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Characteristics of Heart Failure Patients with Reduced Left Ventricular Ejection Fraction (HFrEF) Using Angiotensin Receptor-Neprilysin Inhibitors (ARNI) Compared to Angiotensin Converting Enzyme-Inhibitor (ACE-I)/Angiotensin Receptor Blocker (ARB) Therapy at Haji Adam Malik Hospital, Medan

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ABSTRACT

BACKGROUND: Heart failure with reduced ejection fraction (HFrEF) remains a major cause of cardiovascular morbidity. While guideline-directed medical therapy, including *Angiotensin Receptor Neprylisin Inhibitor (ARNI)* and *Angiotensin Converting Enzyme-Inhibitor (ACE-I)/Angiotensin Receptor Blocker (ARB)*, is well-established, clinical profiling of these patients in Indonesia remains limited.

OBJECTIVES: To evaluate and compare the baseline clinical, demographic, and pharmacological characteristics of HFrEF patients receiving ARNI versus ACE/ARB therapies at Haji Adam Malik Hospital, Medan.

METHODS: This prospective cross-sectional, descriptive study was conducted at the integrated heart center polyclinic from August to December 2025. We consecutively enrolled 50 eligible HFrEF outpatients, consisting of 25 patients receiving ACE/ARB and 25 patients receiving ARNI therapies. Data was recorded during patients' visit and medical history was obtained from patient's medical records. The data were then extracted and analyzed using IBM SPSS.

RESULTS: The cohort had an overall mean age of 57.6 years and was predominantly male (78%). The primary underlying etiology was ischemic cardiomyopathy (86%). Key comorbidities included hypertension (54%) and diabetes mellitus (32%). Overall analysis demonstrated that demographic and clinical parameters, including age, systolic blood pressure, and comorbidities, were not significantly different among patients receiving ACE/ARB and those receiving ARNI (all $p > 0.05$).

CONCLUSION: HFrEF patients are predominantly male with an ischemic etiology and a significant burden of cardiometabolic comorbidities. Baseline clinical profiles are highly comparable between those prescribed ARNI and ACE/ARB therapies, providing valuable real-world data for the optimization of HFrEF management.

Keywords: Angiotensin Receptor Neprylisin Inhibitor; Angiotensin-Converting Enzyme Inhibitors; Angiotensin Receptor Blocker; Heart Failure with Reduced Ejection Fraction.

ABSTRAK

LATAR BELAKANG: Gagal jantung dengan penurunan ejeksi fraksi masih menjadi penyebab utama morbiditas kardiovaskular. Meskipun terapi medis yang sesuai panduan, termasuk *Angiotensin Receptor Neprylisin Inhibitor (ARNI)* dan *Angiotensin Converting Enzyme-Inhibitor (ACE-I)/Angiotensin Receptor Blocker (ARB)*, terbukti efektif, profil klinis pasien di Indonesia masih terbatas.

TUJUAN: Untuk mengevaluasi dan membandingkan karakteristik klinis awal, demografis, dan farmakologis pasien gagal jantung dengan penurunan ejeksi fraksi yang menerima terapi ARNI dibandingkan dengan terapi ACE/ARB di Rumah Sakit Haji Adam Malik, Medan.

METODE: Penelitian deskriptif potong lintang prospektif ini dilaksanakan di poliklinik Pusat Jantung Terpadu (PJT) Rumah Sakit Umum Pusat Haji Adam Malik (RSUP HAM) dari bulan Agustus hingga Desember 2025. Penelitian ini secara konsekutif melibatkan 50 pasien rawat jalan gagal jantung dengan fraksi ejeksi menurun yang memenuhi kriteria, terdiri dari 25 pasien yang menerima terapi ACE/ARB dan 25 pasien yang menerima terapi ARNI. Data pasien diambil saat kunjungan ke poliklinik, dan catatan pengobatan diambil melalui rekam medis. Data yang sudah dikumpulkan akan dianalisis menggunakan IBM SPSS.

