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ORIGINAL ARTICLE

Profile of Patients Hospitalized for Heart Failure in Tertiary Care Hospital

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Abstract

Background: Heart failure is a highly prevalent disease, responsible for many admissions and high mortality rates in our country. The treatment influences patient's mortality and quality of life.

Objective: To identify and compare the clinical and epidemiological survivor's and non-survivor's profiles and treatment of patients hospitalized with heart failure with the international literature.

Methods: Cross-sectional, retrospective study of 816 survivors and non-survivors with heart failure. All patients had their clinical and epidemiological, laboratory and echocardiographic data and treatment recorded.

Results: Most patients were in functional class III/IV. Mean age was 66.5 ± 13.8 years. Half of the patients were men and 88.3% were Caucasians. In-hospital mortality was 11,2%. Highly mortality was associated with old age, Caucasian ethnicity, high functional class, readmissions, prolonged hospitalization, presence of coronary artery disease, chronic atrial fibrillation, severe mitral regurgitation, restrictive diastolic dysfunction, renal dysfunction, and elevated natriuretic peptide levels, as well as with patients who had pulmonary embolism, acute coronary syndrome, pulmonary infection or required dialysis during hospitalization. The use of angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers at admission was significantly higher among survivors.

Conclusion: In-hospital mortality was high when compared to international averages, but it was similar to other Brazilian referral services. Numerous higher severity indicators were observed in the non-survivor group. (Int J Cardiovasc Sci. 2017;30(3):189-198)

Keywords: Heart Failure / mortality; Prevalence; Hospitalization; Restrospective Studies.

Introduction

Heart Failure (HF) is the common final pathway of most heart diseases, and is one of the major current clinical challenges in health.[1] Approximately 23 million individuals have HF, and 2 million new cases are diagnosed every year worldwide,[2] being the main cause of hospitalization in patients older than 60 years of age in Brazil.[3]

The prevalence of HF has been increasing in recent years worldwide,[4] and has become a serious public health problem.[3] The reasons for this include the aging of the population and therapeutic advances in the treatment of acute myocardial infarction (AMI), systemic arterial hypertension (SAH) and even HF, which increase survival and, consequently, promote an increase in its prevalence.[1,4]

In the United States, approximately 550,000 new cases are diagnosed annually, being the fifth most frequent cause of hospitalization.[5] In Brazil, according to data from the Unified Health System Department of Informatics (DATASUS), in 2012, approximately 238,000 hospitalizations occurred due to HF, with 26,000 deaths, accounting for a mortality rate of 9.5% during hospitalization.[6] The BREATHE (Brazilian

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Registry of Acute Heart Failure) trial identified an in-hospital mortality of 12.6%.[7]

Many comorbidities associated with HF worsen its prognosis. Atrial fibrillation (AF) affects approximately 20% to 30% of patients with acute HF.[8] The prevalence of renal failure in outpatients with HF may reach 29.6%,[9] being a marker of poor prognosis.[10] Moreover, hyponatremia, elevated levels of Type B Natriuretic Peptide (BNP), multiple hospitalizations, and associated lung disease are also predictors of poor prognosis.[11]

Currently, there are six classes of therapeutic measures capable of reducing all-cause mortality in HF patients, considered by global guidelines as class I indication measures.[12] However, in Brazil, medications introduced during the in-hospital phase often do not follow the current guidelines, which may contribute to the high morbidity, mortality, and economic costs of this syndrome.[7]

Despite the recent advances in the treatment of HF, the mortality among patients that are hospitalized with this syndrome in Brazil is still high. The objective of this study was to identify and compare the clinical-epidemiological profile and the treatment received by survivors and non-survivors hospitalized with heart failure to the international literature data.

Methods

This is an observational, cross-sectional, and retrospective study of patients with HF who survived or not after being admitted at Instituto de Cardiologia de Santa Catarina (ICSC) between June 2010 and May 2014.

Patients older than 18 years admitted during the study period according to the International Code of Diseases (ICD-10) compatible with HF, namely: I11, I13, I50 and I57, were included in the study. Patients with a clinical, echocardiographic and laboratory picture incompatible with this comorbidity, in addition to those whose medical records were incomplete, were excluded.

