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Screening for Carotid Artery Stenosis

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Introduction

Although stroke-related mortality has been on the decline since the early 20th century, nonfatal stroke remains the most important cause of permanent disability in the United States (US).[1] Within the past decade, stroke mortality has dropped from third to fourth leading cause of death in the US, but the reported age-adjusted mortality owing to cerebrovascular diseases was still 41.9 per 100,000 persons in 2010.[2] Approximately 795,000 people have a new or recurrent stroke every year; 610,000 of these are first events and 185,000 are recurrent attacks.[3] It is estimated that 87% of all strokes are due to ischemic cerebral infarction, 10% intracranial hemorrhage, and 3% subarachnoid hemorrhage.[3] Underlying causes of ischemic strokes can be grouped into 5 subtypes: (1) large artery atherosclerosis, (2) cardioembolic, (3) lacunar (small artery), (4) miscellaneous (eg, nonatherosclerotic vasculopathy, dissection, or hypercoagulable state), and (5) undetermined or cryptogenic.[3,4] The distribution of the causes of ischemic strokes in the US is approximately 16% for large artery, 16% lacunar or small artery, 29% cardioembolic, 3% miscellaneous, and 36% undetermined or cryptogenic, with variations among different races and ethnicities.[4,5]

In population-based studies, ischemic strokes due to large artery atherosclerosis are generally grouped together, including diseases of the common carotid artery, extracranial internal carotid artery (ICA), intracranial ICA and its major branches, and the vertebrobasilar system and its branches. Extracranial atherosclerotic carotid artery bifurcation disease causing moderate to severe stenosis can lead to acute cerebral ischemia owing to distal atheroembolization (Fig. 1), or less commonly, arterial thrombosis. Even though the decline in stroke incidence and mortality is real and encouraging, the overall prevalence of ischemic stroke due to extracranial carotid artery bifurcation disease will likely remain the same or rise, because of the aging of the US baby boomer population in the next decade. In this article, we review the management of carotid artery stenosis and examine the role of screening in primary and secondary stroke prevention. For the remainder of this article, we use the terms stroke and ischemic stroke interchangeably.

Cardiovascular Risk Factors and Causes of Ischemic Stroke

Older age, cigarette smoking, hypertension, and hyperlipidemia are well-established risk factors for atherosclerosis in extracranial carotid arteries and other arterial beds.[1,3,6-8] Other factors well known to be associated with increased incidence of carotid atherosclerosis and ischemic strokes include diabetes mellitus, homocysteinemia, and excessive alcohol consumption.[1,3,6-8] In the United States, the proportion of the population aged ≥65 years is projected to increase from 12.4% in 2000 to 19.6% in 2030.[9] The number of persons aged ≥65 years is expected to double from approximately 35 million in 2000 to an estimated 71 million in 2030, and the number of persons aged ≥80 years is expected to rise from 9.3 million in 2000 to 19.5 million in 2030.[9] According to the US Census Bureau, in the age category of persons aged ≥65 years alive in the US in 2010, there were more women (22,905,024) than men (17,362,960).[9] It follows that stroke prevalence is marginally higher in women than in men, and women tend to be older at the first stroke onset than men are (~75 years compared with 71 years).[3,5] However, sex predilection in the incidence of ischemic stroke due to extracranial carotid bifurcation disease remains debatable. In the Framingham study cohort of 1116 persons, aged 66-93 years, receiving carotid ultrasound examination between 1988 and 1990, the prevalence of "significant" carotid stenosis was similar in both sexes (7% in women and 9% in men).[6] In another population-based study of 454 residents of Rochester, Minnesota, who had sustained an ischemic stroke between 1985 and 1989, the age-adjusted rate of stroke due to large extracranial carotid stenosis was found nearly 4 times higher in men than in

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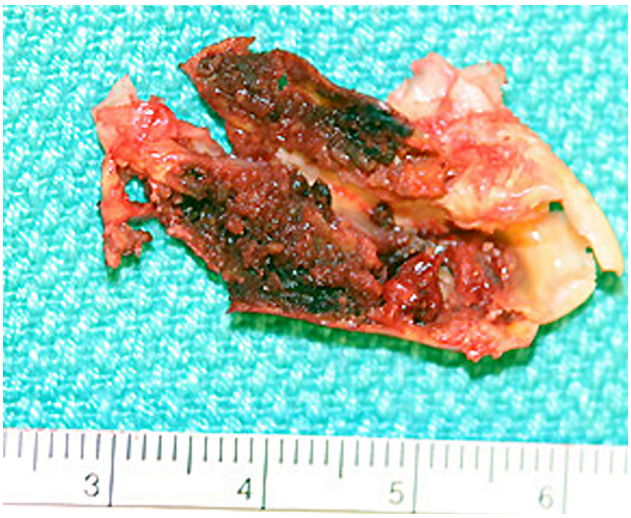

Figure 1 Atherosclerotic hemorrhagic carotid plaque removed from a patient with severe carotid artery stenosis who had an embolic ipsilateral stroke.

women.[10] Consistent with this finding, the majority of reported clinical trials and studies on carotid revascularization interventions to date have disproportionately enrolled more men than women. In addition, across studies of carotid interventions, women appear to have higher periprocedural stroke and death complications compared with men.[11] Direct explanations are lacking for the worse outcome in women compared with men after both carotid endarterectomy (CEA) and stenting, but a possible reason is the typically smaller size of the ICA in women.

