EDITORIAL

Cutting Edge or Cutting Back? What ECST-2 Means for the Vascular Surgeon

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The Second European Carotid Surgery Trial (ECST-2) addresses a critical question: in patients with carotid stenosis ≥50% (whether asymptomatic or low-to-intermediate risk symptomatic), does adding carotid revascularisation (either carotid endarterectomy or stenting) to optimised medical therapy (OMT) yield better outcomes than OMT alone?[1] The trial was conceived in the context that much of the evidence favouring revascularisation (CEA or CAS) comes from trials several decades old — ECST, NASCET, ACST etc. — and medical therapy (lipids, blood pressure control, antithrombotics, risk factor control) has improved substantially since then.

The trial randomised 429 patients between 2012 and 2019: 215 to OMT alone, 214 to OMT + revascularisation. Both symptomatic and asymptomatic patients were included with a carotid stenosis ≥50%. Symptomatic patients had to have a predicted 5-year risk of ipsilateral stroke of less than 20% by the CAR score (Carotid Artery Risk score).[2] The primary outcome for the 2-year, interim analysis was a hierarchical composite endpoint assessed with a win ratio of (1) periprocedural death, fatal stroke, or fatal myocardial infarction; (2) non-fatal stroke; (3) non-fatal myocardial infarction; (4) new silent cerebral infarction on imaging. Analysis was by intention-to-treat.

The study showed that, at 2 years, there was no significant benefit of adding revascularisation in patients meeting the inclusion criteria. The win ratio was 1.01 (95% CI 0.60-1.70; p = 0.97), meaning nearly equal “wins” for OMT alone vs OMT + revascularisation. No heterogeneity (no subgroup with clear benefit) was found in the predefined subgroups (symptomatic vs asymptomatic, degree of stenosis, etc.). Consequently, the authors support treating patients with asymptomatic carotid stenosis, or symptomatic carotid stenosis at low to intermediate risk (by CAR score), with optimised medical management alone, pending further data (5-year follow-up, etc.).

Strengths of ECST-2 include that it is a contemporary trial, offering current OMT. Given improvements in medical therapy (e.g., statins, better control of hypertension, antiplatelet regimens) over the past decades, it’s highly valid to revisit whether revascularisation still adds benefit in lower-risk populations. The trial is responding to a major gap in current evidence. Morover, the use of the CAR score allows stratification by individual risk, rather than treating all patients above a stenosis threshold equally. This constitutes a step toward personalized medicine. The multicentre design (30 centres across several countries) enhances generalizability, the blinded adjudication of outcomes (particularly imaging outcomes) ensures reliability, whereas the use of the hierarchical composite outcome and the win ratio emphasizes clinically more serious outcomes first. This avoids simply adding up events of unequal clinical meaning.

The low event rates underline how good medical therapy has become. The fact that in both arms, stroke (clinical or imaging) occurrences were modest shows that OMT is effective. This underpins the trial’s utility. In addition, monitoring silent cerebral infarction by imaging adds important nuance; many strokes are clinically silent but may have cumulative effects. Including these in the composite outcome improves sensitivity.

While ECST-2 provides highly informative interim data, there are several important limitations (some acknowledged by authors) that should temper how we apply these findings or draw conclusions. First, the 2-year follow-up is short. The risk of stroke in carotid stenosis tends to accumulate over time. Some benefits of revascularisation may not fully manifest until beyond 2 years. The trial is ongoing with planned 5-year follow-up. In the same context, early perioperative risks (stroke, MI, death) might tip the balance against revascularisation in the short term; whether later benefits outweigh early harm may depend on longer follow-up. It should also be emphasized that ECST-2 deliberately excludes patients with high predicted risk (CAR ≥20%) of ipsilateral stroke. Thus, results do *not* apply to higher-risk patients, where benefit of revascularisation may still be substantial.

Statistical issues and power represent another caveat Because event rates are lower than historical trials anticipated, the trial may be underpowered to detect small but clinically meaningful differences, especially for particular subgroups. Subgroup analyses are especially fragile given small numbers. Similarly, the confidence interval of the win ratio is wide (0.60-1.70) meaning substantial uncertainty around effect-size. A possible moderate benefit (or harm) cannot be ruled out.

The generalisability to revascularisation type and proce-

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dural risk is also under question. ECST-2 included both carotid endarterectomies and CAS procedures. The risks and benefits of these two techniques might differ, especially in certain anatomical subtypes or patient comorbidity profiles. Thus, results may not generalize equally to CEA and CAS.

Risk prediction via CAR score is also questionable. The CAR score was recalibrated, but risk prediction always carries uncertainty; improvements in medical therapy may continue, and baseline population characteristics (older age, comorbidity, imaging features) may shift. Thus, the predictions might drift.

Moreover, imaging markers such as plaque vulnerability (e.g. intraplaque hemorrhage, ulceration) might modulate risk substantially; while ECST-2 plans to examine these, the interim results do not yet allow stratification by these imaging features. Some patients otherwise "low risk" may be misclassified.

While inclusion of "silent cerebral infarction" in imaging is a strength, the clinical impact (on cognition, risk of future symptomatic stroke, functional outcome) is still uncertain. The weight given to silent infarcts in the composite (being lowest in the hierarchy) reflects this. But long-term consequences matter, especially in older patients.

ECST-2 was planned initially for a larger sample size (originally ~2000), but recruitment was smaller. This may limit statistical power. Also, during its protracted recruitment period (2012-2019), standards of medical therapy and patient characteristics may have shifted, potentially introducing heterogeneity across enrolment eras.

