

# Does MI Matter?

A critical analysis of the CREST trial results: a surgeon's perspective.

BY WESLEY S. MOORE, MD

**T**he long-awaited CREST trial results were presented at the International Stroke Conference in February 2010 and published in the *New England Journal of Medicine* on July 1, 2010. When we designed the CREST trial more than 10 years ago, we decided to include nonfatal myocardial infarction (MI) as a primary endpoint along with the customary endpoints of death and stroke. The reason for this decision was based on the assumption that carotid artery stenting (CAS) has an advantage over carotid endarterectomy (CEA) because it is less invasive and therefore might show a lower incidence of MI. In fact, this turned out to be the case in this preliminary analysis. The question arises: should nonfatal MI carry the same weight as death and stroke?

## BACKGROUND

The CREST trial is a prospective, multicenter, randomized trial of symptomatic and asymptomatic patients with carotid stenosis carried out in the United States and Canada. The initial analysis was carried out when the last patient had a minimum of 1-year follow-up; the mean follow-up for the entire cohort was 2.5 years. One unique aspect of the CREST trial was the selection process for interventionists. An interventional management committee first screened potential participants based on their documented experience and results with CAS. Those who met stringent criteria were invited to participate in the lead-in phase of the trial. Each selected potential participant was required to prospectively submit up to 20 lead-in cases of CAS. The patients were then carefully examined by the established investigator team at the participating hospital, and the results were submitted to the management committee. If a participant in the lead-in phase met the requirements of the committee, they were then permitted to participate in the randomized

“The good news is that these event rates for both CEA and CAS are the lowest reported to date.”

trial. In this manner, the best of the best interventionists were selected for the trial.

## CREST TRIAL RESULTS

The 30-day event rate combining death, stroke, and MI was 4.5% for CEA versus 5.2% for CAS. These results have been widely circulated by interventionists as showing that CAS and CEA yield equivalent results. However, we must explore the results in more detail before that conclusion can be justified. Because the objective of invasively treating carotid bifurcation disease is to reduce the risk of death or disability from stroke, I submit that these endpoints must be compared separately. The 30-day incidence of death and stroke was 2.3% for CEA versus 4.4% for CAS. That difference was statistically significant ( $P = .005$ ). The good news is that these event rates for both CEA and CAS are the lowest reported to date. However, it must be kept in mind that in this study, as well as in the other European and international studies, CEA is safer than CAS with respect to the endpoints of death and stroke. In the case of CREST, the event rates of death and stroke were twice as high in CAS compared to CEA.

The CREST trial also looked at the effect of age with respect to adverse events of the two procedures. The inflection point occurred at age 70, with patients over the age of 70 having better outcomes with CEA and younger

(Continued on page 90)

(Dr. Moore, continued from page 88)

patients having better outcomes with CAS. In CREST, the higher incidence of MI in the CEA group, when compared to CAS, made the two procedures appear to be equivalent. Is this higher MI rate in CEA important? Apparently not from the patients' perspective.

A quality-of-life analysis was performed on patients who suffered from stroke and MI. At 1 year, neither the physical nor mental components of quality of life were adversely affected in patients experiencing MI compared with those who did not. In contrast, both major and minor stroke had a significant impact on the physical and mental well-being of patients experiencing that event compared to those who did not.

This leaves us to question the long-term consequence of a nonfatal MI. There is literature to suggest that the long-term survival for patients who experience MI is adversely affected. With a median follow-up of 2.5 years, this has not been shown to be the case in CREST to date. CREST is ongoing with respect to long-term follow-up, and the consequence of nonfatal MI will be shown in a future publication.

"Is this higher MI rate in CEA important? Apparently not from the patients' perspective."

### CONCLUSION

There is a possibility for reducing the MI rate with CEA. When the study was designed more than 10 years ago, the benefits of statins and beta-blockers in reducing perioperative cardiac events was not known, and therefore the use of those drugs was not part of the protocol. Today, it is well established that statins and beta-blockers together with an antiplatelet agent should be a part of the preoperative preparation of patients selected for CEA. Also, careful preoperative cardiac evaluation to identify patients who are at an increased risk for MI should be a part of the patient preparation. Using these modern concepts, it is highly likely that future MI rates can be lowered for CEA. In the meantime, the preponderance of evidence favors CEA over CAS, as it is a safer procedure with respect to lower complication rates of death and stroke. ■

*Wesley S. Moore, MD, is Professor of Vascular Surgery, University of California in Los Angeles. He has disclosed that he is a paid consultant to W. L. Gore & Associates. Dr. Moore may be reached at [wmoore@mednet.ucla.edu](mailto:wmoore@mednet.ucla.edu).*