HASIL: Kelompok studi memiliki rata-rata usia keseluruhan 57,6 tahun dan sebagian besar berjenis kelamin laki-laki (78%). Etiologi dasar utama adalah Kardiomiopati Iskemik (86%). Komorbiditas utama meliputi hipertensi (54%) dan diabetes melitus (32%). Analisis keseluruhan menunjukkan bahwa parameter demografis dan klinis, termasuk usia, tekanan darah sistolik, dan komorbiditas, tidak berbeda secara signifikan antara pasien yang menerima ACE/ARB dan mereka yang menerima ARNI (semua $p > 0,05$).

KESIMPULAN: Pasien gagal jantung dengan penurunan ejeksi fraksi di PJT RSUP HAM, sebagian besar adalah laki-laki dengan etiologi iskemik dan beban komorbiditas kardiometabolik yang signifikan. Profil klinis awal sangat sebanding antara mereka yang diberi resep ARNI dan terapi ACE/ARB, sehingga menyediakan data dunia nyata yang berharga untuk optimalisasi tata laksana gagal jantung dengan penurunan ejeksi fraksi.

Kata Kunci: Gagal Jantung dengan Penurunan Ejeksi Fraksi, Angiotensin Receptor Neprylisin Inhibitor, Angiotensin Converting Enzyme-Inhibitor, Angiotensin Receptor Blocker, Profil Klinis

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1. Introduction

Heart failure with reduced ejection fraction (HFrEF) remains a serious health problem and is considered the main cause of cardiovascular morbidity and mortality worldwide [1]. The incidence of heart failure varies globally, ranging from approximately 100 to 500 cases per 100,000 population in developed nations, with a continuously growing burden in Southeast Asia [2]. In Indonesia, the national prevalence of heart failure is estimated to be around 1.5% of the adult population [3]. Moreover, the mortality of the disease is also reported to vary significantly, with 1-year mortality rates ranging from 15% to 20%, and 5-year mortality reaching up to 50% depending on the region and available therapies [4]. Although the management of HFrEF, including the use of Angiotensin Receptor-Neprilysin Inhibitors (ARNI), has been well established and updated periodically, the clinical characteristics and outcomes of the disease were reported varying in each individual [5]. Until now, most of studies only reported general clinical outcomes, and the specific baseline characteristics related to patients' life (quality of life) in clinical settings have been rarely reported [6].

Understanding the detailed clinical profiles of HFrEF patients, including demographic variables, underlying etiologies, and the burden of cardiometabolic comorbidities, is crucial for optimizing guideline-directed medical therapy (GDMT) [7–9]. While randomized controlled trials provide foundational evidence for foundational therapies like ACE/ARBs and ARNIs [10,11], observational data are necessary to understand how these treatments are implemented in daily clinical practice. In Indonesia, comprehensive reports comparing the specific clinical and pharmacological profiles of patients prescribed traditional RAAS inhibitors versus novel agents like ARNI remain severely limited. Comprehensive clinical profiling is essential to identify specific patient phenotypes, recognize potential treatment gaps, and guide tailored clinical decision-making [9].

Our current study, therefore, aimed to evaluate the characteristics of HFrEF patients using Angiotensin Receptor-Neprilysin Inhibitors (ARNI) compared to ACE/ARB therapy at Haji Adam Malik Hospital, Medan. Our results are intended to provide valuable real-world insights to support the targeted management and optimization of therapy for patients with HFrEF in the context of their specific clinical profiles.

2. Methods

Study Design

This investigation is structured as a prospective cross-sectional, analytical observational study. The research setting was located at the integrated heart center polyclinic of the Haji Adam Malik Hospital Medan, from August to December 2025. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist was used to guide the protocols of our study [13]. The retrieval of clinical and demographic characteristics was prioritized, involving the extraction of personal identities, comprehensive medical histories, echocardiogram parameters, and detailed medication records. The accumulated dataset was subsequently prepared for statistical processing

Ethical Approval

The Health Research Ethics Committee of Universitas Sumatera Utara reviewed and granted ethical clearance (No. 1056/KEPK/USU/2025) for this study before any procedures were initiated.

