Low Yield of Extensive Workup for Embolic Sources in Lacunar Stroke Patients

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Objective: We aimed to evaluate the yield of extensive etiologic workup in lacunar stroke patients. *Background:* As lacunar strokes are infrequently caused by thromboembolism, the clinical relevance of extensive workup for thromboembolic sources is questioned. *Methods:* Among consecutive stroke admissions to a single center over 3 years, the 100 cases initially classified as lacunar stroke and a sample of 100 cases classified as non-lacunar ischemic strokes were studied. Review of brain imaging resulted in reclassification of 24 cases, and exclusion of 3 cases, producing a final cohort of 86 confirmed lacunar strokes and 111 confirmed non-lacunar strokes. In each of these cases, results of echocardiographic and vascular imaging studies were evaluated. *Results:* Echocardiography was performed in 93% of both the lacunar stroke cases and non-lacunar stroke cases. High-risk cardiac embolic sources were found less often in lacunar than in non-lacunar stroke cases (19% versus 34%). Findings potentially requiring anticoagulant therapy were found exclusively in the non-lacunar stroke patients. Vascular imaging studies (computed tomography angiography or magnetic resonance angiography) were also performed in similar proportions of lacunar and non-lacunar stroke cases (85% versus 84%). Cerebrovascular occlusions or high-grade stenoses were frequent (62%) in non-lacunar stroke patients but less frequent (25%) in lacunar stroke patients. In the non-lacunar stroke patients, identified vascular lesions were very frequently in a vessel anatomically related to the infarction, but in lacunar stroke patients, this occurred in only 6 cases. *Conclusions:* Echocardiography and vascular imaging studies rarely disclose findings of etiologic relevance, or of likelihood to change management, in patients with lacunar strokes. **Key Words:** Lacunar stroke—lacune—embolism—cardioembolism—large vessel occlusion.

Introduction

Etiologic diagnosis of stroke is important in guiding both acute management and long-term secondary prevention. Thus a goal of admission in acute stroke cases is to gather information providing for identification of likely mechanisms accounting for the strokes. Advances in imaging technologies have allowed for rapid and effective noninvasive evaluation of the heart and cerebral vasculature, supporting diagnosis of stroke mechanisms. The availability of such testing has sometimes resulted in a purely protocol-driven approach to stroke diagnosis and workup, without careful consideration of which diagnostic tests are essential to the management of the individual patient.

Ischemic strokes can occur in cortical or lobar areas of the brain, supplied by the major cerebral arteries and their leptomeningeal branches, or in deep areas of the hemispheres, brainstem, or cerebellum. Thromboembolic events from cardiac or proximal arterial sources

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typically cause large vessel occlusions producing larger infarctions, often in the cortical or lobar distributions. Lacunar strokes are associated with small deep subcortical and brainstem infarctions in areas supplied by the microvasculature. Lacunes have prognostic implications distinct from those of infarctions due to large artery occlusions, and are more commonly caused by intrinsic microvascular disease of the small penetrating arteries. In careful pathological studies by Fisher, lacunar infarctions were typically associated with occlusive segmental "arterial disorganization" in microvessels of 40-200 microns in diameter, with mural destruction and necrosis, microaneurysm formation, deposits of fibrinoid material and hyalinization, and thrombotic occlusion.[1] Fisher opined that the prominent lipid-staining material in areas of segmental disorganization suggested a relationship to atherosclerosis, which was commonly seen in the large cerebral arteries of these patients. Thromboembolism from a proximal source was considered a possibility in rare cases when the supplying artery to a lacune lacked any occlusive lesion on histology; however, no direct evidence of lacunar stroke due to embolus was found.

Although it is important to risk-stratify patients with lacunar stroke in secondary prevention, the clinical relevance of extensive workup for thromboembolic sources in lacunar strokes can thus be questioned. The present study aimed to examine the yield of echocardiography and vascular imaging in lacunar stroke cases, in comparison with their yield in non-lacunar ischemic stroke cases, and to evaluate their impact on inpatient stroke management.

Methods

The study cohort consisted of all admissions to a single hospital of adult patients with a principal discharge diagnosis of stroke over a 3-year period from October 2009 to September 2012. The local institutional review board approved this study. Search of the University of Chicago Medical Center clinical database using a broad set of International Classification of Diseases-9 codes for stroke (325, 342, 430-438, 443.21, 443.24, 671.5, 782.0, 784.3, 784.5, 781.8, and 781.94) yielded 1841 patient admissions. Patient records, including available brain and vascular imaging reports, were reviewed for clinically or radiographically confirmed diagnosis of stroke, and categorized as ischemic, hemorrhagic, or both ischemic and hemorrhagic strokes, or as non-acute strokes. The ischemic strokes were separated into lacunar and non-lacunar strokes. Lacunar strokes were defined as events accompanied by small deep infarctions, of maximum dimension less than 20 mm, in a brain area supplied by penetrating arteries, including deep hemispheric white matter, basal ganglia, deep brainstem, and deep cerebellum, based on magnetic resonance imaging (MRI) diffusion-weighted imaging, when available, or if not, based on computed tomography imaging and clinical assessment. Hemispheric non-lacunar infarctions were either cortical in location, or subcortical and greater than 20 mm in diameter. Brainstem infarctions extending to the ventral surface were considered non-lacunar infarctions. Initial classification of all 1841 cases was made based on review of written notes and reports, whereas final classification was based in addition on review of brain imaging studies.

To further characterize results of diagnostic workup in lacunar strokes, detailed data were collected from all cases initially identified as lacunar strokes, and from a randomly selected matching number of cases initially identified as non-lacunar ischemic strokes. Abstracted data included demographic and clinical patient characteristics (gender, clinical deficits, infarction location, infarction size, and history or presence of atrial fibrillation), results of transthoracic echocardiogram and transesophageal echocardiogram (TEE) studies, results of cerebrovascular imaging studies including computed tomography angiography (CTA), magnetic resonance imaging (MRA), carotid duplex, and admission and discharge patient medications, with stated reasons for any change in medications. Echocardiographic findings classified as findings of potential etiologic relevance included left atrial (LA) or left ventricular (LV) thrombus, moderate or severe LA enlargement, left ventricular ejection fraction (LVEF) below 35%, LV segmental wall motion abnormality, valve vegetation, moderate-to-severe valvular stenosis, and severe valvular regurgitation, or complicated aortic atheroma (>4 mm or mobile). The presence of patent foramen ovale (PFO) or atrial septal aneurysm (ASA) was also noted.

Vascular imaging results were abstracted from reports of MRA, CTA, and carotid duplex ultrasounds. Findings recorded included stenosis, occlusions, irregularities, branch occlusions, calcifications of any major cerebral vessels, or any important incidental findings. Stenoses were classified according to radiological reporting as below 50% or 50%-99%. The anatomic relationship between any affected vessel and the location of the infarction was determined.

The results are expressed as the absolute frequencies for categorical variables and as mean ± SD for continuous variables. For comparisons of categorical variables, chi-squared tests, or, if observation numbers were 5 or less, Fisher exact tests were applied. For continuous variables, independent sample *t* tests were used for analysis. Statistical analysis was performed using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA). A *P* value of <.05 was considered statistically significant.

Results

Clinical Characteristics

Over the 3-year period from September 2009 through August 2012, 1841 patients admitted to the University of Chicago Medical Center were assigned a principal diagnosis of stroke. Of these, 293 cases were confirmed