Patient selection was performed by checking the electronic medical record system (Micromed®). Aiming at a more adequate analysis, the patients were divided into two groups: Group I, of survivors and Group II, of non-survivors. The final sample analyzed 816 patients (724 survivors and 92 non-survivors), as shown in figure 1.

Data collection was performed using the Micromed® system in Laboratório Bioclínico São José and the ICSC Echocardiography Service. Clinical-demographic data, such as age, gender, ethnicity, functional class, presence of comorbidities, complications during hospitalization, mortality and prescribed medications were analyzed. The laboratory tests analyzed were urea, creatinine, sodium, potassium, BNP, and hemoglobin. Among the echocardiographic data, left ventricular ejection fraction (Simpson's method), left ventricular systolic diameter, left ventricular diastolic diameter, valvular heart disease, and left ventricular relaxation alterations were analyzed.

As the study was retrospective, the demographic data were collected by searching the Micromed® system. The patient's ethnicity was the self-declared one when the patient or the companion was registered at the institution. The existence of SAH and diabetes was obtained from data found in the electronic medical record (evolution data, previous diagnoses, and medication use).

This study was approved by the Research Ethics Committee (REC) of ICSC, under registration number 045475/2015.

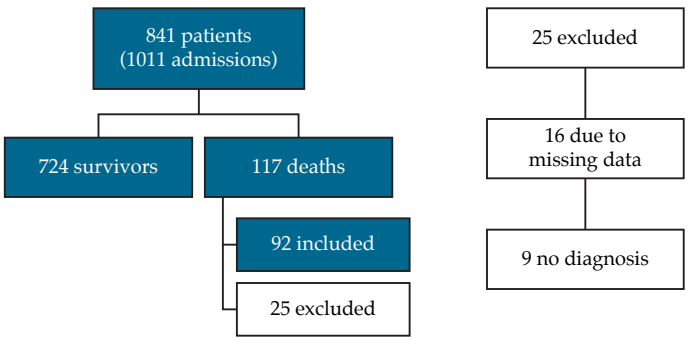

Figure 1 – *Patient selection flow chart*

Statistical Analysis

Data related to categorical variables are described by absolute numbers and percentages, and analyzed using Fisher's exact test or chi-square test.

Data related to continuous variables are described as mean and standard deviation. Intra- and intergroup comparisons of continuous variables, when applicable, were performed using the paired and /or unpaired T test, with *p* values < 0.05 being considered significant. Odds Ratio (OR) was calculated for mortality related to some variables. Data were analyzed using the Microsoft Excel® 2007 program and the GraphPad InStat® statistical analysis program.

Results

A total of 816 patients (971 admissions) were included in the study. There were 92 in-hospital deaths (11.2%). The mean age was 66.5 ± 13.8 years, being significantly older among non-surviving patients (p = 0.03). Males showed a higher prevalence in both groups (52.2% of survivors and 62% of non-survivors), with no statistically significant difference. Regarding ethnicity, most patients were Caucasians, but with a higher prevalence of Caucasians in the non-surviving group (p = 0.01) (Table 1).

When comparing patient groups, it was observed that the non-surviving patients had worse Functional Class (FC) according to the the New York Heart Association (NYHA) at hospital admission (p = 0.004), higher number of previous hospitalizations (p = 0.0001) and longer hospitalizations (p = 0.001).

Regarding the associated comorbidities, the non-survivors had more coronary artery disease (p = 0.01) and chronic AF (p = 0.0001). The presence of SAH, previous AMI, previous ischemic CVA, hypothyroidism, chronic obstructive pulmonary disease (COPD), diabetes and alcohol consumption did not show significant differences between the groups. There were more smokers among the survivors (p = 0.01).

Table 2 shows that, in the group of non-surviving patients, there were more complications during hospitalization, such as pulmonary thromboembolism (p = 0.05), unstable angina (p = 0.01), AMI (p = 0.001), AF (p = 0.0001), need for dialysis (p = 0.0001) and respiratory infection (p = 0.0001), which was the most frequent complication in both groups.

