Atherosclerosis 266 (2017) 16–23

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

High-sensitivity C-reactive protein levels and health status outcomes after myocardial infarction

Yashashwi Pokharel [a, b, *], Puza P. Sharma [c], Mohammed Qintar [a, b], Yuan Lu [d], Yuanyuan Tang [a], Philip Jones [a, b], Rachel P. Dreyer [d], John A. Spertus [a, b]

[a] Saint Luke's Mid America Heart Institute, MO, USA
[b] University of Missouri-Kansas City, Kansas City, MO, USA
[c] Novartis Corporation, East Hanover, NJ, USA
[d] Yale University, New Haven, CT, USA

ARTICLE INFO

Article history:
Received 16 June 2017
Received in revised form
13 September 2017
Accepted 14 September 2017
Available online 18 September 2017

Keywords:
High-sensitivity C-Reactive protein
Health status
Myocardial infarction

ABSTRACT

Background and aims: While high-sensitivity C-reactive protein (hs-CRP) is a marker of inflammation and higher cardiovascular risk, its association with health status (symptoms, function and quality of life) after acute myocardial infarction (AMI) is unknown.

Methods: Among 3410 patients with AMI from the TRIUMPH (N = 1301) and VIRGO (N = 2109) studies, we compared 1-year generic (Medical Outcome Study Short Form-12 and Euro Quality of Life Visual Analog Scale) and disease-specific (Seattle Angina Questionnaire) health status outcomes in those with hs-CRP ≥2 mg/L *vs.* <2 mg/L. In hierarchical linear regression models, we examined the association of 30-day hs-CRP levels with 1-year health status without adjustment, after adjusting for 30-day health status, and after adjusting for demographic, socioeconomic, disease severity/comorbidities and treatment characteristics.

Results: The median (25th, 75th percentiles) 30-day hs-CRP was 2.6 (1.1, 6.1) mg/L and 59% had hs-CRP ≥2 mg/L. Statin therapy was used in 92% of patients at hospital discharge. Thirty-day hs-CRP ≥2 mg/L was inversely associated with all 1-year health status measures in unadjusted and partially adjusted models, but not in fully-adjusted models. Results were similar when hs-CRP was analyzed as a continuous variable.

Conclusions: While elevated hs-CRP 30 days after AMI was associated with worse health status in unadjusted analyses, this was not significant after adjusting for comorbidities, suggesting that hs-CRP may be a marker of comorbidities associated with worse health status. Whether reducing inflammation in AMI patients will improve health status should be tested in ongoing trials.

1. Introduction

Vascular inflammation is a key mechanism in the progression of atherosclerosis and acute coronary syndromes [1]. A common method of assessing vascular inflammation in clinical practice is to measure high-sensitivity C-reactive protein (hs-CRP) levels [2]. Patients with elevated hs-CRP levels (≥2.0 mg/L) 30 days after acute myocardial infarction (AMI) have increased risk for recurrent coronary events and death than those with lower hs-CRP levels [3,4]. Statin therapy is known to lower hs-CRP levels [3–6], and among patients with a history of AMI treated with statin therapy, those who achieved hs-CRP levels <2 mg/L 30 days after AMI had a lower risk for recurrent AMI compared with patients whose hs-CRP levels were ≥2.0 mg/L, independent of achieved low-density lipoprotein cholesterol (LDL-C) levels [4].

Despite the robust literature surrounding hs-CRP and cardiac events, it is unknown whether elevated hs-CRP levels after initial AMI treatment is associated with worse health status (symptoms,

Abbreviations: AMI, acute myocardial infarction; EQ-5D VAS, Euro Quality of Life Visual Analog Scale; hs-CRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; MCS, mental component scale; PCS, physical component scale; SAQ, Seattle Angina Questionnaire; SF-12, The Medical Outcome Study Short Form-12; TRIUMPH, Translational Research Investigating Underlying disparities in acute Myocardial infarction Patients' Health Status registry; VIRGO, Variation in Recovery Role of Gender on Outcomes of Young AMI Patients registry.

* Corresponding author. Saint Luke's Mid America Heart Institute, 4401 Wornall Road, Kansas City, MO 64111, USA.
E-mail address: pokharely@umkc.edu (Y. Pokharel).

https://doi.org/10.1016/j.atherosclerosis.2017.09.019
0021-9150/

function and quality of life), one of the most important outcomes from patients' perspectives [7]. Given that inflammation levels are potentially modifiable, it is particularly important to understand the association of hs-CRP levels after initial AMI treatment with subsequent health status [2,8,9]. To address this gap in knowledge, we compared 30-day post-AMI hs-CRP levels with 1-year health status from 2 large prospective AMI registries. We hypothesized that elevated hs-CRP levels 30 days after recent AMI would be independently associated with poorer general and disease-specific health status outcomes at 1 year.

