Premature atherosclerosis
A major contributor to early-onset ischemic stroke

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Atherosclerosis is an age-dependent process. The prevalence of large-artery atherosclerosis in case series of ischemic stroke in young adults has been substantially less than in older adults.1–4 Historically, data on the role of atherosclerosis in early-onset stroke have been limited for a variety of reasons. First, multi-institutional studies often have inconsistent evaluations of the cerebral vasculature, particularly the intracranial circulation. Second, studies may not report evidence for proximal atherosclerosis less severe than necessary to meet criteria for etiology. Emerging data, however, show a high incidence of modifiable atherosclerosis risk factors such as dyslipidemia, hypertension, diabetes mellitus, and smoking in young adults with ischemic stroke, and worse prognosis and outcomes due to these factors and underlying large-artery atherosclerosis.5–10 A better understanding of the extent of the role of atherosclerosis in ischemic stroke risk in young adults is important for preventive therapy recommendations.

In this issue of Neurology®, a report by von Sarnowski et al.11 provides information on the prevalence of atherosclerosis determined by ultrasound studies in young adults with ischemic stroke. As part of a large European multicenter study, which aimed to determine the prevalence of Fabry disease among patients aged 18 to 55 years (mean age 46 years) with stroke or TIA, the subset with complete data from carotid ultrasound was analyzed. The results that were least susceptible to diagnostic test bias are shown in their table e-2, which includes only patients from sites that examined >90% of their patients with ultrasound. Atherosclerotic disease was greater in the population older than 45 years (table). The authors were careful to note that many of the cases of stenosis or occlusion of intracranial vessels were likely attributable to embolic disease.

The above data, combined with the results of other studies showing a high incidence of angiographic abnormalities in young stroke patients,1–4 highlight the importance of cerebral vascular imaging in early-onset ischemic stroke. Although not the focus of this study, this report supports prior findings2 that nonatherosclerotic large-artery vasculopathies, especially dissection, are at least twice as common as atherosclerotic large-artery disease in those aged 18 to 44 years. Thus, initial imaging evaluation should be designed to be sensitive to this diagnosis. For dissection, optimal imaging may be institution dependent, but could include CT angiography or MRI with gadolinium contrast, and fat-suppressed T1 axial MRI of the neck. Although these authors were careful to exclude dissection, vasculitis, and mobile thrombus, we note that the diagnosis of atherosclerosis was assumed based on ultrasound results. The prevalence of carotid artery plaque was not reported, and nonatherosclerotic arteriopathies (infectious, inflammatory, radiation, moyamoya) also cause arterial flow velocity changes on transcranial Doppler ultrasound. In the future, imaging techniques that discriminate the etiology of arterial narrowing11 may identify atherosclerosis with greater specificity and help to optimize preventive strategies.

As the authors indicate, the findings in this report are applicable only to populations of European origin; however, intracranial atherosclerosis is an important global health problem.5,13 In addition, the patients may not be completely representative of patients within the constituent populations because there could be selection bias based on referral patterns of the participating institutions, which could have either increased or decreased the prevalence of atherosclerotic findings. However, this should not detract from the main finding that there is an appreciable prevalence of detectable large-artery atherosclerosis in early-onset stroke. Atherosclerosis detectable by ultrasound in this age range represents accelerated atherosclerosis and should prompt a search for and treatment of modifiable risk factors. Even among stroke patients aged 18 to 44 years, nearly 10% had detectable extracranial carotid disease, although the proportion with symptomatic disease with stenosis ≥50% or occlusion was only approximately 3%. The prevalence of extracranial and intracranial arterial abnormalities was substantially lower in TIA compared with stroke patients, presumably because patients with nonvascular causes of transient neurologic dysfunction are also classified as TIA. This article provides a valuable service by emphasizing the role of atherosclerosis as an immediate or contributing cause of

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early-onset ischemic stroke, a role that is only likely to increase in countries affected by the epidemics of early-onset diabetes and childhood obesity\textsuperscript{14,15} and the increasing incidence of stroke in young individuals.\textsuperscript{5,6}

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**REFERENCES**

**Table**

<table>
<thead>
<tr>
<th>Vascular imaging abnormalities for ischemic strokes*</th>
<th>Younger (18–44 y), %</th>
<th>Middle aged (45–55 y), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extracranial carotid US (n = 1,095 patients)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any extracranial ICA plaque</td>
<td>9.5</td>
<td>27.6</td>
</tr>
<tr>
<td>Stenosis &gt;50% or occlusion of extracranial ICA</td>
<td>4.6</td>
<td>10.6</td>
</tr>
<tr>
<td>Symptomatic stenosis or occlusion of extracranial ICA</td>
<td>2.8</td>
<td>8.5</td>
</tr>
<tr>
<td>Supratentorial intracranial TCD (n = 904 patients)</td>
<td></td>
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</tr>
<tr>
<td>Any intracranial stenosis or occlusion</td>
<td>10.0</td>
<td>13.7</td>
</tr>
<tr>
<td>Intracranial vertebral or basilar TCD (n = 876 patients)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any intracranial stenosis or occlusion</td>
<td>3.5</td>
<td>6.2</td>
</tr>
</tbody>
</table>

Abbreviations: ICA = internal carotid artery; TCD = transcranial Doppler; US = ultrasound.
* Restricted to centers that examined >90% of their patients with US.