A total of 698 echocardiographic reports was evaluated. Although the ejection fraction and left ventricular systolic and diastolic diameters were similar between the groups, the restrictive diastolic pattern (p = 0.0001) and severe mitral regurgitation (p = 0.005) were more frequent in non-surviving patients, as shown in table 3.

The percentages of patients with BNP > 400 and >1000 pcg/mL were significantly higher among non-survivors (p = 0.03 and 0.02, respectively), according to table 4.

When comparing the results of laboratory tests at hospital admission between the groups of patients, a statistically significant difference was observed for renal dysfunction and hyperkalemia favoring the non-survivor group (Table 5).

The odds ratio (OR) for mortality are shown in Table 6. The findings that increased hospital mortality, among the laboratory variables collected at admission, were urea > 40 mg/dL (OR = 2.13), serum creatinine > 1.4 mg /dL (OR = 4.0), potassium >5.0 mEq/L (OR = 3.0) and BNP > 1000 pg /mL (OR = 2.0).

As for the drugs prescribed at hospital admission, the only statistically significant difference between the groups was Angiotensin-Converting Enzyme inhibitors / Angiotensin Receptor Blocker (ACEI/ARB), with a higher prevalence in the group of survivors (p = 0,04), but their doses showed no statistical difference between the groups (Table 7).

Discussion

HF is one of the leading causes of hospital admission in the world. Data from the literature show that approximately 1 to 2% of the adult population in developed countries has HF, with a higher prevalence (≥ 10%) in the elderly older than 70 years.[13] The American Heart Association has estimated a prevalence of 5.1 million individuals with HF only in the United States, from 2007 to 2012.[1]

The incidence of a first hospitalization for HF in a study carried out in France in 2009 was 0.14%.[14] A recent North-American study observed a reduction in the hospitalization rate for HF,[15] as well as another study carried out in Canada, which analyzed inpatients and outpatients from 1997 and 2007, showing a 32.7% decline in the incidence of HF cases.[16] In Brazil, a reduction in the number of hospitalizations due to HF from 2000 to 2007 was also identified, with a proportional decrease in all geographic regions.[1] The incidence and rates of hospital admission for HF have steadily declined

Table 1 – Basal characteristics of the sample

Clinical factors	Survivors	Non-survivors	p-value
Total of patients, n	724	92	-
Age, mean ± SD, in years	66.1 ± 13.8	70.4 ± 14.2	0.03
Male gender, n (%)	378 (52.2)	57 (62)	ns
Female gender, n (%)	346 (47.8)	35 (38)	ns
Caucasian ethnicity	632 (87.4)	89 (96.7)	0.01
Non-Caucasian ethnicity	53 (7.3)	2 (2.2)	0.01
Functional class, mean	3.4 ± 0.6	3.6 ± 0.5	0.004
Previous hospital admissions, mean ± SD	1.2 ± 0.6	1.7 ± 1.2	0.0001
Days per admission, mean ± SD	11.3 ± 11.5	15.5 ± 14.3	0.001
Diabetes, n (%)	223 (30.9)	26 (28.3)	ns
Arterial hypertension, n (%)	380 (52.5)	55 (59.8)	ns
Previous iCVA, n (%)	49 (6.8)	12 (14.1)	ns
CAD, n (%)	181 (25.1)	34 (38)	0.01
Previous AMI, n (%)	136 (18.9)	25 (27.2)	0.07
Chronic atrial fibrillation, n (%)	170 (23.6)	44 (48.9)	0.0001
AF (ACO), n (%)	117 (16.2)	23 (25)	0.03
Hypothyroidism, n (%)	68 (9.5)	11 (12)	ns
COPD, n (%)	89 (12.3)	13 (15.2)	ns
Smoking, n (%)	217 (30)	13 (15.2)	0.01
Alcohol consumption, n (%)	60 (8.3)	4 (4.3)	ns

SD: standard deviation; Ns: nonsignificant; iCVA: ischemic cerebrovascular accident; CAD: coronary artery disease; AMI: acute myocardial infarction; AF (ACO): atrial fibrillation in anticoagulation; COPD: chronic obstructive pulmonary disease.

