Brazilian Journal of Clinical Medicine and Review

PCAA PUBLICAÇÕES CIENTÍFICAS DE ACESSO ABERTO

Review

Mortality of Individuals with Acute Heart Failure Admitted to the Intensive Care Unit: Integrative Literature Review

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Abstract: Acute heart failure occurs when urgent medical intervention is needed due to signs and symptoms resulting from functional and structural abnormalities of the heart. It is one of the most common causes of hospitalization in Brazil, with a high mortality rate. Thus, this article aims to highlight the aspects related to the mortality of this disease and the factors leading to unfavorable outcomes. An integrative literature review was conducted using the PubMed, Lilacs, and Scielo platforms, covering publications from 2014 to 2024. The search descriptors used were "ICU," "heart failure," and "mortality," combined to refine the search. In total, seven articles were selected at the end of the search stages. Regarding the country of origin of the studies, 28.6% were conducted in Japan, followed by Slovenia, the United States of America, Turkey, Spain, and France, each contributing 14.3%. Evidence points to predictors that increase the chance of mortality after hospitalization, such as male sex, myocardial infarction, chronic kidney disease, and cancer. Other factors that increase the likelihood of in-hospital mortality include stroke and pneumonia. The studies indicate a high admission rate of acute heart failure exacerbations in ICUs and the significant costs this imposes on the healthcare system. Additionally, further aspects related to mortality were observed throughout the research, such as $PaCO_2$ levels, with lower admission levels being associated with higher mortality risk, prognostic scoring systems like NEWS-L, and non-invasive ventilation (NIV), which seemingly does not alter all-cause mortality within 30 days and may be associated with longer hospitalizations, with some exceptions. In conclusion, the predictors that influence and increase the chances of heart failure mortality are evident. Furthermore, the high costs this disease may impose on the healthcare system can be understood if uncertain indications for intensive care persist.

Keywords: Heart failure, Mortality, Neutrophil-to-Lymphocyte Ratio.

Citation: Freitas LNS, Borges LC, Cachapuz ALM, Manfrin IA. Mortality of Individuals with Acute Heart Failure Admitted to the Intensive Care Unit: Integrative Literature Review. Brazilian Journal of Clinical Medicine and Review. 2025:Jan-Dec;03(1):bjcmr17.

https://doi.org/10.52600/2763-583X.bjcmr.2025.3.1.bjcmr17

Received: 4 July 2024
Accept: 6 September 2024
Published: 18 September 2024

1. Introduction

Heart failure occurs when the heart is unable to pump blood adequately to the body's tissues and meet metabolic demands under normal pressure conditions. This can be explained by functional and structural abnormalities that lead to a decrease in cardiac output and filling pressure abnormalities. When there is an abnormality in systolic function, stroke volume is reduced, and when diastolic function is impaired, ventricular filling is compromised. Acute heart failure is characterized by rapid or gradual changes in signs and symptoms that require urgent medical intervention. To classify it, the clinical and hemodynamic aspects must be analyzed, relating to low output and congestion, which are classified as: warm and dry, warm and wet, cold and dry, and cold and wet. Additionally, the disease progression time is divided into a new acute episode or a chronic condition that has acutely worsened. Finally, there are types of clinical syndromes (acute pulmonary edema, cardiogenic shock, congestive heart failure, and left

ventricular failure) and degrees of ventricular dysfunction: preserved ejection fraction (> 50%), intermediate (> 40%), and reduced (< 40%) [1].

Acute heart failure is one of the most common causes of hospitalization in Brazil. According to Arruda et al. [2], from 2008 to 2018, more than 2 million hospitalizations and over 252,000 deaths were recorded. In 2019, heart failure caused 12.9% of hospital admissions (approximately 196,271), with a mortality rate of 11.48 deaths per 100,000 inhabitants. Its high prevalence in the population results in a significant cost to the healthcare system, reaching 3 billion reais. The increase in incidence is associated with therapeutic advances in the treatment of acute myocardial infarction, arterial hypertension, and heart failure itself, as increased survival leads to more frequent hospital admissions [3]. The BREATHE study, conducted by Albuquerque et al. [4], was the first Brazilian registry of acute heart failure in Brazil. It included 1,263 patients from 51 centers in different regions of Brazil in 2011 and 2012.

