

Does MI Matter?

Understanding the endpoint analysis in CREST.

BY WILLIAM A. GRAY, MD

With the recent publication of the CREST trial results, a debate has emerged regarding the relevance of myocardial infarction (MI) in assessing the comparative safety of carotid artery stenting (CAS) and carotid endarterectomy (CEA). This is because CEA had an excess of MI (as determined by conservative criteria and adjudicated by an independent events committee blinded to the treatment given) compared to CAS, and this MI excess roughly cancelled out an excess of minor strokes in the CAS group relative to the CEA group, thus “equalizing” outcomes between the two therapies in the primary endpoint. Predictably, the surgical community would like to minimize the importance of MI as an endpoint, whereas interventionists would rather count these results as originally intended by the trialists and the National Institutes of Health, who constructed and conducted the study, respectively. This article attempts to look at the issue as objectively as possible, and there are several relevant perspectives that deserve mention and discussion.

Probably the most salient argument regarding the MI issue is independent of the particular argument at hand and has more to do with how we interpret trials: revisionist history is not acceptable. MI was a prespecified component of the composite primary endpoint of the CREST trial. Period. Beware the deconstructionists who would selectively include only those components of this or any trial that suit their argument; it is tantamount to changing the handicaps in the middle of a golf match because one does not like how it is going. The incontrovertible interpretation of CREST was and remains that the primary composite endpoint was not different between the therapies and was extraordinarily low compared to historical outcome standards.

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The inclusion of MI in the composite endpoint is not a trivial matter nor an “unequal” outcome vis-à-vis stroke, as some would have us believe. There are multiple studies documenting both the acute and long-term detrimental outcomes of MI after both vascular and other noncardiac surgery.¹ Interestingly, there are no data to suggest that minor stroke affects the patient’s long-term mortality. The recognition of the negative outcomes after perioperative MI has resulted in strategies to reduce the incidence, including beta blockade, statin therapy, antiplatelets, etc. (some to better effect than others). While we currently await the results of the CREST trial’s long-term outcomes in those patients with MI versus those without, the predicate experience would suggest that we not start with a premise that they are inconsequential.

Lastly, the issue of the relative effect on quality of life for the various components of the primary endpoint has been used to support that MI is “preferred” by the patient over stroke (major or minor) and that because minor strokes were greater in the CAS arm, patients would rather have CEA. There are (at least) two perspectives worth mentioning here. First, we have yet to see a similar analysis *by treatment received* from the CREST trial, which will directly answer an important concern from the patient’s point of view:

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the relative impact of the two therapies on quality of life. A recent publication on the SAPPHERE trial reported just such an analysis, and other than a difference in physical scales in the first month (CEA with worse scores), there was no difference between CAS and CEA. Second, although patients did not score MI as a significant quality-of-life issue, it does not mean that it is ultimately not as important to them, as the previous data clearly suggest. It is no different from hypertension or dyslipidemia in that it may not particularly trouble the patient, but they nevertheless carry obvious consequences.

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CONCLUSION

CREST demonstrated excellent outcomes for both CAS and CEA and concluded that there were no differences between these therapies in the composite primary endpoint of death, stroke, and MI. Although there were differences in the components of the primary endpoint from the CREST study, with more MI in the CEA arm and more minor stroke in the CAS arm, it is incorrect to selectively include or exclude these components to draw different conclusions. Any differences in these endpoint components should be viewed as opportunities to improve both treatments and to provide even safer options to patients with carotid bifurcation disease who are at risk of stroke. ■

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1. Landesberg G, Beattie WS, Mosseri M, et al. Perioperative myocardial infarction. *Circulation*. 2009;119:2936-2944.

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