Participants & Eligibility Criteria

The accessible population consisted of outpatients with reduced left ventricular ejection fraction receiving care. To assemble the cohort, a non-probability consecutive sampling approach was implemented. The formula obtained a minimum threshold of 42 participants was established, yielding 21 patients per comparative arm. The selection criteria required participants to be adults over 18 years of age suffering from chronic heart failure with diminished LVEF. It was also mandatory that these patients demonstrated compliance with routine polyclinic visits and had maintained a regimen of either RAAS inhibitors or ARNI for no less than three months. The study excluded any candidates presenting with advanced heart failure, severe valvular pathology, or congenital cardiac conditions.

Measure

A reduced LVEF was defined by the clinical manifestations of heart failure paired with a recorded ejection fraction below 40%. The pharmacological variables, specifically the use of ARNI or ACE/ARBs, were recognized if the patient had been actively utilizing the medication for a duration of at least three months.

Statistical Analysis

All statistical evaluations were performed utilizing the 24th edition of the SPSS software suite. To describe the clinical profiles, categorical data were synthesized into frequency counts and corresponding percentages. Bivariate analysis of categorical variables relied on the Chi-square test, transitioning to the Fisher Exact test whenever the assumption of expected counts (<5 in >20% of cells) was violated. The Shapiro-Wilk analytical test was deployed to verify the normality of the continuous data, classifying distributions as non-normal when the p-value is less than 0.05. Descriptive summaries for numerical data employed the mean and standard deviation for normally distributed variables, or the median and minimum-maximum range for skewed distributions. Comparative inferences regarding the clinical parameters between the independent medication groups (ACE/ARB vs. ARNI) were drawn using an independent samples T-test for parametric data or a Mann-Whitney U test for non-parametric data. A standard alpha level of 0.05 determined statistical significance.

3. Results

Baseline Characteristics

The majority of the participants were men (78%). The overall mean age of the participants was 57.6 years, and the mean systolic blood pressure was 114.4 mmHg. More than half of the participants were having a history of hypertension (54%), and nearly one-third had a history of diabetes (32%). The underlying etiology for the vast majority was ischemic cardiomyopathy (ICM), accounting for 86% of the cohort. Furthermore, 34% of the participants were active smokers, and 92% exhibited a normal sinus rhythm on their electrocardiography (ECG). The baseline characteristics of the participants are described in Table 1.

Table 1. Characteristics of the patients

Variables	Frequency
Age	57.6 (±8.27)
Systolic Blood Pressure	114.4 (±21.8)
Sex	
Male	39 (78%)
Female	11 (22%)
Baseline	
Ischemic Cardiomyopathy (ICM)	43 (86%)
Non-Ischemic Cardiomyopathy (NICM)	7 (14%)
Furosemide	
Furosemide 40 mg	34 (68%)
Without Furosemide	16 (32%)
Bisoprolol	
Bisoprolol (12,5 % Target Dose)	5 (10%)
Bisoprolol (25% Target Dose)	16 (32%)
Bisoprolol (50% Target Dose)	18 (36%)
Bisoprolol (75% Target Dose)	2 (4%)
Bisoprolol (100% Target Dose)	4 (8%)
Carvedilol (12,5% Target Dose)	1 (2%)
Carvedilol (25% Target Dose)	2 (4%)
Without betablocker	2 (4%)
Spironolactone	
Spironolactone (25% Target Dose)	38 (76%)
Spironolactone (50% Target Dose)	10 (20%)
Spironolactone (100% Target Dose)	2 (4%)
SRAA	
Ramipril (25% Target Dose)	2 (4%)
Ramipril 2x2,5 mg (50% Target Dose)	2 (4%)
Ramipril 1x5 mg (50% Target Dose)	3 (6%)
Ramipril 2x5 mg (100% Target Dose)	3 (6%)
Ramipril 1x10 mg (100% Target Dose)	3 (6%)
Candesartan (12,5% Target Dose)	2 (4%)
Candesartan (25% Target Dose)	2 (4%)
Candesartan (50% Target Dose)	3 (6%)
Valsartan 1x80 mg (25% Target Dose)	3 (6%)
Valsartan 2x40 mg (25% Target Dose)	1 (2%)
Valsartan (50% Target Dose)	1 (2%)
Sacubitril + Valsartan (25% Target Dose)	7 (14%)
Sacubitril + Valsartan (37,5% Target Dose)	1 (2%)
Sacubitril + Valsartan (50% Target Dose)	14 (28%)
Sacubitril + Valsartan (75% Target Dose)	2 (4%)
Sacubitril + Valsartan (100% Target Dose)	1 (2%)
History of Diabetes	
Yes	16 (32%)
No	34 (68%)
History of Hypertension	
Yes	27 (54%)
No	23 (46%)
Active Smoker	
Yes	17 (34%)
No	15 (30%)
Ex-Smoker	18 (36%)

