COGNITIVE AND NEUROBEHAVIORAL DYSTUNCTION AFTER CARDIAC BYPASS PROCEDURES

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Since the introduction of cardiopulmonary bypass nearly 5 decades ago, there has been a significant reduction in the morbidity associated with open heart surgery. Nonetheless, adverse neurologic outcomes after cardiac surgery continue to remain a significant concern.[1,2] The spectrum of these outcomes ranges from coma and debilitating stroke to encephalopathy, delirium, and cognitive impairment. Recent studies suggest that the incidence of these adverse outcomes may be closely related to the status of the patient's brain before surgery.[3,4,5] Patients who have had transient ischemic attacks or stroke or who have a history of risk factors for cerebrovascular disease appear to be at greater risk for postoperative neurologic complications.[6] This article focuses on the short- and long-term cognitive changes after coronary artery bypass grafting (CABG).

SHORT - TERMS COGNITIVE CHANGES

Estimates of cognitive change after CABG have been highly variable because of differences in study exclusion criteria, choice of time points for measuring follow-up and statistical criteria used for defining decline. Although early studies focused almost exclusively on the role of surgery-related factors, recent studies have attempted to take into account patient-related variables as well, particularly those patients who have known risk factors for cerebrovascular disease.(7,8,9,10)

PATHOPHYSIOLOGY OF EARLY COGNITIVE CHANGES

No single factor that can account for the early postoperative cognitive changes has yet been identified. The focus of most investigations has been on neural injury secondary to surgery-related factors, including microemboli, hypoperfusion, and the systemic inflammatory response.[11,12] It has proved surprisingly difficult, however, to find direct evidence that any of these variables, individually or in combination with other risk factors, can account of the short-term cognitive changes.

MICROEMBOLI: Patients who have atherosclerosis, especially of the carotid arteries and aortic arch, are known to be at increased risk for cerebral microemboli during the surgery.(13) Several studies using transcranial Doppler have demonstrated that showers of emboli are common during cardiac surgery.[14] particularly during cannulation and clamping/unlamping of the aorta. Some studies have reported that most of these emboli appear to be gaseous rather solid.[15]

It is possible that the cognitive manifestations of microemboli may depend as much on patient-related risk factors (such as the degree of pre-existing cerebrovascular disease) as on the number and size of the embolic load. Patients who do not have significant pre-existing cerebrovascular disease may have a higher tolerance for embolic injury than those who have such disease. Other studies have reported low numbers of emboli in the brains of patients who die shortly after CABG, but cerebral microbleeds are relatively common.[16]

ATRIAL FIBRILLATION: The only variable that has been consistently associated with the development of postoperative atrial fibrillation is older age.[17] Those how have recurrent episodes of atrial fibrillation are at increased risk of stroke and neurocognitive decline.[18,19]

HYPOPERFUSION: Long-standing hypertension and aging are associated with morphologic changes of the brain vascular supply that may predispose the elderly to the effects of hypoperfusion. Abildstrom and colleagues[20] found that candidates for CABG had lower global cerebral blood flow preoperatively than controls. Caplan and

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Hennerici[21] proposed that emboli and hypoperfusion may play a synergistic role (ie, decreased flow during the surgery may result in reduced washout of embolic materials from the brain) and that the watershed areas are particularly susceptible to this combination.

ANESTHESIA: A significant percentage of elderly patients undergoing major noncardiac surgery with general anesthesia also suffer short- or long-term cognitive dysfunction. In a study of patients in the 40- to 60-year age range, 19% were found to have cognitive decline 7 days after surgery with general anesthesia, which is comparable to the incidence reported for patients 60 years or older.[22] There is evidence of some degree of short-term cognitive decline even after major noncardiac surgery with general anesthesia.

DEPRESSION: Mild to moderate depression is common after CABG, but one of the best predictors or postoperative depression is being depressed preoperatively. In prospective studies, however, there is no evidence that new-onset depression after CABG correlates with short- or long-term changes in cognitive performance.[23]

GENETIC FACTORS: The possibility of a link between genetic factors and risk of cognitive decline after CABG was suggested by a study that found a greater likelihood of decline in patients who had the apolipoprotein (apo) E epsilon4 allele.[24] Subsequent studies, however, have not been able to replicate these findings.[25,26,27]

LONG-TERM COGNITIVE CHANGES

Although most studies have focused on short-term cognitive decline after CABG, a study from Duke University raised the possibility of late or delayed cognitive decline after CABG. Newman and colleagues (2) studied 261 patients before surgery and followed them prospectively before discharge and at 6 weeks, 6 months, and 5 years after CABG surgery. The incidence of decline at the time of discharge was 53%, dropping to 24% at 6 months. At 5 years, 66% of the patients were available for follow-up testing, and an unexpected 42% of these patients performed below their baseline performance on global measure of cognition. Predictors of late cognitive decline included older age, fewer years of education, higher baseline score, and cognitive decline at the time of discharge.[25,26,27]

Some studies, however, have not found evidence of late cognitive decline after CABG.[5] The investigators suggested that better control of hypertension, hypercholesterolemia, and other risk factors for cerebrovascular disease during the 5-year follow-up period was a possible explanation for the lack of late decline in their study.

