Perioperative Stroke
Time to Redefine the Impact of Age?

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Perioperative stroke increases the risk of mortality by up to 10-fold after cardiac and noncardiac surgery. In addition to increased disability experienced by the patient, the burden of perioperative stroke significantly impacts healthcare costs. Given the significant consequences imposed by perioperative stroke, it is fortunate that its incidence remains below 10%, even after more complicated cardiac valvular surgery. However, concern has arisen that the burden of perioperative stroke (defined as occurring within 30 days of operation) will increase as a growing number of elderly patients with significant comorbidities are offered cardiac surgery. In this issue of Stroke, Mérie and colleagues approach this important question using a Danish administrative database of 25,159 patients having undergone coronary artery bypass grafting surgery. Their findings challenge the generally accepted notion that elderly patients (age >70 years) should be considered at increased risk of perioperative stroke, and as a result, perhaps be denied surgery. In contrast to advanced age, the authors emphasize the independent role of comorbidities, in particular previous stroke, in increasing the risk of perioperative stroke. This study also demonstrates the importance of considering a contemporary group of patients when determining perioperative risks. With the continued evolution of surgical and anesthetic techniques, perioperative risk may also have changed in recent times. Indeed, their analysis is important, as the traditional perioperative stroke data that they compare their own results with (such as Roach et al) are more than 20 years old and may no longer adequately represent current surgical, anesthetic, or patient factors.

Nonetheless, we must not downplay the importance of age, as there remained a strong association between advanced age and perioperative mortality; age cannot be discounted as an important variable for predicting overall perioperative risk after cardiac surgery. As the EuroSCORE (that integrates age in its index of cardiac surgery risk) was routinely used in Denmark for risk stratification, sicker elderly patients (potentially with more aortic atheroma) may have been denied surgery, creating a selection bias that favored the healthy elderly patient. Indeed, the burden of aortic atheroma (itself a major risk factor for stroke following coronary artery bypass grafting) was not quantified. Furthermore, to achieve a large enough data set to warrant analysis, 10 years of data are included, a time over which clinical care has continuously evolved. Other embedded, and unmeasured, confounders in the article included perioperative variables, such as hemodynamics, acid-base balance, temperature management, and hematocrit.

When interpreting findings from retrospective database studies such as these, we are often faced with the dilemma regarding causality, as well as the potential effects of unaccounted confounders. We have suggested a few of these confounders above; certainly, this study is not immune to this limitation, and hence, we must be cautious in interpreting the data. That said, administrative data could be a powerful initial resource to help us develop insight into important, but uncommon, outcomes. As both perioperative care becomes safer (and with it, overall adverse outcome rates decrease) and simultaneous administrative data collection improves, we will increasingly turn to these types of data sets to gather outcome information. Nonetheless, although administrative database studies provide useful information, they do not abrogate the need for prospective observational studies or randomized controlled trials to confirm their findings. In this light, we suggest that parallel database studies are required to confirm this group’s findings followed by cohort studies to probe further into the interaction of age and stroke.

Although biological plausibility does not circumvent the need to confirm prospectively the findings by Mérie et al, it is of critical importance when interpreting database studies. For example, although the authors found that age modestly increased the risk of stroke (up to age 70 years), this factor was outweighed by the diagnosis of previous stroke. This makes sense, as a previous stroke may indicate other underlying cerebrovascular disease, and also leaves a vulnerable area of the brain with limited autoregulatory capacity. However, previous stroke is a heterogeneous grouping that encompasses patients with varying levels of neurological disability, stroke location, and pathogenesis. Prospective data collection is required to understand the importance of these stroke-related factors in determining perioperative outcomes and whether subtypes of stroke exert higher risk. Furthermore, the finding that previous stroke is not predictive of mortality is of interest given that perioperative stroke imparts...
at least a 2-fold increase in risk of perioperative death. We surmise that for mortality, previous stroke is dwarfed as an important preoperative mortality risk factor by other comorbidities, such as renal failure. Similar to these findings, we recently found that previous stroke did not increase the risk of mortality from abdominal aortic aneurysm repair, but found that the diagnosis of previous stroke did increase the risk of mortality from orthopedic surgery.14 Interestingly, the EuroSCORE avoids the term previous stroke, using neurological dysfunction instead. Additional data are also required to isolate any risk posed by the different conditions grouped under this even broader title.

In their analysis, Mérie et al found that in addition to previous stroke, other vascular risk factors were associated with increased risk of perioperative stroke. This may be because of impaired autoregulation in patients with vascular diseases, such as hypertension and diabetes mellitus,3,12,14 leading to increased risk of ischemia during otherwise normotensive surgery15; clearly, intraoperative variables, such as hemodynamics and hematocrit, would be of use to help discriminate among these issues. Although cerebral oximetry monitors using near infrared spectroscopy are routinely used in some centers to optimize cerebral perfusion, their use is not widespread, largely because of the paucity of data to show their use being associated with improved outcomes. For example, prolonged cerebral hyperperfusion (as determined using near infrared spectroscopy) during cardiac surgery was associated with increased morbidity, but an association with increased risk of stroke.22–24 A complex relationship is evident between risk of stroke and the routine use associated with autoregulation.11,12,14,15

Other interesting observations made by Mérie et al include an association between statin and clopidogrel use and reduced risk of perioperative stroke; in contrast, calcium channel antagonists, thiazide diuretics (both indicators of hypertension), and dipyrohamide (perhaps an indicator of peripheral vascular disease) were associated with increased risk of stroke.1 These results, based on pharmaceutical prescription data, should also prompt prospective study. For example, it is plausible that statins, with pleotropic activities that putatively improve atherosclerotic plaque stability and autoregulation and reduce the inflammatory response, could improve perioperative outcomes.17,18 Statins have also been shown to reduce the risk of perioperative death, myocardial events, renal failure, delirium, and postcardiac surgery atrial fibrillation19–23 in other studies; however, their effects on perioperative stroke are less clear.24 The increased risk of stroke associated with thiazide diuretics and calcium channel antagonists is ascribed to increased use by patients with hypertension (itself a risk factor for stroke); however, we cannot assume this is the only contributing factor. In addition, the association of angiotensin-converting enzyme inhibitors with increased mortality should also be addressed further, as these agents have been associated with perioperative hypotension.25 A complex relationship is evident between risk of stroke and different antiplatelet agents. However, without data on whether these drugs were discontinued, and if so, when they were restarted, these data are hard to interpret. In summary, prospective data collection is required to confirm the results concerning age, comorbidities, and medication on the risk of perioperative stroke and mortality.

Perioperative stroke is a disastrous complication when it occurs, and we are fortunate that data are presented on both nonmodifiable (eg, age) and modifiable (eg, medication) risk factors.1 Although Mérie and colleagues provide good evidence that age should not preclude patients having surgery based on perioperative stroke, elderly patients are at increased risk of perioperative mortality.1 Additional prospective data are required to guide the care of elderly patients undergoing surgery.

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