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ORIGINAL RESEARCH

Impact of Initial Heart Rate, Diastolic Pressure, and Pulse Pressure on Prognostic Outcomes in Heart Failure Patients with Mildly Reduced Ejection Fraction

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Background: Heart rate, diastolic pressure, and pulse pressure are key modifiable factors influencing heart failure prognosis. While heart failure with mildly reduced ejection fraction (HFmrEF) is a distinct subgroup of heart failure, the prognostic impact of these hemodynamic parameters in this population remains unclear, necessitating focused investigation. This study aims to elucidate their effects on HFmrEF patient outcomes.

Methods: We retrospectively analyzed 1,653 hFmrEF patients treated at Xiangtan Central Hospital (2015–2020). Using decision tree classification, patients were categorized based on initial heart rate (≤77 bpm and >77 bpm). The ≤77 bpm group was further divided by pulse pressure (≤37 mmHg and >37 mmHg), and the >77 bpm group by diastolic pressure (≤63 mmHg, 63–100 mmHg, and >100 mmHg). Multivariate COX regression assessed mortality associations.

Results: With a median follow-up of 33 months, overall mortality was 21.7% for heart rates ≤77 bpm and 30.4% for >77 bpm. Multivariate COX regression showed that among patients with heart rates ≤77 bpm, those with pulse pressure >37 mmHg had a higher mortality risk than those with pulse pressure ≤37 mmHg (HR 3.184; 95% CI 1.008–10.058; p=0.048). For patients with heart rates >77 bpm, those with diastolic pressure 63–100 mmHg had a lower mortality risk compared to ≤63 mmHg (HR=0.652, 95% CI: 0.450–0.943, p=0.023), with the lowest risk in patients with diastolic pressure >100 mmHg (HR=0.370, 95% CI: 0.205–0.666, p=0.001).

Conclusion: This study highlights that HFmrEF patients with heart rates ≤77 bpm and pulse pressure ≤37 mmHg had the lowest mortality risk, while those with heart rates >77 bpm and diastolic pressure ≤63 mmHg faced the highest risk. These findings provide valuable insights for risk stratification and may guide personalized management of HFmrEF patients.

Keywords: heart failure with mildly reduced ejection fraction (HFmrEF), initial heart rate, diastolic pressure, pulse pressure, decision tree classification

Introduction

Heart failure (HF) is a significant challenge to global public health, with its prevalence and mortality rates rising sharply. This trend places a tremendous burden on healthcare systems and adversely affects the quality of life of those affected.[1,2] HF can be categorized into three main phenotypes based on left ventricular ejection fraction (LVEF): heart failure with reduced ejection fraction (HFrEF), heart failure with mildly reduced ejection fraction (HFmrEF), and heart failure with preserved ejection fraction (HFpEF).[3] While substantial research has focused on HFrEF and HFpEF, HFmrEF has received relatively less attention despite its distinct clinical characteristics and prognostic implications.[4] Accurate identification and effective management of the HFmrEF population are therefore crucial.[5]

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Traditionally, heart failure research has centered on clinical manifestations, blood-based biomarkers, and electrocardiographic parameters.[6] However, the prognostic significance of vital signs at admission, such as heart rate, diastolic pressure, and pulse pressure, has often been overlooked. These parameters are important modifiable risk factors that can significantly impact the prognosis of heart failure patients.[7–12] Elevated heart rate at the onset of heart failure is strongly associated with increased disease severity, higher readmission rates, and reduced quality of life.[8] Lower diastolic pressure can impair diastolic cardiac function, while variations in pulse pressure may reflect vascular compliance and cardiac pump function, influencing patient outcomes.[9–12]

The prognostic implications of initial heart rate, diastolic pressure, and pulse pressure in HFmrEF patients remain unclear. This study aims to elucidate the specific effects of these parameters on the prognosis of HFmrEF patients. Our goal is to provide clinicians with a more accurate prognostic assessment tool to tailor personalized post-discharge treatment regimens for these patients.

Methods

Study Design and Participant Selection

In this retrospective cohort study, we thoroughly examined the electronic medical records of patients diagnosed with HFmrEF at Xiangtan Central Hospital between 2015 and 2020. The cohort included 1,653 patients with HFmrEF (Figure 1), selected according to the European Society of Cardiology (ESC) Heart Failure Treatment Guidelines.[13] The study was conducted with the approval of the hospital's Institutional Review Board.

Data Acquisition and Defining Variables

We recorded a comprehensive set of baseline characteristics for each patient, including age, sex, comorbidities (such as diabetes mellitus and hypertension), physiological parameters at the time of admission (including heart rate, diastolic pressure, and pulse pressure), and blood biomarker levels. Heart rate, diastolic pressure, and pulse pressure were defined based on the initial measurements recorded upon patient admission.

