Risk of Stroke and Cardiac Events in Medically Treated Asymptomatic Carotid Stenosis

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Background: The risk of stroke in patients with 50% or more asymptomatic carotid stenosis (ACS) on intensive medical treatment is low. Hence, the optimal treatment of ACS remains controversial at this point of time. *Aim:* We assessed the risk of stroke/transient ischemic attack (TIA) and cardiac events in patients with 50% or more ACS on intensive medical treatment. *Methods:* All patients with TIA/minor stroke (National Institutes of Health Stroke Scale score ≤5) who had undergone vessel imaging as part of their evaluation and patients with coronary artery disease who had undergone vessel imaging before cardiac intervention were screened for the presence of asymptomatic carotid stenosis. The risk of TIA/stroke, cardiac events, and vascular deaths were evaluated. *Results:* Of 1,800 patients, 92 patients (.05%) had ACS having 50% to 99% stenosis; 63 had TIA/minor stroke, and 29 had coronary artery disease, of whom 7 patients had bilateral ACS, thus constituting 99 study units of ACS. The mean follow-up was 34.7 months (range 3-120 months). Two patients developed ischemic events on the side ipsilateral to the ACS and 9 patients developed cardiac events during the follow-up. The average annual event rate for cerebral ischemic events was .93% (95% confidence interval [CI], .11-3.37), 4.21% (95% CI, 1.92-7.98) for cardiac events, and 3.27% (95% CI, 1.31-6.74) for death. *Conclusions:* Although the risk of stroke in patients with ACS is low, acute coronary events and vascular deaths were significant. This highlights the importance of intensive risk factor modification to reduce adverse cardiovascular events in ACS rather than revascularization of the carotid stenosis. **Key Words:** Asymptomatic carotid stenosis—cardiac events—stroke—vascular death.

Introduction

In the general population, the prevalence of moderate asymptomatic carotid stenosis (ACS) varied from 0% to 7.5% and the prevalence of severe ACS from 0% to 3.1%. Prevalence estimates increased with age and were slightly higher in men.[1] Although earlier trials showed that carotid endarterectomy is better than medical treatment in patients with ACS,[2-4] the very low operative risk in these trials could not be generalized to routine clinical practice.[5] In addition, the risk of stroke in patients with ACS on intensive medical therapy is decreasing and is less than 1% per year.[6-8] Hence, what constitutes optimal therapy for ACS is still not known. There have been few published studies on the risk of stroke in patients with ACS and that too most of them are in the western population.[6-8] There is a need for studies in

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Indian population to know whether these data can be applied in the Indian context. A patient with ACS is at risk of not only stroke but also major cardiovascular events like myocardial infarction and cardiovascular death. Therefore, management of patients with ACS should be aimed at reducing the overall risk of cardiovascular events rather than carotid revascularization alone. Hence, we performed a hospital-based study to evaluate the risk of cerebral ischemic and cardiac events in patients with medically treated ACS in the Indian population.

Materials and Methods

Patients with ischemic stroke or transient ischemic attack (TIA) attending the outpatient clinic or stroke unit from March 01, 2005, to February 28, 2013, who had undergone vessel imaging as part of their evaluation and patients with coronary artery disease (CAD) who had undergone vessel imaging before cardiac intervention were considered for inclusion in the study. Our study has received the institutional ethics approval. Stroke was defined as acute onset of focal neurologic symptoms of presumed vascular origin lasting more than 24 hours. TIA was defined as a similar event of less than 24 hours.

The baseline demographic characteristics, details of the event, and risk factors were collected. Also the imaging characteristics and vessel imaging details were collected. Only patients with a National Institutes of Health Stroke Scale (NIHSS) score of 5 or less were included in the study to facilitate follow-up and for the ease of reporting new stroke symptoms by the patient. The vessel imaging of patients was done by either neck vessel Doppler, computed tomography angiography, or magnetic resonance angiography. The imaging characteristics, including old and new infarcts and silent infarcts, were recorded. Carotid stenosis was classified by the North American Symptomatic Carotid Endarterectomy trial (NASCET) method of measurement of carotid stenosis.[9] ACS was defined as a reduction in the diameter of the carotid artery of 50% or more without any previous symptoms of stroke or TIA in the respective arterial territory. Patients with carotid occlusions, with stenosis of the proximal common carotid arteries, and those with intracranial atherosclerosis were excluded from the study. In patients who had presented with posterior circulation TIA/stroke or those with CAD who had asymptomatic stenosis of 50% or more of both carotid arteries, each asymptomatic side was included in the study to represent 2 individual units of ACS. To confirm that the asymptomatic stenosis was, indeed, asymptomatic, the patients were specifically interviewed and hospital records verified to identify if any symptoms pertaining to the asymptomatic carotid artery territory were present.

All patients were on intensive medical management including antiplatelet agents, usually aspirin and/or clopidogrel and satins. Antihypertensive medications was initiated and dose modified and titrated to keep the blood pressure less than 140/90 mm Hg. Blood glucose was measured, and antidiabetic medications were initiated and modified as appropriate. Patients were also advised lifestyle modification including abstinence from smoking in relevant cases.

Follow-up details of patients included in the study were recorded by a neurologist in person, by file review or telephonically. Patients were followed up at 3 months, 1 year, and annually thereafter about new or recurrent stroke symptoms, cardiac or other vascular events, medications, drug compliance, and disability in terms of the modified Rankin Scale. Their mean blood pressure, blood glucose levels, and blood lipid levels were recorded to assess if the medical management was intensive. In case of new TIA/stroke symptoms, the characteristics of the event, NIHSS score, and modified Rankin Scale score were recorded in addition to ascertaining that the ACS is responsible for the new symptoms. Any new cardiac event or vascular death in the follow-up period was also recorded. Cardiac event included myocardial infarction or unstable angina. Vascular death was defined as sudden death or unexpected cardiac death occurring within 1 hour after onset of symptoms or within 24 hours given convincing circumstantial evidence—death from ischemic stroke, intracerebral hemorrhage, congestive cardiac failure, myocardial infarction, rupture of aortic aneurysm, or vascular death from other causes like sepsis after stent placement.

Statistical Analysis

The average annual risk of stroke/TIA in the territory of the ACS, new cardiac events, and deaths were defined as events per hundred person-years. Estimations of the annual risks and their 95% confidence intervals were done using the Openepi software, version 3.03 (www.OpenEpi.com; Dean AG et al.).

Results

Of 1,800 patients with TIA/stroke (NIHSS score ≤5) or CAD from March 01, 2005, to February 28, 2013, who underwent carotid imaging, 92 patients (.05%) had 50% or more ACS. Of the 1,800 patients screened, 1,355 had TIA or stroke with an NIHSS score of 5 or less and 455 patients had CAD. Of the 92 patients detected to have ACS, 63 patients had a history of TIA/stroke in the contralateral carotid artery or posterior circulation for which they had undergone a vessel imaging, whereas 29 of the 92 patients (31.52%) had a coronary event and had undergone carotid imaging before cardiac intervention, which had shown 50% or more ACS; 7 patients of the group with the coronary event had 50% or more ACS bilaterally. Because ACS on each side was a risk factor for a TIA/stroke in future, each ACS was considered as a separate unit for the study, hence constituting a total