Techniques of intraoperative cerebral blood flow measurement

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Understanding the physiological mechanisms of cerebral blood flow (CBF) is of great importance to neurosurgeons engaged in the management of patients with cerebrovascular disease. Over the past 50 years, techniques to measure CBF and mathematical methods to calculate CBF have evolved substantially. For the cerebrovascular surgeon, intraoperative CBF monitoring is an important adjunct in certain intra- and extracranial procedures. The authors review current techniques in use for the intraoperative measurement of CBF.

KEY WORDS • cerebral blood flow • intraoperative monitoring • xenon study • transcranial Doppler ultrasonography

The brain uses aerobic metabolism exclusively for energy production. Accordingly, the brain is critically dependent on the nearly continuous delivery of oxygen and glucose to sustain cellular energy production. Resting CBF in the awake patient is approximately 50 ml/100 g brain tissue/min.²⁶ As CBF decreases, neuronal dysfunction and injury occur. At levels of 16 to 18 ml/100 g/min, cortical electrical function fails, as evidenced by attenuation in EEG and SSEP recordings. At levels of approximately 10 ml/100 g/min or less, rapid changes in intracellular and extracellular ion concentrations occur, as well as the development of intracellular acidosis. Persistence of CBF at levels below this threshold of maintaining ionic balance will result in membrane disruption, irreversible neuronal injury, and cell death.

Intraoperative monitoring of CBF, both qualitatively and quantitatively, has contributed to improved outcomes after cerebrovascular procedures.² In patients undergoing CEA, the use of intraoperative CBF measurements has proven to be effective in reducing operative morbidity.^{4,5,43,44} Intraoperative CBF monitoring has also been a useful adjunct in the treatment of complex intracranial aneurysms and arteriovenous malformations, particularly when temporary or permanent vessel occlusion is undertaken.^{2,30} We review the current state-of-the-art techniques for the monitoring of CBF.

QUALITATIVE CBF MONITORING TECHNIQUES

Neurological Examination

The neurological examination is a sensitive, qualitative technique used to assess the adequacy of CBF during cerebrovascular procedures. The primary limitation is that the patient must be awake during the procedure. For patients undergoing CEA, this generally poses no major difficulties. Using a cervical ganglion block, the procedure is performed with ongoing neurological and language-response examination. Because CEA in an awake patient obviates the need for EEG monitoring and allows the patient to be discharged within 24 hours, there is a clear benefit in cost. Furthermore, it is likely that cardiac complications are reduced when regional anesthesia is used compared with general anesthesia for CEA.³⁴ Some patients, however, will not tolerate undergoing an awake procedure.

Transcranial Doppler Ultrasonography

The use of TCD ultrasonography has been advocated as a tool to measure CBF velocity in the ipsilateral middle cerebral artery during carotid endarterectomy.^{17,23,25,27,42} The technique is well established but, because of variations in normal vessel diameter and operative technique, TCD studies can provide only a relative index of CBF based on normal ranges.²⁵ As equipment and surgical experience have evolved, the technique has been used more frequently in intraoperative monitoring. Recently, a very large study reported by Ackerstaff and colleagues¹

Abbreviations used in this paper: CA = carotid artery; CBF = cerebral blood flow; CEA = carotid endarterectomy; EEG = electroencephalogram; SSEP = somatosensory evoked potential; TCD = transcranial Doppler; ¹³³Xe = Xenon-133.

demonstrated that TCD-depicted variables accurately predicted stroke during or immediately following CEA. Furthermore, TCD studies, with high sensitivity, can identify patients at risk for postendarterectomy hyperperfusion syndrome and hemorrhage.^{1,13} Whereas the technique has the advantage of being noninvasive, the cost effectiveness of TCD monitoring during CEA remains unknown.