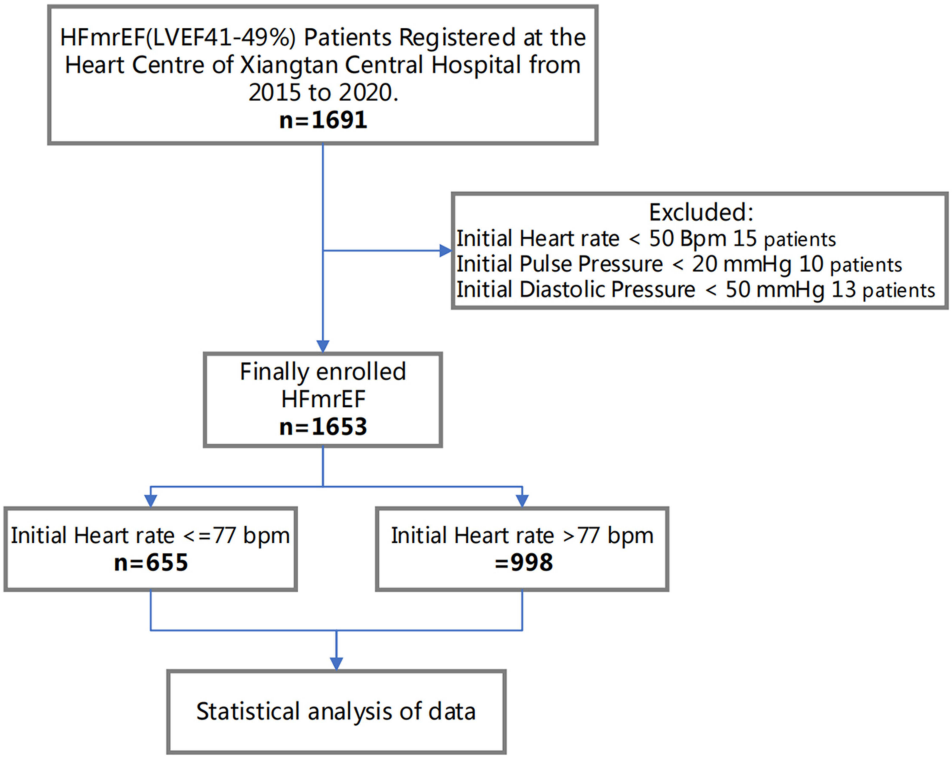

Figure 1 Flowchart of Patient Selection Process.

Patient Stratification

HFmrEF patients were divided into groups using decision tree analysis based on their initial heart rate (≤77 bpm or >77 bpm). Patients with heart rates ≤77 bpm were further stratified into two subcategories based on their pulse pressure at admission (≤37 mmHg or >37 mmHg). Similarly, patients with heart rates >77 bpm were classified into three subgroups based on their initial diastolic pressure (≤63 mmHg, 63–100 mmHg, or >100 mmHg) (Figure 2).

Outcome Assessment

The primary outcome was all-cause mortality, with data obtained from medical records or via telephone follow-ups. The median follow-up period was 33 months (range: 20–50 months).

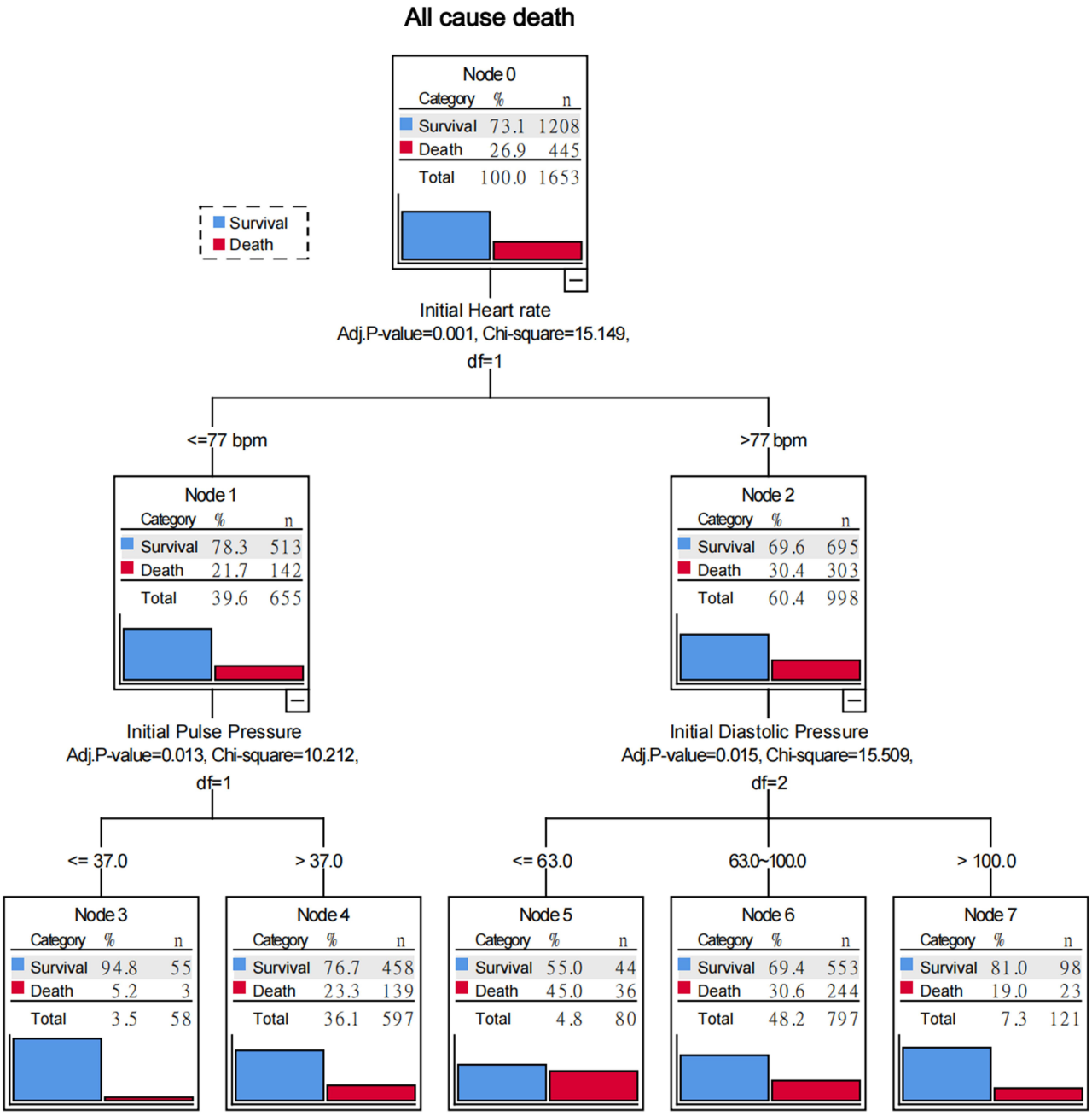

Figure 2 Classification tree by CHAID algorithm for accuracy of the model including potential risk factors associated with All cause death: Initial Heart rate, Pulse Pressure, and Diastolic Pressure.