Given the strengths and the limitations, what does ECST-2's 2-year interim analysis mean for clinicians managing carotid stenosis? For patients with carotid stenosis ≥50%, but otherwise "low risk" (as per CAR score), especially asymptomatic or in whom symptoms are remote, ECST-2 suggests that optimised medical therapy may suffice without the risks of revascularisation. This could spare patients the operative risks (perioperative stroke, MI, death) and costs or morbidity of surgery.

The trial underlines that medical management today is far better than decades ago. High uptake of statins, better control of BP, antiplatelets etc. These therapies matter; any decision about intervention must assume medical therapy is aggressively optimized.

Not all patients with similar degrees of stenosis are the same. Other factors (age, sex, comorbidities, plaque morphology, time since symptoms) affect risk. ECST-2's use of the CAR score and planned plaque imaging point to a more nuanced decision-making framework. Clinicians should adopt risk scores and imaging to identify who might get benefit from revascularisation. Existing guidelines (national and international) that recommend revascularisation based largely on degree of stenosis and symptomatic status may need revising, or at least specifying thresholds for risk under modern therapy. The ECST-2 findings could prompt societies to incorporate risk scores, imaging markers, patient age, comorbidity, and operative risk more explicitly. Patients with "high stroke risk" by CAR (≥20%), recently symptomatic, or with imaging features of vulnerable plaques, may still benefit from intervention. ECST-2 does not include those, so guidelines should still allow revascularisation in those higher-risk categories.

While ECST-2 is important, there are several unanswered questions and areas for further research.

The longer-term data (5-year follow-up) are crucial. Only then can we see whether the modest early disadvantages of revascularisation (perioperative risk) are offset by longer-term reductions in ipsilateral stroke, and to what magnitude.

Plaque imaging (e.g. intraplaque hemorrhage, ulceration, lipid-rich core) may identify patients with low risk by clinical score but high risk by plaque vulnerability. It remains to be seen whether these subgroups derive greater benefit from revascularisation. ECST-2 includes MRI plaque substudies, but these results are not yet mature.

More work is needed to understand how silent infarcts contribute to long-term neurological, cognitive, or functional impairment, and whether preventing them justifies intervention. The choice of hierarchical composite endpoint is good, but what weights do patients give to silent infarcts vs overt stroke vs MI etc?

Quality of life, cognitive decline, functional status—these are not yet fully addressed, especially in those with silent or subclinical infarcts. Also, durability of revascularisation (late restenosis, procedural durability) matters over longer time.

Interventions (especially surgery or stenting) carry cost and resource use. If OMT alone is non-inferior in many low-risk patients, this could shift resource allocation. Economic analyses will be important.

Many trials are done in high-income countries, in centers with high experience. The benefit:risk ratio may differ in lower-income settings, or in centers with less surgical/interventional expertise.

The CAR score is helpful, but further refinement, validation, perhaps integration of imaging, biomarkers (if any) is needed. Also, tracking secular changes in baseline risk (medical therapy improvements) is vital; what is "low risk" now may shift in the future.

Older patients, those with limited life expectancy or comorbidities, may derive less benefit from revascularisation (given procedural risks) and more from medical management. Tailoring by life expectancy is important.

Revascularisation's appeal lies in the idea of removing or bypassing a stenotic lesion, potentially preventing future strokes. But every revascularisation carries risk — surgical morbidity/mortality; for stenting, risks may differ (embolism, restenosis); procedural MI risk; peripheral complications. Conversely, medical therapy also has cost, side effects, adherence issues, but substantially lower immediate procedural risk.

What ECST-2 shows is that, in patients with lower predicted stroke risk under OMT, the immediate procedural risks may not be balanced by enough prevented strokes in a 2-year span. Over time, this balance may shift, or may not; the trial will tell. Thus, the trade-off is highly sensitive to:

- The magnitude of baseline risk of ipsilateral stroke if untreated (or treated just with OMT)
- The procedural risk and the center/surgeon/interventionalist performance
- Patient preferences: e.g. avoidance of even small stroke risk vs desire to avoid surgery
- Life expectancy: someone with longer life more likely to b

ECST-2 is part of a broader trend of re-examining old assumptions. Earlier trials (ECST, NASCET, ACST) established the benefit of carotid revascularisation in symptomatic high grade stenosis, and in some asymptomatic patients. But medical therapy at the time was much less rigorous. Over time, registries and smaller studies have shown that stroke rates under medical therapy have fallen in asymptomatic stenosis to ~1% per annum or less, sometimes even 0.6% in selected cohorts. Other ongoing trials (e.g. CREST-2, SPACE-2, ACTRIS) also aim to clarify the balance of benefits in asymptomatic or lower risk symptomatic carotid disease. ECST-2's contribution is that it gives us randomized controlled data (rather than observational) in modern medical therapy settings, for a well-defined lower risk population. It helps define what "lower risk" may mean in practice, and challenges the practice of automatically revascularizing stenoses above a fixed degree (e.g. ≥70%) regardless of other risk features.

In conclusion, the ECST-2 2-year interim results are a landmark in carotid stenosis management. They suggest that for many patients with moderate carotid stenosis and low-to-intermediate stroke risk, optimised medical therapy alone may perform as well over 2 years as adding carotid revascularisation, considering the risks, costs, and invasiveness of surgery or stenting. Nonetheless, these are interim observations. Longer follow-up, richer imaging subgroup data, better understanding of silent infarcts, and refinement of risk stratification tools are needed before wholesale changes in practice are made. What the trial does immediately is sharpen our awareness that: *not all carotid stenosis is equal*, that *medical treatment today is far more powerful than a few decades ago*, and that *patient-selection matters critically*. Already, in low-risk patients, a more conservative approach seems justified. As with all such pivotal trials, the devil is in the details — patient selection, operator skill, timing, comorbidity — but ECST-2 moves the field forward by providing modern evidence calibrating when carotid revascularization is truly likely to add value beyond best medical care.

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