THE GOAL IS QUANTITATIVE CEREBRAL BLOOD FLOW


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Care directed by data instead of “our best educated guess” has always been the goal of treating physicians, especially for patients in the intensive care unit. Undoubtedly patient specific quantitative information about cerebral blood flow (CBF) is a physiological variable that would be important for clinicians to have in order to meet these goals. Access to this type of information would have clinical relevance for two reasons: first because there are known thresholds of CBF below which reversible [2, 5, 11, 14, 29] and irreversible [4, 12] ischemic injuries occur and second the ability to monitor the response to a proposed intervention conceived to raise CBF would be essential for being able to know if the interventions achieved their goals.

Because the lack of accessibility to reliable CBF measurements alternative approaches have been developed. For example, intracranial pressure (ICP) measurements are commonly made post head injury, in part, to understand the patient’s risk for developing ischemia. Aggressive approaches have developed to “improve CBF” assuming that an elevated ICP meant a compromised CBF. Similarly, transcranial Doppler (TCD) studies are performed on patients post subarachnoid hemorrhage on the assumption that an elevated TCD is indicative of vasospasm and of impending ischemia. Unfortunately, both of these assumptions are not valid in a significant proportion of patients [5, 6].

We have had access to methodologies capable of qualitative patterns of CBF for decades but this information has not won a central role in clinical care. Utility for the measurement of flow patterns has been demonstrated where the goal is identification of a focal elevation or depression of blood flow as a window to coupled changes of metabolism. Utility for flow pattern changes has been demonstrated for defining seizure foci both during and between seizures. Measuring ratios of flow between a presumed to be ischemic brain region and a presumed normal region is another proposed strategy. Unfortunately, using ratio’s to build a series of assumptions is laden with many possible errors. For one, assuming that flow on the “normal” side is 50 ml/100g/min in acute contra lateral MCA ischemia is a false assumption. Using the cerebellum is equally susceptible to the same error. Both regions have flow values closer to 30 ml/100g/min but with much variation between patients. Similarly flow on the “ischemic” side can be absent, reduced or elevated above normal. This approach has yet to win a wide utility for answering critical clinical questions despite the strong advocacy of its proponents.

The use of a qualitative study for assessing the response to proposed therapies involving a physiological challenge are even more problematic. Qualitative studies have been used to assess the response to physiological challenge by measuring ratios between an area of interest and a presumed “normal” region and by measuring the change of the ratio after challenge [16, 18, 20, 21, 26-28]. This approach also requires that assumptions be made about the expected response. For example, with balloon test occlusion if one assumes that the only response that can follow vessel occlusion is lowering of flow on the occluded side one will be wrong in the interpretation of this type of data in over 50% of patients [31]. For example, an error of assignment occurs with ratios when flow elevates bilaterally but with less of an elevation on the side of the test occlusion. This high rate of error at least partially explains the inability of management guided by qualitative studies to significantly lower the risk of carotid sacrifice. This is in contrast the utility demonstrated with quantitative assessments used for guiding carotid occlusion.

Qualitative studies of CBF combined with acetazolamide for the study of patients with occlusive vascular disease failed to identify a group with an increased stroke risk [17]. Conversely, numerous authors have found that quantitative studies do identify a significant population to be at increased stroke risk [25, 30, 33, 35]. Pindzola et al. [34] attempted to answer the question by performing a qualitative assessment of a quantitative data set and thereby identified a 50% error of prediction using a ratio strategy. Ogasawara et al. [24] provided further evidence of the errors that can be made with qualitative data when he performed both types of studies in the same patients with occlusive disease. While a quantitative assessment identified a subgroup with greater than 30% stroke incidence the qualitative study failed to identify any group at increased stroke risk.

Quantitation, however, is not enough. Information that lacks resolution and especially if contaminated by flow within superficial and deeper structures fails to identify even large regions with at or near zero flow. Xenon133 regional flow probes integrate radiation from scalp and from the depths of the brain where there may be high flow. The end result is the inability to identify anything more than the fact that ischemic stroke is accompanied by an asymmetry of flow [1, 3, 13, 19]. The combination of SPECT and xenon133 has improved upon the resolution of the data but there remains a relative
inability to see low flow values especially if below the surface of the brain [22].

CT perfusions as well as MR perfusion studies offer a cluster of three variables with unfortunately the weakest being CBF. It is sufficient to say that the blood volume and transit time data provide utility by providing related variables that overcome the relatively weak quantitative CBF data. Because of their rapid accessibility and high-resolution tomographic format this approach has, however, won considerable support.

Xenon/CT CBF overcomes some of the difficulties of prior technologies but it has other reasons why acceptance has been slow. Sensorial changes induced by xenon have not been insignificant but they have been consistently short lived and benign. Respiratory pauses have been reported but they were self-limiting and not associated with the need for starting external ventilation in any reported case. Both of these types of phenomena have been reduced to rare events by lowering the concentration to 28% xenon, made possible by the improved noise of modern scanners. The ability of xenon to elevate CBF has been an area of concern from the beginning. Numerous studies have, however, demonstrated agreement of Xenon/CT derived values with other established quantitative technologies [7-10, 32]. The explanation for the accuracy of the flow data generated has been explained by a series of articles that demonstrated that significant flow activation occurs late, beyond the time when all gray matter and nearly all white matter flow is already recorded [23].

Other problem areas include the delayed access to Xenon/CT derived flow data that was inherent in earlier systems. In early systems in use in the 1990’s flow data for two or three was usually available for clinical integration for many hours. With modern computers and networking, a completed flow study of 6 or more brain levels is available for integration into prospective decision making within 3 minutes of the inhalation sequence. Thus, a study format in which the baseline flow is reviewed with the patient on the table and a second study performed to answer a specific question: i.e., raise blood pressure if flows are low to check for auto regulation and whether blood pressure changes are efficacious.

Motion remains another problem for high resolution flow imaging with Xenon/CT CBF, thereby limiting consistent access to perfect studies in awake patients that are often confused, apathetic and agitated after ischemic stroke. With a coordinated team often aided by short acting hypnotic agents a high yield of useful studies can, however, be generated in this population. Motion is never a problem in patients that are intubated and paralyzed so that this type of vital CBF data can always be acquired in this population. The ability to correct for motion after study completion is probable in the future.

Until now we have attempted to explain the lack of wide utility of CBF measurements due to the limitation of the available studies. It makes no sense to believe that the goal is anything less than numbers that are real and therefore can be readily integrated into clinical care with a minimal number of assumptions. A central focus has been the inability to provide quantitative information in a user, patient and clinician, friendly manner and deliver the information in a timely manner. With this type of information it is possible to identify not only regions that are reversibly and irreversibly ischemic but also regions that are near ischemic. The ability to repeat a CBF study after elevating blood pressure or lowering pCO2 is essential to be able to assess the efficacy of these and other efforts believed to enhance CBF.

REFERENCES

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