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Statistical Evaluation

Continuous variables with a normal distribution were compared using a *t*-test and are presented as mean ± SD. Continuous variables not conforming to a normal distribution were analyzed using non-parametric testing and are presented as median (interquartile range). Categorical variables were expressed as numbers (percentages) and compared using Pearson's Chi-square test or Fisher's exact test, as appropriate. Survival curves were generated using the Kaplan-Meier method and compared with the Log rank test. The Chi-square Automatic Interaction Detection (CHAID) decision tree algorithm was used to identify potential threshold points for admission heart rate, diastolic pressure, and pulse pressure that were significant for all-cause mortality. The associations of these classifications with mortality rates among HFmrEF patients were evaluated using multivariate Cox regression models, adjusting for potential confounders including age, sex, comorbidities, and blood biomarker levels. Hazard ratios (HRs) and their corresponding 95% confidence intervals (CIs) were computed to assess the relative mortality risk across groups. Stratified analysis was conducted to explore the relationships between admission heart rate stratifications and all-cause mortality across all subtypes, with results graphically represented using forest plots. Statistical significance was defined as a P-value <0.05. Statistical analyses were performed using R 4.2.0 (http://www.R-project.org) and IBM SPSS Statistics 26.0.0 (SPSS Inc., Chicago, IL, USA).

Results

Baseline Characteristics

Our study included 1,653 participants, with 655 patients having an admission heart rate of 77 bpm or below (resulting in 142 fatalities, or 21.68%) and 998 patients having an admission heart rate above 77 bpm (resulting in 303 fatalities, or 30.36%). Significant differences were observed between the two groups in terms of age (68.97 ± 11.41 years vs 67.68 ± 12.93 years, P=0.038), NT-proBNP concentrations (4303.76 ± 6618.37 pg/mL vs 8588.91 ± 10,872.52 pg/mL, P<0.001), initial heart rate (68.73 ± 6.34 bpm vs 94.23 ± 17.46 bpm, P<0.001), initial pulse pressure (55.23 ± 15.98 mmHg vs 56.98 ± 17.68 mmHg, P=0.042), and initial diastolic pressure (76.56 ± 13.11 mmHg vs 83.74 ± 17.12 mmHg, P<0.001). The subset of patients with an admission heart rate above 77 bpm had a higher prevalence of cardiological conditions and a greater rate of all-cause mortality compared to those with a heart rate of 77 bpm or below (Table 1).

Clinical Outcomes Based on Heart Rate Stratification

Without adjusting for potential confounders, categorizing heart rates into two strata showed that the all-cause mortality risk was 49.1% higher [Hazard Ratio (HR) = 1.491, 95% Confidence Interval (CI) = 1.221–1.820, P<0.001] for patients with heart rates above 77 bpm compared to those with heart rates of 77 bpm or below (Table 2, Model I, and Figure 3). When heart rate was treated as a continuous variable, each 1 bpm increase was associated with a 0.7% increase in all-cause mortality risk (HR = 1.007, 95% CI = 1.003–1.011, P=0.002) (Table 2, Model I). Similar trends were observed even after adjusting for age and sex (Table 2, Model II).

Table 1 Baseline Characteristics

	Heart Rate <=77 bpm (n=655)	Heart Rate >77 bpm (n=998)	P-value
Demographics			
Age, years	68.97 ± 11.41	67.68 ± 12.93	0.038
Male, N (%)	436 (66.56%)	631 (63.23%)	0.165
Medical history, N (%)			
Hypertension	447 (68.24%)	697 (69.84%)	0.492
Hyperlipidemia	136 (20.76%)	207 (20.74%)	0.991
Coronary heart disease	546 (83.36%)	746 (74.75%)	<0.001
Atrial fibrillation	86 (13.13%)	199 (19.94%)	<0.001
Renal insufficiency	126 (19.24%)	272 (27.25%)	<0.001
Diabetes mellitus	196 (29.92%)	349 (34.97%)	0.033

(*Continued*)

Table 1 (Continued).

	Heart Rate <=77 bpm (n=655)	Heart Rate >77 bpm (n=998)	P-value
Clinical conditions at admission			
Initial Heart rate, bpm	68.73 ± 6.34	94.23 ± 17.46	<0.001
Initial Pulse Pressure, mmHg	55.23 ± 15.98	56.98 ± 17.68	0.042
Initial Diastolic Pressure, mmHg	76.56 ± 13.11	83.74 ± 17.12	<0.001
NYHA classification III to IV, N (%)	346 (52.82%)	608 (60.92%)	0.001
NT-proBNP, pg/mL	4303.76 ± 6618.37	8588.91 ± 10872.52	<0.001
Treatment, N (%)			
Beta-blocker	529 (80.76%)	793 (79.46%)	0.517
ACEI or ARB	497 (75.88%)	676 (67.74%)	<0.001
ARNI	36 (5.50%)	39 (3.91%)	0.129
SGLT2i	2 (0.31%)	7 (0.70%)	0.284
Diuretics	283 (43.21%)	588 (58.92%)	<0.001
Spironolactone	289 (44.12%)	467 (46.79%)	0.286
Outcome event			
All cause death, N (%)	142 (21.68%)	303 (30.36%)	<0.001

Notes: Results in the table: Mean+SD / N(%). P value: If it is a continuous variable, it is obtained by the Kruskal Wallis rank sum test; if the count variable has a theoretical number <10, it is obtained by the Fisher exact probability test.
Abbreviations: P-value, Probability value; N/n, number; NYHA classification, New York Heart Association classification; NT-proBNP, N-terminal pro-B type natriuretic peptide; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; ARNI, angiotensin receptor - enkephalase inhibitors; SGLT2i, sodium-dependent glucose transporters 2.

