



Late Consequences of Acute Coronary Syndromes: Global Registry of Acute Coronary Events (GRACE) Follow-up

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ABSTRACT

PURPOSE: Short-term outcomes have been well characterized in acute coronary syndromes; however, longer-term follow-up for the entire spectrum of these patients, including ST-segment-elevation myocardial infarction, non-ST-segment-elevation myocardial infarction, and unstable angina, is more limited. Therefore, we describe the longer-term outcomes, procedures, and medication use in Global Registry of Acute Coronary Events (GRACE) hospital survivors undergoing 6-month and 2-year follow-up, and the performance of the discharge GRACE risk score in predicting 2-year mortality.

METHODS: Between 1999 and 2007, 70,395 patients with a suspected acute coronary syndrome were enrolled. In 2004, 2-year prospective follow-up was undertaken in those with a discharge acute coronary syndrome diagnosis in 57 sites.

RESULTS: From 2004 to 2007, 19,122 (87.2%) patients underwent follow-up; by 2 years postdischarge, 14.3% underwent angiography, 8.7% percutaneous coronary intervention, 2.0% coronary bypass surgery, and 24.2% were re-hospitalized. In patients with 2-year follow-up, acetylsalicylic acid (88.7%), beta-blocker (80.4%), renin-angiotensin system inhibitor (69.8%), and statin (80.2%) therapy was used. Heart failure occurred in 6.3%, (re)infarction in 4.4%, and death in 7.1%. Discharge-to-6-month GRACE risk score was highly predictive of all-cause mortality at 2 years (c-statistic 0.80).

CONCLUSION: In this large multinational cohort of acute coronary syndrome patients, there were important later adverse consequences, including frequent morbidity and mortality. These findings were seen in the context of additional coronary procedures and despite continued use of evidence-based therapies in a high proportion of patients. The discriminative accuracy of the GRACE risk score in hospital survivors for predicting longer-term mortality was maintained.

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While the early risks of death and recurrent myocardial infarction have been well characterized following presentation with an acute coronary syndrome,¹⁻¹⁰ the later evidence-based management and consequences in a contemporary patient population remain less clearly defined.¹¹⁻¹⁵ Risk scores are available to predict short-term outcome^{9,16,17} from the Global Registry of Acute Coronary Events (GRACE), an observational study of more than 70,000 acute coronary syndrome patients from 123 hospitals in 14 countries from 1999-2007.¹⁸⁻²⁰ Given the considerable variability that exists among patients across the entire spectrum of acute coronary syndromes (including myocardial infarction and unstable angina), estimation of risk, including beyond the shorter term, may assist in determining optimal longer-term management. Further, the value of risk predictors of short-term outcome (eg, in-hospital¹⁶ and 6-month^{9,17}) from the GRACE models in predicting longer-term outcome (eg, ≥ 1 year) has been limited to date.^{9,13,14,21-24} The purpose of this article is to describe the longer-term outcomes and receipt of coronary intervention procedures and evidence-based medication in selected GRACE patients undergoing 6-month and 2-year follow-up. Our secondary study objective was to determine the value of the GRACE risk score¹⁷ in hospital survivors in predicting 2-year mortality.

METHODS

From 2001 to 2007, 70,395 patients with a suspected acute coronary syndrome were enrolled in the GRACE program. Patients ≥ 18 years old admitted with a presumptive diagnosis of an acute coronary syndrome and electrocardiographic changes consistent with an acute coronary syndrome, abnormal cardiac biomarker, or documentation of coronary artery disease, were included.^{18,20}

Data were collected at each site by a trained coordinator using a standardized case report form. Demographic characteristics, medical history, presenting symptoms, biochemical and electrocardiographic findings, treatment practices, and a variety of hospital outcome data were collected. Standardized definition of all patient-related variables and clinical diagnoses were used.¹⁸ Completed case report forms were faxed to, or entered into, an electronic, Web-based case report form developed by the data-coordinating center.

All cases were assigned to one of the following mutually exclusive categories based on presenting electrocardiographic

characteristics, cardiac biomarker status during hospitalization, and final hospital diagnosis: ST-segment-elevation or new left bundle branch block myocardial infarction, non-ST-segment-elevation myocardial infarction or unstable angina.^{18,20} Patients were diagnosed with ST-elevation myocardial infarction if they had new or presumed new ST-segment elevation ≥ 1 mm in any electrocardiographic location, or new left bundle branch block on the index or qualifying electrocardiogram with at least one positive cardiac biomarker of necrosis (ie, troponin or creatine kinase or creatine kinase-MB elevated above the upper limit of normal/reference limit according to each hospital's laboratory). Non-ST-elevation myocardial infarction was diagnosed in the cases of at least one positive cardiac biomarker of necrosis without new ST-segment elevation seen on the index or qualifying electrocardiogram. Unstable angina was diagnosed when serum cardiac biomarkers of necrosis were within the normal range.

Follow-up at 6 months was prospective and based primarily on individual patient contact; reliance on information from the patient's family, physician(s), and on hospital or central records was used only when direct patient contact was unavailable.^{18,20,25} A one-page standardized data collection form was collected by trained study physicians or coordinators. Questions were asked about rehospitalization for heart disease, development of subsequent stroke, receipt of diagnostic and interventional procedures, and medications currently taken. Subsequent morbidity and mortality, including cause-specific death, were not adjudicated. In 2004, 2-year follow-up was undertaken in a similar fashion to that at 6 months in patients with a discharge acute coronary syndrome diagnosis at 57 sites where ethics approval, patient consent, and logistics allowed; retrospective follow-up was undertaken for some patients in 2004, but was otherwise prospective.

Statistical Analysis

Continuous data are summarized as medians, with 25th and 75th percentiles, and categorical data as frequencies and percentages. The chi-squared test, Wilcoxon rank-sum, and Kruskal-Wallis test were used for group comparisons of categorical and continuous variables, respectively. Multivariable logistic regression was used to examine post-discharge events rates according to final discharge diagnosis. The discriminatory performance of the GRACE risk score was evaluated by the c-statistic (area under the receiver-operating characteristic curve). Cox proportional

CLINICAL SIGNIFICANCE

- Postdischarge follow-up of >19,000 acute coronary syndrome patients revealed that 1 in 14 patients died by 2 years.
- One in 22 patients experienced a myocardial (re)infarction and 1 in 16 developed heart failure.
- One in 4 were readmitted for cardiovascular reasons, including 1 in 6 for a coronary procedure.
- The accuracy of the Global Registry of Acute Coronary Events (GRACE) risk score in hospital survivors for predicting 2-year mortality was maintained.

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