Rationality and Methods of ACCEPT Registry - Brazilian Registry of Clinical Practice in Acute Coronary Syndromes of the Brazilian Society of Cardiology

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Abstract

Background: Assessing the Brazilian clinical practice in patients with acute coronary syndrome, in public and private hospitals to identify gaps in the incorporation of clinical interventions with proven benefit.

Objective: To develop a registry of patients diagnosed with acute coronary syndrome to assess demographics, morbidity, mortality, and standard practice in the care of this condition. Besides, to assess the prescription of evidence-based interventions such as aspirin, statins, beta blockers and reperfusion, among others.

Methods: Registry-type prospective observational study intended to document hospital clinical practices of acute coronary syndrome in public and private hospitals in Brazil. In addition, longitudinal follow-up will be held until discharge and measurement of mortality and occurrence of serious events at 30 days, 6 and 12 months.

Results: The findings will be presented one year after the start of collection (September 2011), and consolidated after a meeting with the population to discuss the objectives sought.

Conclusion: The analysis of this multicenter registry will design a horizontal perspective for the treatment of patients suffering from cardiovascular disease in Brazil. (Arq Bras Cardiol 2011; 97(2) : 94-99)

Keywords: Acute coronary syndrome/epidemiology; evidence-based practice; multicenter studies.

Introduction

Recent data from the World Health Organization reveal that cardiovascular diseases, particularly acute myocardial infarction (AMI), are the main cause of disability and morbidity and mortality in both sexes, both in Brazil and in the world[1-3].

Since it is a major public health problem, the search for interventions that have proven benefits in reducing the incidence of this disease and its complications is a priority. Interventions with proven benefit in reducing major cardiovascular events include drugs such as aspirin, thrombolytics and antiplatelet agents at hospital admission, converting enzyme inhibitors, statins and beta blockers at discharge. These have reduced the relative risk ranging from 6.5 to 25% in previous studies[4-8].

Previous records showed that use of these interventions in the setting of acute coronary syndromes (ACS) is still sub-optimal, suggesting, upon admission, aspirin usage rates ranging from 91 to 92%, and upon discharge, ranging between 90 and 95%, statin usage upon discharge ranging between 26 and 57%, and beta-blocker usage upon discharge in less than 63 to 77% of patients[9-14].

The assessment of its occurrence, through a national registry for controlled collection recently implemented, can thus document the clinical practice in the treatment of patients with ACS, whether hospitalized in public and/or private hospitals in Brazil.

Methods

The registry represents a documentation project of the current clinical practice of service to ACS in Brazil aiming to identify the incorporation of evidence into the clinical practice of treatment of this disease, involving public and private hospitals. Additionally, there will be longitudinal follow-up of patients until their discharge from hospital, besides checking mortality within 30 days, 6 and 12 months.

A. Design

ACS patients treated in public and private hospitals will be compiled to define data related to demographic characteristics, morbidity, mortality and daily practice in the treatment of ACS, and assess patterns of prescription of evidence-based interventions (aspirin, statins, beta blockers, angiotensin-converting enzyme inhibitors and reperfusion).

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Manuscript received December 27, 2010; revised manuscript received March 18, 2011; accepted March 21, 2011.

B. Sample characteristics

Patients whose physician from the medical care suspects of diagnosis of ACS and plan to start treating this condition will be eligible. Thus, the criteria for inclusion and exclusion of patients will be determined not by the protocol but by clinical trial of the assisting doctor. Anyway, it is strongly suggested to include patients presenting the clinical picture as described in Box 1. Patients admitted with the diagnosis of chest pain to be clarified, with suspected coronary origin, allocated in this registry, but not confirmed, after the final diagnosis, will be excluded from it.

C. Hospitals

The centers were selected by invitation sent by the steering committee of this registry and voluntarily after communication about the opportunity to participate in this research on SBC's website for a period of 30 consecutive days. All centers were asked to complete a preliminary inquiry to check the feasibility of having the the participation of the medical center. The participating centers are listed at the end of this article.

