Cardiothoracic Anesthesia, Respiration and Airway

Best evidence in anesthetic practice

Prognosis: cognitive function at hospital discharge predicts long-term cognitive function after coronary artery bypass surgery

Article appraised

Newman MF, Kirchner JL, Phillips-Bute B, et al. for the Neurological Outcome Research Group and the Cardiothoracic Anesthesiology Research Endeavors Investigators. Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery. N Engl J Med 2001; 344: 395–402.

Structured abstract

Question: In patients undergoing elective coronary artery bypass grafting (CABG) with cardiopulmonary bypass, what is the effect of perioperative neurocognitive decline on long-term neurocognitive function?

Design: Prospective cohort followed for five years.

Setting: Single academic centre.

Patients: Two hundred and sixty-one adult patients undergoing elective CABG were enrolled. Patients with symptomatic cerebrovascular disease, psychiatric illness, renal disease, active liver disease, less than seventh grade education, or inability to read were excluded.

Assessment of prognostic factors: Predictors of long-term cognitive decline were determined by multivariate logistic and linear regression methods.

Main outcomes: Overall neurocognitive function and frequency of cognitive decline were the main outcomes. Overall cognitive function was assessed using a composite cognitive index (CCI) score representing the sum of scores of four neurocognitive domains (verbal memory and language comprehension; abstraction and visuospatial orientation; attention, psychomotor speed, and concentration; visual memory). Cognitive decline was defined as a decrease, compared to baseline, of one standard deviation in performance in any of the domains. Domains were derived by factor analysis of test results from nine neurocognitive tests. All tests were administered before surgery (baseline), one day before discharge, and six weeks, six months, and five years post-CABG. The study took place from March 1989 to November 1998.

Main results: By the end of the study, 172 patients had completed five years of follow-up, 23 had died, 14 could not continue due to health problems, and 52 were lost to follow-up. Frequency of cognitive decline was 53% at discharge, 36% at six weeks, 24% at six months, and 42% at five years. CCI scores (means ± SD; positive value = improvement, negative value = decline) were -0.36 ± 2.05 at discharge, 0.99 ± 2.03 at six weeks, 1.37 ± 2.11 at six months, and -1.45 ± 4.09 at five years. Older age, lower level of education, and cognitive decline at time of discharge predicted long-term cognitive decline at five years.

Conclusion: There is a high prevalence of cognitive decline after CABG. Cognitive decline at time of discharge predicts later cognitive decline at five years.

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Commentary by J. Murkin

The recent report by Newman and colleagues has helped further raise the awareness of both clinicians and lay public to what has become an increasingly important impediment to successful outcomes in cardiac surgical patients. A variety of postoperative central nervous system (CNS) abnormalities have been identified in patients after coronary artery bypass graft (CABG) surgery. While both the magnitude and the clinical impact of the apparent recurrence of cognitive dysfunction may be debated, in sum these results are

not qualitatively dissimilar to previous reports.[1,2] Compared to patients without initial neurological decline, Sotaneimi *et al.* observed a significant decline in neurological function three years after aortic valve replacement surgery in patients who exhibited early neurological dysfunction within weeks after their operation, despite improvement one year after surgery.[1] Similarly, Murkin and investigators have reported on the persistence of abnormal neurological signs and cognitive dysfunction in 35% of 97 patients assessed three years after CABG surgery.[2]

There are several potential explanations for these observations: 1) the bimodal appearance of symptoms reflects areas of cortical damage with initial compensation by the remaining brain and subsequent brain aging unmasking the original lesions; or 2) there are patients with an innate susceptibility (ApoE 4 allele), in whom exposure to cardiopulmonary bypass (CPB) unmasks as being unable to withstand the aging process as well as other patients. Both are under intense investigation. Irrespective, the fact remains that significant numbers of CABG patients are experiencing measurable CNS abnormalities, especially cognitive decline, which is often associated with abnormal neurological signs and may be a predictor of magnetic resonance imaging defined loss of brain mass.