One of the results revealed that elderly patients, an important part of the sample, predominated in the South and Southeast regions. The most prominent etiologies were: ischemic (30.1%), hypertensive (20.3%), idiopathic dilated (15%), valvular (12%), and Chagas disease (11%). Regarding the hemodynamic clinical profile, the most admitted cases in hospitals were warm and wet, accounting for 67.4% of cases. The evaluation of heart failure decompensation in this study showed that its main causes were poor medication adherence (30%), infections (23%), and inadequate water and sodium intake (9%). The mortality rate found in the BREATHE study was more than twice that observed in American and European registries.

In Brazil, decompensated heart failure is the leading cause of hospitalization among cardiovascular diseases. In this context, it is important to analyze clinical, laboratory, and hemodynamic parameters to estimate prognosis and reduce the number of deaths. Clinically, profiles with unfavorable prognoses include patients with Chagas heart disease, severe congestion refractory to treatment, and persistent third heart sound [5].

Among routine tests requested for the evaluation of heart failure patients, factors indicating a worse prognosis include elevated creatinine and urea, anemia, hypoalbuminemia, hyperuricemia, and hyponatremia. Moreover, elevated biomarkers in heart failure patients are directly related to the severity of the disease, such as increased BNP/NT pro-BNP, troponin, and C-reactive protein (CRP) [5]. In cases where preventive and treatment measures for heart failure are clinically ineffective, the condition can progress to its acute form. Among hemodynamic parameters, severe low cardiac output, organ hypoperfusion, and cardiogenic shock carry a high risk of death during hospitalization [5]. Additionally, according to Terzi et al. [6], after a two-year study with 90 patients from the Cardiology Intensive Care Unit of the Heart Institute of São Paulo (InCor), pulmonary thromboembolism was highlighted as a contributing factor to acute heart failure decompensation and high mortality. The study suggested that the possibility of anticoagulation in heart failure patients with refractory heart failure should be better discussed. In this analysis, it was also found that nearly two-thirds of patients with class IV heart failure or cardiogenic shock died during their stay in the ICU.

Thus, it can be concluded that when clinical and therapeutic measures are ineffective, a patient with decompensated heart failure can develop a severe prognosis, becoming an emergency situation that requires intensive care. According to PONIKOWSKI et al. [7], the immediate treatment goals for acute heart failure in the ICU include alleviating symptoms, restoring oxygenation, improving hemodynamics and organ perfusion, limiting cardiac and renal damage, preventing thromboembolic events, and minimizing the duration of ICU stays.

Therefore, this study aims to assess how the acute exacerbation of heart failure can lead to hospitalization in which ICU admission becomes necessary, as well as to evaluate mortality among these patients and how they may progress to better or worse prognoses. The proposed review seeks to shed more light on this condition, which is limited by the scarcity of relevant studies. It is important to note that few studies broadly address the

mortality of heart failure patients in the ICU, as most focus on very specific aspects without covering the entire process of disease exacerbation in the ICU and its associated mortality.

2. Methods

In this study, an integrative review was conducted, which consists of research that allows for the evaluation, synthesis, and understanding of a phenomenon based on evidence, aiming to provide an overview of complex concepts, theories, or relevant health problems through existing studies, thus enabling the proposition of interventions [8].

To select the articles, six methodological steps were followed: formulation of the guiding question or research hypothesis, which involved identifying the problem, presenting the search mechanism, and determining the descriptors or keywords; establishment of inclusion and exclusion criteria for articles to be selected for the sample; Exploratory reading of titles and abstracts for pre-selection of articles; analytical reading of the articles to compile, analyze, and categorize the information; interpretation of the results; synthesis followed by the presentation of the identified results, which address the guiding question [9].

Thus, in this study, a search was conducted on the following concepts: Heart Failure, ICU, and Mortality. From these concepts, the guiding question was defined: *What factors influence the mortality of patients with acute heart failure during hospitalization?*.

After formulating the research question, a bibliographic survey was carried out on the PubMed, Lilacs, and Scielo platforms. The study was conducted between January and March 2024, and the selection of texts proceeded with searches on the platforms using filters for texts published between 2014 and 2024, i.e., the last ten years of publications on the subject. The following inclusion criteria were adopted for selecting publications: scientific articles published in English, Portuguese, and Spanish between 2014 and 2024, available online and in full for free. Articles without abstracts in the database or incomplete, editorials, letters to the editor, reflective studies, systematic reviews, or integrative literature reviews were excluded.

