Stroke, delirium, cognitive decline, and depressed mood in the days and weeks after surgery, as well as a late long-term decline in cognitive function, are the most common neurological complications of coronary artery bypass graft (CABG) surgery performed with cardiopulmonary bypass (CPB). Delirium has been reported in 10% to 40% of patients, usually occurring transiently in the immediate postoperative period.1 Brain infarction occurs in 1% to 5% of patients2;3 in 60% of these patients, it is detected in the first 24 postoperative hours, and it occurs during the subsequent 10 days in another 35%-4,5 Cognitive decline occurs in up to 24% of cases at 6 months after CABG.6 Depressive symptoms and self-reported decline in cognitive function are frequently encountered in clinical practice, although they are less well documented in systematic objective testing.7 Although the overall complication rate has decreased over the past 25 years with improved operative techniques, given the more than 400,000 yearly CABG procedures, these adverse effects on the brain are a substantial public health concern. Prevention through a better understanding of their mechanisms remains a desirable and important goal.

Clinical variables associated with these neurological complications include age, prior cerebrovascular or peripheral arterial disease, congestive heart failure, and CPB duration of more than 2 hours.5,8,9 Patient selection, surgical skill, and operative technique also influence the development of these complications.10,11 The mechanisms of neurological complications after CABG performed with CPB (on-pump CABG) remain incompletely understood. Brain infarction secondary to extracranial internal carotid artery stenosis and cerebral hypoperfusion during CPB is rare.12 Brain embolism has repeatedly been demonstrated to be the most common cause of infarction.3 Manual manipulation, cannulation, and clamping of the ascending aorta (which is frequently atherosclerotic and friable) during the course of the operation and emboli generated by the CPB equipment are believed to be the common sources of particles that travel to the brain. In the majority of patients, however, the immediate source of embolism is never identified. This is particularly true in patients who sustain brain infarction more than 24 hours after CABG.

That extensive microembolism can occur during on-pump CABG is supported by pathological data from the brains of patients who had recently undergone CPB. Moody et al13 observed sausagelike small capillary and arteriolar dilatations (SCADs) in arterioles less than 50 μm in diameter. They speculated the particles corresponding to the SCADs were gas microbubbles or fat.13 SCADs were extensively distributed throughout the brain, and in 1 patient, their density was 11.76/mm³ of tissue. Moody et al13 suggested these microvascular events were the anatomic correlate of the neuropsychological deficit observed after CABG. Intraoperative fluorescein angiography shows evidence of retinal microembolism causing microvascular occlusion and leakage of fluorescein in virtually all patients.14 Transcranial Doppler monitoring of the cerebral circulation shows that high-intensity transient signals, which correspond to gaseous or particulate microemboli, are ubiquitous during on-pump CABG operations. The number of high-intensity transient signals has been directly related to the likelihood of a patient having a neuropsychological deficit at 8 weeks.15 Furthermore, new areas of restricted diffusion are detected on postoperative MRI diffusion-weighted imaging sequences in 30%-35% of patients, which suggests that microembolism during the course of the operation is responsible for the brain parenchymal damage. These lesions tend to be small in size (0.2 to 0.8 cm³) and tend to occur in multiples, their number ranging between 1 and 4. They can be detected even in patients without clinically manifest neurological deficits.16

In keeping with the view that CPB is responsible for some of these adverse effects on the brain, off-pump CABG (OPCAB) procedures have become increasingly attractive, when feasible.11 However, definitive evidence that OPCAB is superior in terms of neurological outcomes to on-pump CABG is lacking despite a number of large retrospective analyses, meta-analyses, and randomized trials. The benefit of OPCAB with regard to neurological complications is particularly promising17-19 with lower rates of cerebral embolization on transcranial Doppler monitoring and less of a decline in neurocognitive function in the short term (less than 3 months), although the difference is no longer present at 1 year.19

In this issue of Circulation, Ascione et al20 present their findings from a systematic study comparing 10 patients randomly assigned to OPCAB with 10 assigned to on-pump CABG. They monitored the retinal and brain circulations for evidence suggestive of microembolism and measured laboratory indices for tissue damage in these 2 groups. Although the study sample was small, Ascione et al observed a significantly higher occurrence of retinal microvascular damage and brain microembolism in patients undergoing on-pump CABG surgery. Using the S-100 protein as a marker, they found the extent of brain injury was also more severe in that group.

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Furthermore, they found a correlation between the retinal and brain events in that brain microembolism and injury were higher when there was evidence of retinal microvascular damage. None of their patients had clinical evidence of brain infarction, and the study protocol did not call for neuropsychological testing; thus, the impact of these changes on clinical outcome measures was not assessed.

Are the findings of Ascione et al.²⁰ scientifically and clinically relevant? Are the observations of retinal and brain microembolism and the associated tissue damage sufficient to warrant having physicians and surgeons alter their practice regarding coronary artery surgery today? The findings of the present study add further evidence to an expanding body of knowledge indicating that retinal and brain microembolism frequently occurs during the course of CABG surgery and is associated with tissue injury. Whether the latter is clinically significant is not answered by the present study by Ascione et al.²⁰ and is not sufficiently addressed in other published studies.

Thus, the answer to the second question is “not at this time.” In spite of this negative answer, when technically possible, it would be prudent to avoid CPB during CABG surgery to decrease the potential for intraoperative brain embolism.

The data presented by Ascione et al.²⁰ are scientifically and clinically relevant in 2 ways. First, they confirm the finding of microembolism as a potential mechanism for tissue injury. The lack of postoperative MRI evidence of parenchymal damage in a majority of patients and the relatively limited diffusion-weighted imaging abnormalities in those who develop them¹⁶ are consistent with surprisingly limited brain damage, when the severity of embolism detected by pathological¹³ and ultrasonographic¹⁵ studies and the findings of Ascione et al.²⁰ are taken into consideration. The discrepancy suggests that not all brain microembolism results in infarction or that MRI does not capture the resulting small infarcts. The tissue injury that occurs after brain embolism in on-pump CABG patients probably varies according to the number, size, and composition of embolic particles and the hemodynamic conditions in which embolism occurs, and there is a gradation of resulting laboratory manifestations ranging from increased S-100 protein levels to MRI evidence of brain infarction, and clinical manifestations ranging from cognitive decline to stroke. Future research should identify the specific characteristics of clinically relevant embolism and should stratify patients according to their likely susceptibility to its complications.

Second, the data reported by Ascione et al.²⁰ show substantial differences between OPCAB and on-pump CABG regarding the variables that were measured. Even if the microembolic burden is insufficient to result in readily measurable reduced cognitive performance or adverse neuropsychological outcomes, it is unlikely such microembolism is anything but injurious. This provides additional laboratory evidence confirming the relative merits of OPCAB surgery and supports the clinical findings of some studies showing that OPCAB results in less neuropsychological impairment than the on-pump technique.¹⁸,¹⁹

Disclosures

None.

References


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