Electroencephalography and SSEP Monitoring

Electroencephalography is an indirect, qualitative measurement of CBF in patients undergoing cerebrovascular surgery. It is a highly sensitive marker of CBF, as there is a strong correlation between alterations in the EEG and diminished CBF.^{29,40} The technique has become commonplace for monitoring CBF in patients undergoing CEA.^{12,31,38,48} For intracranial procedures, surface EEG strips can be used. Techniques for intraoperative cerebral protection, such as barbiturate administration or hypothermia, may limit the sensitivity of EEG for the detection of cerebral ischemia, yet EEG is useful in titration of the protective effect when burst suppression is desired.^{3,37,39} Measurement of SSEPs is another neurophysiological monitoring technique currently used in some centers during extracranial vascular surgery.²² Of note, SSEP monitoring may be valuable when reconstructing the vertebral artery circulation, as SSEPs may be more sensitive in detecting brainstem ischemia than EEG.

Intraoperative Angiography

Particularly in the surgical treatment of giant or complex intracranial aneurysms, it is important to have the option of obtaining an intraoperative angiogram; this allows for the qualitative assessment of the presence and adequacy of CBF and the patency of specific cerebral blood vessels following aneurysm repair.^{15,33} Routine use of intraoperative angiography in aneurysm surgery has been reported more frequently of late. In a recent study, intraoperative angiography led to clip repositioning in 10% of 520 consecutive cases.⁴⁵ Accordingly, in all cases in which intraoperative angiography may be required, the head should be fixed with a radiolucent headholder. It is important to position the patient high up on the operating room table so that the shoulders hang over the edge. This will facilitate adequate positioning of the image intensifier. Furthermore, it is advantageous to limit the use of self-retaining retractors, because the retractor bars will obscure good visualization on the intraoperative angiogram. If the cervical CA has been exposed, it can provide an easy route to perform intraoperative angiography through a direct CA puncture. Alternatively, the femoral artery can be cannulated for vascular access.

QUANTITATIVE CBF MONITORING TECHNIQUES

Xenon-133 Study

The most widely used method of intraoperative CBF measurement, and the technique used at our institution, is the intraarterial injection of ¹³³Xe into the internal CA and the extracranial detection of the clearance curve deter-

mined using highly collimated scintillation detectors (Fig. 1). Xenon-133 is a low-energy gamma emitter that diffuses freely through the brain and, thus, is an ideal agent for measurement of CBF.

Xenon-133 is a radionuclide that is chemically related to the element xenon, a nonradioactive gas that is chemically inert. The radionuclide has anesthetic properties at concentrations greater than 33%. It has an unstable nucleus, continuously emitting beta, gamma, and x-ray photons. The emitted photons are of low energy and, as such, can be absorbed by 0.1 ml of lead to reduce exposure by 90%. The physical half-life of ¹³³Xe is 5.27 days. It is distributed as a 5% concentration mixed with 95% CO₂, which is then dissolved in 0.9% sodium chloride for injection.² Xenon-133 freely passes through cell membranes, crosses the blood-brain barrier, and is not metabolized anywhere in the body. After injection into the internal CA, it is retained momentarily in brain tissue and is then released through normal venous outflow channels. Ninety percent of ¹³³Xe is expelled through the lungs on first-pass, thereby minimizing recirculation of the radionuclide through the cerebral vasculature.²

Appropriate safety measures must be taken to minimize radiation exposure to medical staff and patients. In handling ¹³³Xe, care should be taken to avoid direct contact with the hands or any other part of the body. Our standard use involves 0.6 rad/minute of exposure time for the surgeon and less than 5-μrad/minute exposure to surrounding personnel. The maximum permissible exposure, as set by the Nuclear Regulatory Commission, to the hands and body is 75 rads and 5 rads per year, respectively. Thus, the exposure encountered in typical use is well below safe limits. In patients, exposure varies by procedure. For a CEA, the estimated absorbed radiation dose in an average patient from a maximum total dose of 1.6 mCi would be 0.5 mrad to the lungs, 30 mrad to the brain, and 0.9 mrad to the rest of the body. Because of the potential risks, ¹³³Xe should generally be avoided in pregnant women.