The prevalence of ischemic stroke and its subtypes varies among different races and ethnicities. The Atherosclerosis Risk in Communities Study reported approximately 2-3-fold higher age-adjusted relative risk of ischemic strokes in blacks compared with whites, which can be explained in part by the higher prevalence of hypertension, diabetes, and current smoking among blacks than among whites.[4,5,12] In addition, Asians, Hispanics, and blacks are more likely to present with lacunar subtype of infarct or small vessel disease compared with whites.[4,5,12] Most recurrent strokes are thought to be related to the same mechanism as in the incident stroke. The patients with large vessel disease are more likely to experience a recurrent stroke than those with small vessel disease or cardioembolism.[4,13] In general, the patients with lacunar infarcts due to small vessel disease typically have milder impairments and better outcomes, and those who sustained ischemic stroke due to cardioembolic source generally fare the worse.[4,13] The current management of patients with carotid artery plaque disease hinges on the severity of stenosis and whether they are symptomatic (had prior ipsilateral ischemic neurologic symptoms including transient ischemic attack [TIA] or cerebral infarction with or without residual neurologic deficits) or asymptomatic (no symptoms).

Carotid Duplex Ultrasound Imaging

Carotid duplex ultrasound examination is the initial imaging modality of choice to evaluate the extracranial carotid artery bifurcation for the presence of plaque disease and stenosis. Duplex ultrasound is a noninvasive test with high sensitivity and specificity. Duplex ultrasound imaging of the carotid artery incurs no radiation risk and is inexpensive, and as such, it is the ideal test for screening and repeated surveillance. Technologic advances in ultrasound imaging have led to wide use of small portable ultrasound units, which now have a spatial resolution that rivals the larger units. Conversely, the larger ultrasound systems with high resolution have become more compact and are now easily portable. Although vascular ultrasound interrogation is straightforward, the technical details of the study and its interpretation can vary widely.[14,15] The original classification of the severity of ICA stenosis was developed by Strandness and coworkers at the University of Washington and published in 1987.[16] The determination of the severity of carotid artery stenosis by Doppler flow velocities (Fig. 2) is commonly provided in categories (or ranges) rather than as an absolute number or percentage of stenosis. In 2002, the Society of Radiologists in Ultrasound convened a multidisciplinary panel of experts in the field of vascular ultrasonography to come to a consensus, establishing Doppler ultrasound criteria for the diagnosis of carotid artery stenosis.[17] The criteria recommended by the consensus are currently the most commonly cited and clinically used to determine the severity of stenosis of the ICA.[17] To optimize and standardize the quality of vascular ultrasound testing, most institutions mandate both the certification of technologists performing vascular ultrasound and interpreting physicians and the accreditation of the department providing the testing by either the American College of Radiology or the Intersocietal Accreditation Commission (formerly known as Intersocietal Commission for the Accreditation of Vascular Laboratories). Past studies and trials have used varying ranges of carotid stenosis for the assignment of treatment, such as 60%-99% in the Asymptomatic Carotid Artery Surgery trial,[18] 70%-99% stenosis in the North American Symptomatic Carotid Endarterectomy Trial (NASCET),[19] and 80%-99% stenosis for asymptomatic patients in the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE).[20] In our institution, we have adopted modified Doppler criteria for determining the severity of ICA stenosis that can be readily applicable to the current guidelines and clinical management (Table).

Characterization of the carotid bifurcation plaque on gray-scale imaging provides useful information about its morphology and composition (Fig. 3). In general, plaque can be described as low or high in echogenicity and as homogenous or heterogenous. In a study of 293 asymptomatic patients with carotid bifurcation disease followed for an average of 46 months, the authors reported that patients with greater than 75% stenosis and morphologically soft plaque (echolucent) had the greatest risk of TIA or stroke (80%) compared with lesser risk in patients with echogenic plaque and similar severity of stenosis (10%), and no stroke occurred in patients with calcified plaque.[21] Higher incidence of intraplaque hemorrhage has been found in symptomatic than in asymptomatic patients.[22] Intraplaque hemorrhage is thought to be caused by rupture of the plaque neovasculature and has been shown to be a potent atherogenic stimulus by contributing to the deposition of free