After defining the guiding question, locating, and selecting the articles, 1,188 potentially eligible publications were identified for inclusion in this review. After applying the inclusion and exclusion criteria, the sample consisted of 77 publications, and the abstracts of 13 records were analyzed to verify whether they met the eligibility criteria and answered the question guiding this review. Six records were excluded, and only seven were analyzed in full to confirm eligibility for quantitative synthesis and data analysis, according to the selection flowchart (Figure 1).

3. Results and Discussion

During the time frame established for this study (2014-2024), seven articles were found and analyzed, published in the years 2016, 2017, 2018, 2019, 2020, 2021, and 2023, which are summarized in Figure 1. The publications came from different journals, including: Archives of Cardiovascular Diseases, European Journal of Internal Medicine, Nutrients, ESC Heart Failure, European Heart Journal: Acute Cardiovascular Care, and Annals of the American Thoracic Society. Analyzing the study locations, two articles were conducted in Japan (28.6%), while the remaining studies were from the United States, Turkey, France, Spain, and Slovenia.

According to a study by Omersa et al. [10] conducted in Slovenia, male sex, myocardial infarction, chronic kidney disease, and cancer were identified as the strongest predictors of 30-day or one-year mortality after the first hospitalization for heart failure. Additionally, the presence of cancer, stroke, and pneumonia was linked to the highest chances of in-hospital mortality. During the first hospitalization for heart failure (HF), 8,235 (18.9%) patients died, and among those discharged alive, 679 (3.9%) and 7,865

(18.0%) died within 30 days and one year, respectively. Thus, high mortality rates correlated with the high prevalence of HF-related hospitalizations.

Figure 1. Flowchart of the Publication Selection.

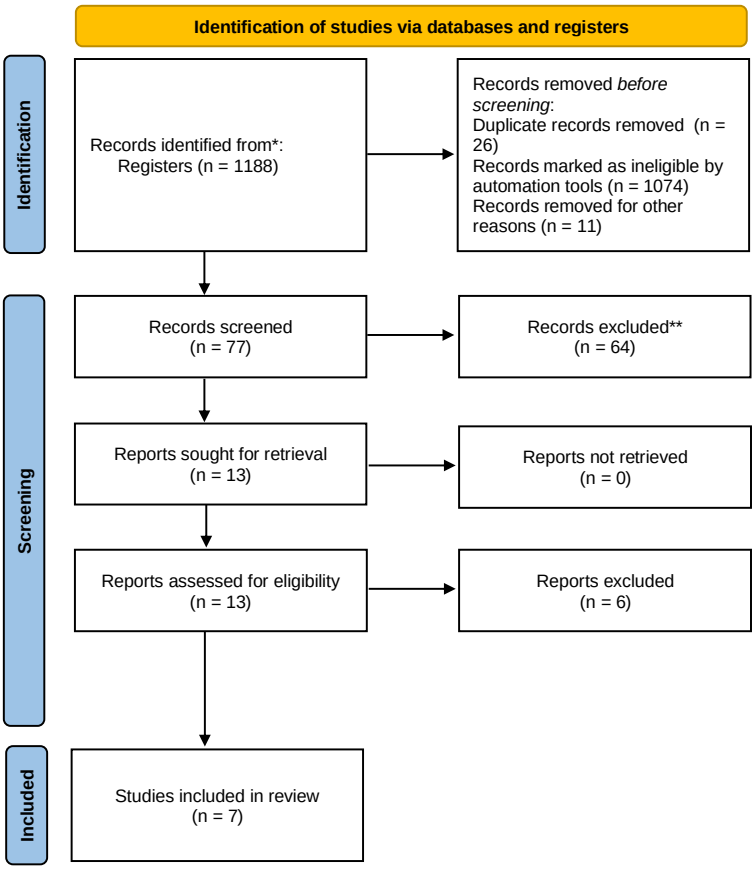

Table 1. Summary of the reviewed articles.