D. Calculation of sample size

In order to detect a proportion of 50% (e.g., rate of usage of statins upon discharge or patients who receive reperfusion), considering a sampling error of 2%, an alpha of 5% and a statistical power of 90%, it will be necessary to include 2,401 patients. This sample size is sufficient to meet the primary objectives of the study, which is feasible within the first year of recruitment. ACCEPT is expected to continue after 12 months, enlisting a larger number of patients, enabling further analysis and inferences about independent predictors of major clinical events.

Box 1 - Inclusion and exclusion criteria for participation in the ACCEPT registry

Inclusion criteria
Acute Coronary Syndrome (ACS) without ST segment elevation Ischemic symptoms suspected as ACS without ST elevation defined as: medical history compatible with the new event or a pattern of worsening chest pain characteristic of ischemia at rest and on minimal exertion (lasting at least 10 minutes)
And at least one of the following: c) Abnormalities in the electrocardiogram (ECG) compatible with new ischemia [ST depression of at least 1.0 mm or transient ST elevation or ST elevation of 1.0 mm or less, or T-wave inversion of more than 3.0 mm in at least two contiguous leads *or* d) Cardiac enzymes (e.g., CKMB) or biomarkers (Troponin I or T) elevated above the upper limit of normal range.
Acute Coronary Syndrome (ACS) with ST segment elevation Presenting signs and symptoms of acute myocardial infarction with duration of at least 20 minutes. With ECG abnormalities defined, compatible with ACS or persisting ST elevation (> 2.0 mm in two contiguous precordial leads or > 1.0 mm in at least two leads of the members) or new left bundle branch block with a Q wave in two contiguous leads.
Exclusion criteria
Patients transferred from other institutions with more than 12 hours of onset of pain

E. Outcomes of interest and definitions

As a primary outcome, the proportion of patients receiving interventions with proven benefits demonstrated by the indicators (e.g., aspirin upon admission and upon discharge, percentage of patients receiving reperfusion, or statins and beta blockers upon discharge).

Secondary outcomes: total mortality and major cardiovascular events (reinfarction, stroke, fatal and nonfatal cardiac arrest, and cardiovascular mortality) during hospitalization, within 30 days, 6 and 12 months.

Cardiovascular mortality

Cardiovascular mortality is defined as any death due to vascular causes and includes deaths that occur after a myocardial infarction, heart failure, stroke, cardiac revascularization procedure (i.e., percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG]), pulmonary embolism, or death from unknown causes.

Reinfarction

Set as a new event (beyond what encouraged the patient's inclusion in the study), includes at least two of the following criteria:

- Ischemic symptoms suspected as ACS without ST elevation defined as: medical history compatible with the new event or a pattern of worsening chest pain characteristic of ischemia (lasting at least 10 minutes).
- Abnormalities in the electrocardiogram (ECG) compatible with new ischemia [ST depression of at least 1.0 mm or transient ST elevation or ST elevation of 1.0 mm or less, or T-wave inversion of more than 3.0 mm in at least two contiguous leads or cardiac enzymes (e.g., CK), or biomarkers (Troponin I or T) elevated above the upper limit of normal range*.

** If at the beginning of the suspicious event the ischemic biomarker was still high as a result of the index event, there should be demonstration of a falling marker level before the suspicious event. Moreover, the subsequent peak of the ischemic biomarker should be 1.5 times the level prior to the start of the event suspected. These criteria do not need to be met if the ischemic biomarker is not high before the event suspected.*

New Q waves, greater than or equal to 0.04 seconds, or pathology distinct from that event that prompted the patient's inclusion (i.e., considered as new since the patient's inclusion in the study).

Nonfatal cardiac arrest

Nonfatal cardiac arrest is defined as the successful resuscitation of a ventricular fibrillation documented or suspected, sustained ventricular tachycardia, asystole or pulseless electrical activity requiring cardiopulmonary resuscitation, drug therapy or cardiac defibrillation.