It is important to obtain baseline measurements of ¹³³Xe for each patient intraoperatively. Accuracy of the instrumentation and measurement devices must also be verified. The main components of the ¹³³Xe CBF measurement system are a scintillation detector, pulse-height amplifier, count-rate meter, power supplies, and a strip chart recorder (Fig. 1). The two types of scintillation detectors in use today are thallium-activated sodium iodide crystal (NaI(TL)), and CdTe. The NaI(TL) detector uses a scintillation crystal that converts the energy of the incoming photons into visible light, and it is coupled to a photomultiplier tube, which then converts these scintillations into electrical pulses. The crystal thickness is usually 6 mm to provide maximum counting efficacy, which is approximately 90 to 99% for ¹³³Xe. The crystal is mounted behind a lead collimator that is 25 mm thick and has a tapered opening from 30 mm at the surface of the crystal to 22 mm at the front end. This detector assembly consisting of the collimator, crystal, photomultiplier tube, and preamplifier is mounted on a stand that can be moved up to the patient's head. The CdTe crystal is 16 mm in diameter by 2 mm thick and is mounted inside a lead collimator that is packaged in a metal cylinder. This unit is attached to the patient's head by means of a strap. The counting efficiency

Fig. 1. Illustration showing the operating and control room layout for ^{133}Xe CBF measurement and EEG monitoring. With permission from the Mayo Foundation.

of this unit with ^{133}Xe is 96%. The detector is lighter weight and operates at a lower voltage than the NaI(TL) system, but it is more expensive.

Signal processing of the electrical pulses generated by the detector assembly requires a preamplifier, amplifier, pulse-height analyzer, and count-rate meter. The preamplifier and amplifier function to match the impedance level between the scintillation detector and the preamplifier and to amplify the low-voltage pulses from the preamplifier to a sufficient level to drive the pulse-height analyzer. The pulse-height analyzer is used to select only those pulses that coincide with the energy level of ^{133}Xe (81 keV) and discriminate against background noise and scattered radiation outside the selected energy range (75–200 keV). The count-rate meter is used to determine the average number of counts per unit time, and the counts are recorded on a strip chart recorder.

Ultimately, the measurements obtained by the scintillation detectors and processed as just described yield clearance curves representing the washout of ^{133}Xe (Fig. 2). These clearance curves can be analyzed by one of several methods for curve analysis to calculate the value of CBF: initial slope index,^{32,35,46} determined from the slope of the first minute of the clearance curve; stochastic method;^{21,22,32,46} and two-compartmental analysis^{20,21,46} to yield both gray and white matter CBF values. The initial slope index is most commonly used, whereas the other two analytical methods require an online computer to determine results.

In using the initial slope index, the primary hypothesis is that blood flow in the cerebral grey matter dominates the first part of the initial fall period of the clearance

Fig. 2. Graph showing CBF curve following intraarterial injection of ^{133}Xe into the internal CA. Cerebral blood flow in milliliters per 100 g per minute is calculated by dividing 3600 by the one-half peak value in seconds—in this example 55.5 ml/100 g/min. cpm = counts per minute. With permission from the Mayo Foundation.

curve. Therefore, the first 1 to 2 minutes of the clearance curve can be regarded as a monoexponential function. The equation for the initial slope can be described as:

$$\text{regional CBF (ml/g/min)} = \lambda \times 2.3 \times F(\text{initial})$$

where λ is the tissue to blood partition coefficient for ^{133}Xe in gray matter, 2.3 is the factor for converting common to natural logarithms, and $F(\text{initial})$ is the numerical value of the slope in semilog (base 10) system. The value for the partition coefficient used is 0.87 because it represents the first descending part of the clearance curve relating to gray matter.^{21,32,35,46} The initial slope analysis does not take into consideration differences in the amount of gray matter being monitored. If a single detector is used and is always placed in the same anatomical location, then the potential for this error is greatly diminished. The advantage of this method is that measurements can be made serially with short wait times, provided that the isotope is adequately cleared from the brain. Because of the simplicity of the equation, a hand-held calculator can be used to compute the blood flow values quickly.²

