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Article

Understanding Mortality in Acute Heart Failure: A Retrospective Study in Santiago, Chile

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Abstract: Backround: Acute heart failure (AHF) is a severe condition with high mortality, with variable data depending on the region. The objective of the study was to describe its mortality in a high-complexity hospital in Santiago, Chile, and the associated factors. Methods: A retrospective study was conducted with 184 patients admitted between 2017 and 2019, aged over 18, and diagnosed with AHF by a cardiology resident. Clinical, sociodemographic, and therapeutic variables were recorded. Regression models and descriptive statistics were used. Results: The 12month mortality rate was 22.7%, of which 35% were due to cardiac causes. The associated risk factors were age (HR 2.28, 95%CI: 1.22-4.23; p<0.05), plasma creatinine at admission (OR 1.87, 95%CI: 1.16-3.40; p<0.05), ProBNP over 4140 pg/mL (RR 2.0, 95%CI: 1.02-4.13; p<0.05), chronic kidney disease (OR 5.44, 95%CI: 1.5-9.3; p<0.05), and atrial fibrillation or flutter (OR 2.74, 95%CI: 1.30-5.76; p<0.05). The use of angiotensin-converting enzyme inhibitors (ACEi) and beta-blockers (BB) at discharge were protective for mortality (OR 0.45, 95%CI: 0.21-0.94; p<0.05 and OR 0.27, 95%CI: 0.09-0.79; p<0.05, respectively), as was a ProBNP level below 3220 pg/mL (RR 0.54, 95%CI: 0.28-0.96; p<0.05). Conclusions: AHF is associated with high one-year mortality in Chile, with significant relevance of patient history and admission tests. The use of ACEi and BB at discharge was associated with improved survival, highlighting the importance of optimized management during hospitalization and at discharge to improve prognosis.

Keywords: Heart Failure; Congestive Heart Failure; Mortality; Acute Heart Failure; Latin América

1. Introduction

Heart failure (HF) is a syndrome characterized by symptoms and signs caused by structural and/or functional cardiac abnormalities, corroborated by elevated levels of natriuretic peptides and evidence of pulmonary or systemic congestion [12]. HF affects 64.3 million people worldwide, representing 1% of the global population. Ischemic heart disease is the most frequent etiology, accounting for 26.5% of cases [3]. The 30-day mortality rate is estimated at 2%, while the five-year mortality rate can reach 50–75% [4].

HF generates high healthcare costs. A systematic review, which included 16 international studies between 2004 and 2016, estimated that the lifetime medical care cost for HF is \$126,819 per patient [5]. In Chile, the situation is similar; in 2014, 1% of all hospital discharges were due to HF, according to the Department of Epidemiology and Health Information (DEIS) [6].

HF can be classified in multiple ways, such as by ejection fraction, affected ventricle, or underlying etiology. However, a key classification is based on the urgency of medical attention required: acute or chronic HF. Acute heart failure (AHF) is defined by the need for urgent medical attention and hospitalization to initiate or optimize treatment [7].

The European Society of Cardiology reports that one-year mortality for AHF patients is 23.6%, while the combined outcome of death or hospitalization within one year of discharge is 40.1% [8]. The rehospitalization rate is up to 25% within 30 days post-discharge [9] and 35–40% at one year [10].

Historically, the main factors associated with mortality in AHF were systolic blood pressure <115 mmHg, blood urea nitrogen >43 mg/dL, and plasma creatinine >2.75 mg/dL [10]. Recently, additional risk factors include male gender, age >80 years, dementia, cancer, atrial fibrillation (AF), kidney injury, severe anemia, and non-use of beta-blockers. Other factors, such as NT-ProBNP and QRS duration, are also predictive of mortality [11], as are echocardiographic parameters like the E/e' ratio and global longitudinal strain [12].

In Chile, there are no specific studies evaluating mortality or risk factors associated with AHF, with most data being extrapolated from international literature.

The primary objective of this study was to describe the mortality of patients hospitalized for AHF at a high-complexity hospital in Santiago, Chile, within 12 months of admission.

Secondary objectives included characterizing the cohort in terms of epidemiology, treatments administered during hospitalization, and discharge prescriptions.