since the 1990s in several countries worldwide,[17,18] and this seems to reflect a real decrease in HF, which can be explained by lower rates of smoking, better SAH control and greater use of reperfusion therapies, such as primary angioplasty.[19]

In the present study, the rate of in-hospital mortality for HF (11.2%) was much higher than that found in studies carried out in other countries,[14,20,21] such as the ICARO registry, in Chile,[22] but it agrees with recent Brazilian studies, such as the BREATHE trial and another performed in the state of São Paulo by Instituto do Coração (InCor), in which the mortality rates were 12.6% and 10%, respectively.[7,23]

Comparing data from the studied population with those from DATASUS,[24] we observed lower mortality rates and length of hospital stay in our institution when compared to two cardiology referral centers in the country, InCor and Instituto Dante Pazzanese. It was also verified that the longer the hospital length of stay, the higher the in-hospital mortality. The Japanese trial ATTEND, which had a mean hospitalization period of 30 days, reported that most sudden cardiac deaths occur within 14 days of hospitalization.[21] Thus, a hospital length of stay of just a few days may be too short to assess mortality.

The mean age of the patients was 66.5 years, that is, similar to the one in the BREATHE trial,[7] but lower than

Table 2 – Events observed in the assessed sample

Complications	Survivors n (%)	Non-survivors n (%)	p-value
Pulmonary thromboembolism	1 (0.1)	3 (3.3)	0.05
Unstable angina	14 (1.9)	6 (6.5)	0.01
Acute myocardial infarction	11 (1.5)	9 (9.8)	0.001
Bradycardia	2 (0.3)	2 (2.2)	ns
Atrial fibrillation	15 (2.1)	26 (28.3)	0.0001
Respiratory infection	156 (21.5)	50 (54.3)	0.0001
Dialysis	2 (0.3)	16 (17.4)	0.0001

ns: non-significant.

Table 3 – Echocardiographic data of patients in the sample

Echocardiographic data	Survivors	Non-survivors	p-value
FEVE, %	39.5 ± 18.9%	39.0 ± 20.0%	ns
LVSD, mm	40.3 ± 14	35.9 ± 12.4	ns
LVDD, mm	57.5 ± 11	58.9 ± 11.8	ns
Diastolic dysfunction grade I (relaxation), %	32.2	17.2	ns
Diastolic dysfunction grade II (pseudonormal), %	29.4	13.8	ns
Diastolic dysfunction grade III (restrictive), %	38.4	69	0.0001
Severe mitral regurgitation, %	6	20	0.005
Severe tricuspid regurgitation, %	10.6	17.8	ns

LVEF: left ventricular ejection fraction; ns: nonsignificant; LVSD: left ventricular systolic diameter; LVDD: left ventricular diastolic diameter.

that of most international studies (69 to 77 years).[16,20-22,25,26] This difference may be related to an earlier manifestation of heart diseases in Brazil, less effective treatment of diseases that lead to HF onset, nonadherence to the recommended treatment or even only represent differences in the studied populations. Another Brazilian study, carried out in a private hospital in Rio de Janeiro, showed an older age group (72.5 years).[27]

Still regarding age, as expected, higher mortality rates were observed among older patients, as shown in the Framingham Heart Study,[28] and confirmed by other trials.[1,14,20,21,26,29]

Although there was no statistically significant difference, there was a predominance of males among non-survivors (62%), being in according to the literature, which reports that HF prognosis is worse in men.[14,28]

The predominance of the Caucasian ethnic group (survivors: 87.4%, non-survivors: 96.7%) can be explained by the demographic difference in our country, with a higher prevalence of Caucasians in the South and Southeast regions;[7] however, the black ethnicity was more prevalent among the survivors (7.3% vs. 2.2%, p = 0.01). The effect of ethnicity on HF prognosis is uncertain, as different studies have shown

Table 4 – Values of type B natriuretic peptide (BNP) in the sample

BNP values (pcg/mL)	Survivors (%)	Non-survivors (%)	p-value
< 100	1.0	1.7	ns
100-400	6.0	10.0	ns
> 400	53.0	88.3	0.03
> 1.000	35.0	58.3	0.02

ns: non-significant.

