Stroke and Intraoperative Hypotension: To Sleep, Perchance to Stroke—Ay, There’s the Rub

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The article by Hsieh et al in this month’s issue of Anesthesia and Analgesia is not the first to suggest that there is not a strong correlation between intraoperative hypotension and postoperative “stroke” (used herein to refer to focal or global ischemic cerebral injury not related to intracerebral or subarachnoid hemorrhage).1–3 Hsieh et al reviewed the electronic medical records of patients at the Cleveland Clinic to identify those in whom strokes, as identified by the International Classification of Diseases, Ninth Revision, codes, had occurred in the postoperative period after nonneurologic, noncardiac, noncarotid surgery. They then examined electronic anesthesia records to extract an area under the curve metric of hypotension, combining duration and degree of mean arterial pressure (MAP) reduction below MAP thresholds of 70, 65, and 60 mm Hg. They propensity-matched 4 nonstroke patients with each of those who had sustained a stroke. They report, “Stroke patients did not experience a greater degree of hypotension than controls”; and they conclude, “There was no association between stroke and intraoperative hypotension.” One hundred four patients (0.11%), of 97,304 with complete data, sustained strokes. Seventeen of those strokes were evident on the day of surgery. The authors note that there is a prothrombotic state that prevails in the postoperative period that may have contributed to the occurrence of the 87 delayed strokes. Ergo, of the limited number of strokes that they identified, many if not most are probably not an immediate consequence of intraoperative hemodynamic management. Ergo, the number of strokes on which this comparison is based is (fortunately) very small, that is, 17.

This editorial commentary is intended to address 2 questions and offer 2 conclusions: (1) Does what we already know about normal cerebral physiology make the observations of Hsieh et al surprising? Absolutely not. (2) Should the present communication make us even more casual about intraoperative hypotension than already appears apparent? Absolutely not.

First, to the matter of normal physiology. The primary definition of “hypotension” used by Hsieh et al was an MAP of less than 70 mm Hg. However, as most of you sit at your desks reading this commentary, the MAP at your circle of Willis is about 70 mm Hg. Were you to be anesthetized in the supine position, an MAP of 70 mm Hg is a normal MAP for at least your cerebrum. Ischemic symptoms do not begin to appear in awake subjects until MAPs reach 40 to 50 mmHg at the circle of Willis.4,5 Even at that threshold, the relative ischemia is not immediately injurious, and probably not injurious at all if MAP does not fall below that threshold.

Why should hypotension cause cerebral injury in the first place? The phenomenon of cerebral blood flow autoregulation maintains CBF across some range of MAPs. However, there is probably much more inherent variability in a normal population than is implied by standard text book diagrams (see Willie et al6 Joshi et al7 and Drummond8). Furthermore, the average lower limit of autoregulation, that is, the MAP below which CBF becomes pressure passive and falls pari passu with declining MAP, is likely to be an MAP much greater than the once prevalent and still reputable9 value of 50 mm Hg. One way or another, in all of us CBF eventually becomes pressure passive and decreases as MAP declines. The threshold for ischemic symptoms (which is not synonymous with the threshold for injury) is a CBF reduction of about 40%.4,5 In volunteer studies, that threshold is reached, as noted previously, at average MAPs of 40 to 50 mm Hg. In one clinical investigation, at MAPs of 50 mm Hg, many sedated, initially normotensive subjects were close to but did not exceed that 40% threshold.10 It should therefore not be surprising therefore that the MAPs observed by Hsieh were not associated with stroke. You can get away with a lot; however, the phenomenon of watershed or boundary zone ischemia12 has taught us that somewhere there is a limit to central nervous system tolerance.4,5 That limit is likely to occur, in most normal adults, at values less than 50 mm Hg.

The other mechanisms by which hypotension might contribute to stroke are largely speculation, albeit reasonable speculation. Surgery is trauma, carefully choreographed trauma to be sure, but trauma nonetheless. Trauma yields a procoagulant state. It is possible that circumstances of low, but nutritively adequate, flow nonetheless result in relative...
stroke and thereby predispose to spontaneous thrombosis, especially in already diseased vessels. I do not believe that the reality of this phenomenon has actually been confirmed but it seems feasible. Most non-watershed strokes, however, are nonetheless probably embolic. Therein lies a second potential contribution of hypotension to stroke. If embolization occurs, as previously suggested, might there be a lesser likelihood of mechanical clearance during periods of low perfusion pressure, or might poorer collateral flow while native clot-clearing mechanisms operate aggrivate the final outcome? Here, for illustration, I will turn to anecdot. A sexagenarian physician friend recently found himself with sufficiently severe spine disease to agree to a lumbar instrumentation. In the preoperative holding area, before any intervention, he abruptly became aphasic. Examination revealed profound right-sided sensory deficits. A stroke code and thrombolyisis ensued. He is now normal. Would that be the case if his spontaneous event had occurred 20 minutes later, at the beginning of 4 or more hours of relative hypotension? (I know. That ignores the issue of no longer being a thrombolyisis candidate. But you grasp the point.)

The second question posed at the outset was, should we be reassured by the report of Hsieh et al that there is a non-relationship, or at worst a very weak one, between intraoperative hypotension and stroke? I doubt it. The number of strokes that actually occurred was very low and that may well be because the data indicate that, at the Cleveland Clinic, blood pressure control is rather more careful than one would think. Yet, there are nonetheless probable embolic. Therein lies a phenomenon of one reviewer’s speculation becoming the next reviewer’s fact.

The avoidance of hypotension that is not necessary for the safe conduct of a surgical procedure. I think that it is reasonable to suspect that even if it requires very significant hypotension to cause stroke in healthy subjects whose nervous systems are not otherwise under threat, strokes that occur spontaneously during anesthesia will be aggravated by sustained hypotension. Until someone proves otherwise, I think that there should be the working assumption and it should influence decisions and encourage caution about intraoperative blood pressure management, at a minimum in individuals perceived to be at increased risk for stroke.

DISCLOSURE
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REFERENCES