Emerging evidence suggests that patients with high-grade asymptomatic carotid stenosis should be revascularized

Christos D. Liapis, MD,[a] Hans-Henning Eckstein, MD,[b] Kosmas I. Paraskevas, MD,[c] *and* Jack L. Cronenwett, MD,[d] *Athens, Greece; Munich, Germany; and Lebanon, NH*

The management of asymptomatic carotid stenosis (ACS) remains a topic of extensive debate. According to the 2009 European Society for Vascular Surgery (ESVS) guidelines for the management of patients with carotid stenosis, carotid endarterectomy (CEA) can be recommended for asymptomatic men below 75 years of age with a 70% to 99% stenosis if the risk associated with surgery is less than 3% (grade A).[1] The 2011 Society for Vascular Surgery (SVS) guidelines similarly recommended that patients with ≥60% ACS should be considered for CEA for reduction of long-term risk of stroke, provided they have a 3- to 5-year life expectancy and perioperative stroke/death rates are ≤3% (grade I; level of evidence: A).[2]

Because of improvements in optimal medical therapy (OMT) since the publication of the landmark randomized controlled trials (RCTs),[3-5] it has been suggested that CEA does not provide a significant benefit for patients with ACS compared with OMT alone.[6-8] As a result, in 2017, the European Society for Vascular Surgery downgraded their previous guidelines for the management of patients with ACS to recommend that for patients with 60% to 99% ACS, CEA should only be considered in the presence of one or more imaging characteristics that may be associated with an increased risk of ipsilateral stroke, projected perioperative stroke/death rates <3%, and life expectancy >5 years (class IIa; level of evidence: B).[9] The basis for this downgrade was two RCTs that demonstrated that increasing stenosis severity (including bilateral stenoses and contralateral occlusion) was not associated with increased rates of late stroke in patients randomized to OMT.[4,5] In addition, a 2014 meta-analysis involving 41 studies (6 RCTs; 35 observational studies) demonstrated that ipsilateral stroke risk was similar in patients with 50% to 70% vs 70% to 99% ACS (1.9/100 vs 2.1/100 person-years, respectively; $P = .427$).[10] As the authors suggested, the lack of difference may have been due to heterogeneity in the definition and measurement of the degree of stenosis across studies. When analyses were stratified by stenosis severity (instead of using meta-regression), the difference became more pronounced (2.4 vs 1.6 per 100 person-years).[10]

In contrast to the 2014 meta-analysis,[10] a recent population-based cohort study, systematic review, and meta-analysis reported opposite results.[11] The Oxford Vascular Study enrolled patients from April 1, 2002, to April 1, 2017, who were referred for carotid imaging and were found to have ACS of any severity (n = 2178).[11] Of these, 154 individuals had 50% to 69% ACS and 53 had 70% to 99% ACS. All patients were started on contemporary OMT including an antiplatelet/anticoagulant, a statin, and at least one blood pressure-lowering agent. After a median follow-up of 5.9 years, there were 16 ischemic events (8 strokes and 8 TIAs) ipsilateral to the side of the 50% to 99% ACS. The 5-year risk of ipsilateral ischemic stroke was significantly greater in patients with 70% to 99% than in patients with 50% to 69% stenosis (14.6% [95% confidence interval (CI): 3.5-25.7] vs 0%, respectively; $P < .0001$) and also greater in patients with 80% to 99% than in those with 50% to 79% stenosis (18.3% [95% CI: 7.7-29.9] vs 1.0% [95% CI: 0.0-2.9], respectively; $P < .0001$).[11] A meta-analysis including 23 studies (n = 8419 patients) reporting ipsilateral stroke risk in patients with moderate and severe stenosis revealed a linear association of stroke risk with degree of stenosis ($P < .0001$), with a >2-fold higher risk for patients with 70% to 99% vs 50% to 69% ACS (odds ratio: 2.1; 95% CI: 1.7-2.5; $P < .0001$) and a 2.5-fold risk for patients with 80% to 99% vs 50% to 79% ACS (odds ratio: 2.5; 95% CI: 1.8-3.5; $P < .0001$).[11] The authors concluded that omitting the degree of stenosis as a selection factor for intervention in patients with ACS and instead advocating the use of other surrogate markers for patient selection (eg, computerized plaque analysis, plaque echolucency, and intraplaque hemorrhage on magnetic resonance imaging) may be inappropriate.[11] It was further concluded that although the reported rates of ipsilateral stroke have fallen over time, the stroke risk is still high for patients with high-grade stenosis on contemporary OMT, "suggesting that the benefits of surgical intervention might be underestimated."[11]

