

EDITORIAL COMMENT

Gaps in Guideline Implementation

A Cause for Concern, Time for Action*



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Lipid-lowering therapy with statins is well established as one of most effective treatments for secondary prevention in patients with established coronary artery disease (CAD) (1). During the past several decades, numerous large, well-designed, randomized, controlled clinical trials as well as subsequent meta-analyses have clearly shown the benefits of statin therapy for reducing major acute cardiovascular events in patients with CAD (1-3). Based on the evidence, the American College of Cardiology/American Heart Association (AHA) guidelines for cholesterol and for acute coronary syndrome (ACS) recommend high-intensity statins for secondary prevention in high-risk CAD patients (4,5). Despite the guidelines' strong recommendations, we continue to see significant gaps in their implementation in clinical practice. The article by Rosenson et al. (6) in this issue of the *Journal* provides the latest documentation of persistent lags in the use of guideline-recommended high-intensity statins in Medicare beneficiaries hospitalized for acute myocardial infarction or myocardial revascularization. Their data add to earlier reports showing poor usage rates for statins and other guideline-directed medical therapy (GDMT) for secondary prevention in high-risk CAD patients (7-9).

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Rosenson et al. (6) performed a retrospective analysis using Medicare pharmacy data to evaluate prescription filling rates and high-intensity statin

use post-discharge in Medicare patients ages 65 to 74 years hospitalized for acute myocardial infarction or revascularization from 2007 to 2009. Disappointingly, only 27% of these patients had their post-discharge first fills for high-intensity statins. Even more disturbing, only 23% of those previously not on any statin and 9.4% of those on prior low/moderate-dose statins had their first high-intensity statin prescription filled post-discharge, compared to 81% of those previously on high-intensity statins. The data presented in their Online Table 1 also show that those >75 years had even lower fill rates for high-intensity statins as well as any statin drugs.

Although their data are inherently limited due to the retrospective study design as well as a lack of information regarding in-hospital medications and those actually prescribed at discharge, the available data are quite concerning regarding the significant gap in the guideline-recommended use of high-intensity statins in these high-risk patients. It is unlikely that most patients after significant cardiac events would have ignored their physician's advice if they were indeed given a prescription for high-intensity statins, so why did most patients end up on lower-dose therapy?

Several possibilities exist. First, treating physicians might simply be unaware of the guideline recommendations, although that appears unlikely. Even if aware, the clinicians may not believe in the recommendations due to widely publicized and still ongoing controversy regarding the 2013 cholesterol guidelines (although most of the controversy relates to primary prevention and removal of low-density lipoprotein cholesterol [LDL-C] targets, with very little, if any, argument regarding high-intensity statin use for secondary prevention). Although the guidelines recommend high-intensity statins in these patients regardless of LDL-C levels, maybe some clinicians did not prescribe higher-intensity statins if the patient's LDL-C level was already low. This could

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not be evaluated in this study due to lack of available information regarding patient lipid levels.

Concern about new-onset diabetes as well as various side effects, especially with high-intensity statins, also might have dissuaded some clinicians from prescribing higher-dose therapy. Although not guideline recommended, it is conceivable that treating physicians wanted to evaluate patient response and tolerance to lower-dose therapy before proceeding to high-intensity statin therapy. Finally, physician inertia and/or lack of adequate discharge planning could explain the observed gaps in GDMT.

COMPARISON WITH PREVIOUS STUDIES

The findings reported by Rosenson et al. (6) echo the results of previous reports documenting similar disappointing findings (7-9). In a large cohort of patients (N = 65,396) admitted with ACS at hospitals participating in the AHA's Get With The Guidelines program, we previously showed that most eligible patients were not discharged on intensive (defined as therapy likely to achieve >50% reduction in LDL-C) lipid-lowering therapy (I-LLT) (7). We assessed I-LLT use at time of discharge in patients admitted with ACS from 2005 to 2009, along with patient and hospital characteristics associated with the use of I-LLT. In contrast to the findings reported by Rosenson et al., the multivariate analyses in our study revealed that prior use of any dose of lipid-lowering therapy was associated with greater use of I-LLT at discharge (6,7). Because of the large cohort and the data's serial nature we were able to evaluate temporal trends and found that after the updated recommendations of the 2004 National Cholesterol Education Program Adult Treatment Panel III, initial use of I-LLT increased from 35.5% to 41.6% (2005 to 2007). Subsequently, we observed an insignificant decrease in I-LLT use with a decline to 35.7% by December 2009 (7), which appeared largely due to a decrease in the use of ezetimibe/simvastatin combination therapy. When we excluded the use of this combination therapy from our analyses, the use of I-LLT decreased to less than one-third (7).

Several other recent reports also have documented significant gaps in GDMT implementation (8,9). An observational study of stable CAD patients in the National Cardiovascular Data Registry compared the rates of guideline-recommended optimal medical therapy (OMT) before percutaneous coronary intervention (PCI) and at discharge in patients undergoing PCI between 2005 and 2009 to evaluate the impact of the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) study,

which provided OMT to all patients and showed no incremental advantage for PCI on outcomes. Comparing the data before and after publication of COURAGE revealed little change in OMT use (8). Overall, nearly one-third of the patients were still not receiving OMT at discharge after PCI (8). These findings are further substantiated in a report by Farkouh et al. assessing 3 large RCTs that evaluated the role of revascularization in patients with stable CAD (9). The trials included COURAGE, BARI-2D (the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial), and FREEDOM (Future Revascularization Evaluation in patients with Diabetes mellitus: Optimal management of Multivessel disease), all of which recommended OMT for all randomized patients. The pooled data for the 5,034 patients participating in these trials revealed that in the highest-risk patients with diabetes and CAD, GDMT and protocol-driven treatment targets for all 4 of the risk factors (LDL-C, systolic blood pressure, smoking cessation, and hemoglobin A1c) were achieved by only 18% of patients in COURAGE, 23% in BARI-2D, and 8% in FREEDOM. Although the percentage of patients achieving LDL-C targets at 1 year improved significantly, a considerable gap still existed in adequate control of LDL-C and all 4 risk factors combined. These data are quite concerning as they reflect real life scenario at most well-established medical centers (9).

WHY IS THERE SUCH A GAP IN IMPLEMENTATION OF GDMT?

The continued lag in implementing GDMT remains worrisome, especially in light of the plethora of recent data clearly showing OMT benefit in CAD patients. In addition to the physician- and system-related issues noted in the preceding text, on the patient side, this lag could reflect real or perceived medication cost issues, polypharmacy (especially in the elderly), noncompliance, and nonadherence. Other important but oft-ignored factors include patients' lack of understanding about the long-term benefits of specific drugs and little, if any, disease-specific education emphasizing the risk of future events and how the drugs prescribed help prevent or decrease event risk. The recommendations of the guidelines in terms of using a cardiac team approach should help alleviate many of these issues (4).

CLINICAL IMPLICATIONS AND FUTURE DIRECTION

The continued lag in GDMT implementation deprives patients of evidence-based therapy and exposes them

to future risk of major acute cardiovascular events that could be significantly reduced with proper secondary prevention. Also, continued use of expensive interventions rather than evidence-based OMT may lead to loss of trust in the physicians involved. Thus, actions must be taken to improve GDMT implementation in clinical practice. Future CAD performance measures should include documentation of evidence for guideline-based therapy use by

clinicians tied to pay for performance. Such a strategy has worked for heart failure and it is time now to apply it to patients with CAD.

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