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istic to believe then that a single dose of dopamine would have the same renal effects in all patients.

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Improving Splanchnic Perfusion during Cardiopulmonary Bypass

IMPAIRED perfusion and distribution of blood flow away from visceral organs during cardiopulmonary bypass (CPB) have been implicated as causing mucosal ischemia, intraluminal acidosis, altered gut permeability, and endotoxemia.[1-8] Although the overall incidence of gastrointestinal complications after cardiac operations is relatively low (0.6–2.0%), associated perioperative mortality can be significantly increased 15% to 63%.[1-3] Accordingly, maintaining or increasing splanchnic perfusion during CPB may be important in selected patients. In this issue of ANESTHESIOLOGY, Bastien et al.[9] use a rabbit CPB model to examine the relative importance of altering blood pressure or pump flow rate on splanchnic perfusion as measured by laser Doppler flowmetry (LDF) in the gastric, jejunal, ileal, and hepatic regions. The authors report that a high pump flow rate (100 ml · kg^{-1} · min^{-1}) improves intestinal mucosal perfusion significantly more than a low pump flow rate (50 ml · kg^{-1} · min^{-1}), whereas altering aortic pressure by infus-

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> ◆ This Editorial View accompanies the following article: Bastien O, Piriou V, Aouifi A, Flamens C, Evans R, Lehot JJ: Relative importance of flow *versus* pressure in splanchnic perfusion during cardiopulmonary bypass in rabbits. ANESTHESIOLOGY 2000; 92:457–64.

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ing vasodilator or vasoconstrictor drugs fails to increase mucosal blood flow. Over the range of 50–500 ml/min, increasing pump flow rate linearly increases gastric and ileal LDF values. The authors conclude that normothermic CPB reduces splanchnic perfusion and attenuates autoregulation so that a linear relationship exists between CPB flow rate and splanchnic LDF. Aortic blood pressure does correlate with LDF in ileal and gastric regions, although the variability of this relationship is so great that any benefit of increasing aortic pressure on intestinal LDF becomes less predictable.

This study does have several limitations, such as: (1) the use of an invasive animal preparation, where lower-extremity circulation is eliminated; (2) lack of confirmatory data using alternative techniques to quantitate blood flow, such as microspheres or electromagnetic flowmetry; (3) bolus drug administration as opposed to constant infusion; (4) an unblinded protocol without concurrent controls; and (5) lack of outcome measures such as animal survival, intraabdominal complications, and long-term effects of altered gut perfusion. Nevertheless, this study illustrates that a major determinant of splanchnic mucosal perfusion during CPB is pump flow rate—not aortic blood pressure—and that altering blood pressure with vasoactive drugs, whether at low or high pump flow rates, fails to improve intestinal LDF.

In reviewing the consequences of nonpulsatile CPB on intestinal perfusion, several important aspects become apparent:

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1. CPB produces variable effects on splanchnic perfusion, with regional intestinal blood flow increasing,[4,10] decreasing,[9] or remaining unchanged[11,12] despite maintenance of acceptable blood pressure and pump flow rates during extracorporeal circulation. Furthermore, CPB may produce heterogenous effects within the gastrointestinal tract by increasing perfusion to some regions (duodenum, jejunum) while decreasing flow to other regions (ileum, colon).[4] Consequently, the level of regional splanchnic blood flow during CPB is difficult to predict.

2. Disparity exists during CPB between regional intestinal perfusion and localized mucosal perfusion.[13,14] Even without changes in regional perfusion to various visceral organs, the intestinal mucosa can become progressively hypoperfused during normothermic CPB.[4] Mucosal hypoperfusion in the stomach is reported to occur commonly in patients.[6]

3. Visceral oxygen delivery decreases during CPB secondary to hemodilution coupled with the narrow range of pressure-flow autoregulation.[4] Unlike renal and cerebral vessels, mesenteric vessels have limited autoregulatory capability[15,16] that may be caused or potentiated by the host of endogenous vasoconstrictor substances released during CPB.

4. Visceral oxygen consumption progressively increases during normothermic CPB, which has been attributed to gut inflammatory responses initiated by CPB.[4] Even with hypothermia, where systemic cooling reduces gut oxygen consumption and extraction,[12] splanchnic oxygen consumption increases during rewarming at a time when regional oxygen delivery remains relatively unchanged.[4]

5. As a result, intestinal mucosal ischemia and hypoxia may occur during CPB, as evidenced by progressive decreases in intraluminal pH in the stomach, jejunum, ileum, and rectum despite otherwise normal indices of global systemic perfusion.[4-6,14]

Hypotension is frequently observed during CPB secondary to contributions from multiple variables, including a reduction in systemic vascular resistance from hemodilution, reduced blood viscosity, dilution of circulating catecholamine concentrations, hyperkalemia, complement activation, and a generalized inflammatory response to extracorporeal circulation.[2] Options to restore aortic pressure during CPB consist of increasing pump flow or administering vasoactive drugs. The rate of pump flow, in particular, is frequently limited by inadequacy of venous return, excessive arterial line pressure, and potential blood trauma.

The use of vasoconstrictors such as phenylephrine or norepinephrine could also be problematic, depending on the relative sensitivities of various capillary beds to α-agonist stimulation. For example, in intact animals, the administration of vasoconstrictive drugs can improve global mesenteric perfusion while causing mucosal vasoconstriction and reduced flow.[17] Furthermore, α-agonists can directly increase gut oxygen consumption secondary to the extra metabolic energy expense of active mucosal vasoconstriction.[18,19] These factors could worsen the potential for mucosal oxygen supply/demand mismatch during CPB.

Results from the study by Bastien et al.[9] concur with other experimental models of CPB in which the infusion of vasoactive drugs fails to improve splanchnic or renal blood flow.[16,20] A study by O'Dwyer et al.[16] found that phenylephrine increased systemic vascular resistance in pigs during CPB, but this vasoconstrictor response occurred more in the splanchnic organs and the kidneys than in the skeletal muscle. These findings contrast animal studies that did not use CPB, where phenylephrine produced greater vasoconstriction in skeletal muscle than in the mesentery,[21,22] and reflect an altered response to vasoactive drugs administered during extracorporeal circulation. Furthermore, these data clearly indicate that the adequacy of visceral perfusion to the intestines and kidneys cannot be assured by monitoring aortic pressure alone.[9,16,20]

The relative importance of splanchnic perfusion during CPB in terms of causing endotoxemia and perioperative morbidity continues to be questioned, and a true causal relationship between CPB, gut hypoperfusion with altered permeability, and endotoxemia has not been established.[23] Nevertheless, normothermic CPB can reduce visceral perfusion, especially to the intestinal mucosa, and increasing pump flow rather than infusing vasoconstrictive drugs to increase aortic pressure can improve both splanchnic and renal perfusion.[9,16,20] Future studies are needed to determine whether these measures actually improve perioperative outcome in patients. These studies should include animal experiments that contrast the effects of fixed CPB flow rate with pharmacologic manipulation of blood pressure, as well as other studies in which only CPB flow rate is manipulated. Outcome measures should include regional intestinal blood flow, mucosal blood flow, and systemic inflammatory mediators, as well as survival and postoperative complications.

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