Critique of the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST): Flaws in CREST and its Interpretation

K.I. Paraskevas, D.P. Mikhailidis, C.D. Liapis, F.J. Veith

Department of Vascular Surgery, Red Cross Hospital, Athens, Greece
Department of Clinical Biochemistry (Vascular Disease Prevention Clinics), Royal Free Hospital Campus, University College London Medical School, University College London (UCL), London, UK
Department of Vascular Surgery, “Attiko” University Hospital, Athens University Medical School, Athens, Greece
Divisions of Vascular Surgery, The Cleveland Clinic and New York University Langone Medical Center, New York, USA

The Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) has been used to support the equivalence of carotid artery stenting (CAS) and carotid endarterectomy (CEA) in the treatment of carotid stenosis in both symptomatic and asymptomatic patients. This inclusion of two different forms of the disease decreased the power and significance of the CREST results and weakened the trial. Other flaws in CREST were the equal weighting of mostly minor myocardial infarctions (MIs) with strokes and death in the peri-procedural, composite ‘end’ point, but not in the 4-year, long-term ‘end’ point. Although CAS was associated with 50% fewer peri-procedural MIs compared with CEA, there were >2.5-fold more MIs than CEA at 4 years. The 4-year MI rate, however, was not a component of the primary ‘end’ point. Additionally, although the initial CREST report indicated that there was no difference in the outcomes of CAS and CEA according to symptomatic status or sex, subsequent subgroup analyses showed that CAS was associated with significantly higher stroke and death rates than CEA in symptomatic patients, in females and in individuals ≥65 years of age. The present article will examine these and other flaws and the details of CREST’s results derived from the trial’s preplanned subanalyses to show why the claims that CREST demonstrates equivalence of the two therapeutic procedures are unjustified.

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In May 2010, the Carotid Revascularization versus Stenting Trial (CREST) investigators reported that the composite ‘end’ point of peri-procedural stroke, myocardial infarction (MI) or death or any ipsilateral stroke within 4 years after randomisation did not differ in patients with carotid artery stenosis (n = 2502) undergoing carotid artery stenting (CAS; n = 1262) or carotid endarterectomy (CEA; n = 1240) (7.2% vs. 6.8%, respectively; hazard ratio (HR) with CAS: 1.11; 95% confidence interval (CI): 0.81–1.51; p = 0.51). CREST included both symptomatic (n = 1321) and asymptomatic (n = 1181) patients. Of these, 872 (34.9%) patients were females and 1630 (65.1%) were males. According to the initial CREST report,1 “there was no differential treatment effect with regard to the primary end-point according to symptomatic status (p = 0.84) or sex (p = 0.34).”

Approximately 5 months later, the American Heart Association (AHA) together with the American Stroke Association (ASA) put forth a guideline indicating that CAS is an ‘alternative’ to CEA for the management of symptomatic carotid stenosis.4 Unfortunately, this AHA/ASA guideline4 did not consider or include the International Carotid Stenting Study (ICSS).5,6 The reason given was that “the timing of publication of ICSS precluded its incorporation into this version of the Guidelines. Publication of 2011 Guidelines was ultimately delayed in order to include the results of CREST”.7 However, ICSS7 was published 4 months before CREST.1

The AHA, the ASA and 12 other important Societies subsequently published a new set of guidelines,8 this time also including ICSS.5 Despite the consideration of ICSS,5 however, these guidelines once again recommended CAS as an ‘alternative’ to CEA in symptomatic patients.8 Additionally, this guideline recommended that prophylactic CAS might be considered in selected asymptomatic patients, but its effectiveness compared with current best medical treatment (BMT) alone for these patients was recognised as not being well established (Class IIb).8 As the AHA/ASA recommendations4,8 were largely based on the initial CREST1 report, they differ substantially from the guidelines published by other societies (e.g., the U.S. and the Australian/New Zealand Societies for Vascular Surgery).9

CREST1 and the AHA/ASA guidelines5,8 have prompted many to conclude that CAS and CEA are generally equivalent and to promote wider use of CAS in standard- and low-risk symptomatic and asymptomatic patients with carotid stenosis.10,11 The present article will make the case that the detailed data from CREST, including its subgroup analyses,5,11 do not support the general equivalence of CAS and CEA. This...
claim of equivalence is especially unjustified in symptomatic patients, females and patients aged 65 years or more. The present case suggesting a wider role for CAS in the management of asymptomatic patients will also be disputed.

