of I/R injury. Specifically, the lungs expressed TNF-α mRNA (12) and protein (12, 22) early in reperfusion, and pretreatment with antibodies to
TNF-α attenuated the I/R-induced increases in pulmonary vascular permeability (12, 22).

We found measurable plasma concentrations of both cytokines in the post-CPB period (Fig. 4), but TNF-α did not increase as a function of time unless the BA was ligated. This indicates that BA perfusion either attenuated TNF-α production or increased TNF-α degradation. Moreover, a direct injurious role for TNF-α was suggested by the significant negative correlation between σ_ab and the final plasma concentration of TNF-α. The fact that IL-6 concentrations did not differ between groups or correlate as tightly with vascular injury parameters suggests that TNF-α may be a more important determinate of vascular barrier dysfunction, but we cannot exclude a role for IL-6 given the presence of a significant correlation between the two cytokines, the unknown relationship between plasma and lung cytokine concentrations, and the relatively small number of observations in this study. Additional studies with administration of anti-cytokine antibodies will be required to test these hypotheses. Anti-TNF-α antibody was shown to alter leukocyte kinetics in a pig model of CPB, but the bronchial circulation was intact and pulmonary vascular permeability was not measured (50).

By providing oxygen, antioxidants, or nutrients to the ischemic lung, BA anastomotic blood flow during PA ischemia may have been adequate to prevent both the PA endothelial barrier dysfunction caused by ischemia alone (4, 5) and the separate injury that occurs at the time of reperfusion (39). Alternatively, BA perfusion of PA vasa vasorum could play an important role in preserving PA endothelial function during either ischemia or reperfusion. Vasa vasorum are present in both PAs and pulmonary veins in sheep (7, 27), supplying pulmonary vessels as small as 100 μm in diameter (47). Hyman et al. (19) showed that ascorbic acid and 5-hydroxydopamine injected into the BA in dogs rapidly appeared in an occluded segment of PA, suggesting that pulmonary vasa vasorum could transport substances to the pulmonary endothelium.

Our laboratory (40) previously examined these possible sources of BA protection in isolated in situ sheep lungs subjected to 45 min of PA ischemia followed by 180 min of blood reperfusion. In these experiments, the bronchial branch of the bronchoesophageal artery was cannulated and either perfused (at 1% of pulmonary flow) continuously throughout PA ischemia and reperfusion, perfused only during PA reperfusion, or never perfused. PA I/R in the absence of BA perfusion caused a significant decrease in pulmonary vascular σ_ab and increases in EVLW and lung lymph flow. These changes were attenuated by BA perfusion. To our surprise, restricting reperfusion of the bronchial circulation to the pulmonary reperfusion phase proved to be most protective. Specifically, measurements of endothelial barrier function and lung water after pulmonary I/R in this limited BA reperfusion group were not different from uninjured control lungs (40).

These data indicated that the presence of BA blood flow limited to the period of PA reperfusion prevented the pulmonary edema from PA I/R injury through a direct effect on pulmonary endothelial barrier function rather than enhancing edema clearance (40). A similar result was recently reported in a canine lung allotransplantation model in which BA revascularization at the time of PA reperfusion significantly reduced endothelial and epithelial cell injury in the transplanted lung during the first 2 h of reperfusion (34). On the basis of these results, it appeared that bronchopulmonary anastomotic flow, which was trivial compared with PA reperfusion flow in either study, was probably not the source of protection. The findings in this transplantation model (34) combined with our previous results (40) suggest that the ameliorating effect of BA perfusion may have been mediated through perfusion of the pulmonary vasa vasorum during PA reperfusion by an as-yet-undetermined mechanism. This scenario would explain how a patent BA can result in such significant protection of PA endothelial barrier dysfunction (Fig. 3) despite the recent observation that BA blood flow decreased by 90% during porcine CPB before returning to pre-CPB levels shortly after CPB termination (45). Thus the presence of adequate BA blood flow in the first minutes after separation from the CPB pump may be all that is necessary to protect the pulmonary circulation from significant injury.

Does BA blood flow attenuate lung injury after CPB in humans? BA blood flow in human CPB, as estimated by anastomotic flow during CPB, was shown to vary over a wide range (2) despite similar pump flow levels, suggesting significant differences in bronchial vascular resistance. This variability was perhaps related to differing amounts of aortic or intercostal artery atherosclerosis. In fact, clinical factors that have been shown to predict severe post-CPB lung injury include cigarette smoking, hypertension, left ventricular heart failure, and low postoperative CO (8). These are all problems that could result in diminished post-CPB BA blood flow from either atherosclerotic vascular obstruction or decreased aortic perfusion pressure. Consistent with this hypothesis, bronchopulmonary anastomotic blood flow during CPB for congenital heart disease repair was recently shown to inversely correlate with post-CPB alveolar-to-arterial oxygen gradient and morphometrically determined interstitial edema and epithelial injury (24). This phenomenon could also contribute to the excessive incidence of respiratory failure complicating CPB for descending aortic aneurysm repair (9). The increasing interest in BA reanastomosis in lung transplant recipients (33) will hopefully provide more direct data on the role of BA blood flow in this related form of human PA I/R lung injury (23).

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