Table 5 – Laboratory results at hospital admission

Laboratory tests	Survivors	Non-survivors	p-value
Urea, mg/dL	61.6	91.1	0.0001
Creatinine, mg/dL	1.40	1.90	0.0001
Sodium, mEq/L	135.8	134.4	ns
Potassium, mEq/L	4.4	5.2	0.0001
Hemoglobin, mg/dL	12.5	12.0	ns

ns: non-significant.

Table 6 – Laboratory tests – odds ratio (OR) for mortality

Laboratory tests at admission	n	OR (CI)	p-value
Urea > 40 mg/dL	376	2.13 (1.3-3.3)	0.001
Creatinine > 1,4 mg/dL	233	4 (1.8-9)	0.0006
Potassium > 5mEq/L	74	3 (1.7-5.4)	0.0001
BNP > 1,000 pg/mL	191	2 (1.1-3.5)	0.01

CI: confidence interval; BNP: type B natriuretic peptide.

divergent results. Dries et al.,[30] in a study comparing HF evolution between Caucasians and blacks, identified higher mortality among blacks; Rathore et al.[31] showed lower mortality among blacks hospitalized for HF; and Mathew et al.[32] showed no difference in mortality between the ethnicities.

The comparative analysis between survivors and non-survivors confirmed some findings of poor prognosis in HF, including elevated NYHA-FC,[1,5,13,25,27,29,33] prolonged length of hospital stay,[21,23] higher number of previous hospitalizations,[1,5,21,29,33] hyperkalemia, elevated BNP,[1,5,33] presence of comorbidities such as coronary artery

Table 7 – Drug treatment instituted at hospital admission

Medication	Survivors (%)	Non-survivors (%)	p-value
Furosemide	81,8	87	ns
Hydrochlorothiazide	4,5	1,1	ns
Spironolactone	56,1	50	ns
Digoxin	36,1	43,5	ns
Nitrate	31,7	23,9	ns
ASA	49,1	50	ns
Hydralazine	6,8	6,5	ns
Amiodarone	6,7	8,7	ns
Beta-blocker	65,8	55,4	0,06
Carvedilol, mean ± SD	14,7 ± 13 mg	12,7 ± 9,3 mg	ns
ACEI / ARB	79,6	62	0,004
Enalapril, mean ± SD	18,2 ± 8,1 mg	17,1 ± 8,2 mg	ns

ns: non-significant; ASA: acetylsalicylic acid; SD: standard deviation; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin-receptor blocker.

disease, chronic AF,[1,5,33] in addition to severe mitral regurgitation[1,33] and diastolic dysfunction with restrictive pattern.[1] The occurrence of acute coronary syndrome,[5,13] pulmonary thromboembolism,[3] respiratory infection,[3] renal dysfunction and / or need for dialysis [1,3,5,13,20,26,29,33,34] during hospitalization is also associated with higher mortality. Contrary to what has been described in the literature, there were fewer smokers among non-survivors. This may be due to a specific feature of this group or to a selection bias. Differences regarding the presence of diabetes,[1,13,29,33] previous AMI,[1] previous stroke,[1] anemia,[1,5,13,33] hyponatremia,[1,27] COPD,[13,33] reduced left ventricular ejection fraction,[1,5,23,33] and severe tricuspid regurgitation,[1] although well established as factors of poor prognosis, were not significant in this study.

The rate of patients who had at least one hospital readmission during the study period was 12%. The ESC-HF Pilot study (Heart Failure Pilot Survey) found a one-year rehospitalization rate of 24.8%.[29] The 60-to-90 day-rehospitalization rate in the OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure) trial was 29.9% in patients with systolic dysfunction and 29.2% in those with preserved ejection fraction.[35] The ADHERE trial indicates that rehospitalization may reach 50% after hospital discharge.[20] Our findings of a lower percentage of hospital readmission may be influenced by the absence of follow-up after hospital discharge, which would identify readmissions at other institutions and death after discharge.