FLAWS IN CREST AND ITS INTERPRETATION

Inclusion of asymptomatic patients

CREST began in December 2000 and initially included only symptomatic patients. Due to a lag in recruitment of symptomatic patients, in 2005 the CREST investigators began enrolling asymptomatic individuals. When the trial stopped enrolling patients in July 2008, it included 1262 CAS and 1240 CEA patients. Of these, 47.1% of CAS and 47.3% of CEA patients were asymptomatic.

In a report of the early results of CREST, it is stated that almost two-thirds of the CAS population (789 of 1262 patients; 62.5%) had already been enrolled in less than the first 3.5 years of the study (December 2000 to 31 March 2004). All these patients were symptomatic. It would be interesting to know why the CREST investigators decided that they could not enrol the remaining 473 (37.5%) symptomatic patients in the remaining 4.5 years of the study (1 April 2004 to July 2008). If almost two-thirds of the CAS population had already been enrolled by 31 March 2004, it is puzzling that the percentage of asymptomatic CAS patients in the final report was as high as 47.1%.

Inclusion of MIs in the primary ‘end’ point

The inclusion of MIs as an ‘end’ point of equal weight to stroke and death should be viewed with some concern. First, no other randomised controlled trial comparing CAS with CEA has included MIs as a primary ‘end’ point (besides CREST and SAPPHIRE (Stenting and Angioplasty With Protection in Patients at High Risk for Endarterectomy)).

The purpose of CAS and CEA is to prevent strokes (as well as death resulting from strokes), not MIs. As CAS is a minimally invasive procedure, it is not a surprise that it is associated with fewer peri-procedural MIs compared with CEA. Interestingly, although CAS was associated with 50% fewer peri-procedural MIs compared with CEA (14 vs. 28, respectively), there were >2.5-fold more MIs after CAS than CEA at 4 years (excluding peri-procedural MIs, 58 vs. 22, respectively; Table 1). The 4-year MI rate, however, was not a component of the primary ‘end’ point.

Second, in CREST “myocardial infarction was defined by a creatine kinase MB or troponin level that was twice the upper limit of the normal range or higher according to the centre’s laboratory, in addition to either chest pain or symptoms consistent with ischemia or ECG evidence of ischemia, including new ST-segment depression or elevation of more than 1 mm in two or more contiguous leads according to the core laboratory." This is an unusual definition of an MI. Besides the fact that no specific duration for the ‘chest pain’ is provided, ‘chest pain’ is a symptom of myocardial ischaemia, not a synonym of infarction. It is incorrect to consider any ‘chest pain’ as an MI. Stable angina pectoris also produces chest pain. The same applies to the electrocardiography (ECG) and biochemical characteristics listed by the CREST investigators. An ST-depression of >1 mm is ‘ECG evidence of ischaemia,’ not an MI.

Third, it is inappropriate to group together as the ‘primary ‘end’ point’ a major stroke or death with a minor MI. The effect an MI has on the patient’s quality of life cannot be equated with the effects of a stroke (even a minor one). By use of the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), it was demonstrated in CREST that major and minor strokes had a considerable effect on the patient’s physical health at 1 year, whereas the effect of peri-procedural MI was less.

| Table 1. Primary end-point, components of the primary end-point and other events in CREST. | | |
|---|---|---|---|---|
| | CAS (n = 1262 pts) | CEA (n = 1240 pts) | HR for CAS vs CEA | p |
| | Nr. of pts (%) | Nr. of pts (%) | (95% CI) | |
| Periprocedural death | 9 (0.7%) | 4 (0.3%) | 2.25 (0.69–7.30) | 0.18 |
| Any periprocedural stroke | 52 (4.1%) | 29 (2.3%) | 1.79 (1.14–2.82) | 0.01 |
| Periprocedural major ipsilateral strokes | 11 (0.9%) | 4 (0.3%) | 2.67 (0.85–8.40) | 0.09 |
| Periprocedural minor ipsilateral strokes | 37 (2.9%) | 17 (1.4%) | 2.16 (1.22–3.83) | 0.009 |
| Periprocedural myocardial infarction | 14 (1.1%) | 28 (2.3%) | 0.50 (0.26–0.94) | 0.03 |
| Any periprocedural stroke or postprocedural ipsilateral stroke | 52 (4.1%) | 29 (2.3%) | 1.79 (1.14–2.82) | 0.01 |
| 4-year death (including periprocedural period) | 94 (7.5%) | 83 (6.7%) | 1.12 (0.83–1.51) | 0.45 |
| Any stroke (periprocedural period + 4-year follow-up) | 105 (10.2%) | 75 (7.9%) | 1.40 (1.04–1.89) | 0.03 |
| Major ipsilateral stroke (periprocedural period + 4-year follow-up) | 16 (1.4%) | 6 (0.5%) | 2.56 (1.00–6.54) | 0.05 |
| Minor ipsilateral stroke (periprocedural period + 4-year follow-up) | 52 (4.5%) | 36 (3.5%) | 1.43 (0.94–2.19) | 0.10 |
| Myocardial infarction (periprocedural period + 4-year follow-up) | 72 (6.2%) | 50 (4.7%) | 1.44 (1.00–2.06) | 0.049 |
| Primary end-point (any periprocedural stroke, myocardial infarction or death or 4-year postprocedural ipsilateral stroke) | 85 (7.2%) | 76 (6.8%) | 1.11 (0.81–1.51) | 0.51 |

