Rationale and Design - BREATHE Registry- I Brazilian Registry of Heart Failure

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Abstract

**Background:** Several local registries have sought to individually depict clinical characteristics of patients hospitalized with heart failure (HF) in Brazilian hospitals and communities. Overall, the analysis of these data suggests that there are important differences in etiology, decompensation factors, treatment and prognosis of patients with HF in different Brazilian regions.

**Objectives:** To evaluate the demographic, clinical and prognostic characteristics of 1,200 patients admitted with a clinical diagnosis of decompensated HF in a group of 60 hospitals representative of the different Brazilian regions.

**Methods:** Transversal observational study (registry) with a longitudinal twelve-month follow-up (admission consultations, hospital discharge, three months, six months and twelve months after inclusion), in which patients admitted to public and private hospitals clinical with a primarily defined HF diagnosis will be studied.

**Results:** The results will be shown soon after data collection completion, quality assessment and statistical analysis.

**Conclusions:** The results of this multicenter registry will allow for a more appropriate planning of financial, technological and personal resource supply for the health care area, as well as the planning of more effective preventive measures in decompensated HF (Arq Bras Cardiol. 2013; 100(5):390-394).

**Keywords:** Heart Failure; Medical Records; Inpatients; Brazil.

Introduction

Heart failure (HF) is a complex systemic clinical syndrome, defined as cardiac dysfunction that causes inadequate blood supply to meet the metabolic tissue needs in the presence of normal venous return, or do so only with elevated filling pressures. The hemodynamic alterations commonly found in HF involve inadequate response of cardiac output and elevated pulmonary and systemic venous pressures\(^1,2\). HF is a major cause of mortality in Brazil and is responsible for a high number of hospital admissions per year (data from the Brazilian Unified Health System Database - DataSUS, 2003). In the United States, HF affects more than five million people and nearly 550,000 new cases occur annually\(^3\); it is estimated that its incidence affects 10/1,000 people after 65 years of age.

In Brazil and in the rest of the world, there is consistent evidence on the high rate of hospital admissions and emergency room visits due to clinical complications associated with the disease. Among patients older than 70 years admitted for HF, 60% are readmitted within 90 days\(^4,6\).

The most comprehensive picture of the situation of hospitalizations for HF in Brazil can be obtained by analyzing DataSUS records with the inherent limitations of an administrative database\(^6\). Data for the year 1997 show that HF was a very frequent cause of hospitalization (3.6% of all admissions and 37% of circulatory system hospitalizations); in addition to causing high rates of in-hospital mortality (6.4 % in 1997). In that year, costs related exclusively to HF admissions represented 4.7% (or approximately 75 million dollars) of the money spent on hospital admissions through SUS.

Data from DataSUS for the year 2007 showed a reduction in the number of hospitalizations in the last ten years, regardless of age range, with increased mortality rate\(^5,6\).

Several local registries have sought to individually depict clinical characteristics of patients hospitalized with heart failure (HF) in Brazilian hospitals and communities. Overall, the analysis of these data suggests that there are important differences in etiology, decompensation factors, treatment and prognosis of patients with HF in different Brazilian regions\(^7-9\).

**Methods**

The Registry represents a project of current clinical practice documentation regarding the care of decompensated heart failure in Brazil, aimed at identifying the incorporation of evidence into clinical practice in the...
treatment of this disease, involving public and private hospitals. Additionally, a longitudinal follow-up of these patients will be carried out, until hospital discharge and mortality at 90, 180 and 365 days.

**Design**

This is a transversal observational study (registry) with longitudinal follow-up.

**Hospital selection**

The hospitals, both public and private, which will participate in the Decompensated Heart Failure Registry of DEIC will be chosen by an investigator committee according to rules defined a priori. A fixed number of patients will be allocated for each of the five regions of the country who will participate in the registry. Each selected hospital will have an institutional coordinator who will be responsible for registry of data on consecutive patients with a clinical diagnosis of IC in up to 12 months.