Several studies have shown the correlation between BNP levels and HF severity.[1,13,25,28,29,33] The ADHERE trial showed that BNP levels at admission were a marker of mortality, [20] as well as a rehospitalization predictor.[28]

As demonstrated in our series, AF is the most frequent arrhythmia in patients with HF,[1,33] and its onset may determine symptom worsening, higher risk of thromboembolism and a worse prognosis. Potential precipitating factors (electrolyte changes, hyperthyroidism, alcohol consumption, mitral valvulopathy, acute ischemia, infection, and uncontrolled hypertension) should be investigated and, if possible, corrected.[1]

As in our study, the OPTIMIZE-HF trial identified a clinical factor that caused HF in approximately 60% of the patients, with pulmonary processes, myocardial ischemia and arrhythmias being the most common ones.[35] Renal dysfunction is a frequent finding among those hospitalized for HF, and approximately 66% of HF patients have some degree of impaired renal function,

which would be one of the main predictors of in-hospital mortality among HF patients.[34] Evidence shows that patients with COPD have a significantly higher risk of congestive HF, and that acute exacerbations of COPD may lead to HF worsening.[25]

Regarding the treatment of systolic HF, guidelines recommend the prescription of ACEI / ARB, followed by the introduction of a beta-blocker. It is also recommended that an aldosterone antagonist be introduced in the presence of an ejection fraction < 35%, if the patient maintains FC II to IV. Diuretics are recommended only to reduce congestion.[5,33]

The percentage of patients receiving ACEI / ARB, beta-blockers and spironolactone, which are measures that decrease HF mortality, was markedly higher than in other studies (Long-Term Registry ESC-HF, ICARO and BREATHE).[7,22,36] Additionally, the use of ACEI/ARB at hospital admission was significantly higher among survivors. However, although the literature shows an increase in HF survival with the use of beta-blockers and/or ACEI/ARB,[1,33] it is probable that non-surviving patients had a more severe clinical and hemodynamic presentation that did not allow the use of these drugs.

In Brazil, there are still considerable failures in the treatment of HF, which may contribute to high morbidity, mortality, and economic costs of this pathology.[7] The analysis of the Euro Heart Survey showed that beta-blockers and ACEI were prescribed to less than half of the eligible patients, and the prescribed doses were below those proven to be effective.[37] The IMPROVE-HF (Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting) trial showed that the addition of each evidence-based therapy is associated with a significant reduction in mortality risk at 1 year.[38]

Limitations

Retrospective data collection, lack of standardization when recording the information in the medical records, possible underreporting of data and the absence of follow-up of patients after hospital discharge can be mentioned as limitations. The use of vasoactive drugs during hospitalization was not addressed, making it impossible to analyze these data.

Conclusion

The results of this study may help improve the management of patients with heart failure, by drawing attention to subgroups with a higher mortality risk, such as patients with older age, previous hospitalizations, high functional class, presence of coronary artery disease, atrial fibrillation, severe mitral regurgitation, renal dysfunction, and/or elevated B-type natriuretic peptide, those with acute coronary syndrome, respiratory infection or need for dialysis during hospitalization.

Patient drug treatment followed the recommended procedures in current heart failure therapy guidelines. The unfavorable clinical profile may have limited the applicability of some of the therapeutic measures considered to be decisive in the prognosis of this syndrome. Despite optimized drug therapy, in-hospital mortality remained high, as it was observed in other Brazilian referral services, when compared to the international average.

Author contributions

Conception and design of the research: Poffo MR, Assis AV. Acquisition of data: Poffo MR, Bald AP, Fracasso M, Londero Filho OM, Alves SMM. Analysis and interpretation of the data: Poffo MR, Assis AV, Fracasso M, Londero Filho OM, Alves SMM. Statistical analysis: Assis AV. Writing of the manuscript: Poffo MR, Bald AP, Schmitt CB, Fracasso M, Londero Filho OM, Alves SMM. Critical revision of the manuscript for intellectual content: Poffo MR, Assis AV, Schmitt CB, Fracasso M. Configuration of Figures and Tables: Alves Filho NR.

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Study Association

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