# CAS in Asymptomatic Patients at High Risk for CEA: Rebuttals

## Rebuttal by Jay S. Yadav, MD

Dr. Comerota's commentary contains multiple misunderstandings and misstatements. He states "CAS has never been shown to reduce stroke risk in any patient category" and asks "Is it not the responsibility of the carotid interventionists to show that CAS is better than the natural course of the disease treated with today's best medical care?" The answer is "no." It would be unethical, as well as completely impractical, to conduct a randomized trial of medical therapy versus carotid stenting in patients who are routinely considered for CEA. Every patient randomized in SAPPHIRE was considered a reasonable candidate for CEA by a panel of physicians, including a vascular surgeon. Given the evidence in favor of CEA over medical management alone in a variety of patient groups, it would be impossible to justify another randomized trial with a medical treatment arm except in perhaps the sickest of patients and certainly no one is advocating any procedures, stent or other, in these patients.

> "It would be unethical . . . to conduct a randomized trial of medical therapy versus carotid stenting in patients who are routinely considered for CEA."

Dr. Comerota also uses the straw man of ACAS to assert that medical management has improved dramatically since ACAS was conducted but fails completely to discuss the ACST trial published last year which was much larger than ACAS, had state-of-the-art medical management (indeed probably better medical management than the average patient in the US), and showed a conclusive benefit for CEA in asymptomatic patients.

He then goes through a litany of the early studies in carotid angioplasty, which had inexperienced operators, did not use embolic protection, and often did not even include stenting. Should we go back to the Fields study when discussing CEA?[1]

Dr. Comerota performs a bizarre analysis of the SAP-

*(**Dr. Yadav,** continues)*

## Rebuttal by Anthony J. Comerota, MD

Dr. Yadav's argument is based upon an "estimated" high stroke risk in patients with asymptomatic carotid disease treated with best medical care. This is a serious overestimation. Important patient care decisions should be based on objective, peer-reviewed data, ideally generated from randomized trials.

> "Eliminating events that occurred prior to operation, the true procedure-related event rate (stroke/death) of CEA in ACAS was 1.5%."

Two large randomized trials of patients with asymptomatic carotid atherosclerosis have established the natural course of the disease in patients treated with best medical care. Both trials have demonstrated that the 30-day to 45-day stroke rate is 0.4%. This is contrasted with a stroke/death rate of 5.4% to 6% in patients undergoing CAS during the same period. The long-term stroke rate of best medical care is approximately 2% per year, based on more than 2,390 patients and more than 7,600 patient years of follow-up. Even in the reports quoted by Dr. Yadav, the overall incidence of cerebral ischemic events was 7.2% (3.7%/y); however, 78% of the events were TIAs. The incidence of stroke at 1 year in patients without TIAs was 1%,[1] increasing to 3.3% in those with >75% stenosis (2.5% ipsilateral stroke).[2]

The data quoted by Dr. Yadav regarding the SAPPHIRE and ARCHeR trials are the best possible spin on these two data sets. A substantial number of patients in SAPPHIRE and ARCHeR had neointimal fibroplasia. Patients with neointimal fibroplasia have a much lower CAS procedure-related event rate compared to patients with atherosclerosis. The important question for the majority of physicians and patients is: "What are the results of CAS in asymptomatic patients with carotid stenosis due to atherosclerosis?" Patients in the ACAS and ACST trials had atherosclerotic disease only; therefore, results of CAS for only atherosclerotic patients should be the comparator.

*(**Dr. Comerota,** continues)*

*(**Dr. Yadav,** continued)*
PHIRE 30-day stroke/death rate in asymptomatic patients stating that the 5.4% event rate was "1,400%" higher than what he would expect with medical management in the same time period. Does this mean that the ACST 30-day surgical stroke/death rate of 2.8% is also unacceptable because it is approximately 700% higher than his calculation of the medical management event rate? As everyone understands, the benefit of revascularization occurs later, and in the 30-day period, medical management always looks better.

> "Vascular surgeons who have dispassionately examined the results of carotid stenting with emboli protection have learned the technique and incorporated it into their armamentarium."

Further obfuscation is present in Dr. Comerota's discussion of the degree of stenosis in SAPPHIRE in which he liberally mixes ultrasound and angiographic stenosis measurements. SAPPHIRE entry criteria were driven by ultrasound because the surgical patients did not get an angiogram, and all patients met the stringent US criteria. In his comments on restenosis, he uses the ultrasound measurements for restenosis but the angiographic core lab data for the baseline stenosis! It is now well understood that the presence of a stent alters flow velocities and new ultrasound criteria are being developed for poststenting measurements. The reintervention rate was less than 1% in the stent arm of SAPPHIRE.

Vascular surgeons who have dispassionately examined the results of carotid stenting with emboli protection have learned the technique and incorporated it into their armamentarium. It should obviously not be used in every patient with carotid disease, but it is clear from the evidence to date that many asymptomatic patients who are at increased surgical risk are well served by this less-invasive procedure. ■

1. Fields WS, Lemak NA. Joint study of extracranial carotid disease. JAMA. 1976;235:2608-2610.

*(**Dr. Comerota,** continued)*
Of course, that escalates CAS morbidity and mortality.

Eliminating events that occurred prior to operation, the true procedure-related event rate (stroke/death) of CEA in ACAS was 1.5%. Even with that admirably low procedure-related event rate, it took 5 years to show a benefit and required that 87 patients have CEA to prevent one stroke. Unfortunately, at present, CAS has a much higher procedure-related event rate and is unlikely to offer any asymptomatic patient benefit, least of all "high-risk" patients. Best medical care offers the most attractive management option.

> ". . . at present, CAS has a much higher procedure-related event rate and is unlikely to offer any asymptomatic patient benefit, least of all 'high-risk' patients."

The SAPPHIRE data set may be the most objectively reported of all CAS trials. It is interesting that in this "high-risk" patient group, fewer than 80% of those undergoing CAS had an arteriographic stenosis of 80% or more. Most physicians would agree that asymptomatic patients with less than 80% stenosis who are considered "high-risk" rightfully should be offered best medical care. Furthermore, Dr. Yadav cannot argue that medical treatment would be associated with an appreciable stroke risk because they did not have a severe carotid stenosis. In the ARCHeR trial, patients undergoing CAS for atherosclerotic disease had a 9.5% procedure-related stroke/death rate. Dialysis-dependent patients had a CAS major morbidity rate three times that of nondialysis-dependent atherosclerotic patients. These event rates cannot justify offering the procedure to asymptomatic patients.

Dr. Yadav needs to address the patient population raising the most concern in the minds of the majority of physicians, namely patients with atherosclerotic occlusive disease. Even the arteriographic figure he uses is designed to divert the reader's attention from the real issue. Postulating that asymptomatic carotid atherosclerosis is associated with a 5% annual stroke rate belies the best data available. Few physicians involved in the management of these patients have witnessed the natural history stroke rate reported by Dr. Yadav, and randomized trials demonstrated an annual stroke rate less than half that postulated by Dr. Yadav. Because this is the entire basis for his argument, and because CAS has higher morbidity in atherosclerotic patients, it appears that CAS cannot be objectively supported for this patient subset. ■

1. Chambers BR, Norris JW. Outcome in patients with asymptomatic neck bruits. N Engl J Med. 1986;315:860-865.
2. Norris JW, Zhu CZ, Bornstein NM, et al. Vascular risks of asymptomatic carotid stenosis. Stroke. 1991;22:1485-1490.