Table 2 Results of a Multivariate Cox Proportional Hazards Model for the Effect of Initial Heart Rate on Death in Patients with HFmrEF

	Non-adjusted Hazard Ratio (95% CI)	P-value	Adjust I Hazard/Risk Ratio (95% CI)	P-value	Adjust II Hazard/Risk Ratio (95% CI)	P-value
Initial Heart rate						
<=77 bpm	Ref.					
>77 bpm	1.491 (1.221, 1.820)	<0.001	1.571 (1.287, 1.918)	<0.001	1.280 (1.023, 1.603)	0.031
Heart rate as a continuous variable	1.007 (1.003, 1.011)	0.002	1.009 (1.005, 1.014)	<0.001	1.004 (0.999, 1.009)	0.127

Notes: Non-adjusted model (Model I) adjust for: None. Adjust I model (Model II) adjust for: Age; Sex. Adjust II model (Model III) adjust for: Age; Sex; Hypertension; Hyperlipidemia; Coronary heart disease; Atrial fibrillation; Renal insufficiency; Diabetes mellitus; NYHA classification; NT-proBNP; Beta-blocker; ACEI or ARB; ARNI; SGLT2i; Diuretics; Spironolactone.
Abbreviations: HFmrEF, heart failure with mildly reduced left ventricular ejection fraction; CI, confidence interval; P-value, Probability value; Ref, reference; NYHA classification, New York Heart Association classification; NT-proBNP, N-terminal pro-B type natriuretic peptide; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; ARNI, angiotensin receptor - enkephalase inhibitors; SGLT2i, sodium-dependent glucose transporters 2.

After comprehensive adjustment for all confounders, patients with heart rates above 77 bpm had a 28.0% higher risk of all-cause mortality (HR = 1.280, 95% CI = 1.023–1.603, P=0.031) compared to those with heart rates of 77 bpm or less. As a continuous variable, each 1 bpm increase in heart rate was associated with a 0.4% increase in all-cause mortality risk, but this was not statistically significant (HR = 1.004, 95% CI = 0.999–1.009, P=0.127). These findings indicate a correlation between an admission heart rate over 77 bpm and higher all-cause mortality risk, although the increase in risk for each additional bpm may not be statistically significant after adjusting for confounders (Table 2, Model III).

Clinical Outcomes

We compared pulse and diastolic pressure in patient cohorts based on admission heart rates of ≤77 bpm and >77 bpm. Without adjusting for covariates, patients with an admission heart rate of ≤77 bpm and pulse pressure above 37 mmHg had a 364% higher risk of all-cause mortality (HR=4.640, 95% CI=1.478–14.563, P=0.009) compared to those with

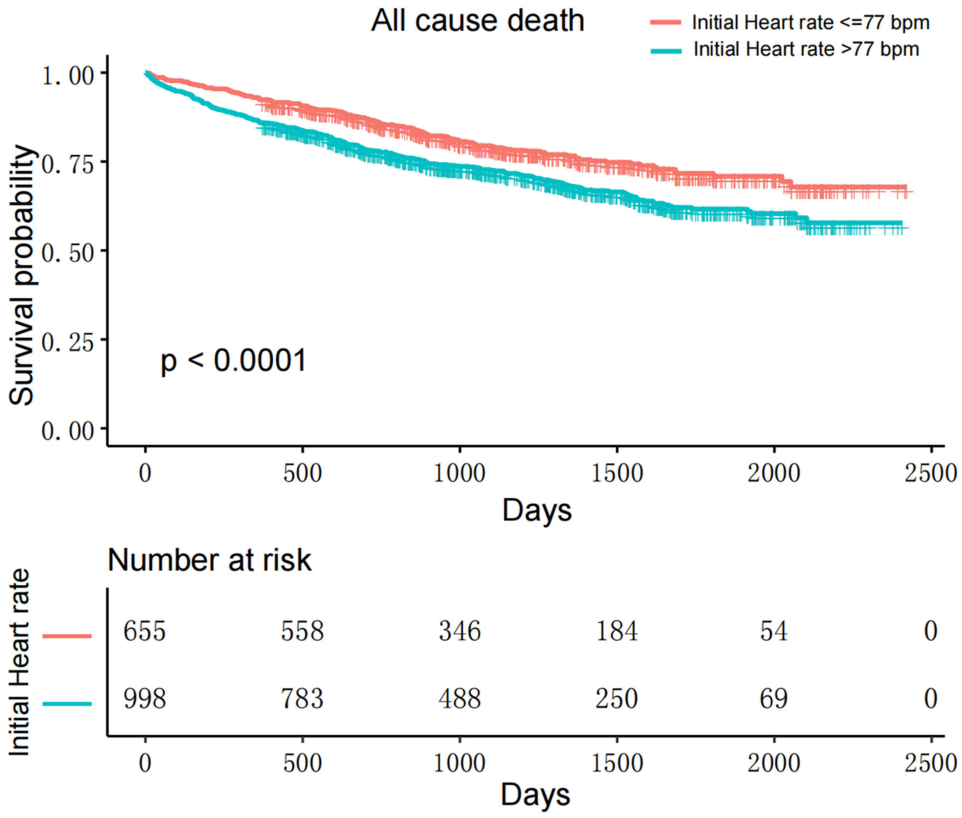

Figure 3 Kaplan-Meier Survival Curves: All-cause mortality stratified by initial heart rate.

