CAS in Asymptomatic Patients at High Risk for CEA:

A Safe Stroke Prevention Treatment in Patients With Comorbid Conditions

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There has traditionally been substantial resistance to the concept of pre-emptive revascularization of severe carotid stenosis in asymptomatic patients. Although the surgical community has embraced carotid endarterectomy (CEA) of asymptomatic carotid disease, the reception has been much less warm in neurological circles. Although the asymptomatic carotid atherosclerosis trial (ACAS) provided clear evidence for the superiority of medical management combined with CEA versus medical management alone in asymptomatic patients with 60% or more stenosis, the benefit was small in absolute terms and was skeptically received.[1]

However, the benefit of CEA in asymptomatic patients was confirmed last year with the publication of the very large asymptomatic carotid stenosis trial (ACST).[2] The ACST trial randomized 3,120 patients to CEA plus best medical treatment versus medical treatment alone. Stenosis >60% on ultrasound had to be present. There was a 2.8% perioperative risk of stroke and death in the surgical arm. At 5 years, the risk of stroke or perioperative death was 11.78% in the medical treatment alone arm versus 6.42% in the surgical treatment arm, with the benefit becoming apparent at approximately 2 years after randomization. For the first time, the ACST trial also demonstrated a benefit for women with surgery. It also demonstrated for the first time a reduction in contralateral stroke after CEA in asymptomatic patients, indicating that improvement in collateral circulation to the contralateral hemisphere can have a benefit in terms of stroke prevention.

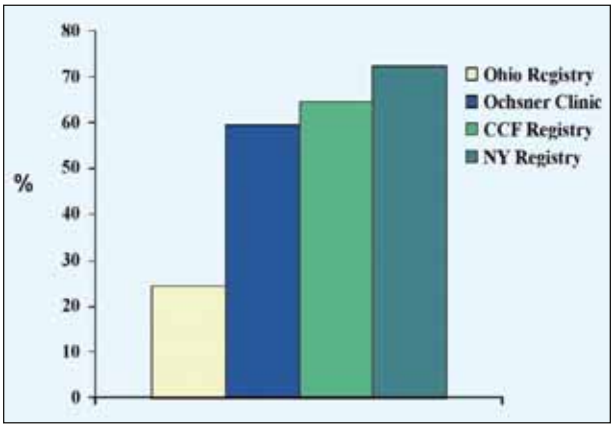

Figure 1. Up to 75% of patients undergoing CEA are asymptomatic.

TABLE 1. PERCENTAGE OF CEA PATIENTS AT MAJOR CENTERS CLASSIFIED AS HIGH RISK

Cleveland Clinic	23%
U of Rochester	16%
U of Michigan	17.5%

Physicians opposed to CEA in asymptomatic patients hypothesize that if all of these patients received adequate medical treatment, there would be no need for revascularization. The ACST trial clearly disproves this sentiment: medical treatment was carefully monitored, and there were very high rates of compliance for antiplatelet therapy, antihypertensive therapy, and lipid-lowering therapy, and yet the surgical arm still did better than medical treatment alone. In summary, the evidence for revascularization for asymptomatic carotid

stenosis with surgery is fairly convincing.

CAROTID STENTING WITH EMBOLI PROTECTION

Let us move on to the use of a less-invasive treatment, carotid artery stenting with emboli protection, for the treatment of asymptomatic carotid disease. I will confine my remarks to patients with comorbid conditions at high risk for surgery because to date , although this has been the most carefully studied set, it is important to note that there are ongoing trials in lower-risk patients. The issue of how to manage asymptomatic carotid disease is of significant public health importance because up to 75% of the patients undergoing CEA in the US are asymptomatic (Figure 1).[3-6]

Many of these patients fall out of the ACAS and ACST criteria due to comorbid conditions, yet are treated with CEA because, in the judgment of their treating physicians, the benefits outweigh the risks (Table 1).[5, 7-8]

In the carotid stenting trials to date, extremely conservative criteria have been used for asymptomatic patients with stenosis having to be ≥80%. This is based on the classic ultrasound studies by Chambers and Norris demonstrating a significant increase in stroke once stenosis reaches 80%, with the risk of stroke rising to approximately 5% in those patients.[9,10] Therefore, the patients in the high-risk carotid trials, such as SAPPHIRE and ARCHeR, had a substantially elevated risk of future stroke compared to the patients in ACAS and ACST based on their degree of stenosis as well as their comorbid conditions.

Figure 2. An asymptomatic patient with 80% stenosis who underwent previous CEA. Should this patient not be stented?

An interesting relationship is evident when one looks at the ACAS and ACST trial results: the 30-day risk of stroke and death in the surgical arm of both trials is comparable to the 1-year risk of stroke in the medical management group (Table 2). Therefore, it appears that if a revascularization procedure has a perioperative risk roughly comparable to the annual risk of medical treatment in that patient population, there are long-term stroke prevention benefits to revascularization. In the SAPPHIRE trial, the 30-day risk of stroke and death was 5.4%; in ARCHeR, it was 4.3%. The estimated risk of stroke in the SAPPHIRE and ARCHeR asymptomatic patients given their degree of stenosis and comorbid conditions would be approximately 5% per year, and therefore it would be expected there would be a stroke prevention benefit in these patients.

Another common objection to the treatment of asymptomatic patients with comorbid conditions is the notion of limited life expectancy. It should be noted that patients in both SAPPHIRE and ARCHeR had been referred for carotid revascularization by their primary care physicians and were patients with a good quality of life. The life expectancy calculations indicate a median life expectancy at 5.5 years for SAPPHIRE and 5 years for ARCHeR. Therefore, these patients would be expected to live long enough to benefit from revascularization. This is not surprising given that many of the conditions that increase their risk for CEA, such as restenosis or previous radiation therapy, have no impact on their long-term survival.

Further evidence that these patients have a good quality of life comes from the baseline modified Rankin scores from the ARCHeR trial, in which 72% had a score of 0 at baseline and 17% had a score of 1,

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TABLE 2. ASYMPTOMATIC DISEASE: THE REVASCULARIZATION RISK SHOULD BE SIMILAR TO ANNUAL STROKE RISK WITH MEDICAL TREATMENT

	Revascularization 30-Day Stroke/Death	Medical Treatment Annual Risk of Stroke
ACAS	2.3%	2.2%
ACST	2.8%	2.3%
SAPPHIRE	5.4%	5%*
ARCHeR	4.3%	5%*
CREST Lead-In	3.1%	not applicable

** Estimated*