Does Ivabradine SIGNIFY Improvements in Quality of Life?

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In his 2015 commencement address to the Columbia College of Physicians and Surgeons, Dr Harlan Krumholz collectively challenged healthcare professionals to “join him in putting the conception of a patient to rest and ushering in a notion of people who we can engage, empower, and strengthen as partners. We are not there to impose our values, we are there to help them pursue a course that is consistent with their wishes”.1 As such, health-related quality of life (QOL) measurement (HRQOL) has become a key tool to help invoke these expectations. Fortunately, this has been made somewhat easier with development of the Seattle Angina Questionnaire (SAQ).2 Developed by Dr John Spertus, the SAQ has been translated into over 80 languages and has become the gold standard for quantifying patient-reported health status and HRQOL in patients with stable coronary artery disease (CAD). The SAQ has become the HRQOL measurement tool used in randomized controlled trials to collect patient-reported health status among tested revascularization and pharmacological strategies. Developed in 1994, the SAQ is a 19-item multi-dimensional, self-administered questionnaire that evaluates 5 dimensions of HRQOL, including physical limitations related to angina symptoms (chest pain, chest tightness, and shortness of breath), angina stability, angina frequency, treatment satisfaction, and QOL.3 Its reliability, validity, and responsiveness have been well established for patients with CAD, including its superiority when compared with previously established patient-reported measures of angina.3

For patients with stable CAD (defined as those with established pattern of angina, a history of myocardial infarction, or angiographically documented coronary plaque burden), the symptoms and functional limitations of angina can significantly impair QOL long term. However, clinical trials evaluating treatments and new therapies for patients with stable angina have traditionally focused on morbidity or mortality related to angina-related QOL in patients participating in the SIGNIFY Quality of Life substudy.5 The results of the SIGNIFY trial, which included 19102 patients with CAD, were neutral with less implication for evidence-based practice. This notion has been highlighted by the COURAGE HRQOL substudy found that PCI demonstrated consistent improvements in important self-reported outcomes related to anginal frequency and overall QOL.5

Several key features of this study deserve further consideration. First, the SIGNIFY HRQOL substudy used a prespecified subgroup of patients with at least Canadian Cardiovascular Class II angina at baseline (ie, having angina symptoms) from the SIGNIFY randomized, double-blind, placebo controlled trial. As such, it was recognized that the presence of angina would have substantial impact on QOL and may accentuate the effects of a tested anti-anginal agent. Second, QOL was assessed using the validated CAD disease-specific SAQ performed at serial time points (at baseline, 6, and 12 months) to record patient-reported QOL and health status. Of note, it is impressive that 12-month QOL measurements were reported for 79% of the Ivabradine group and 80% of the placebo group, which provides a rich source of data.

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Third, the patients completed the SAQ before any other investigations in the main trial—hence, avoids any potential bias. Fourth, the frequency of clinically significant differences in the SAQ dimensional scores between the placebo and treatment groups were reported.

Tendera et al found that anti-anginal treatment with ivabradine significantly improved symptoms of anginal stability/frequency, treatment satisfaction, and overall QOL in patients with angina. These results are even more remarkable because patients in the SIGNIFY population were receiving appropriate levels of evidence-based anti-anginal therapy (87% β-blockers, 54% organic nitrates, 24% dihydropyridine calcium channel blockers) and had no indication for revascularization at study entry. However, ivabradine provides a novel pathway for further reducing the heart rate (inhibits the If current in the sinoatrial node), resulting in decreased demand of the myocardium and enhanced diastolic coronary blood flow. In combination with other antischismic agents, the self-reporting SAQ dimensional scores have identified an additional therapy that improves the HRQOL of patients with stable angina. One may wonder about the incremental benefits that may be accrued in patients without medical optimization (ie, no β-blocker). The results of this study suggest that routine self-reported health status measurement would clearly improve our ability to provide patients with optimal therapy given their own preferences.

It is time that patient-reported outcomes (particularly those measured in randomized controlled trials) receive the prominence and recognition they deserve. And while Tendera et al conducted a subgroup analysis, the significance of these results are no less important. In their editorial in Circulation: Cardiovascular Quality and Outcomes, Sepehrvand and Ezekowitz emphasize the importance of measuring and integrating HRQOL into daily practice, given the emerging importance of QOL over longevity. Better familiarity with HRQOL measurement tools in clinical practice will also add toward greater understanding and appreciation of health status outcomes as those presented by Tendera et al. There is an impressive body of evidence demonstrating that patient involvement leads to increased knowledge about treatment options, more realistic expectations regarding disease course and treatment, improved adherence to therapy, and enhanced patient satisfaction. It is now time to empower clinician’s knowledge of treatment options that have been reported by patients to improve symptoms, angina stability treatment satisfaction, and overall QOL in patients with chronic stable angina. Life or death can become somewhat irrelevant with chronic disease—it is the quality that may matter the most.

Disclosures

None.

References


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