CAS: carotid artery stenting; pts: patients; nr.: number; CEA: carotid endarterectomy; HR: hazard ratio; CI: confidence interval.
Minor strokes also had significant effects on the patient’s mental health at 1 year. As with the enrolment of asymptomatic patients, the inclusion of MIs as equivalent adverse events with stroke and death in the primary ‘end’ point could have improved the CAS composite outcomes.

The initial CREST report mentioned that there was no difference in the primary ‘end’ point between the two groups within the complete cohort (thus including both symptomatic and asymptomatic patients). Further analysis, however, showed that CAS was associated with a >2-fold increase in risk for any peri-procedural stroke, a >2.5-fold increase risk for major ipsilateral stroke and a >2-fold increase risk for minor ipsilateral stroke (Table 1). By contrast, CREST patients undergoing CAS suffered 50% fewer MIs compared with those undergoing CEA. The difference in MIs balanced the difference in strokes and produced the apparent equivalence in the overall primary ‘end’ point.

An argument used to justify the inclusion of MIs in CREST’s primary ‘end’ point was that peri-procedural MIs are associated with a decreased long-term survival. In CREST, the patients who suffered a peri-procedural MI had >3-fold higher 4-year mortality rates compared with those who did not (19.1% vs. 6.7%, respectively; HR: 3.40; 95% CI: 1.67–6.92; \( p < 0.001 \)). The patients who suffered a peri-procedural MI, however, were also older (72.3 ± 8.0 vs. 69.0 ± 8.9 years; \( p = 0.01 \)) and had a higher frequency of prior cardiovascular disease (including a history of MI, angina, coronary insufficiency, intermittent claudication or congestive heart failure; 65.8% vs. 43.3%, respectively; \( p = 0.02 \)) compared with those who did not suffer a peri-procedural MI. By multivariable analysis, the presence of prior cardiovascular disease or coronary artery bypass grafting was a strong risk factor for the occurrence of peri-procedural MI (HR: 2.22; 95% CI: 1.13–4.35; \( p = 0.02 \)).

It is therefore not a surprise that these patients had higher 4-year mortality rates. These high 4-year mortality rates also raise the question of the appropriateness of any carotid intervention in high-risk patients. As the CREST investigators state, “for asymptomatic patients identified to be at higher risk for MI or stroke after CEA or CAS, optimal medical therapy may actually be the preferred option and should be evaluated in a prospective controlled trial.” In addition, the high 4-year mortality of patients after an MI (19.1%) was equalled by the high 4-year mortality after a stroke (21.2%).

Further negating the argument that MIs should have been included in CREST’s primary composite ‘end’ point.

**Differences in anti-platelet treatment between CAS and CEA patients**

Patients undergoing CAS received considerably higher doses of anti-platelet treatment in the peri-procedural period compared with CEA patients (Table 2). This may have accounted, at least in part, for the 50% lower peri-procedural MI rates observed in the CAS compared with the CEA patients. CEA patients continued receiving aspirin 325 mg day\(^{-1}\) (or aspirin 81 mg day\(^{-1}\) or clopidogrel 75 mg day\(^{-1}\)) postoperatively indefinitely (at least for 1 year). By contrast, for CAS patients the continuation of the high anti-platelet treatment (325 mg aspirin once or twice daily for 30 days plus either 75 mg day\(^{-1}\) clopidogrel twice daily for 4 weeks or 250 mg ticlopidine twice daily for 4 weeks) was maintained only for 4 weeks after the procedure (in other words, as long as the 30-day postprocedural period described in the ‘primary ‘end’ point’). After that, the CAS patients received the same anti-platelet treatment as the CEA patients. Possibly as a result, although CAS was associated with 50% fewer peri-procedural MIs compared with CEA, there were >2.5-fold more MIs at 4 years (Table 1). Furthermore, CAS was associated with a higher MI rate at 4 years compared with CEA (HR: 1.44; 95% CI: 1.00–2.06; \( p = 0.049 \)). The 4-year MI rate, however, was not a component of the ‘primary ‘end’ point’. Only ipsilateral strokes within 4 years after randomisation were included in the primary ‘end’ point.