Reference	Study Type	Studied Sample	Studied Variables	Main Results	Conclusions/Limitations
10	pidemiological, observational, retrospective study of national scope.	Patients aged 20 years or older hospitalized with heart failure in Slovenia between 2004 and 2012.	Hospitalization rates, in-hospital mortality, 30-day and 1-year mortality, 30-day and 1-year readmission rates.	Male sex, presence of cancer, chronic kidney disease, lung disease, myocardial infarction, and diabetes mellitus had the highest chances of readmission within 30 days or 1 year after the first hospitalization for heart failure. The presence of cancer,	High mortality and readmission rates correlated with high prevalence of hospitalizations for heart failure. The study was limited by the lack of information on medication use and heart failure severity.

				stroke, and pneumonia had the highest chances of in-hospital mortality.	
11	Retrospective study with instrumental variable analysis.	Medicare patients aged ⩾ 65 years hospitalized with COPD, heart failure, or myocardial infarction between 2010 and 2012.	30-day mortality, hospital cost.	No significant association was found between ICU admission and 30-day mortality for COPD, heart failure, or myocardial infarction. There was a significant increase in hospital costs for heart failure and MI.	ICU admission did not confer a survival advantage for patients with uncertain ICU needs, but it increased hospital costs. There may be overuse of ICU for certain conditions.
12	Retrospective, observational study.	Patients hospitalized in the cardiac ICU with acute heart failure.	PaCO2, long-term mortality, clinical characteristics at admission.	Low PaCO2 (< 31 mmHg) was associated with higher long-term mortality. PaCO2 was an independent predictor of mortality, and low PaCO2 indicated worse prognosis.	Low PaCO2 levels at admission were associated with increased long-term mortality risk. The study was limited by its retrospective nature and single-center analysis.
13	Prospective, observational study.	Patients with decompensated heart failure admitted to the emergency department.	NEWS score, lactate levels, short-term mortality (30 days).	The NEWS score combined with elevated lactate levels was a significant predictor of 30-day mortality. Adding lactate levels to the NEWS score improved the prediction of adverse outcomes.	The study suggests that the NEWS score combined with lactate can be a useful tool for risk stratification in patients with decompensated heart failure in the emergency department. Limitations include being conducted in a single center.
14	Retrospective, observational study.	417 patients hospitalized with acute decompen-	TCB index (triglycerides × total cholesterol	Patients with lower TCBI had higher all-cause and can-	TCBI may be a simple and useful tool for risk stratification in patients

		sated heart failure between 2007 and 2011.	× body weight), all-cause mortality, cardiovascular mortality, cancer mortality.	cer mortality rates. TCBI was an independent predictor of all-cause mortality but not cardiovascular mortality.	with acute decompensated heart failure, but the retrospective design and single-center setting limit the generalization of the results.
15	Observational, retrospective, single-center study.	368 patients aged ⩾ 75 years admitted with acute pulmonary edema between 2007 and 2014.	Use of nitrates (isosorbide dinitrate - ISDN), in-hospital mortality, ICU admission, length of stay.	The use of ISDN increased significantly from 18% in 2007 to 42% in 2014, but there was no significant improvement in outcomes such as mortality or length of stay.	The study observed an increase in nitrate use without a significant impact on clinical outcomes. Limitations include the retrospective design and lack of randomization, which may introduce bias.
16	Observational, retrospective, propensity score-based analysis.	11,152 patients with acute heart failure treated in 41 emergency departments in Spain.	Use of non-invasive ventilation (NIV), 30-day mortality, ICU admission, mechanical ventilation, in-hospital mortality.	NIV use was not associated with a significant reduction in 30-day mortality after propensity score adjustment. Patients older than 85 years with ACS or hypotension had worse prognosis with NIV.	NIV did not demonstrate a benefit in reducing mortality in patients with acute heart failure, except as a symptomatic relief therapy. Patients with ACS, SBP < 100 mmHg, and > 85 years should avoid NIV in the emergency department due to the lack of randomized studies showing clear benefits and its association with worse outcomes, possibly due to advanced age and lack of specific selection criteria for low SBP heart failure.