ECG	
Atrial Fibrillation (AF)	3 (6%)
Sinus Rhythm (SR)	46 (92%)
SR ± PVC (Premature Ventricular Contraction)	1 (2%)

Main Findings

Our findings revealed that age (p = 0.447) and systolic blood pressure (p = 0.382) were statistically comparable between the two groups. While examining the clinical history, comorbidities including diabetes (p = 0.544) and hypertension (p = 0.156) also demonstrated no statistical significance between the ACE/ARB and ARNI groups. The bivariate analysis between the baseline characteristics of the ACE/ARB and ARNI groups is described in Table 2. Our overall analysis found that demographic and clinical parameters were not significantly different between patients receiving ACE/ARB and patients receiving ARNI.

Table 2. Bivariate Analysis between Baseline Characteristics with ACE/ARB and ARNI groups

Variables	**ACE/ARB n (%)**	**ARNI n (%)**	**p value**
Age	56.76 (±8.62)	58.56 (±7.97)	0.447
Systolic Blood Pressure	112.2 (±20.7)	116.8 (22.9)	0.382
Sex			0.306
Male	21 (42%)	18 (36%)	
Female	4 (8%)	7 (14%)	
Baseline			0.684
ICM	21 (42%)	22 (44%)	
NICM	4 (8%)	3 (6%)	
Baseline			0.573

Table 3. Bivariate Analysis between Medication Characteristics with ACE/ARB and ARNI group

Variables	**ACE/ARB n (%)**	**ARNI n (%)**	**p value**
Furosemide			0.544
Furosemide 1×40 mg	18 (36%)	16 (32%)	
Without Furosemide	7 (14%)	9 (18%)	
Beta-blocker			0.649
Without Beta-blocker	1 (2%)	1 (2%)	
Bisoprolol (12,5 % Target Dose)	3 (6%)	2 (4%)	
Bisoprolol (25% Target Dose)	8 (16%)	8 (16%)	
Bisoprolol (50% Target Dose)	11 (22%)	7 (14%)	
Bisoprolol (75% Target Dose)	0 (0%)	2 (4%)	

Bisoprolol (100% Target Dose)	1 (2%)	3 (6%)	
Karvedilol (12,5% Target Dose)	0 (0%)	1 (2%)	
Karvedilol (25% Target Dose)	1 (2%)	1 (2%)	
Spironolactone			0.103
Spironolakton (25% Target Dose)	22 (44%)	16 (32%)	
Spironolakton (50% Target Dose)	3 (6%)	7 (14%)	
Spironolakton (100% Target Dose)	0 (0%)	2 (4%)	

Table 4. Bivariate Analysis between patient history with ACE/ARB and ARNI group

History of Diabetes			0.544
Yes	9 (18%)	7 (14%)	
No	16 (32%)	18 (36%)	
History of Hypertension			0.156
Yes	11 (22%)	16 (32%)	
No	14 (28%)	9 (18%)	
Active Smoker			0.348
Yes	9 (18%)	8 (16%)	
No	8 (16%)	7 (14%)	
Ex-Smoker	8 (16%)	10 (20%)	
ECG			0.513
AF	1 (2%)	2 (4%)	
SR	23 (46%)	23 (46%)	
SR ± PVC	1 (2%)	0 (0%)	