**Table 2.** Routine drug treatment administered to patients undergoing CEA or CAS in CREST. This information is listed in Table 1 of the CREST Supplementary Appendix (available at: http://www.nejm.org/doi/suppl/10.1056/NEJMoa0912321/suppl_file/nejmoa0912321_appendix.pdf).

**CAS patients**

- At least 48 hours before CAS, patients received aspirin 325 mg twice daily and clopidogrel 75 mg twice daily. Instead of ticlopidine, patients could receive aspirin 325 mg twice daily.
- When CAS was scheduled within 48 hours after randomization, patients received 650 mg aspirin and 450 mg clopidogrel 4 or more hours before the procedure.
- After CAS, patients received 325 mg aspirin once or twice daily for 30 days plus either 75 mg/day clopidogrel twice daily for 4 weeks or 250 mg ticlopidine twice daily for 4 weeks.
- The continuation of 325 mg/day aspirin for >4 weeks after the procedure was recommended for all CAS patients.

**CEA patients**

- At least 48 hours before CEA, patients received aspirin 325 mg/day.
- Following CEA, patients remained on aspirin 325 mg/day indefinitely (at least 1 year).
- For those patients intolerant to this dose, acceptable alternatives included ticlopidine 75 mg/day, aspirin 81 mg/day, ticlopidine 250 mg twice daily or aspirin and extended-release dipyridamole twice daily.

CEA: carotid endarterectomy; CAS: carotid artery stenting.
Contradictory results in the initial CREST report and the CREST subgroup analyses

The first CREST subgroup analysis according to symptomatic status (Table 3) showed that the stroke and death rates for all patients (symptomatic and asymptomatic) were almost double for CAS vs CEA (HR: 1.90; p = 0.005). For symptomatic patients, the peri-procedural stroke and death rates were again almost double for CAS versus CEA (HR: 1.89; p = 0.02). Asymptomatic patients undergoing CAS also had almost double the stroke rates compared with those undergoing CEA (HR: 1.88), but due to a wide CI, this difference was not statistically significant (p = 0.15). The finding that in symptomatic patients CAS is associated with significantly higher stroke and death rates compared with CEA was reported in several other multicentre randomised CAS versus CEA trials besides CREST. A recent meta-analysis of these trials showed that CAS is even more likely to cause stroke or death than CEA in patients who are asymptomatic for <2 weeks. CREST also reported another subgroup analysis of the effect of gender on outcomes (Table 3). Although men showed similar peri-procedural stroke rates whether undergoing CAS or CEA, women undergoing CAS had >2.5-fold higher peri-procedural stroke rates compared with CEA. As the CREST authors commented, “women might be at higher risk of periprocedural stroke and death because of technical difficulties related to the fact that they have smaller internal carotid arteries than men.” Therefore, in females CAS was associated with clearly inferior outcomes compared with CEA. A recent, large study of 54,658 carotid revascularisation procedures (94.2% CEA; 5.8% CAS) also supports this finding.

In a third CREST subgroup analysis, it was found that “age acted as a treatment effect modifier for the primary end-point (p = 0.02)” (Table 3). CAS was associated with similar peri-procedural stroke rates with CEA only in patients <65 years of age. For patients aged 65–74 years, CAS was associated with almost double the peri-procedural stroke rates compared with CEA. Due to the wide CI, this difference did not reach statistical significance (p = 0.08). However, for patients ≥75 years, CAS was associated with a significant >2-fold higher peri-procedural stroke rate compared with CEA (p = 0.035). A similar situation was observed at the end of the 4-year follow-up period (Table 3). Regarding the composite primary ‘end’ point, the risk of the two procedures was approximately equal at age 70 years, with CAS demonstrating better results for patients <70 years and with CEA showing better results for patients ≥70 years. As the CREST investigators reported, “for patients 70 years and older, the risk of events in CAS-treated patients was approximately twice that for CEA-treated patients (HR: 2.04; 95% CI: 1.48–2.82).” However, if the MIs were not included, the inflection point for an equal stroke risk for CAS and CEA was at 64 years, that is, 6 years younger than the primary ‘end’ point.

