Fixing the Heart
Must the Brain Pay the Price?

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Coronary artery bypass grafting surgery (CABG) has been persuasively shown to prolong life expectancy in a broad spectrum of patients with severe ischemic heart disease. Improvements in the procedure during the past 2 decades have allowed operative mortality rates to fall while disease severity, comorbidity rate, and procedural complexity have increased. In one area, however, evidence of improvement is harder to discern. Careful studies from a number of groups have now clearly shown that CABG is associated with an increased probability of both short- and long-term (5-year) cognitive dysfunction and consequent reduced quality of life. The cause of this postoperative cognitive dysfunction is most likely multifactorial, with risk factors classified into 2 broad categories: those that are patient related and those that are procedure related. Predominant patient-related factors include the increasing age of the typical CABG patient and the underlying predisposition of older adult patients to develop cognitive dysfunction after any major operation. For example, the International Study of Postoperative Cognitive Dysfunction found that 26% of patients older than age 60 years who underwent major abdominal or orthopedic surgery experienced cognitive dysfunction 1 week after surgery.

Evidence also implicates procedural aspects of CABG surgery in the pathogenesis of cognitive dysfunction, independent of patient predispositions. Procedure-related factors include the use of cardiopulmonary bypass, manipulation of the aorta (especially by cross-clamping), nonpulsatile perfusion or hypoperfusion, and other aspects of management such as hyperthermia during the perioperative period.

A variety of studies have been performed to clarify the extent to which the patient-versus-procedure factors contribute to the highly undesirable outcome of cognitive decline after CABG. If the procedure is primarily responsible, then modifying the way CABG is done may reduce the problem. For example, one proposed advantage of off-pump CABG is the potential for less cerebral injury. Whether this form of CABG does in fact possess this advantage remains controversial. If the patient level of preexisting cerebrovascular disease is the primary cause of long-term cognitive decline, then other remedies must be sought.

An alternative approach to investigating the relationship between CABG and cognitive decline has been to compare CABG with percutaneous revascularization because percutaneous revascularization offers at least the theoretical possibility of achieving equivalent coronary revascularization without the trauma of cardiac surgery. Although the effects of percutaneous coronary intervention (PCI) on cognitive function have not been as extensively investigated as have those after CABG, technical improvements in PCI technology have led to an older adult population with atherosclerosis who are at high risk for central nervous system dysfunction presenting for PCI. In short, the current PCI population would be more likely to show a difference in cognitive outcomes as compared with CABG if procedural factors are the major contributor to such complications, but they would not be expected to show a difference if patient-related factors predominate. This question was examined in a substudy of the Bypass Angioplasty Revascularization Investigation (BARI). At the 5-year follow-up point, 125 patients (64 percutaneous transluminal coronary angioplasty, 61 CABG) underwent a battery of neuropsychological tests. No differences in long-term cognitive function were evident. Limitations of this substudy included the small sample size and the absence of baseline test data.

In this issue of Circulation, Währborg and colleagues provide a contemporary examination of this issue. The investigators examined cognitive functioning in a 145-patient substudy of the Stent or Surgery (SoS) trial. Assessment included a 5-item cognitive function battery administered at baseline, 6 months, and 1 year. Because of the multinational population enrolled in SoS, some standard tests, particularly those that assess aspects of verbal memory and language...
comprehension, were excluded. The investigators failed to
detect any differences in neuropsychological outcomes be-
tween the stent/PCI arm and the CABG arm up to 12 months
after the procedure.

What conclusions, if any, can we draw from the results
of this well-conducted trial and how does the trial compare
to what we already know? As the authors point out in their
Discussion, the small sample size is an important limita-
tion, and the possibility of a type II error must be kept in
mind. The cognitive decline event rate observed in the
CABG arm of this trial appears to be less than has been
previously observed in cohort studies. Although several
possible reasons for this exist, one important reason is that
enrollment in a study in which both PCI and CABG must
be options for each patient likely selects out a lower-risk
subset of CABG patients. This phenomenon was observed in
the BARI trial comparison of randomized versus registry
CABG patients.12

Another possible reason the present study appears to differ
from previous work in the area relates to the use of some
different scales and a different definition of cognitive decline.
Those not directly working in this area may be surprised to
learn that no universally accepted definition of cognitive decline exists. This fundamental lack of consensus clearly has
the potential to greatly affect reported rates of brain injury
after CABG.13 Another difficulty arising from the lack of a
universally accepted definition of cognitive decline is uncer-
tainty about what the absence of a detectable difference in the
SoS trial means. The majority of patients in both arms were
unchanged at 6 and 12 months in their neuropsychological
test results. Is this evidence of preserved cognitive function or
of inadequate sensitivity of the testing battery? Other diffi-
culties in interpreting the results include a less sensitive and
less extensive test battery, as well as the small number of
patients studied at each of the numerous sites, increasing the
variability of results and thus decreasing the standard devia-
tion and event rate.

One final unknown worth at least considering is whether
selective attrition (ie, the greater improvement in myocardial
performance, overall survival advantage, or both demon-
strated with CABG in the larger trial) could serve to bias
neurocognitive differences in the CABG and PCI patients
who are available for follow-up. In addition, as the population
shifts to an older, high-risk group undergoing PCI interven-
tion, and as cardiopulmonary bypass and anesthesia tech-
niques improve, we may witness similar cognitive outcomes
from different interventional procedures that are more rele-
vant to patient risk than to interventional group in determin-
ing clinical outcome.

In conclusion, the study by Währborg and colleagues11
raises some important questions about neurocognitive out-
comes associated with revascularization interventions for
patients with coronary artery disease. In our opinion, the
study should not be justification for complacency about the
possibility of brain injury associated with invasive therapeu-
tic cardiac procedures. Rather, it should stimulate us to seek
the answers that clinicians need to practice thoughtful car-
diovascular medicine and that patients need to make informed
decisions. These answers must come from future well-
conducted, adequately powered, multicenter trials.

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