2. Materials and Methods

2.1 Population and Study Design

The University of Chile's Clinical Hospital is a high-complexity university hospital located in the northern area of Santiago, the capital of Chile. Its cardiovascular center manages highly complex cardiac diseases, including surgical, percutaneous, electrophysiological, and clinical conditions, in patients with both public and private health insurance, sourced from the hospital's own geographic area as well as from other regions of the city and country. A retrospective cohort study was conducted based on records of admissions to the coronary intensive care unit with a diagnosis of AHF between 2017 and 2019. Clinical, social, cardiological, and therapeutic variables were considered, along with respective death records. The study was approved by both the hospital's Clinical Research Support Office and its Scientific Ethics Committee.

2.2. Inclusion and Exclusion Criteria

The main inclusion criterion was the diagnosis of AHF upon admission to the coronary care unit, established by a cardiologist, with patients aged over 18 years. Exclusion criteria included the presence of concomitant severe non-cardiological respiratory conditions (e.g., pneumonia, interstitial lung disease, chronic obstructive pulmonary disease), a condition with a life expectancy of less than one year (e.g., advanced cancer, terminal HF), or death due to SARS-COV2.

2.3. Data Extraction and Variable Recording

Data extraction was performed by the research team from electronic medical records, following strict confidentiality and quality protocols to ensure accuracy and avoid bias. Epidemiological, clinical, cardiological, and therapeutic variables were recorded. Statistical analysis was conducted using R Studio.

2.4. Statistical Analysis

Data cleaning and identification of missing values (NAs) were performed initially. Variables with a significant proportion of missing values (≥50%) were excluded from the analysis due to the potential bias. For variables with less than 50% missing values, imputation was conducted using linear regression for continuous variables and classification for categorical ones. Descriptive statistics were calculated, and inferential analysis was carried out using logistic, logarithmic, or Poisson regression, selecting the best-fit model with the lowest Akaike Information Criterion (AIC). Association measures were calculated (Odds Ratio -OR-, Risk Ratio -RR-, or Hazard Ratio -HR-) according to the type of regression.

3. Results

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A total of 184 patients were included, with a mean age of 72.5 years, 56% male, and a median follow-up of 12 months (Other characteristics are in Table 1). The overall mortality rate at 12 months was 22.7%, with 35% of deaths attributed to cardiac causes. Significant risk factors included advanced age (HR 2.28, 95% CI: 1.22-4.23; p<0.05), elevated plasma creatinine at admission (OR 1.87, 95% CI: 1.16-3.40; p<0.05), and NT-ProBNP levels exceeding 4140 pg/mL (RR 2.0, 95% CI: 1.02-4.13; p<0.05). Additional factors such as chronic kidney disease (OR 5.44, 95% CI: 1.5-9.3; p<0.05), atrial fibrillation/flutter (OR 2.74, 95% CI: 1.30-5.76; p<0.05), and higher daily doses of furosemide (OR 1.03, 95% CI: 1.01-1.04) were also associated with increased mortality.

Table 1. Baseline Characteristics of the Study Population

Group	Variable	Value
Demography and comorbilities	Male gender	59,05%
	Age* (years)	69.46
	Private/Public Insurance	40%/60%
	Hypertension	82.86%
	Diabetes Mellitus	29.9%
Medical History	Atrial Fibrilation or Flutter	37.1%
	Chronic Kidney Disease	12.9%
	Hemodyalisis	5%
	Body Mass Index*	29.48 kg/m ²
	Reduced LVEF ¹	72.12%
	Severe Mitral Regurgitation	23.81%
	Severe Aortic Regurgitation	3.81%
	Severe Aortic Stenosis	1.9%
	Device ²	14.29%
	Prior CABG³	3.81%
In-Hospital Values	APACHE-II	13.7 pts
	Serum Creatinine*	1.33 mg/dL
	Serum Sodium*	137.54 mEq/L
	Ultrasensitive Troponin I*	2.19 ng/dL
	NT-ProBNP*	10447.45 pg/mL
	HbA1C*	6.72 (%)
	Furosemide daily dose*	47.66 mg
	24h Diuresis*	2149.71 cc
	Ultrafiltration	0.95%
	Use of second diuretic	47.3%

¹ Left Ventricular Ejection Fraction. ²Pacemaker, Resincronization, Defibrilation. ³Coronary Artery Bypass Grafting. ^{*}Average.