Cerebrovascular accident

Stroke is the rapid onset of a new neurologic deficit persisting longer than 24 hours. In the case of clinical diagnosis

of stroke, computed tomography (CT) or magnetic resonance imaging (MRI) is highly recommended but not mandatory, at the discretion of the assisting team. Additionally, strokes are classified as "ischemic" or "hemorrhagic", based on image data, or of "unknown cause" if the image data are not available.

The operational flowchart of this record is shown in Figure 1.

F. Details of clinical visits

Index visit - assessment of inclusion/exclusion criteria, demographic data, medical/surgical history, electrocardiogram, myocardial necrosis markers and treatment.

Hospital discharge or day 7 visit (whichever comes first) - assessment of hospital complications and medications.

Day 30 follow-up visit - assessment of cardiovascular events and drugs.

Month 6 follow-up visit - assessment of cardiovascular events and drugs.

Month 12 follow-up visit - assessment of cardiovascular events and drugs.

G. Statistical analysis

Quantitative variables are expressed as mean and standard deviation in the presence of normal or median distribution and interquartile range in the presence of asymmetric distribution. Qualitative variables are presented in absolute frequencies (number of patients) and relative frequencies (percentage).

Considering all centers, the outcomes will be described by an overall percentage and the percentage prescribed in each center and will be expressed by means of proportions and their confidence intervals of 95%. Where there is great variability in prescription, a weighted average variance at each center will be generated.

For regression models, we will report the odds ratio or hazard ratio, the corresponding standard error, confidence

