Lumpers or splitters
Evaluation and management of embolic stroke of undetermined source

For more than 25 years, neurologists and cardiologists have debated the role of transesophageal echocardiography (TEE) in the evaluation of patients with acute ischemic stroke (AIS) of unknown cause. Approximately 1 in 4 stroke patients do not have a specific cause elucidated by routine inpatient evaluations, and mounting data suggest that many of these patients have occult cardiac sources of embolism (CSE). Recently, the new classification of embolic stroke of undetermined source (ESUS) has been proposed to define the subset of patients in whom there is suspicion, but not proof of, a CSE. TEE, however, is not required for a diagnosis of ESUS. Proponents of routine use of TEE in patients with cryptogenic stroke or ESUS note its superiority to transthoracic echocardiography in detection of CSE and the higher morbidity and mortality associated with strokes of cardiac cause. In contrast, detractors point to increased cost and risk with a relatively low yield of management-changing findings.

In this issue of Neurology®, Katsanos et al. present the results of a prospective study of patients who underwent TEE as part of the evaluations of ESUS at 3 referral medical centers. In this cohort, patients meeting criteria for ESUS constituted 6% of all AIS patients; 90% of patients with ESUS underwent evaluation with TEE. There were abnormal findings in 52% of patients with ESUS. The results of the TEE affected secondary stroke prevention management in approximately 1 of every 6 patients. The authors also provide a review of the literature and meta-analysis of similar studies reporting the effect of the results of TEE on the management of patients with AIS.

The debate over TEE in stroke patients typically depends on whether a finding is deemed clinically relevant. Clearly, few would argue that diagnosis of an otherwise unsuspected valvular vegetation, chamber thrombus, or intracardiac mass would affect treatment. TEE findings that are of more debatable value include patent foramen ovale (PFO), atrial septal aneurysm, aortic arch atheroma, and “strands,” among others. Current American Heart Association/American Stroke Association guidelines for secondary prevention do not recommend closure of PFO in the absence of a venous source of embolism or antithrombotic treatment beyond platelet antiaggregants for patients with aortic arch atheroma. The recommendation against routine PFO closure is informed by 3 randomized clinical trials that failed to show benefit for their primary, prespecified endpoints.

In the current cohort, management was changed in 10 patients (16%). Three had PFO with deep venous thrombosis and required anticoagulation for deep venous thrombosis irrespective of the presence of the PFO. One had a chamber thrombus, but atrial fibrillation was discovered during the index hospitalization on routine cardiac monitoring. Three had PFO closure because of repeated cryptogenic cerebrovascular events, and 2 were started on antibiotic drugs after TEE revealed vegetations. A more conservative, but still guideline-based approach, may have resulted in a change in management for only the 2 patients with otherwise unrecognized valvular vegetations (and this assumes they had no other clinical features to suggest endocarditis and that the vegetations were missed with TTE). With this approach, the yield of TEE in changing management decreases from 16% to 3%. It is further worth noting that the prevalence of PFO in this cohort of young patients with ESUS was 28%, which is nearly identical to the prevalence in the general population as described in autopsy series.

Of note, the proposed diagnostic criteria for ESUS (which were used to identify patients who would undergo TEE in this cohort) require only 24 hours of cardiac monitoring to “exclude” atrial fibrillation. This short duration of cardiac monitoring, while clinically practical, has been called into question by the results of the EMBRACE® and CRYSTAL-AF® trials, demonstrating that atrial fibrillation can be detected with more prolonged rhythm monitoring in a subset of patients who would otherwise meet criteria for ESUS. It can be argued that, particularly for patients believed to be at high risk of occult atrial fibrillation, a more prudent approach would be to focus efforts and resources on cardiac rhythm monitoring rather than on TEE. That being said, the patients studied by Katsanos et al. were young, with mean age of 44 years, and therefore perhaps at relatively lower risk
of atrial fibrillation compared with the average ischemic stroke patient.

Clearly, TEE has a role in the evaluation of carefully selected stroke patients. Rather than relying on a standardized, one-size-fits-all approach, it remains important to carefully consider individual patient characteristics to choose the most appropriate diagnostic evaluations. Invasive or costly diagnostic testing should be reserved for situations in which both the pretest suspicion is high enough to warrant this approach and the findings, whether positive, negative, or equivocal, would result in a change of treatment.

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DISCLOSURE
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REFERENCES