Conversely, protective factors included ACEi and BB use at discharge (OR 0.45, 95% CI: 0.21-0.94; p<0.05, and OR 0.27, 95% CI: 0.09-0.79, respectively), NT-ProBNP levels below 3220 pg/mL (RR 0.54, 95% CI: 0.28-0.96; p<0.05), eunatremia (OR 0.91, 95% CI: 0.84-0.97), and high diuresis within the first 24 hours (OR 0.98, 95% CI: 0.97-0.99). Figure 1 summarizes the association measures derived from the univariate regression models.

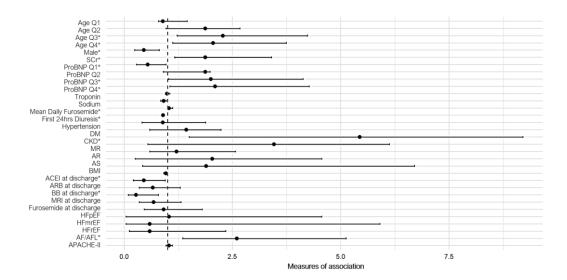


Figure 1. Forest plot of association measures from univariate regression models for 12m-mortality. *: Statistically significant. Q: Quartile, DM: Diabetes Mellitus, MR: Mitral Regurgitation, AR: Aortic regurgitation, AS: Aortic stenosis, BMI: Body Mass Index, ARB: Angiotensin Receptor Blocker, MRI: Mineralocorticoid Receptor Inhibitor, HFpEF: Heart failure with preserved ejection fraction, HFmrEF: Heart failure with middle reduced ejection fraction, HFrEF: Heart failure with reduce ejection fraction.

3.2. Figures, Tables and Schemes

As previously mentioned, age showed a direct association with mortality, with the effect being more pronounced in the upper quartiles. When stratifying each age quartile by gender, women consistently demonstrated a higher mean age compared to men (ANOVA p<0.05, with significant differences confirmed by Tukey post hoc analysis). This finding suggests that the observed protective effect of male gender is likely attributable to differences in age distribution between the groups, rather than an intrinsic protective role of sex. These results are illustrated in Figure 2.

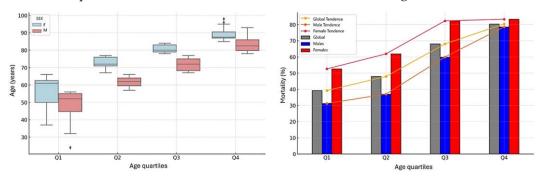


Figure 2. A: Comparison of the mean age between men (M) and women (F) in their respective quartiles. Error bars are shown. B: Comparison of mortality by age quartiles overall and by gender, with tendence lines.

4. Discussion

Our findings align with studies and registries conducted in the United States and Europe. For instance, the ADHERE registry reported a 12-month mortality rate of 36%, compared to the lower but still significant rate observed in our cohort [13, 14]. In Latin America, mortality rates show considerable variability: Venezuela reported a 3-month mortality of 22.7% [15], Argentina observed an 18% 30-day mortality due to combined causes [16], and Brazil documented a one-year mortality of 28.9% [17]. The scarcity of specific data on AHF in other Latin American countries underscores the heterogeneity in regional evidence and the need for more robust datasets.

Key predictors of mortality, including NT-ProBNP levels, advanced age, atrial fibrillation/flutter, and chronic kidney disease, were consistent with previous studies. Elevated NT-ProBNP levels (>5582 pg/mL) have been associated with a higher risk of death (HR 1.6) [18], as have age ≥80 years (HR 1.61), dementia (HR 1.08), and atrial fibrillation (HR 1.71) [10]. Similarly, hyponatremia and elevated plasma creatinine were linked to increased mortality, while lower NT-ProBNP levels were protective.