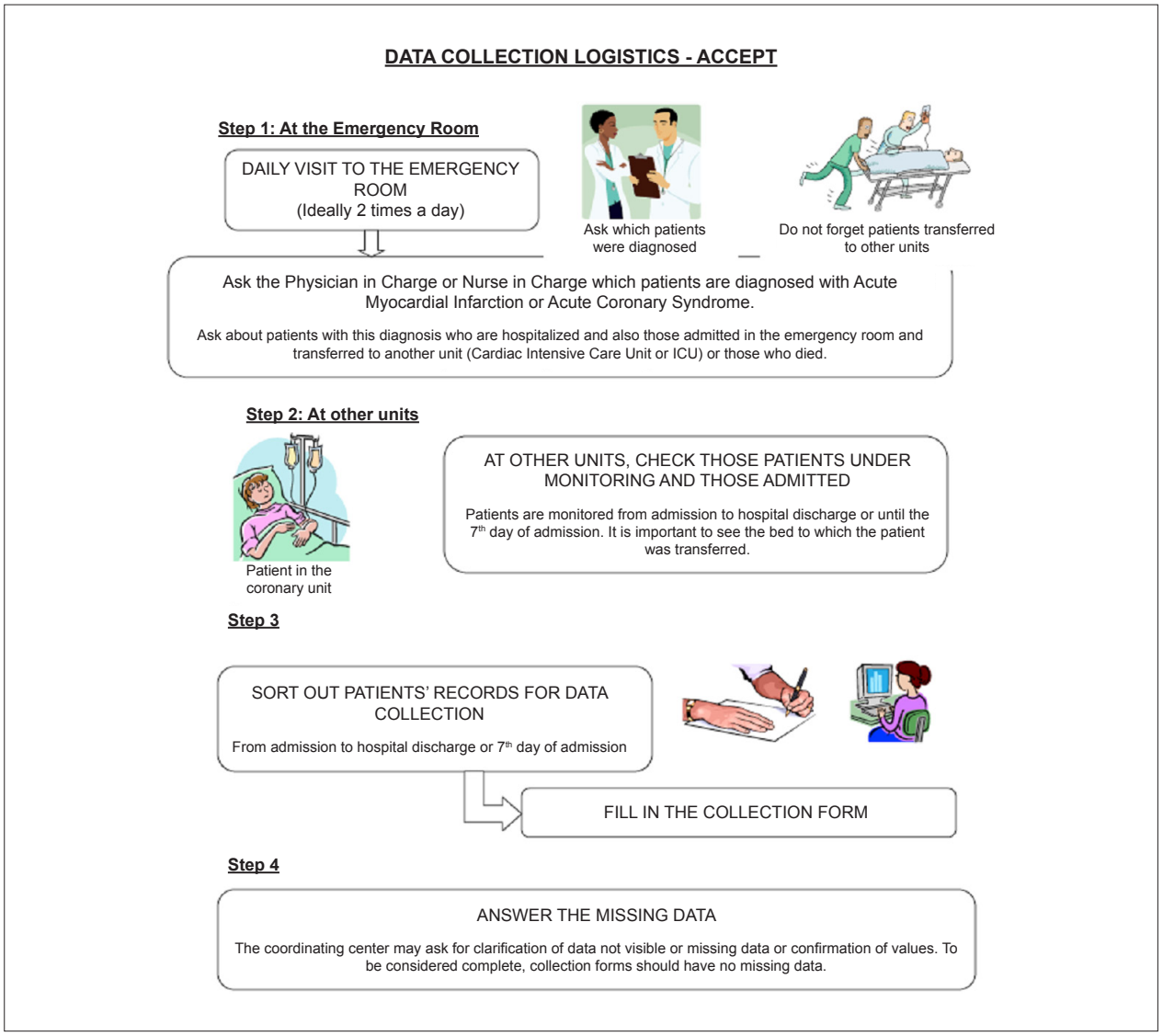

Figure 1 - Operational procedure for inclusion of patients in the ACCEPT Registry.

intervals of 95% and p-values. We will report the p-values up to three decimal places with p-values below 0.001 reported as $p < 0.001$. In all tests, we will use the two-tailed alpha significance level = 0.05. An examination of residues will provide an assessment of model assumptions for the regression analyses. The Goodness-of-fit test for the models will be performed using appropriate Hosmer-Lemeshov tests. The analyses will be performed using Stata version 10.0.

H. Financing

This registry is owned by the Brazilian Society of Cardiology using funds dedicated to this purpose for its implementation. The *Instituto de Ensino e Pesquisa do Hospital do Coração de São Paulo* (HCor/ASS) was contracted to implement this registry, under the coordination of the Brazilian Society of Cardiology. The steering committee of the registry is described later in this article.

I. Data quality control

All centers will receive training on the protocol and on the electronic system in person or by telephone, with the coordination team available to clear doubts.

The quality control of study data will be made by various strategies, such as electronic form for collection of clinical variables, central data checking, in-person monitoring of the 05 centers with larger numbers of patients recruited and random selection of 20% of the centers for in-person monitoring.

J. Ethical aspects

The protocol was approved by the Research Ethics Committee (CEP) of *Hospital do Coração de São Paulo* - SP (HCor/ASS) on June 22, 2010 under registration number 117/2010 and each participating center had it approved in their local CEP.

All patients will sign an informed consent and the clinical trial will be conducted in accordance with the principles of the current revision of the Declaration of Helsinki and the latest version of the Guidelines for Good Clinical Practice (ICH-GCP), as well as Resolution 196/96. The study will be performed according to the local and regulatory legal requirements enforceable in Brazil.

Publishing policy

All presentations of the study and/or publication of findings will be based on clear evidence verified and validated in order to ensure accurate results. Details about the responsibility and sequence of these presentations and/or publications will be defined with the Brazilian Society of Cardiology.

The authorship of the main conclusions of this study will be based on the contributions from the study centers in general. All participants in the registry (investigators and committee members) have make an advance delegation of authority to the Brazilian Society of Cardiology and the *Instituto de Ensino e Pesquisa do Hospital do Coração* - IEP - Hcor for the submission and/or publication of the main findings. Any submission or publication by any participant in the trial should indicate the study and have the approval of the Brazilian Society of Cardiology.