A primary limitation of CBF measurement in ^{133}Xe studies is the "look-through" phenomenon.^{14,18} This is the failure to indicate areas of low- or no-flow regions because the detector can see only areas of perfused tissue. In other words, the detector sees the under- and/or overlying tissue and also tissue peripheral to the area in the field of view. A second limitation is that performing fast serial measurements introduces error. The time interval between CBF measurements at 5 minutes and 10 minutes will result in overestimation of CBF by 10% and 5%, respectively.²⁴ Therefore, a waiting period is recommended between measurements to minimize errors due to a greater than normal background. A third limitation is Compton scattering,³⁶ which may introduce considerable error in the determination of the volume and severity of focal ischemia. Compton-scattered photons can be minimized by setting the lower level of the pulse-height analyzer to 75 keV.³⁵

Ultrasonic Perivascular Flow Probe

An ultrasound-based device historically used in vascular and cardiac surgery, the ultrasonic perivascular flow

probe, has recently been used in cerebrovascular procedures—typically in aneurysm surgery.^{10,11} In this probe a small pencil-like device with a semicircular tip uses ultrasound transit time to measure blood flow. The tip is positioned such that the vessel of interest is contained within the diameter of the semicircle. A quantitative measure of CBF is obtained, and the accuracy of the technique has been convincingly validated.^{19,28,47} With this device, blood flow in individual cerebral vessels can be quantified immediately following placement of an aneurysm clip to verify the sufficiency of flow in the parent artery or nearby perforating arteries.⁹ The technique is fast, easy to perform, and can be repeated after multiple clip applications. We have found it extremely useful in the surgical repair of complex aneurysms, alone or as a quantitative adjunct to intraoperative angiography.¹⁵

Thermal Diffusion Flowmetry

In 1933 Gibbs (unpublished data) first described the use of the thermal diffusion technique to measure CBF. He used a heated thermocoupler to measure flow through the internal jugular vein. However, by nature of its design, it could accurately reflect relative changes but not absolute values. Brawley⁶ furthered the technique by incorporating a Peltier stack to improve the stability of the recording probe, thereby enabling measurement of CBF over extended periods of time as well as measurement quantitation. Carter, et al.,⁷ eliminated the Peltier stack to miniaturize the recording probe so that it could be more easily used postoperatively in a wide variety of cases.

The probe has two gold plates in a thin 3-mm Silastic sheath, one heated and one nonheated. The temperature difference between these plates is monitored constantly by computer, and the resultant difference is converted to a CBF value in milliliters per 100 g per minute. The following is the mathematical formula derived to quantify cerebral flow by thermal diffusion:

$$CBF = K(1/V - 1/V_0),$$

where CBF is the cortical blood flow in milliliters per 100 g per minute, K is the conductivity constant of brain tissue, V is the voltage difference between the two plates, and V₀ is the voltage difference between the two plates at zero flow. The depth range of the measurement of CBF by thermal diffusion in brain tissue is approximately 1.5 mm.¹⁶ Care must be taken not to place the probe on any major surface vessel. The probe must be in contact with the tissue surface to provide valid temperature measurements. Because the placement of the probe must be visually inspected in relation to the cortex, it may be difficult to install the probe at a bedside setting.

The measurement of CBF by thermal diffusion has been used postoperatively to monitor patients who have undergone aneurysm clipping or resection of cerebral arteriovenous malformations.⁸ It has also been used to monitor patients with temporal lobe epilepsy or after severe head injury.^{8,41} The advantage of measuring CBF by thermal diffusion is that real-time continuous monitoring of CBF is possible. The disadvantage is that this technique measures small volumes of tissue and results in possible inaccuracies because of the heterogeneity of blood flow distribution.

CONCLUSIONS

Continued refinement of techniques for the monitoring of CBF has led to an increasing number of clinical applications. Despite these advances, no existing CBF monitoring technique is without certain limitations. Understanding specific advantages and drawbacks of available techniques allows for selection of the most appropriate intraoperative monitoring technique for each patient.

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