Only two long-term follow-up studies published to date have included a control group, Hlatky and colleagues[28] obtained cross-sectional neuropsychologic test performance data for patients who had been randomized to standard coronary artery bypass (N = 125) or angioplasty (N = 64) 5 years earlier. They reported that, at 5 years after the procedure, the cognitive performance of patients who had coronary artery bypass surgery did not differ from that of patients who had angioplasty.

In a study of twins, the postoperative cognitive performance of 232 CABG patients, was compared with that of their twins who did not undergo CABG. Surprisingly, CABG patients who had their surgery at a relatively young age (between age 63 and 70 years) had better cognitive performance 1 to 2 years postoperatively than the co-twin who did not have surgery. No significant differences in cognitive performance were found for the twin pairs in the older age groups.[29]

ETIOLOGY OF LATE COGNITIVE CHANGES

Of the prospective studies that found evidence of late cognitive decline after CABG, none included a control group. It remains unclear, therefore, whether the late cognitive changes are causally related to cardiopulmonary bypass with general anesthesia 5 years earlier, normal aging, development of Alzheimer's disease during the follow-up period, or other causes. The selection of an appropriate control group for patients undergoing CABG has been controversial. Patients undergoing CABG today are known to have a high prevalence of hypertension, diabetes, and other risk factors for cerebrovascular disease. Because these factors by themselves are associated with mild cognitive decline over time, the control group should include subjects who have a similar profile of risk factors for cerebrovascular disease.

Cerebrovascular disease risk factors: There is accumulating evidence from several epidemiologic studies demonstrating that a history of one or more risk factors for cerebrovascular disease may be associated with accelerated cognitive decline even without cardiac surgery.[30,31,32,33] Finally, there is evidence that treatment of these risk factors for vascular disease may prevent any late cognitive consequences.(34,35). These investigators hypothesized that better control of risk factors for vascular disease during the 5 years after surgery may have accounted for the lack of late decline seen in their study.

In summary, there is now considerable evidence from epidemiologic studies demonstrating an association between the duration and degree of vascular disease and the risk of cognitive decline during the later years of life, even in community-dwelling elderly individuals who have not undergone CABG.

PRE-EXISTING MRI ABNORMALITIES: Some studies have found that nearly one third of otherwise asymptomatic individuals have silent brain infarcts on MRI. Several studies have concluded that older age and hypertension are significant risk factors for having such MRI abnormalities.[36] The presence of such lesions may be associated with progressive cognitive decline or late dementia.[37]

Given the high prevalence of silent infarcts in community-dwelling individuals, one would expect such MRI findings to be even more common among candidates or CABG. In a study from Japan, preoperative MRI scans were performed in 421 candidates for CABG.[38] Of these patients, 30% were found to have single, small brain infractions and 20% had multiple infarction. Thus, an unexpected half of this group had evidence of silent brain abnormalities before surgery.

OFF-PUMP CORONARY ARTERY BYPASS GRAFT: Several studies have demonstrated that the use of off-pump surgery is associated with a reduction in the number of emboli to thebrain,[39] but clear-cut benefits in terms of neurocognitive outcomes are less obvious. In the only large-scale prospective randomized study to date, there was no significant difference in the incidence of decline between patients having conventional on-pump versus off-pump surgery at 3 or 12 months.[40]

SUMMARY

From a cognitive standpoint, CABG as currently practiced appears to be safe for the great majority of patients, but transient changes involving memory, executive functions, and motor speed may still occur in a subset of patients during the first few days to weeks after CABG. The etiology most likely is multifactorial and includes a synergistic effect of microemboli, hypoperfusion, and other variables associated with major surgery. The degree of pre-existing cerebrovascular disease have been identified as important risk factors. The short-term cognitive changes appear to be reversible by 3 months after surgery for most patients.

Late cognitive decline after CABG, occurring between 1 and 5 years after the surgery is specifically attributable to the progression of underlying cerebrovascular disease or other age-related changes.

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