a pulse pressure of ≤37 mmHg (Table 3, Model I, and Figure 4A). The all-cause mortality risk did not show significant differences among patients with diastolic pressure in the ranges of 63–100 mmHg and >100 mmHg compared to those with diastolic pressure ≤63 mmHg. When pulse and diastolic pressure were evaluated as continuous variables, each mmHg increase in pulse pressure was associated with a 1.7% increase in all-cause mortality risk, while each mmHg increase in diastolic pressure was associated with a 0.9% decrease, though this latter association was not statistically significant (Table 3, Model I).

For patients with an admission heart rate exceeding 77 bpm, the all-cause mortality risk significantly declined when diastolic pressure was within 63–100 mmHg or above 100 mmHg, compared to those with diastolic pressure ≤63 mmHg. The hazard ratios (HR) were 0.605 (95% CI: 0.426–0.858, P=0.005) and 0.361 (95% CI: 0.214–0.609, P<0.001), respectively (Table 3 and Figure 4B). When diastolic pressure was analyzed as a continuous variable, each unit increase resulted in a 0.992-fold reduction in all-cause mortality risk (95% CI: 0.985–0.999, P=0.033). Conversely, each unit increase in pulse pressure was associated with a 1.008-fold increase in all-cause mortality risk (95% CI: 1.002–1.014, P=0.011) (Table 3, Model I). These findings were consistent after adjusting for age and sex (Table 3, Model II).

After adjusting for all confounding variables, patients with an admission heart rate of ≤77 bpm and a pulse pressure above 37 mmHg had a 218.4% increased risk of all-cause mortality (HR=3.184, 95% CI=1.008–10.058, P=0.048) compared to those with a pulse pressure ≤37 mmHg. The all-cause mortality risk did not significantly vary between patient groups with diastolic pressures of 63–100 mmHg or above 100 mmHg compared to those with diastolic pressure ≤63 mmHg. When pulse and diastolic pressures were assessed as continuous variables, the changes in all-cause mortality risk per mmHg increase were not statistically significant (Table 3, Model III).

In contrast, for patients with an admission heart rate exceeding 77 bpm, the all-cause mortality risk was reduced by 34.8% (HR=0.652, 95% CI=0.450–0.943, P=0.023) and 63.0% (HR=0.370, 95% CI=0.205–0.666, P=0.001) for diastolic pressures within 63–100 mmHg and above 100 mmHg, respectively, compared to those with diastolic pressure ≤63 mmHg. However, for pulse pressure, regardless of its categorization, its association with all-cause mortality risk

Table 3 Association Between HFmrEF Patients and Death After Grouping According to Initial Heart Rate, Pulse Pressure and Diastolic Blood Pressure

Exposure	Initial Heart Rate <=77 bpm	P-value	Initial Heart rate >77 bpm	P-value
Non-adjusted Hazard ratio (95% CI)				
Initial Pulse Pressure				
<= 37 mmHg	Ref.		Ref.	
> 37 mmHg	4.640 (1.478, 14.563)	0.009	1.044 (0.712, 1.531)	0.825
Initial Diastolic Pressure				
<= 63 mmHg	Ref.		Ref.	
63 to 100 mmHg	1.036 (0.631, 1.701)	0.888	0.605 (0.426, 0.858)	0.005
> 100 mmHg	0.633 (0.186, 2.151)	0.464	0.361 (0.214, 0.609)	<0.001
Pulse Pressure as a continuous variable	1.017 (1.007, 1.026)	0.000	1.008 (1.002, 1.014)	0.011
Diastolic Pressure as a continuous variable	0.991 (0.978, 1.004)	0.181	0.992 (0.985, 0.999)	0.033
Adjust I Hazard/Risk ratio (95% CI)				
Initial Pulse Pressure				
<= 37 mmHg	Ref.		Ref.	
> 37 mmHg	3.744 (1.192, 11.762)	0.024	0.954 (0.651, 1.400)	0.811
Initial Diastolic Pressure				
<= 63 mmHg	Ref.		Ref.	
63 to 100 mmHg	1.059 (0.643, 1.743)	0.822	0.637 (0.448, 0.904)	0.012
> 100 mmHg	1.302 (0.378, 4.483)	0.675	0.509 (0.300, 0.864)	0.012
Pulse Pressure as a continuous variable	1.009 (1.000, 1.019)	0.058	1.006 (1.000, 1.013)	0.041
Diastolic Pressure as a continuous variable	0.997 (0.983, 1.011)	0.675	0.999 (0.992, 1.006)	0.784
Adjust II Hazard/Risk ratio (95% CI)				
Initial Pulse Pressure				
<= 37 mmHg	Ref.		Ref.	
> 37 mmHg	3.184 (1.008, 10.058)	0.048	0.911 (0.594, 1.397)	0.668
Initial Diastolic Pressure				
<= 63 mmHg	Ref.		Ref.	
63 to 100 mmHg	0.990 (0.573, 1.711)	0.971	0.652 (0.450, 0.943)	0.023
> 100 mmHg	0.875 (0.193, 3.979)	0.863	0.370 (0.205, 0.666)	0.001
Pulse Pressure as a continuous variable	1.003 (0.992, 1.015)	0.554	1.002 (0.995, 1.010)	0.512
Diastolic Pressure as a continuous variable	0.995 (0.979, 1.011)	0.563	0.992 (0.984, 1.001)	0.079

Notes: Non-adjusted model (Model I) adjust for: None. Adjust I model (Model II) adjust for: Age; Sex. Adjust II model (Model III) adjust for: Age; Sex; Hypertension; Hyperlipidemia; Coronary heart disease; Atrial fibrillation; Renal insufficiency; Diabetes mellitus; NYHA classification; NT-proBNP; Beta-blocker; ACEI or ARB; ARNI; SGLT2i; Diuretics; Spironolactone.