Patients hospitalized for HF may deteriorate and require intensive care, often leading to transfer to the ICU. According to a study by Valley et al. [11], which evaluated 626,174 patients admitted with heart failure exacerbation across 2,691 hospitals between 2010 and 2012, 154,445 (24.7%) of these patients were admitted to the Intensive Care Unit. Over 30 days, no significant difference in mortality was observed between ICU admissions and those admitted to general wards (95% CI for absolute difference, –0.4 to 2.6; P = 0.14). They also found that ICU admissions were associated with significantly higher hospital costs for HF patients, highlighting the need to avoid unnecessary admissions

and, more importantly, to implement preventive programs in regions with higher disease prevalence. However, when ICU admission is indicated, certain parameters must be assessed to improve outcomes and analyze mortality. Acid-base balance is an important factor in patient prognosis. Kato et al. [12] observed the relationship between blood carbon dioxide levels and mortality in HF patients admitted to the ICU. They found that patients with $PaCO_2 > 31$ mmHg had a mortality rate of 21.8%, while those with PaCO2 < 31 mmHg had a mortality rate of 39.5% (p=0.032). Thus, lower PaCO2 levels at admission were associated with a higher long-term mortality risk in patients with acute HF.

Similarly, in the metabolic evaluation of ICU patients with HF, Guzelce et al. [13] assessed lactate status using the NEWS+L scale as a prognostic measure. They found that higher scores on the scale indicated a more unfavorable prognosis. The AUC values for predicting unfavorable outcomes were 0.719 for NEWS, 0.734 for NEWS+L, and 0.601 for lactate values, suggesting greater sensitivity and specificity for the scale that included lactate values. Nutritional status may also be related to mortality in ICU patients with acute HF. Ishiwata et al. [14] found that patients with a lower nutritional index, as calculated by the TCB index (triglycerides × total cholesterol × body weight), had a higher risk of death. Event-free survival curves showed that the cumulative incidence of cardiovascular mortality was significantly higher in patients with a lower TCBI ($p = 0.041$). Another crucial component of recovery for ICU patients with acute HF is support measures, including ventilation. Non-invasive ventilation (NIV) and pharmacological treatment with vasodilators were identified in studies as not significantly altering mortality rates. In fact, patients using NIV were more frequently associated with prolonged hospitalizations ($p<0.004$). A study by Lemanchatti et al. [15] noted an increase in vasodilator use, but there were no significant differences in outcomes, with similar ICU admission rates (17% vs. 13%; $P = 0.3$) and in-hospital mortality (11% vs. 8%; $P = 0.5$) [15, 16].

This article, although offering valuable insights, has several limitations that should be acknowledged. First, the heterogeneity of the variables in the reviewed studies may have influenced the consistency and generalizability of the conclusions. Variations in data collection methods, inclusion and exclusion criteria, and treatment protocols may have introduced bias and affected the comparability between studies. Additionally, the scarcity of studies related to the topic may have limited the statistical power of the analyses and, consequently, the robustness of the conclusions. Another point to consider is the absence of longitudinal data, which could have provided a more comprehensive temporal view of the studied phenomena. Dependence on secondary data, when present, may have introduced limitations related to the quality and accuracy of the information. Future research should seek to overcome these limitations by using studies with consistent variables, larger samples, and longitudinal data to strengthen the evidence and improve the applicability of findings in diverse clinical contexts.

4. Conclusion

This study aimed to highlight the mortality of patients with heart failure within the Intensive Care Unit setting, as well as to explore other aspects of the disease's progression and factors that can influence clinical outcomes or provide more accurate prognostic assessments. Among the findings, the predictors that increase mortality following the first hospitalization were: male sex, myocardial infarction, chronic kidney disease, and cancer. Additionally, stroke and pneumonia were highlighted as factors with a higher chance of in-hospital mortality. Furthermore, the high prevalence of hospitalizations itself correlated with high mortality rates.

These findings allow medical professionals to pay closer attention to the predictors that genuinely increase heart failure mortality in the ICU, apply prognostic indicators to patient evaluations, and reflect on measures that may be avoided due to their lack of impact on mortality. Since there is limited uniformity among studies, it would be beneficial if the recruited parameters, predictors, and other criteria discovered in future research were standardized and applied with more consistency, rather than being treated

as isolated variables that are difficult to apply. Hence, there is a need for more research and analysis on additional parameters.

Based on the results presented, it is important to consider increased investment in preventive programs, especially in regions with a high prevalence of heart failure. Besides the preventive aspect, it is also important to consider the high costs that this disease imposes on the healthcare system. These costs can be reduced by minimizing unnecessary and uncertain ICU admissions. More research is needed on other factors that increase the mortality of hospitalized patients, as well as ways to avoid them, to improve patient management and prognoses.

Funding: None.

Research Ethics Committee Approval: None.

Acknowledgments: None.

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

Supplementary Materials: None.

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