

## Pro: During Cardiopulmonary Bypass for Elective Coronary Artery Bypass Grafting, Perfusion Pressure Should Routinely Be Greater Than 70 mmHg

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**I**F DURING THE COURSE of a noncardiac surgical procedure under routine general anesthesia, a blood pressure of 75/35 mmHg was obtained, the common responses would include a decrease in the depth of anesthesia, administration of fluids, and possible infusion of vasopressors and/or inotropic agents. In contrast, a mean arterial blood pressure (MAP) of 50 mmHg during cardiopulmonary bypass (CPB) elicits no such response; rather, it is accepted as normal in many cardiac centers. Why are the responses to hypotension so radically different in these two settings?

The controversy over the optimal or even safe MAP during CPB is certainly not new. Keats,<sup>1</sup> in his 1983 Rovenstine lecture reviewing his 30 years in cardiac anesthesia, defined "a group of problems that were perceived as serious but never were solved,"<sup>1</sup> listing MAP on CPB as one such question. This question was further discussed in this Journal in 1991,<sup>2,3</sup> and is now being revisited in part because of recent data from the author's institution, in an admittedly small number of patients (n = 248), which suggest that higher MAP may reduce central nervous system complications during CPB.<sup>4,5</sup> It is interesting to note that the current debate is not confined to the CPB setting, as evidenced by a recent letter to the editor of *Anesthesiology*<sup>6</sup> suggesting a rethinking of the concept of the lower limit of autoregulation.

### AUTOREGULATION

Autoregulation has been the cornerstone on which the defense of MAPs of 50 mmHg has been built. The concept of autoregulation has been overapplied as a defense of CPB at an MAP of 50 mmHg.<sup>7-10</sup> The autoregulation curve, introduced into the anesthesia literature by Shapiro<sup>11</sup> in 1981, has been repeatedly referred to in textbooks, papers, and lectures. The data for the original curve, as depicted in *Anesthesia*,<sup>11</sup> were likely derived (J.C. Drummond, personal communication, February 10, 1996) from a review article by Lassen,<sup>12</sup> in which the lower limit of autoregulation was defined in pregnant women receiving hydralazine (a recognized cerebral vasodilator) and veratrum (cerebral action undefined). Although there appears to be widespread acceptance in humans of a range in which cerebral blood flow is relatively independent of MAP, the limits of a population study are not definitive for any specific

individual. The raw data show extensive variations above and below the mean regression line. Close inspection of the raw data from one such article reveals a scatter of data points around a regression line. Cerebral blood flow differences between individual patients can vary by as much as threefold (Fig 1). Though the lower inflection point of this regression line for the population may occur at 50 mmHg, is it true for all patients? Articles describing the effects of temperature,<sup>13</sup> pH,<sup>8,9</sup> cerebral vascular disease,<sup>10</sup> and aging,<sup>7,10</sup> on autoregulation are punctuated by disclaimers to the effect that the data cannot be applied with certainty to a particular patient, or to patients with hypertension or known alterations in neurovasculature.<sup>10,14</sup> Therefore, because it is then difficult to categorize patients, should the data be indiscriminately applied in clinical practice? Applying such population-based definitions of autoregulation to the cerebral blood pressure-flow relationships of an individual may not be accurate. Drummond<sup>6</sup> has summarized other studies in humans showing a large individual variation in the lower limit that suggests the lower limit of autoregulation is much greater than 50 mmHg, more in the range of 70 to 85 mmHg.<sup>15-17</sup> Hypertensive patients have alterations in their cerebral blood flow-pressure relationship.<sup>10,16,17</sup> In these patients, arterial pressure may be the single most important determinant of perfusion. Using a pressure that is within 25% of their normal value, elevated MAP may be essential to the preservation of cerebral function. Patients currently presenting for cardiac surgery are older and sicker and at greater risk for morbidity or mortality than patients from previous decades.<sup>7</sup> The cerebral vasculature is known to undergo age-related changes with impact on postoperative dysfunction,<sup>7</sup> yet little is done routinely to alter CPB technique in the older patient. Opponents to an MAP greater than 50 mmHg have pointed to data in which preservation of autoregulation appears, even in the elderly. These data were derived from global measures of cerebral blood flow. To assume that regional areas of the cerebral vasculature are necessarily reflected in global measures of flow seems unfounded.

### Why MAP of 50 mmHg?

Why then has an MAP well below the range commonly accepted in noncardiac settings become the standard for MAP on CPB? Low arterial pressures were easily achieved with the initial extracorporeal circuitry minimizing derangements to blood elements. Lower pressure permitted the use of smaller venous and arterial cannulae and conferred less stress on the pump components and cannulation sites. It provided excellent operating conditions by minimizing collateral coronary blood flow, which can obscure the surgical field. Hypothermia (mild to marked), providing cerebral protection, and hemodilution, which decreases MAP by lowering viscosity, were usually used.

