Back to the Future

Improving the Use of Guidelines-Recommended Coronary Disease Secondary Prevention at the Dawn of the Precision Medicine Era

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This is an interesting and exciting time in medicine. The confluence of high-throughput molecular assay platforms, sophisticated informatics capabilities, and cloud computing has us poised for the advent of an era of medical therapy in which it will be possible to define more precisely which patients are most likely to benefit from treatment with a given drug or have the best benefit-to-risk profile and then tailor therapy accordingly. Yet, even as we revel in the promise and future possibilities of precision medicine in cardiovascular disease, it is important not to lose our focus on what we can and should do for our patients with coronary artery disease today. Although it is true that the current process of developing and testing new therapies and the resultant treatment recommendations has followed a "one-size-fits-all" approach, we have learned much about adherence to evidence-based medicine and performance improvement and their relationships to improved clinical outcomes at the population level.

A handful of medications demonstrated to improve outcomes in randomized, controlled trials and given Class I indications in multiple treatment guidelines have been collectively referred to as optimal medical therapy when used concurrently. The power of optimal medical therapy was clearly demonstrated in 2 large, randomized, clinical trials that showed that, as a strategy, there was no difference in mortality or major adverse cardiac events after 5 years of follow-up among patients with documented coronary artery disease treated with optimal medical therapy versus optimal medical therapy plus revascularization with percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG). Furthermore, from these trials, we learned that, with the concerted efforts of patients and physicians, rates of use of each of aspirin, β-blocker, statin, and angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (ACEI/ARB) from 85% to 95% could be achieved in secondary prevention. However, reports from population registries consistently demonstrate a wide variability in rates of use and much lower overall rates of use of optimal medical therapy in practice: in hospital, at hospital discharge, and during longitudinal follow-up. These same reports have also solidified the relationship between adherence to optimal medical therapy in hospital and during secondary prevention and outcomes, with as much as 10% lower mortality for each 10% increase in composite adherence to guidelines-recommended therapies in hospital and a 33% reduction in mortality overall with consistent use of optimal medical therapy in secondary prevention.

In this light, the study by Iqbal and colleagues in this issue of Circulation should give us all a sense of discomfort and encourage us to redouble our efforts to ensure that we are using optimal medical therapy as we know it today, even as we work to understand how to tailor cardiovascular therapy in the future. With the use of a strict definition of optimal medical therapy (use of at least 1 drug from each of antiplatelet therapy, β-blocker, statin, and ACEI/ARB classes concurrently), in their study of >1700 patients randomized in the Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) trial of PCI versus CABG among patients with complex coronary artery disease, just over 41% of all post-CABG and post-PCI patients were discharged on optimal medical therapy, and only about one third of all patients received optimal medical therapy at 5 years. Importantly, consistent with prior studies, the use of optimal medical therapy at discharge was associated with significantly lower 5-year mortality. The rates of use in the SYNTAX cohort were much lower than demonstrated among 156 145 outpatients treated at clinical practices participating in the National Cardiovascular Data Registry Practice Innovation and Clinical Excellence (NCDR PINNACLE) registry, in which optimal medical therapy was prescribed as appropriate for eligible patients in 66.5% of visits. Some of the difference between the SYNTAX study observations and NCDR PINNACLE registry results may be explained by the inability to account for contraindications to treatment in the SYNTAX cohort, which is supported by the much lower rates use of ACEI/ARB and β-blocker, for which absolute and relative contraindications are more frequent, than the rates of use of antiplatelet therapy and statins. However, this is unlikely to be the sole explanation.

Rates of use of optimal medical therapy at discharge among SYNTAX patients were significantly lower among post-CABG patients (31.2%) compared with post-PCI patients (50.2%) but were similar at 5 years. The early differences in rates of use of optimal medical therapy among CABG patients compared with PCI patients are interesting. In 1 study, only 74% of patients filled all of their evidence-based cardiac medications within 120 days of discharge, influenced by factors such as age, income, and discharge counseling.
and there is some evidence that post-CABG patients are less likely to fill a prescription for a statin or an ACEI/ARB than post-PCI patients. Furthermore, medication possession ratios for statins, ACEI/ARBs, and β-blockers were lower among post-CABG patients. These observations may reflect both prescribing practices and patient adherence and may be driven by a number of factors, including absolute and relative contraindications or side effects. Regardless, in both the SYNTAX and NCDR Pinnacle cohorts, rates of use of all agents were much lower than the high benchmarks for treatment set in the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) and Bypass Angioplasty Revascularization Investigation-2 Diabetes (BARI-2D) trials, in which there was a focus on use of optimal medical therapy. This suggests that, with attention by providers and patients, better performance is possible, a contention that is supported by results of performance improvement programs such as the Acute Coronary Treatment and Intervention Outcomes Network Registry–Get With The Guidelines. Iqbal and colleagues noted several differences among patients discharged on optimal medical therapy and those who were not, which could inform where to focus efforts to understand gaps in treatment and to improve use of secondary prevention medications. Patients with peripheral vascular disease, higher EuroSCORE and SYNTAX scores, and chronic obstructive pulmonary disease were less likely to be discharged on optimal medical therapy. The EuroSCORE weights as a part of its score age, poor mobility, renal insufficiency, and chronic lung disease. Many of these characteristics have been associated with treatment gaps in other studies. For example, even after myocardial infarction, patients with chronic obstructive pulmonary disease or asthma are significantly less likely to be prescribed β-blockers, although 1-year survival benefit has been demonstrated in myocardial infarction patients with chronic obstructive pulmonary disease or asthma except those who concurrently take β-agonists or who have severe chronic obstructive pulmonary disease or asthma. The work of Iqbal and colleagues adds additional information to a large body of literature on deficits in the use of secondary prevention and, in particular, should heighten our awareness that patients who have undergone revascularization are vulnerable to undertreatment with evidence-based medication. This work also reminds us that even though blood flow is restored, these patients have substantial atherosclerotic burden and remain at risk for future ischemic events. There is substantial evidence that use of optimal medical therapy is an important component in mitigating this risk and that performance improvement programs work to increase use. Thus, even as we pursue the dream of “precision cardiovascular medicine,” remaining focused on applying available evidence and proven approaches to lessen the burden of cardiovascular disease morbidity and mortality at the population level is our present and our immediate future.

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