Lipids in High-Risk Patients Presenting With Ischemic Stroke or Transient Ischemic Attack

Are We Missing the Target?

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See related article, p 3343.

Prospective clinical registries can serve a variety of important purposes, including providing data for quality improvement programs, monitoring real-world benefits and complications of interventions expected based on the results of clinical trials (ie, clinical effectiveness), furnishing consistent information for selected groups of patients not available from administrative databases or other sources, identifying practice gaps, contributing to assessments of provider and institutional performance, and developing hypotheses to be tested in subsequent studies. Such registries also have inherent limitations. The data may be subject to selection and other biases and, because collection requires an underlying commitment and dedication of resources to support the program, may not be generalizable to nonregistry settings. As a result of these and other issues, registry and nonregistry patients may have important differences in characteristics and outcomes. With this background, in this issue of Stroke, Saposnik et al report on an analysis of data from the high-quality, prospective American Heart Association Get-With-The-Guidelines-Stroke (GWTG) Registry finding that, of patients with an acute ischemic stroke or transient ischemic attack (TIA), only 62% with existing coronary artery disease, 52% with diabetes mellitus, and 55% with a prior cerebrovascular event had an admission low-density lipoprotein-cholesterol (LDL-C) <100 mg/dL and only 21% had an LDL-C <70 mg/dL. The authors conclude that, “This large study is unique in providing evidence that those high-risk patients with preexisting cerebrovascular disease alone or concomitant cerebrovascular disease and coronary artery disease received suboptimal therapy.” Given the proven reductions in stroke risk with lipid-lowering therapy, particularly with statins, in these and other high-risk populations, the implication is that better adherence to treatment targets would reduce the incidence of cerebrovascular events. The interpretation of the data and consequences for current practice, however, are not entirely straightforward.

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The analysis by Saposnik et al is based on data from patients admitted to GWTG-Stroke hospitals between 2003 and 2012. The 2001 National Cholesterol Education Panel III guidelines set an LDL-C target of <100 mg/dL for patients with coronary heart disease, other forms of atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm, symptomatic carotid artery disease), diabetes mellitus, or having a 10-year coronary heart disease risk >20%. A subsequent interim National Cholesterol Education Panel report reviewing the results of additional trials indicated that an LDL-C goal of <70 mg/dL was a therapeutic option for high-risk patients. For patients with stroke or TIA, in particular, an LDL-C goal of <100 mg/dL was suggested in AHA guidelines as early as 1999. The 2006 AHA secondary stroke prevention guidelines recommended an LDL-C target of <100 mg/dL for stroke patients with coronary heart disease or symptomatic atherosclerotic disease and an LDL-C goal of <70 mg/dL for high-risk persons with multiple risk factors. Therefore, over the study period, the target LDL-C for patients with established coronary heart disease, diabetes mellitus, or stroke/TIA related to atherosclerotic disease was <100 mg/dL. The goal of <70 mg/dL was generally considered a therapeutic option rather than a specific recommendation and applied only to particularly high-risk patients.

The analysis by Saposnik et al revealed that 60% of stroke patients with prior coronary artery disease, 50% with diabetes mellitus, and 48% with prior stroke/TIA were receiving lipid-lowering agents at the time of the stroke/TIA that prompted admission to a GWTG-Stroke hospital, raising concern that these medications were being underused, irrespective of their admission LDL-C. It is noteworthy that the proportion of treated patients with stroke/TIA was considerably lower than in some other reports. For example, another retrospective study found that 70% of patients with prior stroke were receiving lipid-lowering therapy. A more recent study found an even higher rate of statin use after stroke (84.6%), although few met guideline-based targets. The reason for the particularly low use of lipid-lowering therapies in patients with prior stroke/TIA in the Saposnik et al study is not clear.

