

Carotid Disease: What the Clinician Wants

Thomas S. Hatsukami, MD

Professor of Surgery, University of Washington, Seattle, WA

Improved methods of patient selection for carotid intervention: Stroke is the second leading global cause of death and the leading preventable cause of disability. Amongst ischemic stroke survivors 65 years of age and older, 50% have some hemiparesis, 30% are unable to walk without assistance, 19% have aphasia, and 26% are institutionalized in a nursing home six months following their ischemic event. In 2011, the direct and indirect cost of stroke in the U.S. alone was \$33.6 billion and projected costs in 2050 exceed \$2.2 trillion.

As a means for ischemic stroke prevention, an estimated 100,000 carotid endarterectomy (CEA) procedures were performed in the U.S. in 2010. Carotid stenting (CAS) procedures increased from <3% of all carotid vascular procedures in 1998 to 13% in 2008. However, the role of CEA and CAS amongst patients with asymptomatic carotid atherosclerosis, and symptomatic patients with moderate, <70% stenosis is debated. Clinical trials have shown that the benefit provided by CEA and CAS in these groups is relatively small, and there are many individuals who are subjected to the risks of the procedure unnecessarily. However, to deny carotid surgery or stenting to all such patients may subject a subgroup of these individuals to the devastating consequences of stroke. In order to better select individuals for carotid intervention, improved methods for identifying the high risk carotid plaque are needed.

The current paradigm for the management of carotid atherosclerosis is guided by severity of stenosis. With carotid magnetic resonance imaging, we now have the opportunity to shift the focus from the flow channel to the diseased arterial wall itself. Given the heterogeneity of carotid plaque types, a method that can reliably characterize the carotid atheroma *in vivo* may lead to improved risk stratification for new or recurrent stroke.

Histological findings of CEA specimens suggest that plaques with a disrupted luminal surface (DLS) and intraplaque hemorrhage (IPH) characterize the high-risk carotid plaque. Recently published meta-analyses of studies utilizing carotid MRI have shown that individuals with MRI-detected carotid IPH and DLS have a significantly higher risk for future transient ischemic attack (TIA) or stroke. In order to translate this promising imaging technology to clinical practice, larger multi-center natural history studies and randomized clinical trials incorporating vessel wall imaging with MRI are needed.

Vessel wall imaging in cryptogenic stroke: Despite extensive diagnostic evaluation, the etiology of ischemic events is indeterminate in approximately 30% of stroke survivors. A number of studies utilizing vessel wall imaging with MRI have shown that angiography underestimates plaque burden, due to the geometry of the carotid bulb and compensatory expansive remodeling. As such, there may be a subset of symptomatic patients and mild-to-moderate stenosis who may benefit from carotid intervention. Prospective studies are underway to identify the prevalence of disrupted plaque amongst those with cryptogenic stroke, and whether these individuals are at greater risk for recurrent stroke. Furthermore, vessel wall imaging techniques to examine high-risk features of intracranial atherosclerosis show promise. Identifying the location of the culprit plaque responsible for the ischemic event (extra- vs. intracranial) will help guide appropriate therapy.

Guiding medical management: Further research is needed to determine which individuals are appropriate for screening with vessel wall imaging, and which patients are high-risk for progression to plaque disruption, in whom closer follow-up surveillance imaging would be appropriate. Additionally, further investigation is needed to assess whether outcomes improve when the intensity of medical therapy is guided by the response of the atherosclerotic lesion to treatment, as measured by vessel wall imaging.

In summary, better criteria to identify individuals appropriate for carotid intervention will lead to a reduction in overall health care costs by reserving surgical procedures for individuals at greatest risk for future stroke. Furthermore, a better understanding of the nature of the high-risk carotid plaque will serve as a foundation for further research into the mechanisms of initiation and progression toward development of high-risk lesions of atherosclerosis, and perhaps lead to development of novel pharmacological therapy.