Editorial

Can Cognition Survive Heart Surgery?

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In this issue of Circulation, Jensen et al1 report that cognitive difficulties were no fewer when off-pump (OPCAB) versus conventional (CCAB) coronary artery bypass grafting was used. This important investigation, a substudy of the Best Bypass Surgery Trial, is a randomized prospective controlled trial that compares OPCAB with CCAB. Although the numbers seem relatively small (ie, 120 elderly patients with a mean age of 76 years), the study was carefully powered to show differences in cognitive function at a mean of 103 days of follow-up. Although one could quibble with the details of the neuropsychological tests chosen (mini-mental state examination as a screening test for dementia after randomization but before inclusion, visual verbal learning, concept shifting, Stroop color word interference test, letter-digit coding), the main result is unequivocal. The incidence of cognitive decline was roughly 8%, and no difference between OPCAB and CCAB was found. This disappointing result raises important questions about the mechanisms of neurological injury caused by cardiac surgery and what future strategies might entail.

Early in the development of cardiac surgery, it was psychiatrists who first reported difficulties with thought content and process. Rizzo et al2 reported on 32 patients under the care of Lewis Dexter (cardiologist) and Dwight Harken (cardiac surgeon) who underwent “finger fracture” valvuloplasty surgery for rheumatic mitral valve disease at the Peter Bent Brigham Hospital in Boston. These psychiatrists applied analytical explanations (eg, hysterical fantasies as the heart as a sexual organ, transference to the surgeon, depersonalization, narcissism) to their findings of disordered thinking in many of their patients. Only 50 years later, these explanations sound amusingly antique, but they mark the first organized recognition that the brain could suffer serious damage as a result of cardiac surgery.

The neurological complications of cardiac surgery fall into 2 major categories: those affecting the peripheral nervous system and those affecting the central nervous system. Although common and important, peripheral nervous system complications are not the subject of the Jensen et al1 study. The central nervous system complications fall into 3 major categories: acute encephalopathy as a result of a disorder in the neurological systems that subserve consciousness (inattention, confusion, delirium, drowsiness, stupor, and coma, sometimes with seizures and/or myoclonus), overt stroke (the sudden or rapid onset of a neurological deficit in a vascular territory as a result of a cerebrovascular disease), and a chronic syndrome of cognitive decline (inattention, amnesia, aphasia, apraxia) that is often, but not always, associated with symptoms of depression (apathy, sadness, sleep disorder, anhedonia). As cardiac surgery has matured and become technically better, the incidence of acute encephalopathy and overt stroke has progressively declined to current levels in the best hands of <10% and <3%, respectively, but the problem of chronic cognitive decline has remained and in many ways has become the most important complication that plagues a significant minority of patients who have otherwise successfully survived heart surgery.

When extracorporeal circulation was introduced, it was implicated in the mechanism of brain damage from heart surgery,3-5 and many efforts were made to protect the brain through the use of inline filtration systems meant to deal with what was believed to be the major mechanism of neurological damage, namely cerebral emboli.6-7 Soon it became clear that central neurological complications of heart surgery were not limited to intracardiac (open heart) surgery but were seen in extracardiac (coronary artery bypass surgery) as well.8 The precise prevalence of cognitive decline after coronary artery bypass grafting varies widely, presumably depending on the sensitivity of the neuropsychological tests used, but have been found by some to be much more prevalent than the roughly 8% found in the present study by Jensen et al.1 Newman and colleagues,9 who defined a significant decline as a 20% reduction from baseline, found a cognitive decline in 53% of patients at discharge, 36% at 6 weeks, 24% at 6 months, and 42% at 5 years. This interesting finding of late cognitive decline correlated with early cognitive impairment, indicating that that those patients who suffer cognitive deficits from the stress of cardiac surgery may have had an early form of a degenerative dementia (eg, Alzheimer disease). Others have not found an increased incidence in Alzheimer disease among those who suffer cognitive decline after cardiac surgery. Knopman et al10 retrospectively analyzed 557 patients with dementia compared with age- and sex-matched control subjects; 24 dementia patients and 28 control subjects who had undergone CCAB. There was no association between cardiac surgery and Alzheimer disease. McKhann et al11 compared 140 patients who underwent CCAB and 72 patients who underwent OPCAB with 2 control groups, 1 comprising 99 patients who had vascular disease but did not undergo surgery and 1 consisting of 69 age-matched normal control subjects. All groups except the normal control subjects showed a mild reduction in neuro-

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psychological scores, but there was no evidence of a surgically correlated dementia at 3 months or 1 year. In the study in this issue of Circulation, Jensen and colleagues tried to exclude a premorbid early dementia before including patients in the study, but the mini-mental state examination could be too coarse an instrument with which to detect such patients. Jensen et al did not address the issue of whether there was a late progressive cognitive decline.

