Management of Carotid Stenosis in Women

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The management of carotid stenosis in women remains a topic of controversy. In this review article, we aimed to define carotid disease burden in women, review outcomes of carotid endarterectomy and carotid artery stenting in women, discuss differences in practice patterns based on sex, and provide guidelines for management of women with carotid stenosis. Symptomatic women with high-grade stenosis derive benefit from carotid endarterectomy, although they have different risk profiles than men and are often not taking appropriate medical therapy. Women with asymptomatic carotid artery stenosis have less stroke risk reduction with CEA than their male counterparts; therefore, they should be screened for other treatable risk factors for stroke, with the institution of lifestyle changes and the appropriate medical therapy. After medical optimization, the decision to proceed with CEA in asymptomatic women must be made by carefully assessing that the benefits of stroke risk reduction outweigh perioperative risks.

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Methods

We performed a PubMed review of the published literature regarding sex-based differences in carotid disease and outcomes of CEA and CAS.

Results

Demographics of Stroke and Carotid Artery Stenosis in Women

Women have a similar lifetime risk for stroke as men (16.1% vs 14.5%) but a greater risk of disabling stroke (58% vs 48%) and stroke-related mortality (20% vs 14%). While the stroke-related mortality rate has fallen over the past 50 years in men (from 23% to 14%, P = .01), it has not changed in women (from 21% to 20%, P = .32). This is attributed to an older age at onset of stroke among women than men (81 vs 76 years).\(^3\)

The American Vascular Association National Screening Program found carotid stenosis in 9% of the overall population, but higher prevalence in men than women (8% vs 6%, P = .03).\(^4\) Among those patients with carotid stenosis, women were less likely to be taking antiplatelet medications (32% vs 58%, P < .001). This difference in antiplatelet therapy between women and men was also observed in a study of CEA patients in the Netherlands, with women being found less likely to be taking aspirin (66.9% vs 75.9%, P = .032), but there was no difference in statin use.\(^5\) In patients with coronary artery disease, women were also less likely than men to be taking statins.\(^6\)

Outcomes of CEA and CAS in Women

The North American Symptomatic Carotid Endarterectomy Trial (NASCET), Asymptomatic Carotid Atherosclerosis Study (ACAS), and European Carotid Surgery Trial (ECST) have all demonstrated that CEA reduces the risk for stroke in selected patients with symptomatic internal carotid artery stenosis (NASCET and ECST) and, to a lesser extent, in those with asymptomatic carotid disease (ACAS), with acceptably low perioperative (30-day) stroke and death risks.\(^7-9\) However, women comprised only a third of patients in these trials (between 28%-34%). Also, a subgroup analysis of NASCET, ACAS, and ECST suggested that CEA may not be as efficacious in women as it is in men. In ACAS, CEA reduced the 5-year rate of ipsilateral...
stroke or perioperative death by 66% in asymptomatic men but only 17% in asymptomatic women.

Alamowitch et al\textsuperscript{10} examined symptomatic patients using data from NASCET and the Aspirin and Carotid Endarterectomy Trial. Overall, the 30-day risk for death was higher in women than in men (2.3% vs 0.8%, \(P = .002\)), which was owing to the higher risk for fatal stroke in women (2.1% vs 1.5%, \(P = .26\)). Among symptomatic patients with more than 70% stenosis, both men and women benefited from CEA for stroke prevention. The 5-year absolute risk reduction (ARR) in stroke after CEA was similar between women (15.1%) and men (17.3%), corresponding to a 5-year number needed to treat of 7 women and 6 men to prevent one stroke. Among symptomatic patients with 50% to 69% stenosis, CEA was found to be beneficial in men but not in women. This may be because medically treated women with 50% to 69% stenosis had a lower risk for stroke than men. The 5-year risk for ipsilateral stroke in women in this group was 16.1%, if medically treated, compared with 13.1%, if surgically treated, with an ARR of 3%. Their male counterparts who were medically treated had a 5-year risk for stroke of 25.3%, which decreased to 15.3%, if surgically treated, with an ARR of 10%. This corresponds to a 5-year number needed to treat of 33 women vs only 10 men.

Rothwell et al\textsuperscript{11} pooled data from ECST and NASCET and found that the risk for stroke or death within 30 days after CEA in men was 6.8% compared with 8.7% in women. The benefit from CEA in symptomatic patients was greater in men because the ARR with CEA was 11% in men vs 2.8% in women. In addition, in a systematic review of 36 studies published from 1980-1997, Rothwell et al\textsuperscript{12} found that women had higher odds of stroke and death following CEA (odds ratio, 1.50; 95% CI, 1.14-1.97).

