



What do the results of CREST-2 offer us?

¿Qué nos aportan los resultados del CREST-2?

The publication of the CREST-2 trial results in the *New England Journal of Medicine* on November 21st, 2025 (1) quickly resonated in non-scientific vascular media with headlines such as: "The long-awaited CREST-2 results support stenting for asymptomatic carotid stenosis," "The CREST-2 study highlights the benefits of carotid artery stenting," or "Historic: CREST-2 data show a reduction in stroke risk with carotid stenting compared with medical therapy alone."

Almost simultaneously, WhatsApp groups related to the specialty were flooded with messages taking positions on the matter; academic centers discussed it internally and adopted extreme stances, ranging from complete disqualification of the trial results to calls for immediate changes in clinical practice guidelines. It is worth recalling that the most recent guidelines from the Society for Vascular Surgery (SVS) (2), the European Stroke Organisation (ESO) (3), and the European Society for Vascular Surgery (ESVS) (4) almost completely relegate transfemoral carotid stenting.

In an effort to contribute to this debate within the international vascular community regarding the optimal management of asymptomatic extracranial carotid stenosis, this editorial aims to analyze the main concerns raised by the SVS in its official commentary (5) and to discuss their implications for the angiologist and vascular surgeon.

CREST-2 is a clinical trial designed to compare best medical therapy (BMT) vs revascularization (via carotid endarterectomy—CEA—or transfemoral carotid artery stenting—TF-CAS). It provides valuable data in a strictly controlled setting. However, as noted by the SVS, a critical interpretation of these findings in light of accumulated evidence and real-world clinical practice is imperative.

ANALYSIS OF THE CREST-2 FINDINGS AND LIMITATIONS

1. *The gap between controlled trials and the real world.* One of the key points highlighted by the SVS is the difficulty of translating the CREST-2 BMT regimen into routine clinical practice. The trial achieved an annual stroke rate of 1.5-1.7% with BMT, a remarkable accomplishment that required exceptional resources: telephone follow-up, lifestyle coaching, and close medication monitoring. In real-world practice, adherence and resources are limited, and stroke risk with BMT may be variable and not always as low (6).

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Therefore, if the BMT arm of the trial is difficult to replicate, the absolute benefit of revascularization (which already showed a modest advantage in CREST-2) could be significantly greater in the general population. This reinforces the concept that optimal BMT is the cornerstone but does not invalidate the role of revascularization in selected patients.

2. *The absence of TCAR in the equation.* CREST-2 did not evaluate transcarotid artery revascularization with flow reversal (TCAR), a technology that has transformed practice in the United States. Evidence from the Vascular Quality Initiative (VQI) registry consistently shows that TCAR has stroke/death rates equivalent to CEA and significantly lower than TF-CAS, with the added benefit of reducing the risk of myocardial infarction and cranial nerve injury (7). Any modern evaluation of revascularization options that omits TCAR excludes a fundamental tool, particularly valuable in patients with high anatomical risk (unfavorable aortic arch) or in octogenarians, in whom its safety is well documented.
3. *Biases in patient and operator selection.* The CREST-2 design introduced stricter and more complex exclusion criteria for the TF-CAS arm than for the CEA arm. Unfavorable aortic arch anatomy, tortuosity, or severe calcification were excluded—precisely the scenarios where TF-CAS carries increased risk. In addition, TF-CAS operators were selected more rigorously (50% acceptance) than surgeons (90%) (8). This filtering creates an “ideal” TF-CAS cohort that does not reflect real-world practice, where less experienced operators may incorrectly extrapolate results to higher-risk anatomies. The TF-CAS “learning curve” is long (> 50-100 cases) (9), unlike TCAR, where early risk does not appear to be increased (10).
4. Favorable for CEA (5). Furthermore, previous meta-analyses consistently demonstrate a higher rate of perioperative stroke with TF-CAS vs CEA, particularly minor strokes (11,12). The recent ACST-2 also reflected this pattern (13). The SVS argues that some late events in the CEA arm of CREST-2 (strokes occurring years later, unrelated to restenosis) may have distorted long-term comparisons in a setting where event rates are very low.

THE CURRENT LANDSCAPE: A PERSONALIZED AND MULTIMODAL APPROACH

The main conclusion drawn from the SVS commentary is that CREST-2 does not change the standard of care. Rather than promoting one therapy over another, it reinforces the need for a personalized and multimodal approach:

- Optimal BMT is the cornerstone for all patients.
- The choice of revascularization technique should be based on individual risk stratification considering:
 - Anatomy: aortic arch, tortuosity, calcification, and lesion length.
 - Patient comorbidities: cardiac and pulmonary risks and prior cervical radiotherapy.
 - Center and operator experience.
- CEA remains the reference treatment for many patients, with robust and durable evidence.
- TCAR has become established as a safe and effective alternative, especially in patients at high risk for CEA or with unfavorable anatomy for TF-CAS.
- TF-CAS may be an option in carefully selected patients with favorable anatomy, provided it is performed by highly experienced operators.

CONCLUSION

CREST-2 is an important contribution to the literature, highlighting the value of intensive BMT and confirming that revascularization continues to provide benefit in asymptomatic carotid stenosis. However, its results must be interpreted within the limitations of a highly controlled trial. For the angiologist and vascular surgeon, the key message is that the therapeutic arsenal is broader than ever (BMT, CEA, TCAR, and TF-CAS). Excellence in the care

of patients with carotid disease does not lie in the dogmatic adoption of a single technique, but in the ability to select—collaboratively and based on real-world evidence (such as that from the VQI registry)—the safest and most effective strategy for each individual. Clinical practice should be guided by the totality of evidence, clinical guidelines, and, above all, the principle of personalizing therapy to optimize outcomes.

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