More modern techniques to assess the mechanism of central nervous system injury such as intraoperative transcranial Doppler12 and diffusion-weighted MRI13 have shown that cerebral emboli are the dominant mechanism of brain injury during cardiac surgery, even in the vast majority of patients who do not demonstrate the syndrome of overt stroke. Border-zone ischemia, resulting from hypotension, is a relatively rare mechanism of intraoperative brain injury, seen in only the most obvious cases of systemic hypotension during the procedure. Usually ischemic lesions, detected by diffusion-weighted MRI, seen in the so-called border zones are actually emboli in the terminal arterial territories, in which case the lesions are often strikingly asymmetrical, a finding that is rare in true border-zone (or watershed) regions affected during systemic hyperfusion. Metabolic insults almost never explain the nature and persistence of the neurological deficits.

If, as Jensen et al have shown in the present study, the incidence of cognitive decline is not reduced by performing OPCAB and if, as the overwhelming bulk of the evidence has shown, emboli are the major cause of the deficits, one is forced to inquire about the source and nature of the emboli. Clearly, the persistent problem with microemboli cannot be attributed to extracorporeal circulation as was originally believed. The use of inline filtration systems probably has had a beneficial effect by reducing embolic burden, but a persistent risk of stroke and more subtle brain damage persists despite the widespread use of these systems. It seems likely that manipulation of the heart and great vessels and clamping of the aorta, required to implant the grafts in OPCAB, even without breaching the cardiac chambers, is enough to release showers of microemboli. Only the fairly rare macroembolism produces an overt stroke (incidence <3%), whereas the nearly ubiquitous microemboli produce the more common acute syndrome of inattention, confusion, and delirium (agitated confusion) and the chronic syndrome of depression, apathy, inattention, and frank dementia. This hypothesis is supported by the evidence that the major risk factors for postoperative cognitive decline are age, hypertension, known cerebrovascular disease, and preoperative cognitive difficulties. It is likely that cardiac surgery is indeed a stress test for cerebral reserve, producing more cognitive difficulties in those destined to develop a dementia, even if that dementia is not classic Alzheimer disease.

Cardiac surgery is one of the great triumphs of 20th century medicine. It has become so apparently safe that coronary artery bypass grafting is now a routine procedure. The last remaining major complication is subtle cognitive failure that can lead to disabling loss of the ability to enjoy intellectual pursuits. As coronary artery bypass grafting is challenged by interventional methods for revascularization of the myocardium, perhaps all but the most emergent preoperative patients should be investigated using sophisticated neurocognitive tests and neuroimaging to identify those who may not be able to withstand the challenge of an inevitable shower of microemboli. Interventional techniques probably also produce some emboli, but the dose is likely to be much less, perhaps making these procedures safer for the high-risk patient who requires myocardial revascularization. Intraoperative measures that may affect the incidence of neurological deficit include ultrasonic assessment of the aorta to determine where mobile atheromatous material may reside to avoid these areas when placing the clamp and grafts, transcranial Doppler to monitor embolic activity in real time, and minimization of movement of the heart and great vessels during the procedure. Use of devices (eg, suction) that help to immobilize the heart during OPCAB so that the surgeon can sew in the grafts may paradoxically increase the risk of emboli and thus neurological deficit. Perhaps the trend to use OPCAB in high-risk patients has reached its peak and is declining. This study by Jensen et al removes another apparent advantage of coronary artery bypass grafting on the beating heart, a procedure that is more difficult technically than CCAB, may result in less viable grafts, is challenging to teach to the next generation of cardiac surgeons, and apparently does not reduce the risk of the last remaining major side effect of surgical myocardial revascularization, that of cognitive decline.

In summary, the problem has been reduced to a rather simple one. Stroke, produced mostly by arterial source emboli, is the cause of heart surgery–induced cognitive failure. The clinical syndromes fall on a continuum. A few strokes (<3%) are gross and singular, producing an obvious deficit (eg, hemiplegia), but most are multiple. When the embolic burden is high (~10%), an acute encephalopathy ensues. When the burden is lower, no deficit is noted in the acute period, but if the cerebral reserve is low (ie, there is an invidious premorbid brain disease such as hypertensive cerebrovasculopathy), then the patient suffers a nonprogressive cognitive deficit (~8%). In the subgroup of patients in whom the premorbid disease is an inherently progressive disorder (eg, presymptomatic Alzheimer disease that is made manifest by the stress of cardiac surgery), the patient later undergoes a progressive cognitive decline (dementia). This continuum hypothesis explains the disparate results of many studies, because very much like the aphorism of the wise men and the elephant, each investigator was examining a separate part of the problem, but none could see the problem as a whole. All we have to do to deal with the problem of cognitive failure in cardiac surgery survivors is to reduce the burden of cerebral ischemia in those who are selected to undergo the procedure. OPCAB does not address the major issue, arterial source emboli, and thus, not surprisingly, does not address the problem. By selecting patients more carefully with preoperative cognitive and brain imaging methods and then by minimizing intraoperative cerebral emboli using methods that require less manipulation of the heart and aorta, the neurocardiologists of the future might finally save the mind of the cardiac surgery survivor.
Disclosures

None.

References


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