There are several reasons in addition to potentially suboptimal prescription of lipid-lowering medications that could have contributed to the observed disparity in the use of these medications. The recommendations for lipid-lowering treatment for patients with coronary artery disease and diabetes mellitus are well-defined, but the proportion of patients with prior stroke/TIA who should have been treated with lipid-lowering therapy is less clear. Information reflecting the subtype and other features of the prior stroke are not available in the GWTG-Stroke registry. Depending on race-ethnicity and other factors, ≈45%
to 80% of strokes are cryptogenic, with 4% to 44% attributed to atherosclerosis. 11 Therefore, the proportion of patients with a prior stroke/TIA caused by atherosclerosis in the GWTG-Stroke registry (ie, those who should have been treated with lipid-lowering therapy) is not known.

There are a variety of factors, including costs, side-effects, and other issues, outside of the control of the provider that may contribute to the lack of persistence or adherence to prescribed medications. 12 Consistent with the 81% rate found by Saposnik et al, an analysis of data from the Adherence Evaluation After Ischemic Stroke—Longitudinal (AVAIL) registry, a GWTG-Stroke substudy, found that 75% of stroke patients were discharged on a statin. 13 AVAIL followed stroke patients over the year after the index hospitalization to assess medication use and compliance. The 1-year persistence rate for statin therapy was 76%; in 75% of cases, the statin was discontinued by a physician, presumably for appropriate medical reasons, with only a small proportion stopped by the patient. The extent to which lipid-lowering therapy was initially prescribed and then discontinued for valid medical reasons in the study by Saposnik et al is undetermined.

Although a gap between optimal and actual treatment undoubtedly exists, the most effective (and cost effective) strategies for reducing the discrepancy is uncertain. Saposnik et al suggest that because a high proportion of stroke patients are discharged from the hospital on a statin, that medication persistence could be improved through better access to post-stroke ambulatory care. GWTG-Stroke, however, has no data reflecting a patient’s posthospitalization course, and the degree to which lack of access alone leads to suboptimal therapy is not known. The previously cited retrospective study did find that stroke patients referred to an organized stroke clinic compared with those who were not referred had minimally higher rates of use of antiplatelet agents (49% versus 45%; P<0.001) and lipid lowering therapy (73% versus 68%; P<0.001). 14 The study, however, did not randomize patients to the alternative care settings and, despite propensity matching, was subject to residual confounding. A randomized trial found improvements in risk factor control in patients with a prior stroke or TIA with directed case management by either a nurse (who provided risk factor evaluation, counseling, and feedback to primary care providers) or a pharmacist (who also prescribed medications according to treatment algorithms), with relatively better control among those managed by a pharmacist. 10 Additional work is needed to better understand the reasons for the potential gaps between guideline-recommended therapies and their use in clinical practice and the most appropriate strategies for optimizing care delivery.

With the caveats discussed above, the report by Saposnik et al raises concern that at least 1 component of secondary prevention, targeted lipid-lowering therapy, may have been suboptimal in the past. It is nonetheless encouraging that they also found increasing proportions of patients were being treated with this intervention over time. Because randomized trials do not provide adequate data on titration of lipid-lowering therapy to specific goals, the most recent US national guidelines give no recommendations for or against specific LDL-C or non–HDL-C goals for the primary or secondary prevention of atherosclerotic vascular disease. 14 The new guideline-recommended treatment algorithms, however, do include monitoring for an anticipated therapeutic response and do not obviate the need for follow-up lipid testing. Whether the new approach results in higher proportions of appropriate high-risk patients receiving lipid-lowering therapy can only be addressed with ongoing monitoring to determine the degree to which the new target is being missed.

Disclosures

Member Stroke Prevention With the Aggressive Reduction in Cholesterol Levels (SPARCL) trial steering committee and Pfizer sponsored meeting speaker; Guideline Committee Member, National Lipid Association.

References


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Page 3180, second column, second paragraph, there is a word missing. It should be "...revealed that 60% of stroke patients...."

This correction has been made to the online and print version of the article, which is available at http://stroke.ahajournals.org/content/45/11/3180.
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