

Lecture

Cerebral Blood Flow During Cardiopulmonary Bypass

John M. Murkin, MD, FRCPC*

Department of Anaesthesia, University Hospital
University of Western Ontario, London, Ontario

*Associate Professor of Anaesthesia

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Abstract

This article reviews the development of cerebral blood flow techniques as used both clinically and experimentally for measurement of cerebral blood flow (CBF) and cerebral metabolic rate for oxygen (CMRO₂) during cardiopulmonary bypass (CPB). The limitations associated with the various techniques for measurement of CBF during

cardiopulmonary bypass are discussed, as well as considering the influence of some of the management options, including pH management and use of pulsatile or nonpulsatile perfusion, on CBF and CMRO₂. The impact of various perfusion techniques on neurological outcome following cardiopulmonary bypass is also considered.

CBF Techniques

Within a few years of the first successful use of cardiopulmonary bypass (CPB) by Gibbon et al in 1953,¹ investigators were applying techniques first elucidated by Seymour Kety and Carl Schmidt in 1945² to examine the influence of CPB on cerebral blood flow (CBF) and cerebral metabolism, with a view towards helping to understand some of the neurological syndromes that too often accompanied extracorporeal circulation.³

In 1958 Creech et al^{4,5} utilized magnetic rotameters to record CBF and cerebral metabolic rates for oxygen (CMRO₂) during normothermic CPB in dogs. This technique assumes that the resistive load imposed by the intracarotid catheters does not significantly reduce blood flow. Whether this assumption is still valid as perfusion pressure decreases is not certain. With this preparation they observed a linear relationship between

CBF and arterial blood pressure, and a reduction in CMRO₂ of at least 50% in each of the animals during CPB. Because of the type of experimental preparation used, however, they were unable to assess the reversibility of these changes in CBF and CMRO₂ after discontinuation of CPB.

By the mid 1960s, Woolman and colleagues⁶, prior to the publication of their classic investigations of CBF and CMRO₂ during anesthesia, used changes in the arterial and jugular venous oxygen content difference (AVDO₂) to estimate changes in CBF during alterations of mean arterial pressure (MAP) and arterial carbon dioxide tensions (PaCO₂) in patients undergoing CPB. This technique presupposes the constancy of cerebral metabolic rate during the experimental period, thus changes in AVDO₂ were inversely related to alterations in CBF. They observed a linear correlation between PaCO₂ and AVDO₂ (CBF), and no relationship between AVDO₂ (CBF) and MAP.⁶ Although the concepts of alpha-stat and pH-stat pH management during hypothermia had not been elucidated at this time, these authors recommended a pH strategy aimed at maintaining temperature corrected PaCO₂ mid way between 30 and 40 mmHg during hypothermic CPB.

Using a modified N₂O saturation method (Kety Schmidt), Horecky et al⁷ reported in 1966 that cerebral metabolic rate

Address Correspondence to:

Dr. John M. Murkin,
Department of Anaesthesia
University Hospital
339 Windermere Road
London, Ontario,
N6A 5A5

decreased by 11% during normothermic nonpulsatile CPB in dogs, and by 94% during profoundly hypothermic (20°C) CPB. This investigation supported the view that nonpulsatile CPB produced derangements of cerebrovascular physiology, although once again the reversibility of these derangements of CBF and $CMRO_2$ were not re-assessed after separation from CPB.

In 1968, a Japanese investigator using the recently developed technique of radioisotopic clearance, measured CBF and $CMRO_2$ during CPB.⁸ As shall become evident, this remarkable report by Yasukazu Kubota presaged by nearly two decades studies using similar techniques in the West. In a series of 40 patients, ^{85}Kr clearance, in conjunction with cannulation of the superior jugular bulb, was used to determine CBF and $CMRO_2$ and, in conjunction with retinal photomicrography, the impact of nonpulsatile CPB on the cerebral vasculature. While the study suffers somewhat because of fluctuations in uncontrolled variables, i.e. $PaCO_2$, and critical data such as esophageal temperatures and hematocrits were not reported, these observations, i.e. decreases in CBF of 35% with institution of CPB, decreases in $CMRO_2$ of 63% during hypothermia and 23% during rewarming, and retinal venous engorgement during rewarming, are both qualitatively and quantitatively consistent with what subsequent investigators have observed. This paper apparently also marked the first observations in man of retinal microembolism occurring during CPB, again markedly preceding the reports by Blauth et al.^{9,10}

Despite these remarkable observations, there were few if any radioisotopic CBF studies during CPB in man reported for the next 15 years. Other investigators relied upon indirect estimates of CBF, e.g. $AVDO_2$, Doppler scans, or thermodilution techniques,¹¹⁻¹³ producing results that were of limited interpretability and that precluded the essential examinations of concomitant cerebral metabolic activity.