**Inclusion and exclusion criteria**

Patients admitted to public and private hospitals with a primarily defined HF diagnosis will be studied. The criteria used to diagnose HF have been previously described, validated and applied in our country in similar studies in the past (Table 1)[10]. To be included in the study, patients must have a score > 7, attaining a definitive HF diagnosis.

Patients who underwent myocardial revascularization procedures (angioplasty or surgery) in the last month and patients with signs of HF secondary to a sepsis picture will be excluded.

**Patient identification at each hospital**

Each institutional coordinator will be responsible to enroll patients during a maximum period of 12 months. It is essential that the registry patients reliably represent the population treated at each institution. Thus, patients must be registered consecutively, according to the possibility of local logistics, following an active search in different sectors of the Hospital (Emergency Room, Internal Medicine groups and Cardiology and Intensive Care Units). An institution, for instance, which registers only patients from the Cardiology Team will be demonstrating a biased depiction of the sample’s characteristics.

After identification, according to the above defined the inclusion criteria, patients will be invited to participate in the study and sign the informed consent form. The local researchers will then fill the Individual Registration Form that will be available in an electronic address, accessed through the Brazilian Society of Cardiology website. Questions that arise during the filling of forms can be answered with the use of online dictionary or electronically through the intranet.

Demographic data, as well as data on HF characteristics, associated diseases and drugs used in patient management during hospitalization will be collected. It is suggested that physicians routinely in charge of patients be informed through a letter, at each institution, of the study objectives, inclusion and exclusion criteria and how patients will be enrolled. It should be clear that the aim of this registry is exclusively descriptive, will not influence patient care in any way and that the collected information will be used confidentially, solely for research purposes.

**Patient follow-up**

Patients will be reassessed through medical consultation and, when unable to return for reassessment, will be contacted by telephone after 90, 180 and 365 days of the initial evaluation to determine the occurrence of clinical outcomes and hospital readmissions.

**Sample size**

In the first phase, 1,200 hospitalizations in public and private hospitals are expected to be evaluated. The sample size definition will identify the primary descriptive goal - hospital mortality (demonstrate event rate), in addition to respecting the enrollment of other international registries. As is the case with other SBC registries, the BREATHE study aims to be continued after the 12-month period, enrolling a greater number of patients, which will allow future analyses and inferences on independent predictors of major clinical events.

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**Table 1 - Boston criteria for heart failure**

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. History</td>
<td></td>
</tr>
<tr>
<td>Dyspnea at rest</td>
<td>4</td>
</tr>
<tr>
<td>Orthopnea</td>
<td>4</td>
</tr>
<tr>
<td>Paroxysmal nocturnal dyspnea</td>
<td>3</td>
</tr>
<tr>
<td>Dyspnea with ambulation</td>
<td>2</td>
</tr>
<tr>
<td>Dyspnea with stair climbing</td>
<td>1</td>
</tr>
<tr>
<td>II. Physical Examination</td>
<td></td>
</tr>
<tr>
<td>Heart rate alteration</td>
<td>1-2</td>
</tr>
<tr>
<td>91-110 bpm= 1</td>
<td></td>
</tr>
<tr>
<td>&gt; 110 bpm=2</td>
<td></td>
</tr>
<tr>
<td>Jugular venous distension</td>
<td></td>
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<tr>
<td>&gt; 6 cm H2O 2</td>
<td></td>
</tr>
<tr>
<td>&gt; 6 cm H2O plus edema or hepatomegaly</td>
<td>3</td>
</tr>
<tr>
<td>III. Chest X-ray</td>
<td></td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td></td>
</tr>
<tr>
<td>Basal</td>
<td>1</td>
</tr>
<tr>
<td>&gt; basal</td>
<td>2</td>
</tr>
<tr>
<td>Wheezing</td>
<td>3</td>
</tr>
<tr>
<td>Gallop rhythm S3</td>
<td>3</td>
</tr>
<tr>
<td>Kerley’s B lines</td>
<td>2</td>
</tr>
</tbody>
</table>
Outcomes of interest

Primary outcome: Overall mortality.

Secondary Outcomes: It is the proportion of patients undergoing interventions with proven benefits demonstrated by several indicators of quality of care (e.g., use of ACE inhibitors in target dose, use of beta-blockers in target dose), rehospitalization due to HF, length of hospital stay, cardiovascular mortality, sudden death, quality of life.

