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

Em nome dos Investigadores do BREATHE

Sociedade Brasileira de Cardiologia – Departamento de Insuficiência Cardíaca (DEIC)

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

Mailing Address: Denilson Albuquerque •
Rua Voluntários da Pátria 445 Sala 1402, Botafogo. Postal Code 24240-670, Rio de Janeiro - RJ - Brazil
E-mail: albuquerque@cardiol.br
Manuscript received March 01, 2013, revised March 06, 2013, accepted March 28, 2013.

DOI: 10.5935/abc.20130093

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.

Table 1 - Boston criteria for heart failure

Criterion	Score
I. History	
Dyspnea at rest	4
Orthopnea	4
Paroxysmal nocturnal dyspnea	3
Dyspnea with ambulation	2
Dyspnea with stair climbing	1
II. Physical Examination	
Heart rate alteration	1-2
91-110 bpm= 1	
> 110 bpm=2	
Jugular venous distension	
> 6 cm H2O 2	
> 6 cm H2O plus edema or hepatomegaly	3
Pulmonary rales	
Basal	1
> basal	2
Wheezing	3
Gallop rhythm S3	3
III. Chest X-ray	
Pulmonary alveolar edema	4
Interstitial alveolar edema	3
Bilateral pleural effusion	3
Cardiothoracic index > 0.50	3
Kerley's B lines	2

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.

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 with p-values < 0.001 reported as $p < 0.001$. 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, relaease 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).

Intellectual Property: DEIC/Sociedade Brasileira de Cardiologia.

Participating Investigation Centers:

Hospital de Clínicas de Porto Alegre/UFRGS, Porto Alegre/RS: Dr. Luis 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 Hoffmann Filho; Instituto

Dante Pazzanese de Cardiologia, São Paulo/SP: Dr. Abilio Augusto Fragata Filho; Total Cor, São Paulo/SP: Dr. Antonio Baruzzi; Hospital Auxiliar de Cotoxó/InCor/HCFMUSP, São Paulo/SP: Dr. Antonio Carlos Pereira-Barretto; Hospital das Clínicas/Faculdade de Medicina de Botucatu/Unesp, Botucatu/SP: Dra. Beatriz Bojikian Matsubara; Unidade de Miocardiopatia e Doenças da Aorta InCor/HCFMUSP, São Paulo/SP: Dr. Charles Mady; Hospital Copa D'Or, Rio de Janeiro/RJ: Dr. Denilson Campos de Albuquerque; Unidade de Insuficiência Cardíaca – InCor/HCFMUSP, São Paulo/SP: Dr. Edimar Alcides Bocchi; Hospital Rios D´Or, Rio de Janeiro/RJ: Dr. Elias Pimentel Gouvea; Instituto Dante Pazzanese de Cardiologia, São Paulo/SP: Dra. Elizabete Silva dos Santos; Hospital Lifecenter, Belo Horizonte/MG: Dr. Estevão Lanna Figueiredo; Hospital Escola Alvaro Alvim, Campos dos Goytacazes/RJ: Dr. Felipe Montes Pena; Hospital Vera Cruz, Belo Horizonte/MG: Dr. Fernando Carvalho Neuenschwander; Casa de Saúde São José, Rio de Janeiro/RJ: Dr. Gustavo Luiz Gouvea de Almeida Jr.; Hospital Universitário Antônio Pedro – UFF, Rio de Janeiro/RJ: Dr. Humberto Villacorta Jr.; Hospital Quinta D'Or, Rio de Janeiro/RJ: Dra. Jacqueline Sampaio; São Bernardo Apart Hospital, Colatina/ES: Dr. João Miguel de Malta Dantas; Instituto Nacional de Cardiologia, Rio de Janeiro/RJ: Dr. Marcelo Imbroinise Bittencourt; Hospital Universitário Clementino Fraga Filho/UFRJ, Rio de Janeiro/RJ: Dr. Marcelo Iorio Garcia; Santa Casa de Votuporanga, Votuporanga/SP: Dr. Mauro Esteves Hernandes; Hospital das Clínicas de Ribeirão Preto/ USP-FMRP, Ribeirão Preto/SP: Dr Marcus Vinícius Simões; Instituto do Coração/HCFMUSP, São Paulo/SP: Dr. Mucio Tavares de Oliveira Filho; Hospital Santa Paula, São Paulo/SP: Dr. Otávio Gebara; Hospital de Base/Famerp, São José do Rio Preto/SP: Dr. Paulo Roberto Nogueira; Santa Casa de São Paulo, São Paulo/SP: Dr. Renato Jorge Alves; Centro de Pesquisa da Clínica Médica e Cardiologia da Unifesp, São Paulo/SP: Dr. Renato Delascio Lopes; Hospital Barra D'Or, Rio de Janeiro/RJ: Dr. Ricardo Gusmão; Hospital Universitário Pedro Ernesto/UERJ, Rio de Janeiro/RJ: Dr. Ricardo Mourilhe Rocha; Hospital do Coração, São Paulo/SP: Dr. Ricardo Pavanello; Hospital do Coração de Goiás, Goiânia/GO: Dr. Aguinaldo Freitas Júnior; Hospital das Clínicas da UFMG, Belo Horizonte/MG: Dra. Maria da Consolação Vieira Moreira; Hospital Madre Teresa, Belo Horizonte/MG: Dr. Roberto Luiz Marino; Hospital das Clínicas UFG, Goiânia/GO: Dr. Salvador Rassi; Instituto de Cardiologia do Distrito Federal, Brasília/DF: Dr. Carlos V. Nascimento; Hospital Universitário São José/FCMMG, Belo Horizonte/MG: Dr. Sidney Araújo São José; Fundação Bahiana de Cardiologia, Salvador/BA: Dr. Alvaro Rabelo; São Lucas Médico Hospitalar, Aracaju/SE: Dr. Antonio Carlos Sobral Sousa; Instituto Cardiopulmonar, Salvador/BA: Dr. Eduardo Darzé; Fundação Beneficência Hospital de Cirurgia/Hospital do Coração, Aracaju/SE: Dr. Fabio Serra Silveira; Hospital Santa Izabel, Salvador/BA: Dr. Gilson Soares Feitosa; Hospital Espanhol, Salvador/BA: Dr. Fabio Villas-Boas; Hospital de Messejana, Fortaleza/CE: Dr. João David de Souza Neto; Hospital Universitário Presidente Dutra/UFMA, São Luís/MA: Dr. José Albuquerque de Figueiredo Neto; Hospital da Cidade, Salvador/BA: Dr. Marcelo Silveira Teixeira; Real Hospital Português de Beneficência em Pernambuco, Recife/PE: Dra. Silvia Marinho Martins; Hospital Universitário Professor Alberto Antunes HUPAA, Maceió/AL: Dra. Maria Alayde Mendonça da Silva; Hospital Universitário João de Barros Barreto – UFPA, Belém/PA: Dr. Eduardo Costa; Fundação Hospital de Clínicas Gaspar Vianna, Belém/PA: Dr. Helder José Lima Reis.