Abbreviations: HFmrEF, heart failure with mildly reduced left ventricular ejection fraction; CI, confidence interval; P-value, Probability value; Ref, reference; NYHA classification, New York Heart Association classification; NT-proBNP, N-terminal pro-B type natriuretic peptide; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; ARNI, angiotensin receptor - enkephalase inhibitors; SGLT2i, sodium-dependent glucose transporters 2.

was not statistically significant (Table 3, Model III). These findings highlight significant differences in the impact of pulse and diastolic pressure on all-cause mortality risk among different heart rate groups, providing crucial insights for clinical decision-making.

Stratified Analysis

In the stratified analysis presented in the forest plot, we investigated the correlation between heart rate, divided into two groups (≤77 bpm and >77 bpm), and the incidence of all-cause mortality. Our study showed that, across various demographic and clinical subgroups, there was a significant increase in the risk of all-cause mortality in patients with a heart rate >77 bpm compared to those with a heart rate ≤77 bpm (see Figure 5 for details).

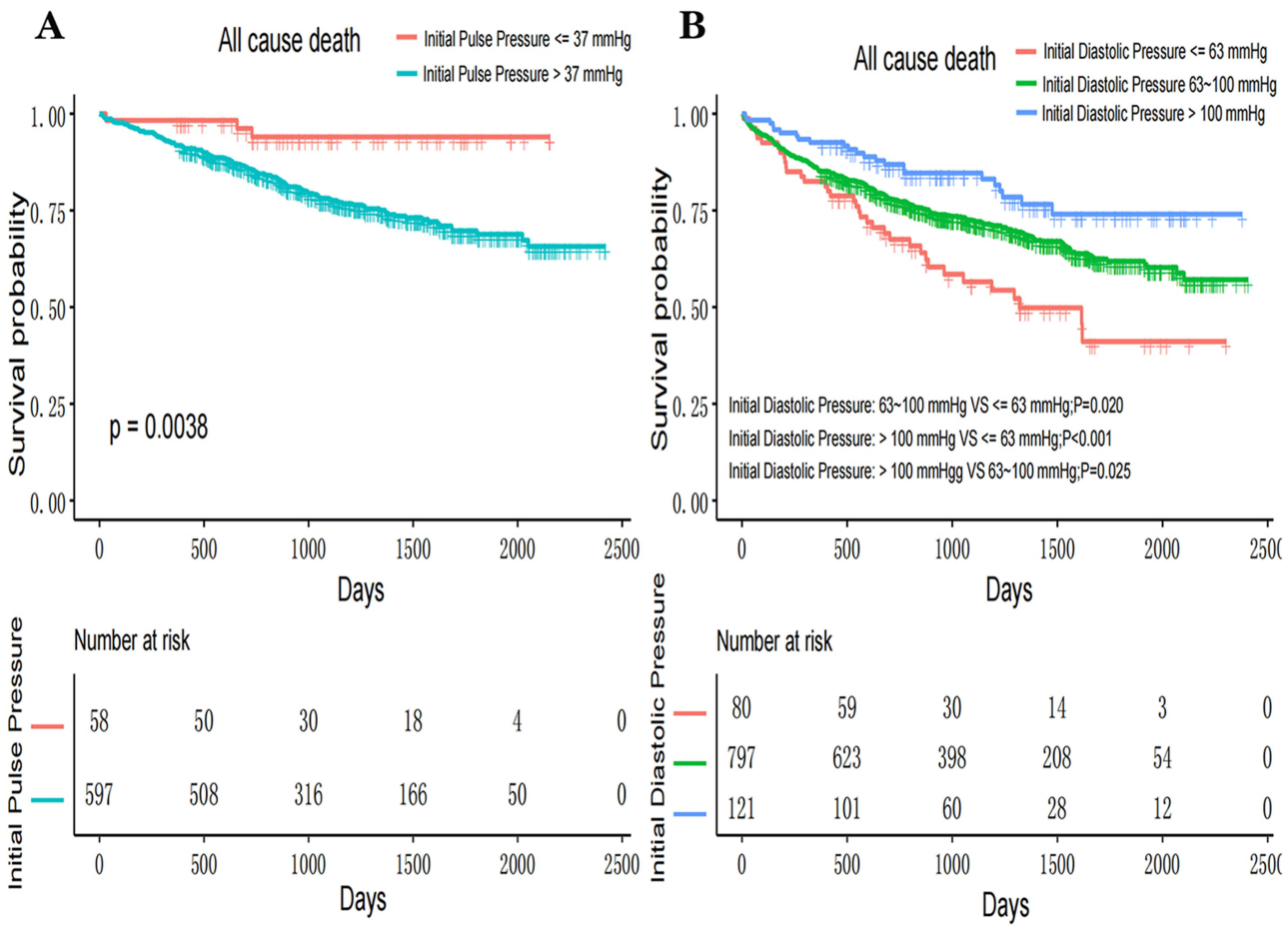

Figure 4 Kaplan-Meier Survival Curves. (**A**) Comparison of mortality trends in patients with an initial heart rate <=77 bpm according to the Initial Pulse Pressure subgroup. (**B**) Comparison of mortality trends for patients with an initial heart rate >77 bpm according to the Initial Diastolic Pressure subgroup.

