ORIGINAL ARTICLE

COMPARISON OF IN-HOSPITAL OUTCOMES BETWEEN HEART FAILURE PATIENTS WITH REDUCED AND PRESERVED EJECTION FRACTION: A SINGLE-CENTER CROSS-SECTIONAL STUDY

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Objectives: Heart failure (HF) poses a significant global health burden, characterized by inadequate cardiac output and systemic organ dysfunction. This study aimed to compare in-hospital outcomes between patients with reduced (HFrEF) and preserved (HFpEF) ejection fraction presenting with congestive heart failure.

Methodology: A cross-sectional, prospective study was conducted at the Department of Cardiology, National Institute of Cardiovascular Diseases, Karachi, Pakistan, from July 2022 to January 2023. Patients aged 35 to 80 years with congestive heart failure were included. Ejection fraction status, demographic data, and clinical parameters were assessed, with in-hospital mortality as the primary outcome.

Results: Among 196 patients, 91 (46.4%) had HFrEF, and 105 (53.6%) had HFpEF. In-hospital mortality occurred in 23 (11.7%) patients. Mortality rates were significantly higher in HFrEF patients compared to HFpEF patients (17.6% vs. 6.7%, p=0.018). Age (>60 years) and diabetes mellitus were significantly associated with in-hospital mortality (p=0.001 and p=0.036, respectively).

Conclusion: This study highlights significantly higher in-hospital mortality rates in patients with reduced ejection fraction compared to preserved ejection fraction, underscoring the importance of considering ejection fraction status in assessing prognosis and guiding management strategies for patients with congestive heart failure.

Keywords: Heart Failure; In-Hospital Mortality; Preserved Ejection Fraction; Reduced Ejection Fraction

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INTRODUCTION

Heart failure (HF) represents a significant clinical challenge worldwide, characterized by inadequate cardiac output leading to systemic organ dysfunction. The progressive alteration in cardiac structure and function contributes to systolic and/or diastolic contractile dysfunction, ultimately culminating in HF.[1] Risk factors such as age, hypertension, obesity, diabetes, atrial fibrillation, and coronary artery disease (CAD), especially when complicated by myocardial infarction, are strongly associated with the prevalence and incidence of HF.[2]

Despite advancements in therapeutic modalities, HF remains associated with high rates of morbidity, mortality, and hospitalization. The one-year mortality rate post-diagnosis is approximately 20%, rising to 53% at five years.[3] Within hospitalized patients, mortality rates range from 17% to 45% within a year of admission, with roughly 50% of HF patients surviving beyond five years.[1,4] Age-related comorbidities like type 2 diabetes mellitus, renal impairment, myocardial infarction, and hypertension contribute to the increasing incidence and prevalence of HF in an aging population globally.[5]

Approximately 50% of HF cases exhibit preserved ejection fraction (HFpEF), which is associated with comparable rates of morbidity and mortality to HF with reduced EF (HFrEF).[6] Current treatment options for HFpEF are limited, prompting researchers to explore biomarkers indicative of the syndrome's pathogenesis for diagnostic and therapeutic advancements.[7]

While prognosis for HF with reduced left ventricular ejection fraction (LVEF) has improved with advancements in treatment, no established therapy exists for HF with preserved LVEF (HFpEF).[8-10] The prognosis for HFpEF remains unchanged.[9] A significant proportion of HF patients exhibit mildly impaired LVEF (40-50%), while those with intermediate or mid-range LVEF (HFmrEF) may fall into either the HFrEF or HFpEF category, depending on LVEF cutoffs used in clinical studies.[11,12] A 2016 study reported mortality rates of 14.0% for HFpEF and 14.3% for HFrEF.[13]

The aim of the current study was to assess and compare in-hospital mortality rates between patients with reduced (HFrEF) and preserved (HFpEF) ejection fraction presenting with congestive heart failure, while also exploring associations between demographic and clinical variables (such as age, diabetes mellitus, and hypertension) and in-hospital mortality within each ejection fraction group. Notably, research on the clinical outcomes of HF with varying ejection fractions remains limited in South Asian nations, including Pakistan. This study addresses this gap by examining the outcomes of HFrEF and HFpEF in a Pakistani population. By elucidating the differences in outcomes between these two groups, this study contributes to the understanding of HF management strategies in this region.

METHODOLOGY

Study Design: This cross-sectional, prospective study aimed to assess and compare in-hospital mortality rates between patients with reduced (HFrEF) and preserved (HFpEF) ejection fraction presenting with congestive heart failure.