A recent report using data from the Society for Vascular Surgery (SVS) Vascular Registry compared the outcomes of 1347 CEAs and 861 CAS procedures performed on patients aged <65 years versus 4169 CEAs and 2536 CAS procedures performed on patients aged ≥65 years. In patients <65 years, CAS was associated with a higher incidence (but not significantly so) of the primary ‘end’ point consisting of 30-day stroke, death or MI rates compared with CEA (5.23% vs. 3.36%, respectively; p = 0.065). In patients ≥65 years included in the SVS Registry, however, CAS, when compared with CEA, was associated with a significantly higher incidence of not only the primary ‘end’ point (30-day stroke, death or MI rates: 7.14% vs. 4.27%, respectively; p < 0.01), but also of death (1.97% vs. 0.91%, respectively; p < 0.01) and stroke (4.89% vs. 2.52%, respectively; p < 0.01). In patients aged ≥65 years, CAS was associated with higher rates of the composite outcome of 30-day death, stroke or MI in both symptomatic (9.52% vs. 5.27%; p < 0.01) and asymptomatic (5.27% vs. 3.31%; p < 0.01) subgroups. The conclusion reached by the SVS Outcomes Committee was that “compared with CEA, CAS resulted in inferior 30-day outcomes in symptomatic and asymptomatic patients aged ≥65 years. These findings do not support the widespread use of CAS in patients aged ≥65 years.”

Strokes after CAS and CEA

The CREST investigators recently reported that “stroke is a more frequent complication of CAS compared to CEA. In CREST, this greater occurrence of stroke in the CAS arm was offset by the greater occurrence of MI in the CEA arm.” An analysis of the baseline and plaque characteristics of those patients who did suffer a stroke versus those who did not showed that CAS patients who suffered a stroke were more likely to be older (73.0 ± 7.7 vs. 68.5 ± 9.0 years, respectively; p < 0.001) and symptomatic (70.8% vs. 52.3%, respectively; p = 0.01). Furthermore, patients with specific plaque characteristics undergoing CAS were more likely to suffer a stroke, namely those with ulcerated (54.2% vs. 36.0%, respectively; p = 0.01) or eccentric plaques (70.8% vs. 56.6%, respectively; p = 0.051) and those with long carotid lesions (20.9 ± 7.6 vs. 17.6 ± 8.5 mm, respectively; p = 0.01). By contrast, there was no difference in patient and carotid plaque baseline characteristics of those suffering a stroke in the CEA arm. Finally, the 4-year mortality rates were almost 3-fold higher in the stroke group compared with the stroke-free group (21.2% vs. 11.6%, respectively; HR: 2.78; 95% CI: 1.63–4.76; p value not provided).

CAS FOR ASYMPTOMATIC CAROTID STENOSIS

Although almost double, the stroke and death rates of asymptomatic patients in CREST undergoing CAS did not differ significantly from those undergoing CEA (2.5% ± 0.6% vs. 1.4% ± 0.5%, respectively; HR: 1.88; 95% CI, 0.79–4.42; p = 0.15). According to the AHA/ASA guideline, CAS might be considered in selected asymptomatic patients, but its effectiveness compared with current BMT alone for these patients is not well established (Class IIb). However, it has been proposed that current BMT alone may be the...
treatment of choice for most asymptomatic patients and that no invasive treatment is required for the majority. Unt

till appropriately designed trials have compared the effectiveness of CAS versus CEA versus current BMT alone in asy

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tomatic patients, it may be inappropriate to recommend CAS for most of these patients.

CONCLUSIONS

Although the CREST data were initially interpreted as showing that there were no differences in outcomes between the two procedures, subsequent subgroup analyses showed that CAS was associated with higher stroke and death rates in symptomatic patients, females and patients ≥65 years compared with CEA. If these groups are removed, the only patients left in whom CAS was associated with similar stroke and death rates with CEA were asymptomatic males <65 years of age. However, current BMT alone may be the treatment of choice for most asymptomatic patients. If this concept is verified, there may be even fewer indications for CAS. CAS may be restricted to symptomatic patients in whom CEA is more

Table 3. Summary of the results of CREST and its subgroup analyses.