Specifically, considering sex, both male and female patients with a heart rate >77 bpm demonstrated a significant increase in the risk of all-cause mortality, with hazard ratios of 1.45 (95% CI: 1.13–1.86, P=0.003) and 1.55 (95% CI: 1.11–2.16, P=0.011), respectively. A similar trend was observed across age groups (<75 years and ≥75 years), pulse pressure, diastolic pressure, NT-proBNP concentrations, NYHA classification, and subgroups with hypertension, hyperlipidemia, coronary artery disease, atrial fibrillation, renal dysfunction, diabetes, and specific medication use.

Notably, within the subgroup with pulse pressure ≤37 mmHg, patients with a heart rate >77 bpm had a significantly higher risk of all-cause mortality, with an HR of 6.42 (95% CI: 1.95–21.11, P=0.002). Similarly, within the subgroup with diastolic pressure ≤63 mmHg, those with a high heart rate exhibited a notable increase in all-cause mortality risk, with an HR of 2.53 (95% CI: 1.44–4.46, P=0.001).

In summary, across all demographic and clinical subgroups, patients with heart rates >77 bpm showed a significantly higher risk of all-cause mortality compared to those with heart rates ≤77 bpm, with an HR of 1.49 (95% CI: 1.22–1.82, P<0.001). This evidence supports the hypothesis that an elevated heart rate may serve as a significant prognostic marker for all-cause mortality in the context of HFmrEF.

Discussion

In this investigation, we elucidated the important prognostic implications of heart rate, diastolic blood pressure, and pulse pressure in patients with HFmrEF. Our findings show that, within the HFmrEF cohort, individuals with an initial heart rate of ≤77 bpm face a significantly lower mortality risk compared to those with an initial heart rate of >77 bpm. Furthermore, the mortality risk is minimized among patients with an initial heart rate of ≤77 bpm and a pulse pressure of

Characteristic Strata	Events/Total Heart rate <=77 bpm	Events/Total Heart rate >77 bpm	HR(95%CI)	P−value
Female	48/219	118/367	1.55 (1.11, 2.16)	0.011
Male	94/436	185/631	1.45 (1.13, 1.86)	0.003
Age < 75 years	65/422	161/673	1.67 (1.25, 2.23)	<0.001
Age >= 75 years	77/233	142/325	1.40 (1.06, 1.85)	0.017
Pulse pressur <= 37 mmHg	3/58	29/102	6.42 (1.95, 21.11)	0.002
Pulse pressure > 37 mmHg	139/597	274/896	1.39 (1.13, 1.70)	0.002
Diastolic blood pressure <= 63 mmHg	18/87	36/80	2.53 (1.44, 4.46)	0.001
Diastolic blood pressure 63 to 100 mmHg	121/544	244/797	1.47 (1.18, 1.83)	<0.001
Diastolic blood pressure > 100 mmHg	3/24	23/121	1.48 (0.45, 4.94)	0.521
NT−proBNP < 900 pg/ml	24/208	21/183	1.00 (0.56, 1.80)	0.991
NT−proBNP >= 900 pg/ml	95/349	250/702	1.40 (1.11, 1.77)	0.005
NYHA classification I to II	54/309	91/390	1.36 (0.97, 1.90)	0.077
NYHA classification III to IV	88/346	212/608	1.50 (1.17, 1.92)	0.001
Hypertension:No	39/208	71/301	1.26 (0.85, 1.87)	0.241
Hypertension:Yes	103/447)	232/697	1.57 (1.25, 1.98)	<0.001
Hyperlipidemia:No	121/519	250/791	1.43 (1.15, 1.77)	0.001
Hyperlipidemia:Yes	21/136	53/207	1.84 (1.11, 3.05)	0.018
Coronary heart disease:No	28/109	79/252	1.36 (0.88, 2.10)	0.161
Coronary heart disease:Yes	114/546	224/746	1.51 (1.21, 1.90)	<0.001
Atrial fibrillation:No	121/569	219/799	1.36 (1.09, 1.70)	0.007
Atrial fibrillation:Yes	21/86	84/199	1.88 (1.17, 3.04)	0.010
Renal insufficiency:No	104/529	185/726	1.34 (1.05, 1.70)	0.018
Renal insufficiency:Yes	38/126	118/272	1.65 (1.14, 2.37)	0.008
Diabetes mellitus:No	102/459	177/649	1.25 (0.98, 1.60)	0.068
Diabetes mellitus:Yes	40/196	126/349	2.05 (1.44, 2.93)	<0.001
Beta−blocker:No	47/126	75/205	0.99 (0.69, 1.42)	0.954
Beta−blocker:Yes	95/529	228/793	1.72 (1.35, 2.18)	<0.001
ACEI or ARB:No	57/158	130/322	1.11 (0.81, 1.52)	0.506
ACEI or ARB:Yes	85/497	173/676	1.59 (1.23, 2.06)	<0.001
ARNI:No	139/619	291/959	1.45 (1.19, 1.78)	<0.001
ARNI:Yes	3/36	12/39	3.14 (0.87, 11.37)	0.081
SGLT2i:No	142/653	302/991	1.49 (1.22, 1.82)	<0.001
SGLT2i:Yes	**0/2**	**1/7**	**NA**	
Diuretics:No	74/372	109/410	1.34 (1.00, 1.80)	0.051
Diuretics:Yes	68/283	194/588	1.53 (1.16, 2.02)	0.003
Spironolactone:No	74/366	176/531	1.81 (1.38, 2.38)	<0.001
Spironolactone:Yes	68/289	127/467	1.19 (0.89, 1.60)	0.251
Summary	**142/655**	**303/998**	**1.49 (1.22, 1.82)**	**<0.001**