Setting: The study was conducted from July 2022 to January 2023 at the National Institute of Cardiovascular Diseases, Karachi, Pakistan.

Participants: The study included patients of either gender aged between 35 to 80 years presenting with congestive heart failure. Patients with known coagulation disorders, congenital heart disease, valvular heart disease-induced heart failure, certain types of anemia, advanced liver disease, renal failure, or who had undergone previous cardiac interventions were excluded. Lactating and pregnant women were also excluded.

Variables: The independent variable of interest was the ejection fraction status, categorized as reduced (HFrEF) or preserved (HFpEF). The dependent variable was in-hospital mortality. Other variables included demographics (age, gender, weight, height), body mass index (BMI), comorbidities (diabetes mellitus, hypertension), and relevant clinical parameters.

Data Sources/Measurement: Data collection involved obtaining informed and written consent from patients or guardians. Demographic data were recorded, and BMI was calculated using standard methods. Echocardiography was performed to determine ejection fraction status. CHF diagnosis was based on clinical criteria and confirmed by NT-pro-BNP levels. In-hospital mortality was confirmed by clinical assessment.

Bias: To minimize bias, non-probability consecutive sampling technique was employed. Additionally, exclusion criteria were established to ensure homogeneity within the study population. The study was approved by the Institutional Ethical Committee, and informed consent was obtained from all participants or their guardians.

Study Size: The sample size was determined using the WHO sample size calculator, yielding a total of 196 participants based on the frequency of HFrEF among CHF patients, with a 95% confidence level and 7% margin of error.

Quantitative Variables: Quantitative variables included age, weight, height, BMI, and duration of hospital stay. These variables were summarized using mean and standard deviation or median with interquartile range, as appropriate.

Statistical Methods: Data analysis was performed using Statistical Package for Social Sciences (SPSS), version 26.0. Normality of continuous data was assessed using the Shapiro-Wilk test. Chi-square and independent sample t-tests were utilized to compare in-hospital mortality and hospital stay between HFrEF and HFpEF patients. Stratification analysis was conducted to assess effect modifiers/confounders, with appropriate statistical tests applied at a significance level of 0.05.

RESULTS

Participants: The study included a total of 196 patients, comprising 93 (47.4%) males and 103 (52.6%) females. The mean age of the participants was 56.40 years, with a standard deviation of 12.90 years. Among them, 43 (21.9%) had a family history of coronary artery disease (CAD), 85 (43.4%) had a history of smoking, 72 (36.7%) had diabetes mellitus, and 111 (56.6%) had hypertension.

Descriptive Data: The descriptive statistics of quantitative data are presented in Table 1. The mean

weight of the participants was 77.04 kg, with a standard deviation of 11.43 kg. The mean height was 1.69 meters, with a standard deviation of 0.08 meters. The mean body mass index (BMI) was 27.20 kg/m², with a standard deviation of 4.34 kg/m². The average duration of hospitalization was 4.47 days, with a standard deviation of 1.50 days.

Table 1: Descriptive statistics of quantitative data

Variables	Summary
Total (N)	**196**
Age (years)	56.40±12.90
Weight (kg)	77.04±11.43
Height (cm)	1.69±0.08
Body mass index (kg/m^2)	27.20±4.34
Duration of hospitalization (days)	4.47±1.50

Outcome Data: Among the participants, 91 (46.4%) had reduced ejection fraction (HFrEF), while 105 (53.6%) had preserved ejection fraction (HFpEF). In-hospital mortality occurred in 23 (11.7%) patients. In the comparison of ejection fraction, in-hospital mortality was noted in 16 (17.6%) patients with HFrEF and 7 (6.7%) patients with HFpEF, with a statistically significant difference (p=0.018).

Main Results: Older age (>60 years) was significantly associated with in-hospital mortality, with 16 (69.6%) of patients aged over 60 experiencing mortality compared to 7 (30.6%) in the age group of 35-60 years (p=0.001). Additionally, diabetes mellitus showed a significant association with in-hospital mortality, with 13 (56.5%) diabetic patients experiencing mortality compared to 59 (34.1%) non-diabetic patients (p=0.036). Other factors such as gender, BMI, family history of CAD, hypertension, and history of smoking did not show significant associations with in-hospital mortality. The detailed stratification of study variables with respect to in-hospital mortality is presented in Table 2.