Health insurance (public vs. private) did not significantly influence 12- or 60-month mortality in our cohort. While patients with public insurance were, on average, older by eight years, no notable differences in comorbidities or disease severity were found. This contrasts with Japanese studies showing public insurance as an independent risk factor for mortality (HR 2.15) [20]. A systematic review by Enard similarly reported mixed results, highlighting the influence of geographic and population contexts [21]. In Chile, health insurance appears unrelated to long-term AHF outcomes.

The COVID-19 pandemic introduced challenges in AHF management, with reported doubling of 30-day mortality and reduced hospitalizations, likely contributing to higher in-hospital mortality [22]. These changes emphasize the need for adaptive strategies in acute care.

Regarding prognostic tools, the APACHE II score is widely used in intensive care units but shows variable correlations with outcomes in critically ill cardiology patients. While models like APACHE-HF address cardiogenic shock, no scoring systems specifically tailored to AHF exist [23]. In our study, APACHE II was used solely for classification and characterization, showing no significant association with mortality.

Treatment guidelines emphasize early diuretic response, with the European Society of Cardiology recommending 3 to 5 liters of diuresis within 24 hours [24]. Poor diuretic response correlates with higher 180-day mortality (HR 1.24) [25], and rapid response has been linked to reduced 30-day mortality [26]. However, the relationship between intravenous diuretic doses and mortality remains unclear. Sub-analyses from ADHERE suggested that higher diuretic doses increase in-hospital mortality, while greater diuresis improves symptoms and reduces rehospitalization, as shown in the ROSE-AHF study [27, 28]. Our findings indicate that higher diuretic doses were associated with increased mortality, whereas higher diuresis was protective. This highlights the complexity of diuretic response, warranting alternative definitions based on furosemide mg/kg and achieved diuresis.

5. Conclusions

AHF presents a significant and high mortality rate one year after discharge in Chile. Mortality was associated with age, NT-ProBNP levels, plasma sodium and creatinine at admission, as well as a history of CKD and AF/FLA. Additionally, the average dose of furosemide administered and diuresis during the first 24 hours were significantly related to outcomes. Notably, health insurance type (public or private) was not associated with mortality.

This study highlights key factors linked to mortality in AHF at a center in Santiago, Chile, providing valuable insights into their relative contributions. Furthermore, it enabled the development of predictive models that may improve patient stratification upon admission.

It is important to acknowledge that the study included a relatively small number of patients, which might limit how well these results apply to larger populations or different healthcare settings. Despite this, the findings provide valuable information and are consistent with international studies, which adds confidence to their relevance.

Prospective studies are needed to address potential biases and incorporate contemporary cardiological variables of interest, such as urinary sodium, quantitative LVEF, additional biomarkers, and social determinants of health. Such research is essential to develop strategies for optimizing inpatient and outpatient care for AHF patients6. Patents

Author Contributions: For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Conceptualization, X.X. and Y.Y.; methodology, X.X.; software, X.X.; validation, X.X., Y.Y. and Z.Z.; formal analysis, X.X.; investigation, X.X.; resources, X.X.; data curation, X.X.; writing—original draft preparation, X.X.; writing—review and editing, X.X.; visualization, X.X.; supervision, X.X.; project administration, X.X.; funding acquisition, Y.Y. All authors have

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read and agreed to the published version of the manuscript." Please turn to the <u>CRediT taxonomy</u> for the term explanation. Authorship must be limited to those who have contributed substantially to the work reported.

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Institutional Review Board Statement: This research was reviewed and approved by the Ethics Committee of the Clinical Hospital of the University of Chile, under Resolution Number 59, issued during the session held on October 8, 2024.

Informed Consent Statement: This was a retrospective study with anonymized data, conducted under a confidentiality agreement and in compliance with Chilean legislation on human research, so informed consent was not required. Nonetheless, all collected data were handled with the highest level of confidentiality, without recording any personal identifiers.

Data Availability Statement: Chilean legislation stipulates that patient information collected exclusively for research purposes cannot be shared. Additionally, the Ethics Committee only authorized access to this information for research objectives. Therefore, the authors are unable to share the data.

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Conflicts of Interest: The authors declare no conflicts of interest.

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