JACC: Heart Failure
© 2014 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 2, No. 2, 2014
ISSN 2213-1779/$36.00
http://dx.doi.org/10.1016/j.jchf.2013.12.003

Impact of Cardiovascular Events on Change in Quality of Life and Utilities in Patients After Myocardial Infarction

A VALIANT Study (Valsartan In Acute Myocardial Infarction)

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Objectives The objective of this study was to determine the impact of nonfatal cardiovascular (CV) events on changes in health-related quality of life (HRQL).

Background There is limited understanding of the impact of nonfatal CV events on long-term changes in HRQL in survivors of myocardial infarction (MI).

Methods The VALIANT (Valsartan In Acute Myocardial Infarction) trial enrolled 14,703 patients post-MI complicated by Killip class II or higher (scale measuring heart failure severity post-MI ranging from class I to IV) and/or reduced ejection fraction. The HRQL substudy included 2,556 (17.4%) patients who completed the EQ-5D with 5 questions, with responses mapped to utility weight on a scale of 0 to 1 and a visual analog scale (VAS) ranging from 0 (worst) to 100 (best) imaginable health state. EQ-5D was administered at baseline and 6, 12, 20, and 24 months. The trajectory of EQ-5D scores was developed by using linear mixed effects regression models with calculation of deviation from this trajectory after nonfatal CV events. Patients who died before the next EQ-5D assessment were excluded.

Results Over a 2-year period, 597 patients experienced a nonfatal CV event and survived to have another EQ-5D assessment. Their baseline EQ-5D scores were lower than patients without a subsequent nonfatal CV event (VAS 61.0 $\pm$ 19 vs 68.2 $\pm$ 18 [$p < 0.001$] and US-based utility score 0.76 $\pm$ 0.22 vs 0.83 $\pm$ 0.17 [$p < 0.001$]). These patients with CV events experienced a trajectory-adjusted 6.6 point decrease ($p < 0.001$) in VAS scores and a 0.07 decrease ($p < 0.001$) in utility score after the nonfatal CV event.

Conclusions MI survivors suffering a CV event experienced significantly worse HRQL than their previous trajectory, suggesting that generic instruments can be responsive to nonfatal events. Reduction in nonfatal CV events may affect longitudinal changes in HRQL. (J Am Coll Cardiol HF 2014;2:159–65) © 2014 by the American College of Cardiology Foundation

Advances in therapies for acute myocardial infarction (MI) have increased the numbers of survivors living with chronic coronary artery disease (CAD) and impaired left ventricular function (1). These patients are at heightened risk for subsequent nonfatal and fatal events (2–4). From a medical perspective, providers are often focused on secondary preventive efforts and attenuation of the risk of consequences of the infarct such as heart failure, recurrent MI, and sudden

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Manuscript received February 19, 2013; revised manuscript received October 8, 2013, accepted December 3, 2013.

JACC: Heart Failure Vol. 2, No. 2, 2014
April 2014:159–65

Abbreviations and Acronyms

CAD = coronary artery disease

CI = confidence Interval

CV = cardiovascular

HRQL = health-related quality of life

LVEF = left ventricular ejection fraction

MI = myocardial infarction

VAS = visual analog scale

death. Although these efforts are of utmost importance, health-related quality of life (HRQL) has emerged as an additional target of therapy and outcome measure for large clinical trials in post-MI patients (5). Given the expanding therapies for patients with CAD, often without clear survival benefit, understanding patient-reported outcomes in this population is becoming even more important.

