Contemporary Clinical Trials 44 (2015) 11–19

Contents lists available at ScienceDirect

Contemporary Clinical Trials

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

Design and baseline data from the Gratitude Research in Acute Coronary Events (GRACE) study

Jeff C. Huffman [a,b,*], Eleanor E. Beale [b], Scott R. Beach [a,b], Christopher M. Celano [a,b], Arianna M. Belcher [c], Shannon V. Moore [b], Laura Suarez [a,b], Parul U. Gandhi [a,c], Shweta R. Motiwala [a,d], Hanna Gaggin [a,c], James L. Januzzi [a,c]

[a] Harvard Medical School, Boston, MA, United States
[b] Department of Psychiatry, Massachusetts General Hospital, Boston, MA, United States
[c] Department of Medicine, Division of Cardiology, Massachusetts General Hospital, Boston, MA, United States
[d] Department of Medicine, Division of Cardiology, Beth Israel Deaconess Medical Center, Boston, MA, United States

ARTICLE INFO

Article history:
Received 13 May 2015
Received in revised form 2 July 2015
Accepted 3 July 2015
Available online 10 July 2015

Keywords:
Optimism
Gratitude
Physical activity
Acute coronary syndrome
Coronary artery disease

ABSTRACT

Background: Positive psychological constructs, especially optimism, have been linked with superior cardiovascular health. However, there has been minimal study of positive constructs in patients with acute coronary syndrome (ACS), despite the prevalence and importance of this condition. Furthermore, few studies have examined multiple positive psychological constructs and multiple cardiac-related outcomes within the same cohort to determine specifically which positive construct may affect a particular cardiac outcome.
Materials and methods: The Gratitude Research in Acute Coronary Events (GRACE) study examines the association between optimism/gratitude 2 weeks post-ACS and subsequent clinical outcomes. The primary outcome measure is physical activity at 6 months, measured via accelerometer, and key secondary outcome measures include levels of prognostic biomarkers and rates of nonelective cardiac rehospitalization at 6 months. These relationships will be analyzed using multivariable linear regression, controlling for sociodemographic, medical, and negative psychological factors; associations between baseline positive constructs and subsequent rehospitalizations will be assessed via Cox regression.
Results: Overall, 164 participants enrolled and completed the baseline 2-week assessment; the cohort had a mean age of 61.5 +/− 10.5 years and was 84% men; this was the first ACS for 58% of participants.
Conclusion: The GRACE study will determine whether optimism and gratitude are prospectively and independently associated with physical activity and other critical outcomes in the 6 months following an ACS. If these constructs are associated with superior outcomes, this may highlight the importance of these constructs as independent prognostic factors post-ACS.

1. Introduction

Each year, 1.1 million Americans are hospitalized for an acute coronary syndrome (ACS; myocardial infarction [MI] or unstable angina [UA]) [1]. Among post-ACS patients, approximately 20% will be re-hospitalized for ischemic heart disease or suffer mortality within the next year [2]. It is therefore critical to identify factors that may protect against adverse events and improve overall prognosis during the high risk post-ACS period.

Psychological factors may play an important role in post-ACS prognosis. Depression following ACS has been associated with recurrent cardiac events, rehospitalizations, and death, independent of sociodemographic factors or medical illness severity [3], and has been declared an official risk factor for poor prognosis following ACS by the American Heart Association [4]. Likewise, elevated anxiety symptoms and formal anxiety disorders have been associated with adverse events in patients with cardiovascular disease, including those with an ACS [5,6].

In contrast, positive psychological factors may have a beneficial impact on cardiac prognosis. Several syntheses of the literature have found that positive psychological well-being is associated with superior cardiac health [7,8] and reduced mortality in patients with medical illness [9]; such connections are typically independent of traditional risk factors and above and beyond the adverse effects of depression. Optimism (a general expectation that the future will be favorable) in particular may be associated with superior medical outcomes in those with and without known heart disease, with several large longitudinal studies and a large meta-analysis finding links between optimism and superior cardiac prognosis [8,10,11]. These positive constructs may be especially related to physical activity and other cardiac health

* Corresponding author at: Massachusetts General Hospital/Blake 11, 55 Fruit Street Boston, MA 02114, United States.
E-mail address: jhuffman@partners.org (J.C. Huffman).

http://dx.doi.org/10.1016/j.cct.2015.07.002
1551-7144/

behaviors, as several prior studies have found links between positive psychological well-being and increased activity, healthier diet, and reduced rates of smoking [12–14].

However, critical gaps in the literature exist. First, there has been minimal study of the prognostic impact of positive psychological constructs following an ACS, despite the high rates of adverse events in this population. Such studies could inform post-ACS assessment and interventions. Second, gratitude (a general disposition to appreciate and be thankful for people, events, and experiences in one's life) is a commonly experienced psychological state following an ACS; approximately one-half of post-ACS patients experience increased gratitude [15]. However, there has been minimal study of the association of gratitude with cardiac prognosis. Third, relatively few studies exploring positive psychological constructs and health outcomes have examined more than one positive state to assess whether one construct may be more or less prognostically important. Finally, very few investigations in this field have simultaneously examined the prospective effects of positive psychological well-being on biological, behavioral, and clinical outcomes to parse the potential mechanistic effects of positive constructs.