In animals, however, the influence of pulsatile perfusion on cerebrovascular responses during CPB was assessed by Matsumoto et al¹² in 1971, using a perfused dog head model with external electromagnetic flow probes to assess changes in carotid flow. They also directly observed cerebral and retinal capillaries and noted marked decreases in cerebral blood flow, and evidence of capillary closure and microcirculatory sludging during nonpulsatile perfusion.

pH Management and CBF

Relatively little new information regarding the cerebral circulation in man during CPB occurred until 1983 when Lief Henriksen published his remarkable observations of cerebral hyperemia during CPB.¹³ This report was followed in 1984 by a classic paper from Govier et al.¹⁴ This latter study is noteworthy not only for its observations of CBF during CPB, but also for its remarkable economy of design. Not only did these

investigators spark a controversy with their observations of ischemic-threshold levels of CBF during CPB — in direct contrast to the hyperperfusion reported by Henriksen — but they also made preliminary observations on virtually all of the critical variables felt to influence CBF during CPB.¹⁴

What was missing from both of these studies, however, was the investigation of concomitant cerebral metabolism, without which these various discordant observations of CBF could not be meaningfully reconciled. In 1987 Murkin et al reported their observations of both CBF and $CMRO_2$ during hypothermic CPB in man, using a ^{133}Xe clearance technique for measurement of CBF, similar to those reported by Kubota, Govier, and Henriksen and their colleagues, and with the addition of a jugular bulb catheter for sampling effluent cerebral venous blood for measurement of cerebral metabolic activity.¹⁵ The working hypothesis was that differences in pH management accounted for the apparently divergent values reported for CBF during hypothermic CPB. Accordingly, patients were managed with either alpha-stat or pH-stat pH management during hypothermic CPB. Not only was a similar and pronounced reduction in $CMRO_2$ observed in both groups during hypothermia, but in the alpha-stat group global cerebral flow/metabolism coupling was better preserved in comparison to the group managed with pH-stat. Also of note were the decreases in CBF and $CMRO_2$ that were still evident after rewarming during normothermic nonpulsatile CPB. These values for CBF and $CMRO_2$ returned to control levels shortly after separation from CPB, and were consistent with the observations of decreased CBF and $CMRO_2$ during nonpulsatile perfusion made previously during normothermic CPB.^{4,5,7,8}

Normothermic CPB

The cerebrovascular and metabolic effects of normothermic CPB have been elegantly investigated in studies by Anderson and Sorensen and coworkers.^{16,17} Using radioisotopic microspheres, they reported that CBF and the cerebral metabolic rate for glucose (CMR_{glu}) were decreased by 32% and 22% respectively during normothermic nonpulsatile CPB, and that there was a pronounced decrease in calculated cerebral capillary diffusion of 80%. Again CBF and CMR_{glu} were not assessed after separation from CPB and the authors speculated that cerebral microembolization was responsible for the changes observed. These decreases in CBF and cerebral metabolism were remarkably similar to those we measured during normothermic CPB, and which returned to control levels shortly after separation from CPB.¹⁸ Our further studies using thiopental-induced EEG suppression suggest that functional cerebral capillary closure during nonpulsatile CPB may be a mechanism for these decreases.¹⁹

This is not to downplay the potential for embolization of micro and macro debris into the cerebral circulation during

CPB. Blauth et al reported retinal microembolizations occurring during CPB in all 20 patients whom they examined using intraoperative fluorescein retinal angiography.^{9,10} It is worth noting that bubble oxygenators were utilized in all the cases reported. In a study using a transcranial Doppler for detection of cerebral emboli, Padayachee et al²⁰ demonstrated continuous generation of cerebral emboli in all patients managed using bubble oxygenators and none in whom a membrane oxygenator was used. In addition, specific events during CPB, i.e. aortic cross-clamping, were associated with generation of detectable cerebral emboli. It is apparent that these investigations not only point out modifications of equipment and technique that might decrease cerebral risk, but also illustrate a potential risk of cerebral hyperperfusion with its attendant increase in delivery of embolic debris into the cerebral circulation.

Pulsatile Perfusion

The influence of pulsatility during normothermic CPB was assessed by Tranmer et al²¹ in a series of dogs before and after the production of an ischemic hemispheric lesion. In the nonischemic brain, the institution of pulsatile perfusion during CPB increased CBF by 19% over the nonpulsatile CPB control, while it increased CBF by 55% in relation to nonpulsatile control after the production of an ischemic brain lesion. Murkin et al have demonstrated increases in CBF of 15% with pulsatile perfusion during hypothermic CPB in man.²² When assessed in the context of the other investigations outlined above, these studies should not be interpreted as showing increases in CBF during pulsatile CPB, but rather that nonpulsatile perfusion decreases CBF, and presumably CMRO₂, by some as yet undetermined mechanism with pulsatile perfusion restoring CBF towards normal.

Clinical Implications

Currently, these and other questions are all being actively pursued by several groups of investigators, including the most important question of whether modifications in the conduct of CPB, e.g. pulsatile or nonpulsatile perfusion, or various forms of pH management, have any impact upon neurological outcomes after CPB. At least one study, that by Bashein et al,²³ has been unable to demonstrate differences in psychobehavioural outcome after randomization to either alpha-stat or pH-stat management during hypothermic CPB, although whether this study truly assessed pH-stat management is controversial.²⁴ Similarly, the prophylactic administration of thiopental to patients undergoing coronary artery surgery has not been shown to favorably influence neurological outcomes.²⁵ Whether other such interventions or modifications of technique will be similarly unrewarding remains to be seen, but the important aspect of all of these investigations is that clinical management

techniques that are optimal for the patient continue to be actively sought so that the reported incidences of neurological and psychobehavioural dysfunction of 40 to 60% following CPB²⁶⁻²⁹ can hopefully be reduced.

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