Clinical visit characteristics

Baseline Visit: assessment of HF etiology, cause of decompensation, physical and clinical examination, hemodynamic profile, risk factors, laboratory tests, imaging tests, medications for use at home and during hospitalization.

Hospital discharge visit: assessment of treatment indicators in HF patients, in-hospital cardiac procedures, current medications and imaging tests.

90-day follow-up visit: assessment of major cardiovascular events and current medications, laboratory and imaging tests.

180-day follow-up visit: assessment of major cardiovascular events and current medications, cardiological procedures, laboratory and imaging tests.

365-day follow-up visit: assessment of major cardiovascular events and current medications, cardiological procedures, laboratory and imaging tests.

Predicted statistical analysis

Quantitative variables will be expressed as mean and standard deviation in the presence of normal distribution or median and interquartile range in the presence of asymmetric distribution. Qualitative variables are expressed as absolute (number of patients) and relative (percentage) frequencies. Primary and secondary outcomes will be described by overall percentage, considering all the centers as well as by the percentage prescribed in each center and will be expressed by proportions and their respective 95% confidence intervals.

In case of great variability in the prescription, a variance-weighted mean will be generated in each center. For the regression models, the odds ratios [OR] (for logistic regression) or hazard ratio [HR] (for Cox proportional hazard regression), the corresponding standard error, the 95% confidence intervals and the associated p-values will be reported. P-values will be reported up to three decimal places. The two-tailed alpha significance level = 0.05 will be used in all tests. Residual analysis will provide an assessment of model assumptions for the regression analyses. The goodness-of-fit test of the models will be performed using appropriate Hosmer-Lemeshow Tests. All analyzes will be performed using Stata software, release 10.0 (StataCorp. 2007. College Station, TX: StataCorp LP).

Financial support

This Registry is owned by the Department of Heart Failure (DEIC) of 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 (IEP-HCor) was employed to operationalize the performance of this registry under the coordination of DEIC. The directive committees of this registry are described at the end of this article.

Data quality control

All centers will receive protocol and electronic system training in person or by phone and the coordination team will be available to answer any questions that might arise.

The study data quality control will be performed through several strategies, such as electronic CRF, central data checking, monitoring of the five centers with the highest numbers of enrolled patients.

Ethical aspects

The protocol was approved by the Research Ethics Committee (REC) of Hospital do Coração de São Paulo, SP (HCor), on the 1st of February, 2011, under registration number 144/2011 and subsequently, each participating center was also approved locally.

All patients will sign the Free and Informed Consent Form and the clinical trial will be carried out in accordance with the principles of the current revision of the Declaration of Helsinki and Good Clinical Practice Guidelines, in its latest version, and according to Resolution 196/96. Additionally, it will follow the local legal and regulatory requirements of Brazil.

Publication policy

All study presentations and/or result publications will be based on objective data, verified and validated beforehand, to ensure result accuracy.

The publication of the main findings will have authorship based on the contributions of the participating centers. All registry participants (researchers and committee members) have previously delegated the authority for the presentation and/or publication of the main results to DEIC/SBC. Any presentation or publication by any participant of the trial should mention the study and have the approval of DEIC / SBC.

Organization

The study will be carried out and coordinated by DEIC / Brazilian Society of Cardiology (SBC) and the Instituto de Ensino e Pesquisa do Hospital do Coração (IEP-HCor).


Participating Investigation Centers:

Hospital de Clínicas de Porto Alegre/UFRGS, Porto Alegre/RS: Dr. Luiz Eduardo Paim Rohde; Hospital São Lucas/PUCRS, Porto Alegre/RS: Dr. Luiz Claudio Danzmann; Hospital Universitário de Londrina/UEL, Londrina/PR: Dr. Manoel Fernandes Canesin; Hospital Regional Hans Dieter Schmidt, Joinville/SC: Dr. Conrado Roberto Hofmann Filho; Instituto de Ensino e Pesquisa do Hospital do Coração de São Paulo (IEP-HCor).
References


