Does the brain need an enema during deep hypothermic circulatory arrest?

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We are pleased to comment on the article, “Adjunct Retrograde Cerebral Perfusion Provides Superior Outcomes Compared With Hypothermic Circulatory Arrest Alone: A Meta-Analysis,” by Tian and colleagues,¹ appearing in this issue of the *Journal*.

Dr Denton Cooley famously referred to retrograde cardioplegia as “an enema of the heart”—reflecting without camouflage his disfavor of that technique for protection of the heart during ischemia. The article by Tian and colleagues¹ examines a similar issue of backwards perfusion of, not the heart, but rather the brain during the global ischemia of deep hypothermic arrest.

Tian and colleagues¹ have done a superb job of addressing this issue through meta-analysis. Their study involved an extreme amount of work in identifying, examining, categorizing, and analyzing nearly 1000 studies that report clinical results after aortic arch operations done with straight deep hypothermic circulatory arrest (HCA) or deep HCA supplemented by retrograde cerebral perfusion (HCA + RCP). They applied advanced meta-analytic techniques to the distillate of most relevant and most complete articles. For this tremendous effort, the aortic surgical community is grateful.

The meta-analysis reveals that (1) HCA + RCP leads to lower operative mortality, and (2) HCA + RCP leads to lower perioperative stroke rate. These are important findings. The lower operative mortality disappears when meta-regression statistical techniques are applied, however, and the stroke benefit disappears when only medium- to high-quality studies are included in the meta-analysis. Wikipedia defines meta-regression techniques as “a tool used in meta-analysis to examine the impact of moderator variables on study effect size using regression-based techniques.”² Thus the main findings of this study, although meaningful, are not statistically robust.

The meticulous review conducted by Tian and colleagues¹ identified only 2 randomized, controlled trials, which totaled only 31 patients in each arm of the study

Long-term survival for elective arch replacement cases compared with reference population.

Central Message

Tian and colleagues¹ show benefit of retrograde brain perfusion relative to straight hypothermia for arch surgery; however, the findings are not statistically robust.

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(only 1.1% of the entire meta-analysis). The remaining studies were retrospective and observational in nature.

We have published extensively on aortic arch surgery, demonstrating high safety in terms of mortality and stroke.^{3,4} In our articles published in *The Journal of Thoracic and Cardiothoracic Surgery* in 2014 and 2017, we found low mortality (2.9%), low stroke rate (2.0%), and excellent long-term survival (Figure 1). In our experience, neither antegrade nor retrograde brain perfusion has been necessary to secure good clinical outcomes. Straight

FIGURE 1. Long-term survival of patients undergoing elective aortic arch surgery under straight deep hypothermic circulatory arrest is not statistically different from that of an age- and sex-matched control population. Reprinted with permission.⁴

deep HCA has afforded us a clean, bloodless, clutter-free surgical field. That said, we have no objection to adjunctive brain perfusion, whether antegrade or retrograde.

Our *Journal*-published experience of 613 patients was not included among the studies tabulated in this meta-analysis. Our article seems to meet all the criteria outlined by Tian and colleagues¹ (human study, English language, adult patients, arch surgery, either HCA or HCA + RCP, specific primary outcome data) except for the lack of patients in the RCP category (we used only deep HCA in all patients). Our article, were it included, would have expanded the HCA group in the Tian and colleagues¹ article by more than 30%—and likely skewed the mortality and stroke comparisons into “nonsignificant” territory.

In an effort to generate more generalizable data in regard to the cerebral protection techniques, Drs Tian and Yan have devised and launched a multicenter registry—the International Aortic Arch Surgery Study Group (IAASSG)⁵—which may help elucidate the specific benefits of each cerebral protection strategy. We look forward to studies from the IAASSG evaluating the risks and benefits of

HCA alone compared with the perfusion strategies, and specifically RCP.

We thank Tian and colleagues¹ for their important contribution, which adds additional clarity to a surgical controversy in which a specific surgeon’s practice pattern seems to be determined (appropriately) in large part by his or her individual training and experience.

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