Accordingly, in the Gratitude Research in Acute Coronary Events (GRACE) study, we will examine the prospective effect of optimism and gratitude, measured 2 weeks post-ACS, on subsequent health behaviors, prognostic biomarkers, and clinical outcomes over the subsequent 6 months.

2. Study methods

2.1. Overview

This is a prospective observational study of the impact of baseline gratitude and optimism over a 6 month follow-up period on health-related outcomes of patients hospitalized for an ACS. Patients were enrolled in the hospital, will have in-person study visits 2 weeks post-ACS and 6 months later, and will complete interim self-report assessments by phone at 3 months (Fig. 1).

The primary outcome measure for the study is physical activity, measured by accelerometer, at 6 months. The enrollment goal for the project was a minimum of 150 patients; enrollment is now complete. Approval from the Partners Healthcare Institutional Review Board (IRB) for the full protocol was obtained prior to commencement of study procedures.

2.2. Eligibility criteria

To be potentially eligible, patients were required to be admitted to one of three cardiac units at MGH, an urban academic medical center, for an ACS.

2.2.1. Cardiac inclusion criteria

To receive a diagnosis of ACS, patients had to meet criteria for MI or UA. For MI, potential subjects met established consensus criteria [16], specifically: (1) elevation of cardiac biomarkers (cardiac troponin) in addition to: (2) symptoms of ischemia (e.g., acute chest pain), (3) ischemic changes on electrocardiogram (e.g., ST-segment elevation or ST-depression and T-wave inversions), or (4) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality. For UA, subjects met formal standardized criteria used in prior cardiac studies [17,18]: (1) crescendo angina, (2) new onset (within 1 month) angina with minimal exertion, or (3) angina with minimal exertion or at rest. When unclear, diagnoses were adjudicated by the study cardiologist (J.J.).

2.2.2. Exclusion criteria

Patients were excluded if they had: (1) a periprocedural ACS (ACS occurring in the setting of another medical procedure), (2) a condition likely to alter biomarkers of interest, (3) a medical condition likely to be terminal within the timeframe of the study, (4) an unrelated condition limiting physical activity, (5) an inability to communicate in English, or (6) a cognitive disturbance that precluded participation or informed consent, as identified using a six-item cognitive screen designed to assess suitability for research participation [19].

Patients with a periprocedural ACS (e.g., type 4 or type 5 MI [16]) were excluded due to concerns that such events may occur in the absence of structural heart disease and likely represent a different pathophysiology, course, and prognosis than those with 'endogenous' ACS. It is true that such patients, who may have cardiovascular systems that are especially prone to (physical or emotional) stress-related cardiac events, may have even greater associations between well-being and cardiac outcomes. However, to maintain the most homogeneous cohort for this project, they were excluded from this initial trial.

Conditions likely to alter biomarkers of interest included renal failure requiring hemodialysis, and some inflammatory illnesses (systemic lupus erythematosus, inflammatory bowel disease, and Wegener's

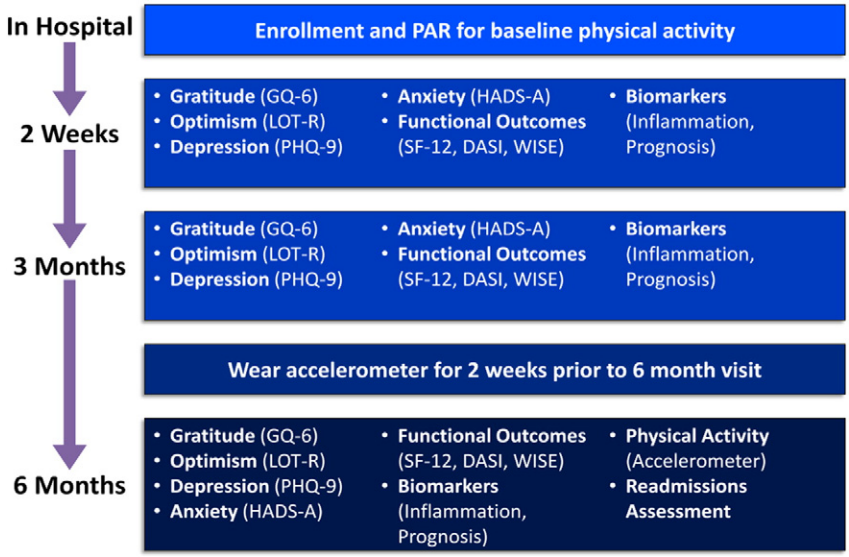

Fig. 1. Timeline of study assessments. DASI = Duke Activity Status Index; GQ-6 = Gratitude Questionnaire Six Item Form; HADS-A = Hospital Anxiety and Depression Scale—Anxiety Subscale; LOT-R = Life Orientation Test-Revised; MOS-SAS = Medical Outcomes Study Specific Adherence Scale; PAR = Physical activity recall; PHQ-9 = Patient Health Questionnaire-9; SF-12 = Short Form 12; WISE = Women's Ischemia Symptom Evaluation Scale.