Since the seminal NASCET and ACAS trials, conflicting data regarding sex differences in the efficacy of CEA for carotid stenosis and perioperative complications have emerged from multiple retrospective and prospective series, as well as national- and state-level database analyses. For example, the retrospective single-institution review by Yavas et al\textsuperscript{13} demonstrated no statistically significant difference between women and men in rates of neurological complications or in-hospital mortality following CEA, which was also seen in prospective studies by Rockman et al\textsuperscript{14} and Baracchini et al\textsuperscript{15}. This lack of difference in outcome by sex is also seen in population-based studies using state-level and national-level databases.\textsuperscript{15,16}

Several studies have examined CAS and found that women have worse outcomes with CAS than CEA. Vouyouka et al\textsuperscript{17} found that women had higher rates of in-hospital mortality and stroke with CAS than CEA, regardless of symptomatic status. The risk for stroke or mortality was 1.7-fold higher in symptomatic women and 3.4-fold higher in asymptomatic women with CAS than CEA. Bisdas et al\textsuperscript{18} found that among symptomatic women, CAS was associated with higher mortality (4.19% vs 0.47%, \(P = .01\)) and combined stroke/mortality (12.09% vs 6.05%) than CEA. Asymptomatic women experienced worse outcomes than asymptomatic men, with higher stroke rates than men after CEA (1.38% vs 1.16%, \(P = .03\)) and higher myocardial infarction rates than men after both CEA (0.75% vs 0.51%, \(P < .001\)) and CAS (0.96% vs 0.28%, \(P = .01\)).

### Sex Differences in Practice Patterns

These conflicting findings can influence medical practice. Poisson et al\textsuperscript{19} examined patients with transient ischemic attack and 70% or greater carotid stenosis, half of whom were women. Women were less likely to undergo CEA than men (36.4% vs 53.8%, \(P = .004\)), independent of other factors. Among women who did undergo CEA, surgery was significantly delayed compared with men (mean, 35 days vs 18 days; \(P = .03\)), despite adjusting for patient-related covariates, clinical presentation, and degree of carotid stenosis. In a single-institution retrospective study, Amaranto et al\textsuperscript{20} examined vascular studies from 2006-2008, looking at 253 patients with carotid stenosis and found that 52.7% of men underwent CEA compared with 41% of women (\(P = .07\)). These studies suggest a difference in practice patterns for the surgical management of carotid disease may exist for women, but further studies are warranted to determine whether disparities are related to the health care system, the health care provider, or factors inherent to the patient.

### Guidelines for Management of Carotid Stenosis in Women

The updated Society for Vascular Surgery guidelines for the management of extracranial carotid disease recommend CEA as the first-line treatment for most symptomatic patients with stenosis of 50% to 99% and asymptomatic patients with stenosis of 60% to 99%.\textsuperscript{21} However, the perioperative risk for stroke and death in asymptomatic patients must be less than 3% to provide benefit. Women and individuals with small internal carotid arteries are at most risk for early neurological events and late restenosis, if standard CEA is performed. The Society for Vascular Surgery guidelines also state that beyond the acute phase of ischemic stroke, it remains unclear whether women benefit as much as men from CEA, and further studies must recruit sufficient numbers of women to address treatment of women with asymptomatic extracranial carotid artery disease.\textsuperscript{22} In addition, the American Heart Association concluded that the benefit of CEA in asymptomatic women remains controversial and stated that it remains uncertain whether asymptomatic women should undergo any revascularization procedure.\textsuperscript{23}

### Conclusions

Women with carotid stenosis have a lower stroke risk reduction benefit from CEA than men. Despite this, symptomatic women with high-grade carotid stenosis clearly benefit from CEA. Surgeons should be aware of this benefit, and current surgical practice patterns should be amended to offer timely CEA to symptomatic women with high-grade carotid stenosis.

However, the data remains mixed on how much the benefit outweighs risk for CEA in asymptomatic women compared with men, particularly in patients with moderate stenosis. Based on the available data, in the asymptomatic population, one can be more liberal with men than women in choosing to proceed with CEA. Intervention in asymptomatic women should be done with careful attention to which patients are good surgical candidates, with optimization of co-
morbidities and minimizing perioperative risk. Asymptomatic women with carotid stenosis need to be carefully selected for CEA and counseled that their risk-reduction benefit from CEA is lower than in their male counterparts. In addition, women with asymptomatic carotid artery stenosis should be screened for other treatable risk factors for stroke, with the institution of lifestyle changes and the appropriate medical therapy.

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