

Time to Widen Our Horizons in Perioperative Medicine

A Plea in Favor of Using Patient-centered Outcomes

IN this issue of *ANESTHESIOLOGY*, Bateman *et al.* use the Nationwide Inpatient Sample database to estimate the incidence of perioperative acute ischemic stroke (AIS) as 0.7%, 0.2%, and 0.6% for patients who underwent hemicolectomy, total hip replacement, and lobectomy/segmental lung resection, respectively.¹ Apart from the high incidence and severity of this complication, a striking feature of this study is the surgical population in which it occurred, one that most anesthesiologists would see in daily practice. In their conclusion, the authors “hope that their study will draw attention to this issue and promote further investigation of this topic.” Our focus in this editorial is to underscore the likelihood that such a high incidence of AIS does indeed exist and to expand on this statement by Bateman *et al.*¹

Should We Believe These Results? Is Perioperative AIS Really This Common?

There are two ways to address these questions. One relates to our individual perception as anesthesiologists of risk in the perioperative period, and the other relates to the methodological biases of the Bateman *et al.*¹ study. With an incidence of AIS approaching 1% in this study, our first reaction is to doubt the validity of such a result because it disagrees with our own personal experience. Our personal understanding of risk accumulates progressively from our daily clinical experience, but not in a linear way because we don't psychologically add each complication encountered in practice; we may not even be aware of them. Although we cannot precisely know from the study of Bateman *et al.*¹ when in the perioperative period these AIS's occurred, they most likely occurred several days after surgery. Such devastating events may not be seen by most anesthesiologists who work mainly in the operating room environment and remain unaware of delayed complications. Moreover, patients suffering from cerebrovascular accidents are likely transferred to special units for care^{2,3} and are therefore extracted from the normal flow of surgical

patients and disappear from the anesthesiologist's radar. Also, many anesthesiologists in general practice cover a wide variety of surgical procedures and would not care for a large number of cases of each of the types described by Bateman *et al.*¹ in a brief period of time. In other words, they would not anesthetize 100 patients for hip replacement before months or years pass and would consequently not see an AIS in such a patient for a similarly long period. The complication thus becomes diluted in our personal experience of the several hundred patients we care for during that period.

Another factor might cause us to neglect or minimize this complication. Patients who undergo the three surgical procedures studied by Bateman *et al.*¹ are getting older and sicker, and the occurrence of AIS in this population is not rare. Healthcare providers might be less surprised that this complication occurred because it may be considered unavoidable in this population. Comparing the incidence of AIS in the perioperative period with that found in similar populations of individuals not undergoing surgery is an interesting way to assess if an additional risk exists in surgical patients. Kleindorfer *et al.* have, for example, demonstrated an annual incidence of first-ever stroke to be at 0.163% for residents of the Greater Cincinnati/Northern Kentucky area,⁴ an incidence only slightly lower than that found by Bateman *et al.*¹ in patients undergoing major surgery. Yet, differences in methods used to collect data preclude direct comparison, and we cannot conclude that the high incidence of AIS observed by Bateman *et al.*¹ represents the baseline occurrence of this event.

A third factor that colors our view of perioperative risk relates to our perception of the role of anesthesia in the occurrence of a given disorder or complication. It is often difficult to ascribe precisely the complication to a single factor or event, and this is even more difficult when the time interval between the complication and the anesthetic increases. We must, therefore, widen our window of search to include both the intraoperative and postoperative periods and all the different services that impact patient care during this time.⁵ Most of us look at our field of practice and concentrate our search for causes among those related to anesthesia care, thus forgetting other plausible causes because they are linked to a different place and time period (*i.e.*, on the postoperative surgical wards). There is, after all, no formal reason to say today that anesthetic factors play a role in the occurrence of AIS after surgery.

Our personal experience, which tends to dismiss a high incidence of AIS, might be reinforced by an uncon-

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scious rationalization or search for methodological weaknesses of the study by Bateman *et al.*¹ Without getting lost in the minutiae of their methods, several important questions arise, primarily due to the retrospective nature of their study, which was based on administrative data.^{6,7} Were all strokes collected? Are we certain that all neurologic complications included were indeed due to AIS? Did these events occur in the perioperative period or later in a prolonged hospital stay? Can their occurrence be linked to surgery or anesthesia? The authors have adequately discussed these questions and have provided reasonable arguments that their results likely reflect the true incidence of perioperative AIS in their database. However, it remains possible that some complications were not captured. Interestingly, if this were the case, their estimate, which may be shockingly high to many of us, actually represents an underestimation of the true rate of AIS in these surgical patients. It is also possible that some strokes occurred very late after surgery and have no link with the procedure and the associated actions such as anesthesia. Also, because of the confidential nature of the process, internal validation could not be done, and verification of medical diagnoses after extraction of a statistically relevant sample of medical files was not possible. This is in contrast with data obtained in mortality studies in which a posteriori questioning of the medical examiner can validate data collected in death certificates.⁸

It seems likely, therefore, that the incidence of AIS after these common types of surgery lies between 0.2 and 0.7%. Yet, it remains impossible from this observation to state that the occurrence of a postoperative AIS has any link with anesthesia or surgery itself. This is not because of the absence of perioperative information collected, but rather because of the intrinsic nature of the epidemiologic research process, which cannot prove the causal role of any factor but can only disclose factors that are associated with the occurrence of a given complication.