Newman *et al.* suggest that CABG surgery is associated with a decline in cognitive function that is two to three times higher than the baseline incidence; however, their study did not include a suitable control group. At least one large prospective study, an investigation of 8,000 Japanese-Hawaiian patients suffering myocardial infarction (MI), CABG surgery, or stroke, was unable to confirm either MI or CABG surgery as predictors of late cognitive impairment.[3] Forty-five percent of patients with previous stroke, compared to 16% with prior MI and 10% of men with previous CABG, were cognitively impaired.[3] However, patients in the CABG cohort had relatively low surgical risk, came from higher socioeconomic classes, and had high education. Other sociogenetic factors may have also altered the risk profile of this group. Thus, confounders in the CABG cohort may have obscured any adverse impact of CABG on cognitive function.

Despite these uncertainties, CABG surgery with CPB is associated with a degree of increased CNS risk that is amenable to changes in intraoperative management: arterial line filtration and membrane oxygenation,[3] alpha-stat pH management,[4] and CABG without CPB.[5] As CPB is a very important modality for circulatory support in a variety of clinical and therapeutic settings, the challenge is to enhance the circulatory support characteristics, with their attendant potential for powerful therapeutic extracorporeal blood and organ treatments, while minimizing CNS morbidity. The important work of Newman and colleagues underscores the need for further research in this area.

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Commentary by R. Hall

Newman *et al.*'s prospective, longitudinal, five-year observational study examines changes in neurocognitive function in 261 patients (172 completed all assessments) following coronary artery bypass graft (CABG) surgery. Subjects were given nine validated neuropsychometric tests of cognitive function (using previously defined standards)[1] at baseline preoperatively and over time postoperatively. Factor analysis of the baseline scores for the nine tests suggested that 86% of the variability among patients could be accounted for by four factors representing the cognitive domains of verbal memory and language comprehension (short-term and delayed); abstraction and visuospatial orientation; attention, psychomotor processing speed, and concentration; and visual memory. Each of the scores for each factor and a composite score comprised of the total scores for these factors were calculated and determined over time. Cognitive decline was evident in 42% of patients at five years.

This study is important as it describes the magnitude of ongoing neurocognitive dysfunction following

CABG surgery. The major criticism of the study design is the failure to follow a group of patients, who did not undergo CABG surgery, of similar age and disease burden over time to determine the degree to which non-surgical variables, such as age, influence the results. Does a change of one standard deviation in cognitive scores represent an important clinical difference? Evidence from a previous study suggests that, in the short-term, it does[2] and anecdotal reports of patient outcomes suggest the same is true in the long-term (*"Dad was never the same after his heart surgery"*).

What is the mechanism and what can be done to prevent the problem? Current wisdom suggests that cognitive decline is a combination of cerebral embolization, hypoperfusion, and the systemic inflammatory response.[3] The independent role of cardiopulmonary bypass (CPB) should be evident from comparative studies of "off-pump" *vs* "on-pump" surgery. Preliminary results[4] suggest that the role of CPB may not be as large as previously thought.

Efforts to reduce atheroemboli (use of epiaortic scanning to detect plaques, blood flow diversion using different types of arterial cannulation, or avoidance of aortic manipulation altogether), to monitor and maintain cerebral perfusion with avoidance of hyperthermia, and to avoid unprocessed blood from cardiotomy suction may all be useful manoeuvers.[3] Preliminary observations suggest that pharmacological manipulation of the systemic inflammatory response using aprotinin may also prove useful.[5]

Arguably, improvement in neurological outcomes is the next major challenge facing cardiac surgery. By demonstrating that the neurocognitive component of central nervous system dysfunction is present in a significant number of patients at five years postsurgery, Newman *et al.* have helped to define the problem and establish a research agenda that must examine strategies to improve neurological outcomes.

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