Rationale and design of the GRACE (Global Registry of Acute Coronary Events) project: a multinational registry of patients hospitalized with acute coronary syndromes

Acute coronary syndromes range from UA to STEMI. Although they have a common underlying pathophysiology, the ACS represent a spectrum of conditions in terms of diagnosis, treatment, and prognosis. Significant progress has been made in the development of effective treatment strategies for ACS and yet relatively little is known about the extent to which these strategies are used in daily clinical practice. Many data are available from industrialized countries, in which ACS are a major cause of morbidity and mortality, but much less information is available from the developing world, where an epidemic of cardiovascular disease is starting to emerge.[1,2] To improve the outcomes of patients with ACS, up-to-date data on the world-wide management of these individuals are needed. By examining and reporting on current patterns of therapy, we aim to improve the treatment and outcomes of patients with ACS.

GRACE is a large, ongoing, multinational, observational study of patients hospitalized with suspected ACS. The aim of this registry is to improve in-hospital and long-term outcomes for ACS patients.

Table. Criteria for inclusion in GRACE

- ACS as a presumptive diagnosis
- At least 18 years old
- Alive at the time of hospital presentation
- Qualifying ACS must not have been precipitated or accompanied by a significant comorbidity such as trauma or surgery. Inpatients who are already hospitalized when they develop symptoms of ACS are not eligible for enrollment
- Patients transferred into or out of a registry hospital can be enrolled regardless of the time spent at the transferring hospital
- For patients transferred out of a registry hospital, data collection for the initial case report form ends with the transfer
- Patients may be re-enrolled provided that at least 6 months have elapsed since their previous enrollment
- Patients hospitalized for less than 1 day who die and do not meet the criteria for ACS may be enrolled provided that the cause of death is confirmed to be ACS

Methodology

A total of 14 countries across four continents are represented in GRACE – Argentina, Australia, Austria, Belgium, Brazil, Canada, France, Germany, Italy, New Zealand, Poland, Spain, United Kingdom, and the USA (Figure). Data collection began in April 1999, with the aim of collecting data from around 10 000 patients each year. During the first year, data were collected from patients hospitalized with ACS in 18 cluster geographic sites, which were chosen to represent populations with different demographic, clinical and treatment characteristics. Each cluster of hospitals enrolls approximately 600 patients per annum.

In order to allow the study findings to be generalized and to describe systematically the clinical epidemiology, natural history and management practices of patients from a multisite, community-wide perspective, a population-based approach to the study has been adopted at half of the sites. Patients must reside in a defined geographic catchment area to be included in these community-wide sites. In the remaining clusters, where a population-based perspective was considered to be neither feasible nor cost-effective, a sample of hospitals was selected which was representative of those from that region or country. Cases of ACS were included irrespective of the patient's residence. Approval from the local hospital's ethics or institutional review board was obtained where necessary, and signed, informed consent for follow-up contact was obtained from the patients at enrollment.

At each site a trained coordinator collects data on the following using a standardized case report form: patient demographic and clinical characteristics, medical history, duration of prehospital delay, presenting symptoms, electrocardiographic findings, use of cardiac medications and interventional procedures, and hospital-associated outcomes. A standardized set of definitions for patient-related variables and clinical diagnoses is used. Patients are followed up by telephone 6 months after discharge from hospital, using a standardized case report form on long-term mortality, occurrence of various clinical events, rehospitalization for coronary heart disease, receipt of cardiac interventions, and use of various therapies after discharge.

The GRACE Investigators

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Figure.
Location of participating clusters in GRACE (core, restricted group)

Inclusion criteria

The criteria for inclusion in GRACE are outlined in the Table. To be eligible for inclusion, patients must be at least 18 years of age, alive at the time of presentation, hospitalized with a presumed diagnosis of ACS, and have at least one of the following:

- electrocardiographic changes consistent with ACS
- elevated serum biochemical markers of cardiac necrosis
- documentary evidence of coronary artery disease.

The qualifying ACS must not have been precipitated or accompanied by a significant comorbidity such as trauma or surgery. Patients who died out of hospital from sudden cardiac death, or before informed consent could be obtained, were excluded from enrollment in the study.

Patient identification

To aid the review of medical records and to facilitate data collection, prospective ('warm') and retrospective ('cold') surveillance approaches, similar to those used in the MONICA project, are used to identify cases of ACS.[3,4] In sites using warm pursuit, patients are identified during the index admission and, once informed consent has been obtained, their medical records are reviewed on an ongoing basis. In sites using cold pursuit, hospital listings of discharged patients are used to identify potentially eligible ACS patients, and all data are obtained from hospital charts.

Quality control

The database is audited periodically to identify potential outlying fields and discrepancies in the data. Random periodic audits of the cluster sites are also carried out. Completed case-report forms are faxed to the data management organization, where they are reviewed for completeness and clinical validity. Resulting queries are referred back to the originating site before the forms are processed. The data are scanned into the electronic database and checked manually. Cleaned data sets are sent to the international coordinating center for analysis.

Each study site receives a quarterly report, with a profile of its data along with a summary profile of the overall data. A website has been set up to facilitate communication between investigators and coordinators, to provide updates about the study's progress, and to enhance quality-control measures. The website includes the GRACE Member's Room, which is password protected, and a public section, with an overview of GRACE, an up-to-date bibliography, and a list of participating hospitals.

This large, observational registry will provide important and wide-ranging insights into current and evolving practice patterns for patients hospitalized with ACS, and the impact of these practice patterns on short- and long-term outcomes. In time, the findings of this study will reveal both regional and national variations in practice, and will generate hypotheses for investigation in other large observational databases or in randomized clinical trials.

References

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