Health status and HRQL are independent predictors of adverse events in a variety of study groups, including those with CAD (6) and heart failure (7). Characterization of HRQL commonly has focused on the clinical and psychosocial determinants of these perceptions immediately after the MI (8–10). Patients with a history of CAD have significantly impaired HRQL compared with the general U.S. population (11). However, there are gaps in our understanding of the long-term change in HRQL, especially beyond the first few months. Researchers have identified several baseline predictors of worsening HRQL post-MI, including persistence and severity of angina (10), depression, inadequate social support, adverse effects of therapies, and anxiety about the uncertainty of their prognosis (8,12). Much of the variance in HRQL response is unexplained by baseline clinical factors (13). One potential explanation of decreased HRQL could be the occurrence of recurrent MI, heart failure, and stroke. However, little is known about the quantitative impact of subsequent nonfatal cardiovascular (CV) events on changes in HRQL. Identification of the impact of these nonfatal CV events on change in HRQL will provide a potential explanation for some of the unexplained variance in HRQL responses in clinical practice and clinical trials, and possibly aid researchers in the design of future trials assessing patient-reported outcomes. Thus, the aim of the present study was to determine the impact of nonfatal CV events on change in the trajectory of visual analog scale (VAS) and utility scores in a cohort of patients who had experienced an acute MI.

Methods

The details of the enrollment and exclusion criteria, follow-up, and results of the VALIANT (Valsartan In Acute Myocardial Infarction) trial have been reported elsewhere (14,15). Briefly, the study included 14,703 patients age ≥18 years of age with an acute MI occurring between 12 hours and 10 days before randomization with clinical evidence of acute heart failure, radiological evidence of heart failure, or left ventricular ejection fraction (LVEF) ≤35% as assessed by echocardiogram or left ventriculogram or LVEF <40% as assessed by radionuclide scan. The patients were randomly assigned to receive captopril (up to 50 mg 3 times daily), valsartan (up to 160 mg twice daily), or the combination of these 2 drugs (up to captopril 50 mg 3 times daily and valsartan 80 mg twice daily).

Health status measurement. Of the 24 countries participating in VALIANT, patients from sites in 10 countries (Argentina, Australia, Canada, Denmark, France, Germany, Italy, Sweden, the United Kingdom, and the United States) were eligible to participate in the HRQL substudy. Health status was measured by using the EQ-5D, a self-administered instrument comprising 2 components: a descriptive profile and a single-index VAS (16). The instrument has excellent psychometric properties in patients with a previous MI (17). The descriptive profile assesses health status on 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Respondents were asked to indicate whether they have: 1) no problems; 2) some/moderate problems; or 3) extreme problems with each of the 5 dimensions. Their responses were then mapped to previously derived utility weights for each of the 243 possible combinations (18). These utility weights are intended to represent society's ratings of the desirability of a given health state. Utility weights have been derived from populations in numerous countries, including the United Kingdom and the United States (19,20). The VAS records the patient's personal perspective of their current health status on a vertical rating scale with scores ranging from 0 to 100, with 0 representing the worst imaginable health status and 100 representing the best imaginable health state (18). The VAS has been considered a representation of patients' overall HRQL.

The EQ-5D was administered at baseline, which was either at the time of discharge from the hospital after the acute MI or at 15 days' post-randomization, whichever came first. It was then repeated at 6, 12, 20, and 24 months for the first 2 years of follow-up and annually thereafter throughout the trial follow-up period.

CV events. The trial case report form documented the following CV events: 1) hospitalization for heart failure, defined as the unplanned treatment of new or worsening heart failure requiring the use of intravenous diuretic agents, inotropes, or vasodilators during any hospital admission or overnight stay in a health care facility; 2) recurrent MI, defined as an increase in cardiac enzyme levels and either typical clinical presentation or typical electrocardiograph changes (evolving ST-segment or T-wave changes, new left bundle branch block, or new Q/QS waves in contiguous leads); 3) stroke, defined as a focal neurological deficit lasting >24 hours; and 4) sudden death/cardiac arrest, defined as the occurrence of sudden death or cardiac arrest with or without premonitory heart failure or MI. In addition, each event was adjudicated by a central clinical endpoints committee to ensure consistent adjudication of the first nonfatal CV event. The primary analysis focused all unadjudicated nonfatal CV events as reported by the site investigator. A secondary analysis focused on only the nonfatal CV events that were adjudicated by the clinical endpoints committee.