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<th>Study</th>
<th>Results</th>
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<td>CREST</td>
<td>- For 2502 pts over a median follow-up period of 2.5 years, there was no significant difference in the estimated 4-year rates of the primary end-point between the CAS and the CEA groups (7.2% vs 6.8%, respectively; HR with CAS: 1.11; 95% CI: 0.81–1.51; p = 0.51). - There was no differential treatment effect with regard to the primary end-point according to symptomatic status (p = 0.84) or sex (p = 0.34).</td>
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CREST subgroup analysis by symptomatic status

- Periprocedural stroke and death rates: 4.4% vs 2.3%, for CAS vs CEA, respectively; HR: 1.90; 95% CI: 1.21–2.98; p = 0.005.
- Periprocedural stroke and death rates for symptomatic pts: 6.0% ± 0.9% vs 3.2% ± 0.7%, for CAS vs CEA, respectively; HR: 1.89; 95% CI: 1.11–3.21; p = 0.02.
- Periprocedural stroke and death rates for asymptomatic pts: 2.5% ± 0.6% vs 1.4% ± 0.5%, for CAS vs CEA, respectively; HR: 1.88; 95% CI: 0.79–4.42; p = 0.15.

CREST sub-group analysis by sex

- Periprocedural strokes for men: 27 vs 20 events (3.7% vs 2.4%), for CAS vs CEA, respectively; HR for CAS: 1.39; 95% CI: 0.78–2.48; p = 0.26.
- Periprocedural strokes for women: 25 vs 9 events (5.5% vs 2.2%), for CAS vs CEA, respectively; HR for CAS: 2.63; 95% CI: 1.23–5.65; p = 0.013.

CREST subgroup analysis by age

- Periprocedural strokes in pts <65 yrs: 9 vs 8 (2.2% vs 2.1%), for CAS vs CEA, respectively; HR for CAS: 1.10; 95% CI: 0.42–2.84; p = 0.85.
- Periprocedural strokes in pts 65–74 yrs: 20 vs 10 (3.8% vs 2.0%), for CAS vs CEA, respectively; HR for CAS: 1.98; 95% CI: 0.93–4.23; p = 0.08.
- Periprocedural strokes in pts ≥75 yrs: 23 vs 11 (6.9% vs 3.1%), for CAS vs CEA, respectively; HR for CAS: 2.17; 95% CI: 1.06–4.45; p = 0.035.
- Stroke end-point in pts <65 yrs: 13 vs 16 (3.7% vs 4.5%), for CAS vs CEA, respectively; HR for CAS 0.78; 95% CI: 0.37–1.62; p = 0.50.
- Stroke end-point in pts 65–74 yrs: 26 vs 18 (5.1% vs 4.6%), for CAS vs CEA, respectively; HR for CAS 1.42; 95% CI: 0.78–2.60; p = 0.25.
- Stroke end-point in pts ≥75 yrs: 33 vs 16 (10.9% vs 4.9%), for CAS vs CEA, respectively; HR for CAS 2.15; 95% CI: 1.19–3.91; p = 0.01.

CAS: carotid artery stenting; CEA: carotid endarterectomy; HR: hazard ratio; CI: confidence interval; yrs: years.

Any stroke within the periprocedural period.

Any stroke within the periprocedural period and 4-year postprocedural ipsilateral stroke.
risky (e.g., surgically inaccessible carotid lesions, those with scarred or infected necks, recurrent laryngeal nerve injury or contralateral internal carotid occlusion, etc.)

Importantly, the outcomes of CEA versus CAS versus current BMT alone have not been studied in these high-risk symptomatic patients.

Thus, current data suggest that CEA and CAS are not equivalent for the management of symptomatic patients. Although CAS has up until now been associated with higher stroke and death rates compared with CEA, it is important to emphasise that CREST used CAS technology and indications that are now outdated. With current and future improvements, such as better embolic protection methods (reversal and cessation of flow devices), better stents (membrane or mesh covered) and better patient selection, it is likely that CAS outcomes will improve and CAS will become increasingly competitive compared with CEA. It is also likely that the two procedures will have a complementary role in certain patients. However, further trials are needed to justify this assumption and to document the equivalence or superiority of CAS to CEA in various patient groups that will show a benefit beyond current BMT.

CONFLICTS OF INTEREST/FUNDING

None.

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