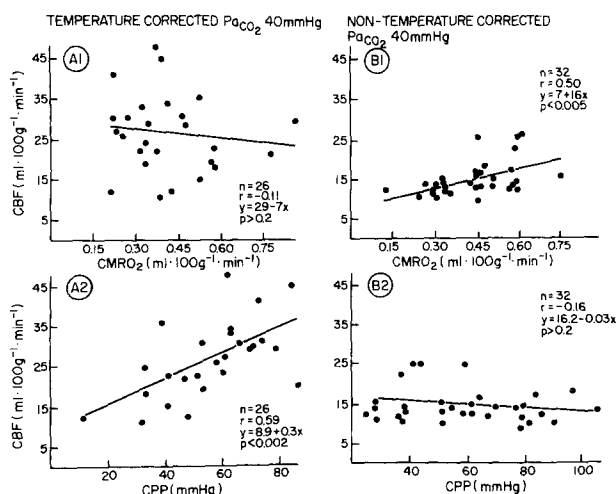
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**Fig 1. Simple linear regression of cerebral blood flow versus cerebral perfusion pressure or cerebral oxygen consumption for temperature-corrected and non-temperature-corrected groups. Upper panel: There is no significant correlation between CBF and CMRO<sub>2</sub> in the temperature-corrected group (A1), whereas CBF significantly correlates with CMRO<sub>2</sub> in the non-temperature-corrected group (B1). Lower panel: CBF is significantly correlated with CPP in the temperature-corrected group (A2), whereas CBF is independent of CPP in the non-temperature-corrected group (B2). Abbreviations: CBF, cerebral blood flow; CPP, cerebral perfusion pressure; CMRO<sub>2</sub>, cerebral metabolic rate for oxygen. (Reprinted with permission from Murkin JM, Farrar JK, Tweed WA, et al: Cerebral autoregulation and flow/metabolism coupling during cardiopulmonary bypass: The influence of PaCO<sub>2</sub>. *Anesth Analg* 66:825-832, 1987)**

Cardiac patients have commonly received anesthetic agents that decrease cerebral oxygen requirements. Hence, an MAP of 50 mmHg was widely accepted as the lower limit of normal autoregulation for cerebral blood flow.

#### Is It Essential?

Is an MAP of 50 mmHg essential to facilitate surgery? There are good outcomes with cardiac surgery performed at higher pressures.<sup>18</sup> In the new era of noninvasive cardiac surgery, anastomoses are constructed on a beating heart with maintained systemic perfusion pressures. Adequate conditions and exposure have been facilitated by ingenious suspension clamps, suction devices, and irrigators. Although designed to facilitate beating-heart surgery, an alteration in practice to use these advances may reduce the real or perceived problem of blood in the surgical field when coronary artery bypass on the arrested heart is performed at higher pressure.

#### HYPOTHERMIA AND HEMODILUTION

Hypothermia may afford some preservation of autoregulation or at least cerebral protection. Deep hypothermic circulatory arrest is performed with excellent results.<sup>10</sup> However, warm CPB is also being used in many centers. Even with hypothermia, there are significant temperature fluxes during cooling and especially during rewarming. It is a paradox of the routine that during the period of great risk for embolic load to the central nervous system (clamp removal and partial-occlusion clamp application), rewarming of the blood and brain has typically commenced and thus any protective effect from hypothermia

attenuated. The role of MAP under these changing conditions is conjectural. Further, hemodilution is known to alter the usual relationship between MAP and flow.<sup>10</sup> Studies to define how much and specifically in what way hemodilution affects oxygen delivery to focal areas of the human brain during nonpulsatile normothermic CPB are needed.

#### MAP GREATER THAN 50 mmHg

Two recent papers from the author's research group investigated the role of higher MAP in patients undergoing elective coronary artery bypass grafting surgery. Decreased combined neurologic and cardiac morbidity was shown in a subset of patients managed at high MAP on CPB (80 to 100 mmHg) compared with those managed at conventional (50 to 60 mmHg) MAP on CPB.<sup>4</sup> Transesophageal ultrasound of the aorta performed on a subset confirmed the importance of atheroma grade in determining adverse outcome. Although the number of patients was too small to achieve statistical significance, a striking trend was shown in stroke rate for patients who underwent coronary artery bypass grafting managed at different pressures.<sup>5</sup> Does aortic atheroma grade serve as a marker for those patients with alterations in the normal cerebrovascular relationship between MAP and cerebral flow? Are these patients a subset in whom the margin of safety with respect to cerebral blood flow is diminished? Should MAP be maintained with vasoconstrictors or flow? Can different pressures be used at hypothermic and normothermic periods of CPB? The topic remains controversial. It is hoped that these data may serve as a platform to reexamine the role of pressure management of CPB. Only large-scale, randomized, controlled studies can answer these compelling questions.

#### SUBGROUP DEFINITION

The issue of routine use on CPB of an MAP greater than 70 mmHg needs clarification. Critics of elevating blood pressure to greater than 50 mmHg on CPB have themselves argued that there is a subset of patients who likely would benefit from elevated MAP on CPB.<sup>19</sup> Definition of this subgroup then becomes of utmost importance. Identification of patients at increased stroke risk and the use of ultrasonography of the thoracic aorta have been suggested as stratification criteria. It seems logical to include patients with chronic, poorly controlled hypertension in this subset. Definition of the optimal pressure at which to perfuse a given individual awaits further outcome studies in which variable MAPs greater than 50 mmHg are used on CPB.

#### CNS INJURY FROM EMBOLISM

A large portion of neurologic injury after CPB is attributable to embolic phenomena. It is reasonable to question why these patients would benefit from an MAP of 70 versus 50 mmHg. Higher pressure should predispose to more turbulence, increasing the likelihood of dislodging intravascular debris. However, elevations in pressure may be of benefit by reducing the area at risk for ischemia secondary to emboli because collateral flow in this setting is known to be pressure dependent.<sup>20,21</sup>

## CONCLUSION

The persistence of neurologic injury after CPB suggests that the final word is not in. Reexamination of the concept of autoregulation is warranted. Perfusion at MAPs greater than 50 mmHg may benefit a high-risk subset of patients. Unless

controlled studies show poorer outcomes (cardiac, neurologic, pulmonary, renal, or hematologic) from an elevated MAP on CPB, it might be asked, "Why not routinely perfuse at greater than 70 mmHg when possible?"

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