Response to Letter Regarding Article, “Comparative Effectiveness of Carotid Revascularization Therapies: Evidence From a National Hospital Discharge Database”

We appreciate Dr Giri’s interest in our work and the opportunity to clarify the purpose, strengths and limitations, and validity of the methodologies used in our article.

We sought to determine whether the outcomes achieved in randomized controlled trials (RCTs) of carotid revascularization therapies are recapitulated in the real-world clinical setting. Central to this investigation is the concern that the presumed clinical equipoise and apparent equivalence in outcomes after carotid angioplasty and stenting (CAS) compared with carotid endarterectomy may be a manifestation of the operator experience screening in the CAS arm of prior RCTs. Such screening bias confounds the generalizability of RCTs to the large number of patients who do not undergo carotid revascularization at larger tertiary care centers.

To study real-world outcomes on a national scale, we used the Premier perspective national hospital registry. Such databases provide extremely useful epidemiological data and complement RCTs by overcoming small size limitations in the detection of uncommon adverse outcomes. Propensity score matching is a robust statistical method to mitigate the often-cited limitation of retrospective data, selection, and treatment bias. By pairing patients between study arms by clinical similarity as it relates to the probability of receiving treatment, propensity score matching approximates the randomization event of an RCT.

As our data originate from US hospitalizations, the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST) was the most logical RCT to emulate using propensity score matching. The Premier data set permitted inclusion of all but one of the patient assignment/randomization variables of CREST in our statistical model, resulting in a favorable improvement in covariate balance between carotid endarterectomy and CAS recipients after matching. The absence of the degree of carotid stenosis from our model is not expected to be a major source of confounding bias because of standardized thresholds of clinically significant carotid stenosis between therapies. Furthermore, Premier uniquely identifies chronic from acute comorbidities, allowing us to build a more accurate statistical model.

Stenting recipients are commonly enrolled in manufacturer-sponsored device trials. Such trials benefit the manufacturer by providing longitudinal outcome data and benefit patients by providing a mechanism to defray the cost of the procedure. Although trial enrollment status was absent from the Premier database, there are no data to suggest that trial enrollment favorably influences short-term outcomes or enhances detection of death or unfavorable discharges. Post–revascularization stroke detection is also unlikely to benefit from trial enrollment during hospitalization as providers are well trained to detect this outcome. Accordingly, the higher incidence of adverse outcomes after CAS in our data set is unlikely to be a manifestation of detection bias.

The 2- to 3-fold lower rates of myocardial infarction reported in our study are likely explained by the exhaustive efforts of CREST to identify post–revascularization myocardial infarction that are not routinely performed either in real-world clinical practice or in older carotid revascularization trials. These differences in detection are a study limitation but do not invalidate our findings, as severe cases of post–revascularization myocardial infarction are likely to be detected without rigorous screening efforts. Furthermore, there is no expectation for systematic detection bias, as undetected milder myocardial infarctions are likely equally distributed between therapies.

Among centers participating in the Carotid Artery Revascularization and Endarterectomy registry, embolic protection device utilization exceeds 95%. As this registry draws from a disproportionate fraction of tertiary care facilities, these data may not reflect clinical practice patterns at smaller medical centers that may be slower to adapt to changes in standards of care. However, we do acknowledge that the strategy of conditioning reimbursement on the use of embolic protection devices during CAS procedures in Medicare patients likely attenuates differences in utilization.

Notwithstanding these limitations, we feel that our study reasonably approximates CREST, yet demonstrates a higher frequency of adverse outcomes after CAS when compared with carotid endarterectomy. The outcomes of CREST seem to be a manifestation of the operator screening that is absent from retrospective data. These findings argue for continued research of the safety of carotid artery stenting.

Disclosures
None.

Robert J. McDonald, MD, PhD
Jennifer S. McDonald, PhD
Harry J. Cloft, MD, PhD
Department of Radiology, College of Medicine
Mayo Clinic
Rochester, MN

References
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Robert J. McDonald, Jennifer S. McDonald and Harry J. Cloft

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