From the Department of Vascular and Endovascular Surgery, Athens Medical Center, Athens[a]; the Department of Vascular and Endovascular Surgery, Klinikum rechts der Isar, Technical University of Munich, Munich[b]; the Department of General and Vascular Surgery, Central Clinic of Athens, Athens[c]; and the Section of Vascular Surgery, Dartmouth-Hitchcock Medical Center, Lebanon.[d]

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Correspondence: Christos D. Liapis, MD, Department of Vascular and Endovascular Surgery, Athens Medical Center 56, Kifissias Ave & Delfon St, 15125 Marousi, Athens, Greece (e-mail: liapis@med.uoa.gr).

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A similar conclusion was reached in a population-based cohort study inviting all 65-year-old men living in the county of Uppsala, Sweden (n = 3057), to a carotid ultrasound examination.[12] Individuals were grouped according to the presence of carotid atherosclerosis (normal carotids, plaque without significant stenosis, moderate [50%-79%] and severe [80%-99%] ACS). The same individuals were re-screened at age 70. Among those with plaque but not significant stenosis (n = 696), 25 (3.6%) progressed to moderate stenosis and 8 (1.1%) to severe stenosis, of whom 4 (0.6%) developed neurological symptoms. Of 31 men with 50% to 79% ACS, 4 (12.9%) progressed to a severe stenosis, of whom 2 (6.5%) developed symptoms. Finally, 5 of 12 individuals (42%) with 80% to 99% ACS developed symptoms. This independent study demonstrated a high risk of neurological events in patients with severe ACS.[12]

So what are the issues guiding the selection of specific ACS patients for consideration for intervention? Severe stenosis appears to be important. As demonstrated in the two independent recent reports,[11,12] severe (80%-99%) but not moderate (50%-79%) ACS is a prerequisite for recommending CEA. Patients with moderate degrees of ACS do not have a high enough stroke risk to justify a prophylactic carotid intervention.[11,12] This key issue was recognized in the updated 2021 SVS guidelines for the management of extracranial cerebrovascular disease.[13] After evaluation of the available evidence, a strong recommendation was provided for CEA plus OMT over OMT alone for the long-term prevention of stroke and death in low-surgical risk patients with >70% ACS (grade I; level of evidence: B).[13]

Another crucial issue is the standardization of carotid duplex ultrasound criteria to guide duplex classification of disease severity. The substantial variation in institutional protocols for determining the degree of ACS and consequently the threshold for intervention results in a large percentage of under- or overestimation of ACS and has a profound effect not only on patient outcomes but also on health care costs.[14,15] Offering a prophylactic carotid intervention to selected asymptomatic patients with >80% ACS, few negative prognostic factors for long-term survival (eg, congestive heart failure, dialysis dependence, and insulin-dependent diabetes) and a good life expectancy are essential to ensure that these patients with ACS will benefit from intervention.[16,17]

An issue that may need to be re-assessed is that the recommended perioperative stroke/death rate threshold (<3%)[9,13] in patients with ACS undergoing an intervention may be too high. The recently updated German-Austrian clinical practice guidelines strongly recommended that periprocedural stroke/death rates for ACS should be as low as possible after CEA/carotid artery stenting.[18] According to these guidelines, the periprocedural stroke/death rates should be monitored by neurologists and should not exceed 2% for ACS.[18]

Transcarotid artery revascularization (TCAR) with dynamic cerebral blood flow reversal has emerged as an alternative to CEA and transfermoral carotid artery stenting for the management of both symptomatic and asymptomatic carotid patients.[19,20] TCAR has gained popularity and is being increasingly used in everyday clinical practice, yet its role in the management of carotid patients has not yet been defined by guidelines. The role of TCAR and other topics is addressed in a separate comprehensive implementation document by the SVS guidelines committee.[13]

In conclusion, recent key articles appear to clarify the optimal management of patients with ACS.[11-13] Clearly, it is essential that all patients with ACS should be placed on OMT. However, emerging evidence suggests that patients with severe asymptomatic stenosis (80%-99%) are at high stroke risk with OMT alone and should be considered for a prophylactic procedure to reduce the risk of a future cerebrovascular event.[11,12] This fact is expressed with a strong recommendation in the updated 2021 SVS guidelines.[13]

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