Turning guidelines into outcomes

Compliance with guideline-based treatment of acute coronary syndromes improves long-term patient outcomes, including survival (1). The most recent American College of Cardiology/American Heart Association (ACC/AHA) guidelines for non–ST-elevation acute coronary syndromes were published in 2014 (2), with additional recommendations published in 2015 (3) and 2016 (4). These guidelines are comprehensive, comprising 150 pages and 363 referenced citations. Changes to the ACC/AHA guidelines are not uncommon, and as many as 20% of all class I recommendations are downgraded or omitted in subsequent versions. Downgrades, reversals, and omissions are most common among recommendations not supported by multiple randomized clinical trials (RCTs) (5).

In this issue of Baylor University Medical Center Proceedings, Gill and colleagues report on their center’s compliance with recommended medical therapy following acute coronary syndromes/acute myocardial infarction (6). They assessed whether, at discharge, patients received the five drug classes recommended by current ACC/AHA guidelines: 1) aspirin, 2) thienopyridine inhibitors, 3) beta-blockers, 4) angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and 5) high-intensity HMG-CoA reductase inhibitors. All drug classes carry class I indications, meaning that they are recommended and should be administered. The level of evidence for aspirin, thienopyridine inhibitors, and high statin therapy is strong, with level of evidence A, meaning that there is evidence from multiple RCTs that use improves patient outcomes. Gill and colleagues found that >90% of patients left the hospital with prescriptions for aspirin, thienopyridine inhibitors, beta-blockers, and statins.

Of interest, only 69% of patients were prescribed high-intensity statins. This is disappointing given that high-intensity therapy is safe and is associated with better patient outcomes than low- or moderate-intensity therapy (2). Both physicians and patients appear to remain cautious and may worry about perceived side effects, especially myalgias. My hope is that future guidelines will refocus on reduction of low-density lipoprotein (LDL). The use of additional agents such as ezetimibe and PCSK-9 inhibitors to achieve the lowest possible serum LDL offers an opportunity to improve patient outcomes beyond what can be achieved with statin therapy alone.

Gill and colleagues report lower compliance for ACEIs/ARBs at 67%. However, there is debate as to whether or not routine ACEI/ARB use improves patient outcomes. There is good evidence (level A) that use in patients with heart failure or reduced ejection fractions (<0.40) improves outcomes but little evidence of benefit in patients with preserved ejection fractions (level C). If these agents had no side effects, this might be a purely academic point, but their use exposes patients to side effects including hypotension, hyperkalemia, and rare cases of angioedema.

The good news is that while there is some room for improvement, the majority of patients evaluated by Gill et al are being discharged on the agents they investigated. The relatively lower rate of ACEI/ARB prescribing may be appropriate based on current guidelines, and that rate combined with use of low- and moderate-, as opposed to high-intensity, statin therapy is largely responsible for reducing the compliance rate for all five agents to 50%, making overall compliance appear worse than it is. Of interest, the investigators chose to omit analysis of other agents with class I recommendations. There is proven benefit for aldosterone antagonists in select patients with reduced ejection fraction but preserved renal function and normal serum potassium following myocardial infarction. Use carries a class I indication in current guidelines and comes with strong evidence that therapy improves outcomes (level A).

It may surprise some that a prescription for sublingual or nitroglycerine spray also has a class I recommendation, though this is based on weak evidence (level C). Class I recommendations also exist for prescribing nondihydropyridine calcium antagonists for patients with ischemic symptoms, either in addition to or in place of beta-blockers. Again, there is little evidence for improved patient outcomes (level C). There is even a guideline-directed class I indication to use proton pump inhibitors in patients with a history of gastrointestinal bleeding who require triple antithrombotic therapy (level C). This recommendation may be revisited in future guidelines given growing evidence that long-term proton pump inhibitor use can negatively impact patient outcomes (7).

Left out of the study by Gill and colleagues is an analysis of agents thought to either offer no benefit or cause harm (class III recommendations). These include vitamins E, C, B6, and B12, beta-carotene, and folic acid. High-quality data from RCTs has shown no benefit (level A). Of greater concern, it appears that both hormone therapy and nonsteroidal antiinflammatory drugs can worsen outcomes. It is a class III recommendation that hormone therapy should not be initiated and chronic use stopped if feasible (level A). Nonsteroidal antiinflammatory drugs also appear to cause harm, though the supporting evidence is less strong (level B).

Current ACC/AHA guidelines seek to be both thorough and comprehensive. This is an admirable goal but one that may undermine their purpose, which is to improve patient outcomes. How many physicians will read a 150-page guideline? One option would be for future guidelines to only include...
recommendations based on high-quality data (level A). Such guidelines could further limit themselves to making recommendations either for or against (currently class I and III). Class II recommendations might be dispensed with altogether. The resulting guidelines might fit on a single page and be easily referenced. Perhaps we could trust physicians to navigate treatments and therapies of unclear benefit? After all, physicians have done this for years through shared decision-making with their patients. And shared decision-making between physicians and patients is a class I recommendation.

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