Table 2: Stratification of study variables with respect to in-hospital mortality

Study Variables	In-hospital mortality		P-value
	Yes	No	
Total (N)	**24**	**173**	**-**
Age (years)			
35-60	7 (30.4%)	120 (69.4%)	0.001
>60	16 (69.6%)	53 (30.6%)	
Gender			
Male	12 (52.2%)	81 (46.8%)	0.629
Female	11 (47.8%)	92 (53.2%)	
Body mass index (kg/m^2)			
19-27	13 (56.5%)	100 (57.8%)	0.907
>27	10 (43.5%)	73 (42.2%)	
Diabetes	13 (56.5%)	59 (34.1%)	0.036
Family history of coronary artery disease	6 (26.1%)	37 (21.4%)	0.609
Hypertension	13 (56.5%)	98 (56.6%)	0.991
History of Smoking	14 (60.9%)	71 (41.0%)	0.071

DISCUSSION

HF remains a substantial cardiovascular disease burden worldwide, characterized by significant morbidity, mortality, and escalating healthcare costs.[14,15] Its prevalence increases notably with age, particularly among individuals over 60 years old.[16] Approximately 50% of HF cases present with preserved ejection fraction (HFpEF), exhibiting mortality and morbidity rates akin to those with reduced EF (HFrEF). However, diagnosing HFpEF proves challenging and varies across studies, posing a significant issue in clinical trials.[17-19] Symptoms such as fatigue or dyspnea in patients with preserved LVEF may not solely originate from HFpEF, with some patients exhibiting co-morbidities that drive symptoms and events, potentially limiting the benefits of HF treatment when cardiac event risk is low.[20-23]

In our study, the mean age of patients with congestive heart failure (CHF) was 56.40±12.90 years. This finding is consistent with previous studies reporting varying mean ages, ranging from 53.58±16.90 years to 76.1±7.5 years.[13,24,25] Gender distribution also differed across studies, with 47.4% males and 52.6% females in our study, compared to 49% males and 51% females in other studies.[24,25] These variations may reflect disparities in healthcare access, facilities, and awareness of CHF symptoms.

Our study documented in-hospital mortality in 11.7% of patients with CHF. We found a significant difference in mortality rates between patients with HFrEF (17.6%) and HFpEF (6.7%). This aligns with prior research reporting mortality rates ranging from 13% to 33% in HFpEF and 33% to 42% in HFrEF.[24,25] Despite similar hospital stays between the HFrEF and HFpEF groups in our study, mortality discrepancies highlight the need for aggressive management strategies in both HF subtypes.

Echocardiography emerged as a valuable tool for assessing left ventricular function and guiding HF management. Its accuracy, accessibility, safety, and cost-effectiveness make it the preferred diagnostic approach, particularly in suspected HF cases, as recommended by the European Society of Cardiology guidelines[17].

LIMITATION

Limitations of our study include its single-center design, modest sample size, and lack of prospective analysis. Furthermore, our study only observed short-term outcomes, warranting further prospective trials to elucidate long-term prognosis in CHF patients.

CONCLUSION

In conclusion, our study highlights significantly higher mortality rates in patients with reduced (HFrEF) compared to preserved (HFpEF) ejection fraction, while hospital stay differences were insignificant. Further well-controlled prospective trials are warranted to validate these findings and inform optimal management strategies. Aggressive treatment approaches are warranted for both HFrEF and HFpEF patients, with similar mortality rates observed across genders, particularly in the HFpEF group.

AUTHORS' CONTRIBUTION

HS and KK: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work HS, KK, GI, and KA: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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REFERENCES