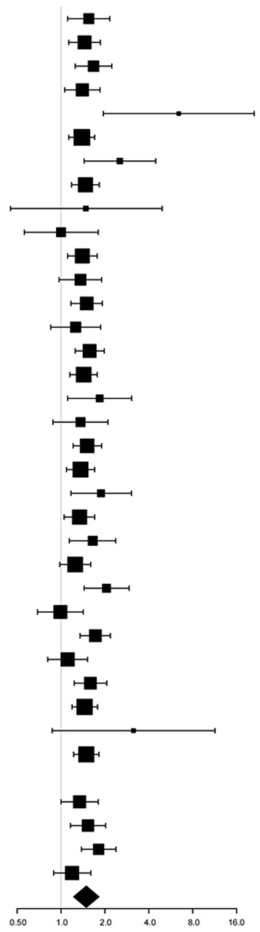

Figure 5 Forest Plot for Stratified Analysis Based on Initial Heart Rate Groups.

≤37 mmHg. In stark contrast, patients with an initial heart rate of >77 bpm and a diastolic blood pressure of ≤63 mmHg bear the highest mortality risk.

Pathophysiological Basis of Findings

The observed association between a high heart rate and poor prognosis can be attributed to increased myocardial oxygen consumption and reduced coronary perfusion time during diastole, both of which are exacerbated in heart failure patients.[14,15] These mechanisms align with prior studies that emphasize the importance of heart rate control in heart failure management.[7,8,14,16–18] However, while existing studies focus on general heart failure populations, our research specifically identifies 77 bpm as a critical threshold for HFmrEF patients, thus filling a gap in current knowledge.

While heart rate >77 bpm was significantly associated with increased mortality as a categorical variable, heart rate as a continuous variable was not statistically significant after full adjustment (Model II). This finding suggests that heart rate's prognostic impact may be threshold-dependent rather than linear across all ranges, underscoring the importance of using clinically relevant cutoffs for risk stratification.

Similarly, pulse pressure plays a pivotal role in the prognosis of HFmrEF patients, reflecting arterial stiffness and the interaction between left ventricular ejection and vascular compliance. Patients with a pulse pressure >37 mmHg and heart rates ≤77 bpm demonstrated significantly higher mortality risks, possibly due to increased afterload and ventricular wall stress, which adversely affect cardiac function.[11,12,19–21] The identification of 37 mmHg as a cutoff adds granularity to risk stratification, aiding clinicians in better assessing patient outcomes.

For diastolic pressure, our results suggest that pressures within the range of 63–100 mmHg or above 100 mmHg may indicate better coronary perfusion and reduced afterload, mitigating heart failure progression.[22,23] Conversely, a diastolic pressure ≤63 mmHg likely reflects inadequate coronary perfusion, contributing to higher mortality risks in patients with elevated heart rates.[9,10,24,25] This novel stratification approach highlights the combined prognostic influence of heart rate and diastolic pressure.

Explanation of Research Methods and Outcomes

Using the decision tree classification method, we stratified patients into discrete cohorts based on their baseline heart rate and the diastolic and pulse pressures recorded upon hospital admission. This methodology enhances our ability to perform detailed risk stratification within each cohort, beyond evaluations limited to single variables.

Clinical Significance and Utility

Our findings have direct clinical implications. Identifying patients with high heart rates and low diastolic pressure as a high-risk group enables targeted interventions, such as optimizing β-blocker therapy or using novel agents like Ivabradine to achieve better rate control. Similarly, monitoring pulse pressure and managing it through appropriate antihypertensive therapies can further improve outcomes. These insights offer clinicians practical tools for individualized risk assessment and management in HFmrEF patients.

Study Limitations and Proposed Resolutions

As with any retrospective study, potential selection bias cannot be excluded, and single-center data may limit generalizability. Future multicenter prospective studies are essential to validate our findings. Additionally, further research is needed to explore the molecular mechanisms underlying the observed associations and to develop specific clinical guidelines for managing HFmrEF patients based on these parameters.

Future Research Directions and Emerging Questions

Future research should focus on prospective validation of our results and exploring other potential factors that could influence the prognosis of HFmrEF patients. Additionally, we need to determine how our findings can be integrated into clinical practice. For instance, if we identify an optimal combination of heart rate, diastolic pressure, and pulse pressure, can we then implement targeted interventions to improve survival prospects for HFmrEF patients? This question warrants thorough investigation.

Conclusion

Our investigation confirms the link between elevated initial heart rate and increased all-cause mortality risk in HFmrEF patients. Patients with high initial heart rates and low diastolic pressure face the highest mortality risk, while those with low heart rates and low pulse pressure have the lowest risk. These findings underscore the importance of heart rate, diastolic pressure, and pulse pressure as key prognostic factors, offering a basis for improved risk stratification and individualized management in HFmrEF patients. Further studies are needed to validate these results and explore targeted interventions to improve outcomes.

Data Sharing Statement

Data are available on reasonable request. If anyone wishes to request the data pertaining to this study, please contact the corresponding author, Mingyan Jiang or Jianping Zeng.

Ethics Statement

This study is a retrospective observational study, and all data were obtained from previously completed clinical treatment records without any intervention in the patients' treatment plans. All patient information was kept strictly confidential, and no identifiable information was used during the data analysis. This study was approved by the Ethics Committee of Xiangtan Central Hospital (Xiangtan, China, No.20211036). According to the regulations of the Ethics Committee of

Xiangtan Central Hospital, informed consent was waived due to the retrospective nature of the data analysis, and the committee has formally approved the waiver of informed consent. Our study complies with the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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