2. Materials and methods

2.1. Study population

We used data from the Translational Research Investigating Underlying disparities in acute Myocardial infarction Patients' Health Status (TRIUMPH) [10] and Variation in Recovery Role of Gender on Outcomes of Young AMI Patients (VIRGO) [11] studies. Study investigators obtained institutional review board approval at each participating institution and informed consent from study participants. The methodologies of TRIUMPH [10] and VIRGO [11] have been previously described. In brief, TRIUMPH was a prospective observational, 24-center AMI registry of 4340 patients with AMI from diverse geographical regions throughout the US between April 2005 and December 2008. An optional component of the TRIUMPH study was to participate in a blood sample sub-study, with collection of fasting blood samples at baseline and, optionally, at 30 days and 6 months after a patient's AMI. Therefore, 30-days hs-CRP levels were available in 1301 patients, who comprised the TRIUMPH portion of our analytic cohort (Fig. 1). The VIRGO study prospectively enrolled 18-55 year-old patients recovering from an AMI between August 2008 and May 2012. To enrich the recruitment of young women, a 2:1 female:male ratio was used to enroll 2985 participants from 103 US hospitals [11]. Similar to the TRIUMPH study, participation in blood sample collection in VIRGO was also an optional component, and 2109 patients had their hs-CRP assessed 30 days after their AMI and were included in our analyses (Fig. 1).

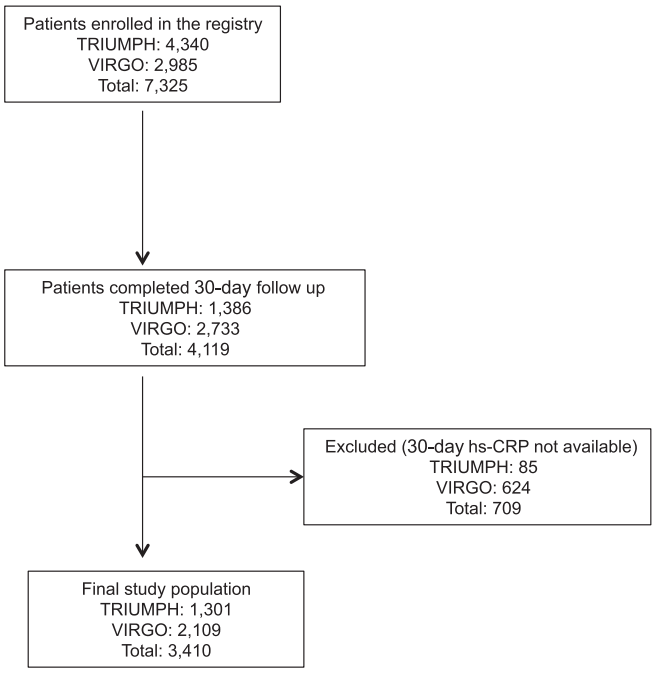

Fig. 1. Study population.
For the VIRGO registry, only patients enrolled from the US hospitals were included in the current analysis. hs-CRP, high-sensitivity C-reactive protein; TRIUMPH, Translational Research Investigating Underlying disparities in acute Myocardial infarction Patients' Health Status registry; VIRGO, Variation in Recovery Role of Gender on Outcomes of Young AMI Patients registry.

2.2. Assessment of hs-CRP and other study variables

Clinical Reference Laboratories and Quest Diagnostics measured hs-CRP levels in TRIUMPH and VIRGO, respectively. In TRIUMPH, this was accomplished using Tina-quant CRP-Latex HS assay, Cat#11972855 216, an approved assay in the US market using a Roche Modular P automated clinical chemistry analyzer. It has a coefficient of variation of 3% at an hs-CRP level of 2 mg/L. The assays used and their coefficients of variation in VIRGO were quantitatively determined using a fixed-time nephelometric, turbidity method that has a coefficient of variation of 4.7% at an hs-CRP level of 1.84 mg/L.

Details about study variables have been described previously [10,11]. Briefly, study variables were abstracted from medical records and patient interviews using similar protocols in both TRIUMPH and VIRGO. Lipids and cholesterol were measured using Vertical Auto Profile in both registries [12]. Lipid lowering therapy was defined as use of statin or non-statin (cholesterol binding resins, ezetimibe, fibrates or niacin therapy) therapy.

2.3. Study outcomes and definitions

2.3.1. Medical Outcome Study Short Form-12

The Medical Outcome Study Short Form-12 (SF-12) is a valid and reliable instrument and one of the most widely used generic health status measures of patients' mental and physical functional status [13]. This instrument measures overall physical (Physical Component Summary [SF-12 PCS]) and mental (Mental Component Summary [SF-12 MCS]) health through 12 items scored and transformed to a 0 to 100-point scale. The population median is 50 and higher scores indicate better functioning.

2.3.2. Euro quality of life visual analog scale

The Euro Quality of Life Visual Analog Scale (EQ-5D VAS) is a standardized, validated measure of health status that provides a simple and generic measure of overall health for clinical assessment [14]. The scale ranges from best (100) to worst (0) imaginable state.

2.3.3. Seattle Angina Questionnaire

The Seattle Angina Questionnaire (SAQ) is a 19-item disease-specific health-related quality-of-life measure for patients with coronary artery disease that has demonstrated validity, reliability, and clinical responsiveness and is predictive of mortality and rehospitalization [15–17]. The 5 domains of the SAQ include physical limitation, angina stability, angina frequency, treatment satisfaction, and quality of life and can be summarized into an overall summary score [18]. For the purposes of this study, angina-related physical limitation, angina frequency, angina-related quality-of-life and the summary scores were used. Each domain ranges from 0 to 100 points, with higher scores indicating higher levels of functioning, fewer symptoms, and greater quality of life.

All health status measures (SF-12, EQ-5D VAS and SAQ) were collected during the index AMI hospitalization, 30 days and 1 year after hospital discharge in both studies.