Can we influence postoperative cognitive dysfunction?

C. KALKMAN

More than 50 years ago Bedford wrote in the *Lancet* that cognitive dysfunction occurred frequently after anesthesia and surgery in the elderly (1). Severe postoperative cognitive dysfunction (POCD) can have a considerable impact on quality of life and may result in withdrawal from society, which – in turn – is a strong predictor of mortality in the elderly. POCD has been studied most extensively in cardiac surgery, because the incidence was thought to be particularly high after procedures where cardiopulmonary bypass (CPB) is used. There are several potential cerebral injury mechanisms in cardiac surgery, including hypoperfusion, cerebral embolization of air and atheromatous material from the ascending aorta, and a systemic inflammatory response resulting from interaction of blood with the artificial surfaces in the cardiopulmonary bypass system. Newman et al. reported that after an initial decrease in the incidence of POCD one year after surgery the proportion of patients with decline increased again after 5 years, suggesting that even mild insults render the brain more vulnerable to the effects of natural aging (2). Embolization is also a relevant injury mechanism during and after carotid endarterectomy and major joint replacement. In contrast, global cerebral ischemia caused by hypoperfusion is more relevant during aortic arch procedures and severe perioperative hypotension. Focal ischemia may occur during intracranial neurosurgical procedures (temporary clipping, retractor ischemia).

**Detecting POCD**

To detect POCD the patient needs to undergo a battery of neuropsychological tests each designed to test one or more aspects (domains) of cognitive function. Such domains include: visual/verbal memory, psychomotor skills or attention. These tests are typically administered by a trained neuropsychologist and a full battery may take up to 90 min to complete. In recent years computerized test batteries have been developed with the aim to reduce test times and increase reproducibility. Such computerized tests may be as sensitive in detecting POCD as the traditional ‘pen and paper’ test batteries (3). A major issue in detection of POCD is the use of concurrent control groups. Repeated application of the same tests (even when variants are used) results in better performance over time. It is therefore necessary to correct for such ‘practice-effects’. More importantly, when a cohort of patients is followed up over a period of years, it becomes important to control for the effects of normal aging. It is therefore necessary to subject a relevant control group (for example, patients with a similar age distribution and level of education) to the same tests. Only then can reliably be established to what extent a particular surgical procedure causes long term cognitive decline (4).

**Postoperative Cognitive decline in cardiac surgery**

The incidence of POCD after cardiac surgery was reported in some studies to be as high as 50%. Newman et al. performed neurocognitive tests preoperatively (at base line), before discharge, and six weeks, six months, and five years after CABG surgery.Decline in postoperative function was defined as a drop of 1 SD or more in the scores on tests of any one of four domains of cognitive function. The incidence of cognitive decline was 53 percent at discharge, 36 percent at six weeks, 24 percent at six months, and 42 percent at five years. This study has been criticized because there was no concurrent control group, which could have resulted in ‘regression to the mean’ (5). If CPB is a major causative factor in cognitive decline after cardiac surgery, it is logical to assume that avoiding CPB should lead to a decrease in the incidence of POCD. In the Octopus trial 281 patients were randomized to conventional coronary artery bypass graft procedure (CABG) with CPB or to ‘off-pump’ CABG. Although a small difference in POCD in favor of off-pump surgery was observed 3 months after surgery, one year and 5 years after the procedure the incidence of POCD was similar in both groups (6, 7). These results suggest that modern CPB-techniques are not likely to be most dominant factor for development of POCD.
Postoperative cognitive decline after non-cardiac surgery

In recent years POCD after non-cardiac surgery has been systematically studied. In particular the ISPOCD (International Study group of Postoperative Cognitive Dysfunction) has been successful in uncovering the extent of the problem and defining risk factors by using rigid study methodology and use of appropriate control patients. Early POCD occurs in approximately 25% of patients one week after surgery, and then declines to less than 10% after 3 months (8). Increasing age and duration of anesthesia, limited education, a second operation, postoperative infections, and respiratory complications are risk factors for early postoperative cognitive dysfunction, but only age was a risk factor for late postoperative cognitive dysfunction. Unexpectedly, neither intraoperative hypoxemia nor hypotension appeared to be predictors of POCD.

It is at present unknown what the contribution of anesthesia is to the incidence of POCD. In a randomized trial (ISPOCD2) elderly patients undergoing non-cardiac surgery were randomized to either general or regional anesthesia. There was no difference in the incidence of POCD after 3 months (general anesthesia : 14.3 vs. 13.9% after regional anesthesia).

Obviously, loss of cerebral tissue (either by surgical removal of as a result of cerebral ischemia) can result in neurological deficits and/or cognitive dysfunction. HEYER et al. recently compared POCD in patients undergoing carotid endarterectomy (CEA, n = 80) and lumbar spine surgery (n = 25) (9). A battery of neuropsychological tests was administered preoperatively and on postoperative days 1 and 30. Significant cognitive dysfunction was defined as performance that exceeded 2 SDs above the mean performance of patients in the control group. The CEA group performed significantly worse than the spine surgery patients. Cognitive dysfunction was seen in 22 patients (28%) in the CEA group on day 1 and in 11 (23%) of 48 patients on day 30. The same authors recently found that in 16% of patients there is a genetic predisposition for developing POCD after CEA (10). The presence of the APOE-epsilon4 allele increased the risk of neurocognitive dysfunction at 1 month 62-fold. Diabetes and obesity also predisposed to injury. The APOE-epsilon4 allele appears to be a robust independent predictor of neurocognitive decline 1 month following CEA.

SAMRA et al. recently presented results of a POCD substudy of the IHAST2 – International Hypothermia for Aneurysm Surgery randomized trial (Samra S., et al., Stroke, 38, 1864-72, 2007). In that study 1001 ‘good grade’ subarachnoid hemorrhage patients undergoing aneurysm clipping surgery were randomized to mild intraoperative hypothermia or normothermia. Hypothermia did not result in significant cerebral protection (11). Mild intraoperative hypothermia did also not result in a reduced incidence of POCD after aneurysm clipping surgery.

In conclusion, POCD appears to be a real phenomenon that may result in considerable reductions in quality of life for some patients. Nonetheless, it should be remembered that not all patients with ‘decline’ based on neuropsychological test scores are hindered or even aware of their declined performance. Conversely, the proportion of patients reporting subjective cognitive complaints postoperatively is larger than the proportion of patients who actually perform worse in tests after surgery. Until we have a better understanding of the pathophysiological mechanisms of POCD, specific preventive strategies can not be recommended. In the meantime, high quality anesthesia care (optimizing delivery of anesthetics and analgesics by careful titration, maintaining adequate oxygenation of neuronal tissue (by assuring normovolemia, adequate Hb, normoxia, normotension and normocarbia) will remain the basis of our approach to minimize neurological (and cognitive) deficits after surgical procedures.

References