BREATHE Directive Committee: Denilson Campos de Albuquerque, João David de Souza Neto, Fernando Bacal, Otávio Berwanger, Hélio Penna Guimarães.

SBC Directive Committee: Fernando Bacal, Otávio Berwanger, Luiz Alberto Piva de Matos, Jadelson Andrade.

National Coordinator Center Team: Hélio Penna Guimarães, Karina Normilio da Silva, Katia Cristina Leite, Juliana Trench Ciampone, Sabrina Bernardez Pereira, Matheus de Oliveira Abreu.

Intellectual Property: DEIC/Sociedade Brasileira de Cardiologia.

References

1. Bocchi EA, Marcondes-Braga FG, Ayub-Ferreira SM, Rohde LE, Oliveira WA, Almeida DR, et al; Sociedade Brasileira de Cardiologia. III Diretriz brasileira de insuficiência cardíaca crônica. Arq Bras Cardiol. 2009;93(1 supl.1):1-71.
2. Bocchi EA, Marcondes-Braga FG, Bacal F, Ferraz AS, Albuquerque D, Rodrigues D, et al; Sociedade Brasileira de Cardiologia. Atualização da Diretriz brasileira de insuficiência cardíaca crônica - 2012. Arq Bras Cardiol. 2012;98(1 supl. 1):1-33.
3. American Heart Association. 2004 Heart Disease and Stroke Statistical update. [Accessed on 2004 Feb 02]. Available from: http://www.americanheart.org/statistics
4. Krumholz HM, Parent EM, Tu N, Vaccarino V, Wang Y, Radford MJ, et al. Readmission after hospitalization for congestive heart failure among Medicare beneficiaries. Arch Intern Med. 1997;157(1):99-104.
5. Montera MW, Almeida RA, Tinoco EM, Rocha RM, Moura LZ, Réa-Neto A, et al; Sociedade Brasileira de Cardiologia. II Diretriz brasileira de insuficiência cardíaca aguda. Arq Bras Cardiol. 2009;93(3 supl.3):1-65.
6. Albanesi Filho FA. Insuficiência cardíaca no Brasil. Arq Bras Cardiol. 1998;71(4):561-2.
7. Stewart S, Blue L, Capewell S, Horowitz JD, McMurray JJ. Poles apart, but are they the same? A comparative study of Australia and Scottish patients with chronic heart failure. Eur J Heart Fail. 2001;3(2):249-55.
8. Tavares LR, Victer H, Linhares JM, de Barros CM, Oliveira MV, Pacheco LC, et al. Epidemiologia da insuficiência cardíaca avançada em Niterói- Projeto EPICA Niterói. Arq Bras Cardiol. 2004;82(2):125-8, 121-4.

9. Tavares L, Silva GP, Pereira SB, Souza G, Pozam R, Victer H, et al. Co-morbidades e fatores de descompensação dos pacientes internados por insuficiência cardíaca descompesada na cidade de Niterói. In: 57 Congresso Brasileiro de Cardiologia, São Paulo, 21-24 set.; 2002. Arq Bras Cardiol. 2002;78(supl 4):35,79.

10. Marantz PR, Tobin JN, Wassertheil-Smoller S, Steingart RM, Wexler JP, Budner N, et al. The relationship between left ventricular systolic function and congestive heart failure diagnosed by clinical criteria. Circulation. 1988;77(3):607-12.