LETTERS TO THE EDITOR

Improvement of outcomes after coronary artery bypass

To the Editor:

We wish to draw attention to serious problems in the reports by Gold and associates^{1,2} regarding the effects of cerebral perfusion pressure on neurologic outcome after cardiac operations. Our first concern is that the original study has inadequate power to discern a difference in stroke outcome resulting from an intervention, inasmuch as there were only 248 patients in the study. This small sample size is combined with a stroke rate of 7.2% in the "control" group. This is an unexpectedly high rate, inconsistent with the generally expected rate of about 3% to 5% or the recently reported rate of 0.8% in the Bypass Angioplasty Revascularization Investigation (BARI),³ which was conducted in 18 centers in North America with perfusion pressures similar to those used in Gold's control group. The combination of a small sample size and an abnormally high event rate raises serious questions about the general applicability of Gold's results and almost certainly leads to the creation of a type I statistical error (i.e., finding an effect when one did not exist). With a stroke rate liberally assigned at approximately 5%, it would take an estimated 2000-patient study to detect a 50% reduction,^{4,5} a difference less than purported to have been found in the 248-patient study of Gold and associates.

Also of serious statistical concern is the issue of multiple comparisons. Although Gold identified the five major outcomes in advance, there is no license to test each one at the overall unadjusted alpha of 0.05, especially considering that the outcomes are clearly strongly related and not mutually exclusive. Even without any adjustment, none of the five major outcomes showed a significant difference between the mean arterial pressure groups. Most disturbing is that selected endpoints were combined in post hoc analysis to create another outcome for comparison (mortality + cardiac morbidity + neurologic morbidity). This combination, which ignored the variables that were similar between groups, requires a penalty for multiple comparisons that would place the observed difference inside the cutoff for significance.

A final mechanistic issue relating to the presumed effect of mean arterial pressure on cerebral perfusion is the authors' apparent ignorance of the rather large amount of literature regarding autoregulation of cerebral circulation during cardiac surgery, a subject recently reviewed by Schell and coworkers.⁶ There is abundant information from many clinical studies that show clearly that cerebral perfusion pressure has little effect on cerebral blood flow in the range of pressures used in the study by Gold and coworkers.¹ Contrary to the comments of Gold,² this has been shown during hypothermic, nonpulsatile cardiopulmonary bypass. Similar findings have been shown in the more elderly patient population as well.⁷

We believe the report of Gold and coworkers that

higher perfusion pressure during cardiopulmonary bypass improves outcome should be considered at best as a preliminary, incomplete scientific study and the conclusion in defiance of current knowledge concerning cerebral physiology during cardiopulmonary bypass.

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Reply to the Editor:

The members of the Cornell Coronary Artery Bypass Outcomes Trial (CCABOT) Group appreciate the opportunity to expand on the points raised by Reves and colleagues. The authors have raised three major concerns. The first issue is the "high event" rate. The overall rate of stroke in our cohort was 4.8%, with 7.2% occurring in the control group. Few studies have formally trained neurologic observers blinded to intraoperative randomization performing serial evaluations, as were done in our cohort. Our study neurologists performed neurologic evaluations before the operations, 24 to 28 hours after the operations, 6 days after the operations, and 6 months after the operations. Such uniform surveillance has been shown unequivocally to increase detection rates.¹

In many ways, our patients were similar demographically and clinically to those in the Bypass Angioplasty