Delayed Complications after Anesthesia: A Challenge for a Specialty in Constant Search of Increased Performance

Ischemic stroke is an important problem for perioperative physicians, not only because of the high incidence reported here, but also because this is a major complication that can endanger the patient's life or significantly degrade quality of life.⁹ Previous studies evaluating the incidence of perioperative AIS after noncardiac surgery are rather old and few, most of which are included in the Bateman *et al.*¹ reference list. Why is there a renewed interest in this complication? The most obvious answer is that anesthesiologists have mainly concentrated their

efforts until now on adverse events, which are frequently observed in the core of their job, *i.e.*, those occurring during anesthesia or immediately thereafter. Our focus on this time period has led to an improved understanding of factors causing these complications and a large reduction in the incidence of such complications.⁸ Because of the large reduction of these most visible complications during the intraoperative period, it is logical that we now open our eyes to complications, which are either even less common or less obviously related to our practice. Anesthesia research has already begun this widened view, with a growing interest in ischemic heart disease and prevention of coronary complications after surgery. Anesthesiologists are already experts in understanding the role of and prescribing β -adrenergic blockers in the perioperative period¹⁰ and are becoming more familiar with in the perioperative use of statins,¹¹ although these drugs are not necessary to provide anesthesia. The scope of our clinical activities progressively enlarges, blurring the limits of anesthesia practice.¹² How far the practice of anesthesia and perioperative medicine grows will depend on how large a role we choose to play in recovery after surgery and mitigation of critical postoperative events.¹³

What Should Be Our Strategy Now?

As regards perioperative AIS, the results of Bateman *et al.*¹ require confirmation by additional studies. The next step will include studies to analyze risk factors and to identify those that are avoidable. Such studies may uncover inadequate quality of care in the occurrence of this complication. It is both completely remarkable and logical that Bateman *et al.*¹ suggest the possible role of intraoperative arterial hypotension as a factor causing perioperative AIS. Zahara *et al.* have recently reported a mean incidence of perioperative stroke of 0.7% but have also shown that hypotension increases the risk of postoperative stroke more than sevenfold (odds ratio, 7.35 [1.7-32.5]).¹⁴ This study and the comment by Bateman *et al.*¹ again show our propensity to focus on factors that are related to intraoperative anesthesia practice and quality of care in perioperative adverse events. Although anesthesia might play a role in the occurrence of perioperative AIS, we may just as well find other factors that are more important. Odds ratios are values that are relative to parameters included in the analysis. Controlling for a major risk factor artificially increases the weight of those of smaller importance and may lead to inappropriate attention and action directed toward minor factors. There are indeed several other non-anesthetic factors that may be of importance. These factors may take place during the intraoperative period, but they could and are perhaps more likely to occur during the whole postoperative period.

Trials measuring surrogate end points or process measures are often preferred by researchers and funding agencies to obtain results more quickly with fewer patients and at lower costs.¹⁵ Unfortunately, these trials do not provide results that are definitive in our care of patients.¹⁵ Rather, it is of utmost importance to scrutinize both the overall process of care and the pathophysiologic changes, which are situated between the surgical procedure and the time at which the adverse event occurs. Postoperative inflammatory responses and/or anticoagulant administration might well play a role in perioperative AIS as discussed by Bateman *et al.*¹ This also reminds us that additional studies in other practices or countries are necessary. The ENDORSE study showed, for example, the wide variability of anticoagulant use after orthopedic surgery,¹⁶ and US surgeons are well known to use anticoagulants less frequently than their European counterparts. US surgeons have also been shown to use anticoagulants for a shorter period of time than recommended, potentially exposing their patients to late venous thromboembolic events¹⁷ but also possibly to an increased rate of arterial events.

The study by Bateman *et al.*¹ in this issue of ANESTHESIOLOGY is important and interesting in many aspects. It highlights the utility of large databases to probe rare, or not so rare, adverse events in the perioperative period, and it gives rise to some fresh thinking about a major perioperative complication that had been somewhat neglected in research. It also raises important questions relative to our specialty and patient safety. Finally, it focuses our efforts on patient-centered outcomes, which are clearly more important than process outcomes^{15,18}; it does so by widening our horizons as perioperative physicians on three dimensions: the surgical procedure, the entire perioperative hospital stay, and the disease itself. Integrating these notions will change our view of patient safety and our ability to advance perioperative medicine.

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