Stenting versus Endarterectomy for Treatment of Carotid-Artery Stenosis (CREST trial)

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At the time of this trial, carotid endarterectomy (CEA) was well-established as an effective treatment for both symptomatic and asymptomatic carotid artery atherosclerosis. Carotid artery stenting (CAS) was also established as an effective treatment, though results from prior comparative studies between the two treatment modalities were conflicting. For this reason, this study was undertaken to directly compare CEA vs. CAS in extracranial carotid artery atherosclerotic disease, on a larger scale.

Experimental design and statistics: This was a randomized, controlled trial with blinded end-point adjudication, conducted in the US and Canada. Patients were considered to have **symptomatic** carotid artery disease if they had experienced amaurosis fugax, TIAs, or non-disabling strokes corresponding to the index artery in the 180 days prior to randomization. Eligible patients with symptomatic carotid disease had to have carotid stenosis >50% on angio, >70% on U/S, or >70% on CTA or MRA if U/S stenosis was 50-69%. A few years into the study, patients with **asymptomatic** carotid disease were also enrolled, with their eligibility criteria including carotid stenosis >60% on angio, >70% on U/S, or >80% on CTA or MRA if U/S stenosis was 50-69%. Major exclusion criteria included a history of Afib in the prior 6mos. or Afib requiring anti-coagulation, a recent MI, or unstable angina. Eligible patients were randomly assigned to undergo either CEA or CAS by a participating interventionist,[1] performed via published guidelines. Protocols for anti-platelet and/or dual anti-platelet therapy around CEA or CAS are outlined on pp.13-14, and appropriate medical therapy for HTN + HLD was provided to all patients. Following each treatment, assessments were performed at 18 + 54hrs, 1 month, and 6 months[2]. The primary endpoint was the composite of any stroke, MI, or death in the peri-procedural period (randomization to post-op day 30-36) and w/in 4 yrs post-op. Statistical analyses were aimed at the superiority of one treatment: hazard ratios of CAS v. CEA were calculated for the primary outcome, and freedom from the primary outcome was plotted via Kaplan Meier survival curves. Sex, age, and symptomatic status were included in statistical models as interaction terms.

Results: From 2000 to 2008, a total of 2522 patients were randomized, with a final, analyzed sample size of N = 1262 in CEA and N = 1240 in CAS; baseline patient characteristics were similar, other than more dyslipidemia in the CEA group (**Table 1**). In terms of the primary outcome (**Table 2, Fig. 2A**), there were no group differences in the composite of stroke, MI, or death in the peri-procedural (5.2% v. 4.5%, CAS v. CEA, HR: 1.18, p = 0.38) or full 4yr study period (7.2% v. 6.8%, CAS v. CEA, HR: 1.11, p = 0.51). However, there were group differences in individual end points. The rate of peri-procedural death was slightly higher in the CAS v CEA group (0.7% v. 0.3%, p = 0.18). The rate of peri-procedural stroke was also higher in CAS v CEA (4.1% v. 2.3%, p = 0.01), but no group differences existed after the peri-procedural period (estimated 4yr CAS v CEA rates of 2.0% and 2.4%, p = 0.85). Finally, peri-procedural MI was higher with CEA (2.3%) v. CAS (1.1%, p = 0.03). There were no treatment effect modifications by sex or symptomatic status, though CAS was more efficacious in those <70 y/o, and CEA in those >70 y/o (**Fig. 2B**). Secondary analyses also showed that the rates of the primary endpoint did not differ between CAS and CEA, among both symptomatic and asymptomatic patients (**Table 3**)[3]. Finally, major and minor stroke seemed to have a greater effect on the overall physical health status at 1yr than did MI.

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[1] All participating interventionalists were screened for appropriate and standardized certification in CEA or stenting procedures.

[2] Assessments included NIHSS, TIA questionnaires, health status, EKG, Carotid U/S, and mRS

[3] An additional secondary analysis showed that CEA was associated with a higher rate of peri-procedural cranial nerve palsies vs. CAS.

Conclusions: Overall, this study showed that although the composite outcome of death, stroke, and MI did not differ between CAS and CEA for carotid artery disease, the individual rates of stroke and MI did differ, with higher rates of peri-procedural stroke in CAS and higher rates of MI in CEA. Regarding stroke risk, however, group differences were seen only peri-procedurally, and were not apparent during the subsequent 4yr follow up period; stroke did have a greater effect on overall quality of life at 1yr. The greater efficacy of CAS in those <70 and CEA in those >70 also suggested that age could be a factor when assessing the appropriate treatment modality. Finally, the authors noted that this study had lower rates of the specified end points than in prior trials, perhaps owing to strict interventionalist credentialing and evolving techniques. This study did have limitations, (strict operator credentialing, one stenting system used reduced generalizability; lack of a medical therapy alone group), but ultimately suggested that both CAS and CEA are safe and effective treatments. The low, absolute risk of stroke (outside of the peri-procedural period) also suggested that both techniques were likely durable long-term.

Additional reading, if interested:

1) Brott, T.G et al., Long-Term Results of Stenting vs. Endarterectomy for Carotid-Artery Stenosis, NEJM (2016), 374: 1021 -1031. This study reported the results from the above patient population at 10yrs of follow up, showing generally similar outcomes.

Summary created by Elaine Sinclair, D.O.