1. Schwinger RHG. Pathophysiology of heart failure. Cardiovasc Diagn Ther. 2021;11(1):263-76.
2. Conrad N, Judge A, Tran J, Mohseni H, Hedgecott D, Crespillo AP, et al. Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals. Lancet. 2018;391:572-80.
3. Ziaeian B, Fonarow GC. Epidemiology and aetiology of heart failure. Nat Rev Cardiol. 2016;13:368-78.
4. Ponikowski P, Anker SD, AlHabib KF, Cowie MR, Force TL, Hu S, et al. Heart failure: preventing disease and death worldwide. ESC Heart Fail. 2014;1:4-25.
5. Zhang J, Begley A, Jackson R, Harrison M, Pellicori P, Clark AL, et al. Body mass index and all-cause mortality in heart failure patients with normal and reduced ventricular ejection fraction: a dose-response meta-analysis. Clin Res Cardiol. 2019;108(2):119-32.
6. Hage C, Michaëlsson E, Linde C, Donal E, Daubert JC, Gan LM, et al. Inflammatory biomarkers predict heart failure severity and prognosis in patients with heart failure with preserved ejection fraction: a holistic proteomic approach. Circ Cardiovasc Genet. 2017;10:e001633.
7. Iorio A, Senni M, Barbati G, Greene SJ, Poli S, Zambon E, et al. Prevalence and prognostic impact of non-cardiac co-morbidities in heart failure outpatients with preserved and reduced ejection fraction: a community-based study. Eur J Heart Fail. 2018;20(9):1257-66.
8. Berliner D, Hänselmann A, Bauersachs J. The Treatment of Heart Failure with Reduced Ejection Fraction. Dtsch Arztebl Int. 2020;117(21):376-86.
9. Li Q, Qiao Y, Tang J, Guo Y, Liu K, Yang B, et al. Frequency, predictors, and prognosis of heart failure with improved left ventricular ejection fraction: a single-centre retrospective observational cohort study. ESC Heart Fail. 2021;8(4):2755-64.
10. Henning RJ. Diagnosis and treatment of heart failure with preserved left ventricular ejection fraction. World J Cardiol. 2020;12(1):7-25.
11. Mauro C, Chianese S, Cocchia R, Arcopinto M, Auciello S, Capone V, et al. Acute Heart Failure: Diagnostic-Therapeutic Pathways and Preventive Strategies-A Real-World Clinician's Guide. J Clin Med. 2023;12(3):846.
12. Raffaello WM, Henrina J, Huang I, Lim MA, Suciadi LP, Siswanto BB, et al. Clinical Characteristics of De Novo Heart Failure and Acute Decompensated Chronic Heart Failure: Are They Distinctive Phenotypes That Contribute to Different Outcomes?. Card Fail Rev. 2021;7:e02.
13. Abebe TB, Gebreyohannes EA, Tefera YG, Abegaz TM. Patients with HFpEF and HFrEF have different clinical characteristics but similar prognosis: a retrospective cohort study. BMC Cardiovasc Disord. 2016;16:1-8.
14. Ong SC, Low JZ. Financial burden of heart failure in Malaysia: A perspective from the public healthcare system. PLoS One. 2023;18(7):e0288035.
15. Alghamdi A, Algarni E, Balkhi B, Altowaijri A, Alhossan A. Healthcare Expenditures Associated with Heart Failure in Saudi Arabia: A Cost of Illness Study. Healthcare (Basel). 2021;9(8):988.
16. Groenewegen A, Rutten FH, Mosterd A, Hoes AW. Epidemiology of heart failure. Eur J Heart Fail. 2020;22(8):1342-56.
17. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Bohm M, Dickstein K, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail. 2012;14(8):803-69.
18. Pfeffer MA, Shah AM, Borlaug BA. Heart Failure With Preserved Ejection Fraction In Perspective. Circ Res. 2019;124(11):1598-617.
19. Naing P, Forrester D, Kangaharan N, Muthumala A, Mon Myint S, Playford D. Heart failure with preserved ejection fraction: A growing global epidemic. Aust J Gen Pract. 2019;48(7):465-71.
20. Paulus WJ, Tschope C, Sanderson JE, Rusconi C, Flachskampf FA, Rademakers FE, et al. How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology. Eur Heart J. 2007;28:2539-50.
21. Bavishi A, Patel RB. Addressing Comorbidities in Heart Failure: Hypertension, Atrial Fibrillation, and Diabetes. Heart Fail Clin. 2020;16(4):441-56.
22. Takeda A, Martin N, Taylor RS, Taylor SJ. Disease management interventions for heart failure. Cochrane Database Syst Rev. 2019;1(1):CD002752.
23. O'Connor CM, Whellan DJ, Wojdyla D, Leifer E, Clare RM, Ellis SJ, et al. Factors related to morbidity and mortality in patients with chronic heart failure with systolic dysfunction: the HF-ACTION Predictive Risk Score Model. Circ Heart Fail. 2012;5:63-71.
24. Najjar E, Faxén UL, Hage C, Donal E, Daubert JC, Linde C, et al. ST2 in heart failure with preserved and reduced ejection fraction. Scand Cardiovasc J. 2019;53:21-7.
25. Maeder MT, Rickenbacher P, Rickli H, Abbühl H, Gutmann M, Erne P, et al. N-terminal pro brain natriuretic peptide-guided

management in patients with heart failure and preserved ejection fraction: findings from the Trial of Intensified versus standard medical therapy in elderly patients with congestive heart failure (TIME-CHF). Eur J Heart Fail. 2013;15(10):1148-56.

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