Data collection

Until February 15, 2011, we recorded 51 participating centers, of which 38 are already active, with a total of 850 patients included, since August 2010 (35.4% of the total desired). The end of the inclusion is estimated for the end of the first half of 2011.

Organization

Main investigators - Luiz Alberto Piva e Mattos and Otávio Berwanger.

Steering committee - Luiz Alberto Piva e Mattos, Otávio Berwanger, Jorge Ilha Guimarães, Fábio Sândoli de Brito, Renato A. Kalil, Ângelo V. de Paola, Hélio Penna Guimarães and Alexandre Biasi Cavalcanti.

Coordinators of HCor Institute for Teaching and Research - Hélio Penna Guimarães, Eliana Vieira Santucci, Luis Paulo Duprat, Karina Normilio da Silva, Alessandra Akiko Kodama, Marcos Thadeu de Tenuta Junior e Ana Denise Zazula.

Intellectual property - Brazilian Society of Cardiology.

Coordination and supervision - Brazilian Society of Cardiology and IEP-HCor.

Research centers

IMV Mãe de Deus, Porto Alegre/RS: Euler Roberto Fernandes Manenti; Hospital Moinhos de Vento, Porto Alegre/RS: Eduardo Costa Duarte Barbosa; Instituto de Cardiologia-Fundação Universitária de Cardiologia, Porto Alegre/RS: Oscar Pereira Dutra; Irmandade Santa Casa de Misericórdia de Porto Alegre/Hospital São Francisco, Porto Alegre/RS: Paulo Ernesto Leães; Hospital de Clínicas de Porto Alegre, Porto Alegre/RS: Carisi Anne Polanckzyk; Instituto de Cardiologia Uruguaiana, Uruguaiana/RS: Sidney Campodonico Filho; Hospital São Vicente, Passo Fundo/RS: Hugo Vargas Filho; Hospital Santa Izabel, Blumenau/SC: Sérgio Luiz Zimmermann; Instituto de Cardiologia São José, São José/SC: Ilnei Pereira Filho; Centro Hospitalar UNIMED, Joinville/SC: Rogério Carregoza Dantas; Sociedade Hospitalar Angelina Caron, Campina Grande do Sul/PR: Dalton Bertolim Précoma; Irmandade Santa Casa de Misericórdia de Curitiba, Curitiba/PR: José Augusto Ribas Fortes; Associação Bom Samaritano-Hospital e Maternidade Santa Rita, Maringá/PR: Raul D'Aurea Mora Junior; Hospital de Caridade São Vicente de Paulo, Guarapuava/PR: Stefan Wolanski Negrão; Hospital São Paulo, São Paulo/SP: Antônio Carlos de Camargo Carvalho; Hospital do Coração, São Paulo/SP: Edson Renato Romano; Instituto Dante Pazzanese de Cardiologia, São Paulo/SP: Elizabete Silva dos Santos; Hospital Santa Paula, São Paulo/SP: Otavio Celso Eluf Gebara; Hospital Bandeirantes, São Paulo/SP: Hélio Castello; Hospital Sírio Libanês, São Paulo/SP: Roberto Kalil Filho; Hospital Maternidade Celso Pierro-PUCCAMP, Campinas/SP: José Francisco Kerr Saraiva; Hospital Vera Cruz, Campinas/SP: Sílvio Giopatto; Santa Casa de Votuporanga, Votuporanga/SP: Mauro Esteves Hernandes; Instituto de Moléstias Cardiovasculares, São José do Rio Preto/SP: Gilmar Valdir Greque; Santa Casa de Marília, Marília/SP: Pedro Beraldo de Andrade; Hospital Regional de Presidente Prudente, Presidente Prudente/SP: Margaret Assad Cavalcante; Instituto Nacional de Cardiologia

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Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

This study was funded by *Sociedade Brasileira de Cardiologia*.

Study Association

This study is not associated with any post-graduation program.

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