4. Discussion

The baseline characteristics analysis revealed that heart failure patients with a reduced left ventricular ejection fraction (HFrEF) had a mean age of 57.6 years. This aligns with several studies on HFrEF patients, which demonstrate a strong association with age; older patients experience higher mortality, greater hospitalization, and different underlying causes of the disease compared to younger patients [14–17]. Age is an independent predictor of worse outcomes in HFrEF, including increased long-term mortality and the risk of heart failure rehospitalization [14]. Patients over 80 years of age bear the highest risk, even after adjusting for various comorbidities and other health factors [15]. The impact of a reduced ejection fraction on poor outcomes is evident in both younger and older patients; however, the relative risk is often lower in the younger age group due to fewer comorbiditie [16]. Furthermore, a mild reduction in left ventricular ejection fraction or

the presence of subclinical systolic dysfunction in the elderly population is independently associated with an increased risk of developing heart failure and high mortality rates [14].

In this study, male patients predominated at 78%, while females accounted for only 22%. This indicates that men have a higher risk of developing HFrEF compared to women. The etiology of HFrEF was most frequently attributed to ischemic heart disease, accounting for 80%. Ischemic heart disease, particularly myocardial infarction, is the most common cause of HFrEF, and its prevalence is significantly higher in men than in women, especially in older age groups [18,19]. Estrogen in premenopausal women provides cardioprotection by reducing fibrosis, improving vascular function, and limiting adverse cardiac remodeling. This makes women less susceptible to developing HFrEF until after they enter menopause. Following menopause, the risk of heart failure in women increases, but they still more frequently experience HFpEF rather than HfrEF [20]. Conversely, men are more prone to eccentric left ventricular remodeling and have risk factors such as smoking and myocardial infarction, both of which contribute to the development of HfrEF [21]. Women generally have a higher proportion of hypertension and diabetes, two conditions more closely associated with HFpEF than HfrEF [19]. Ischemic heart disease, primarily due to coronary artery disease and myocardial infarction, is the most frequent cause of HFrEF. This condition accounts for approximately 50–60% of all HFrEF cases [22]. HFrEF caused by an ischemic etiology generally has a lower likelihood of ejection fraction recovery and exhibits higher levels of cardiac stress markers (NT-proBNP) [23]. Prolonged or recurrent myocardial ischemia causes a reduction in blood flow to the heart muscle, ultimately triggering irreversible myocardial cell death. The necrotic area is replaced by scar tissue that lacks contractile capability, thereby directly reducing the left ventricular ejection fraction [24]. Following an infarction, the heart also undergoes structural changes (remodeling) that further decrease the heart's pumping ability and exacerbate heart failure symptoms [25].

The mean systolic blood pressure in this study sample was 114.4 mmHg with a standard deviation of 21.8. This result is consistent with findings from various large-scale clinical studies. This systolic blood pressure data holds important clinical significance because both low and high systolic blood pressures are associated with clinical outcomes in HFrEF patients. Several studies indicate that a lower systolic blood pressure in HFrEF, specifically below 120 mmHg, is linked to an increased risk of all-cause and cardiovascular mortality, as well as an increased rate of heart failure rehospitalization. For instance, patients with a systolic blood pressure <120 mmHg known to have a long-term mortality risk 1.81 times higher than patients with higher systolic blood pressures [26,27]. In other studies, the relationship between systolic blood pressure and clinical outcomes in HFrEF follows a J-shaped pattern, where very low systolic blood pressure is associated with worse outcomes, whereas higher systolic blood pressure does not significantly increase the risk (in contrast to HFpEF) [28]. The optimal systolic blood pressure range for HFrEF patients generally falls between 120–130 mmHg, with values below this threshold associated with a poorer prognosis [27–29]

Regarding HFrEF therapy in accordance with guideline-directed medical therapy (GDMT), furosemide use was observed in the majority of heart failure patients, amounting to 68%, while 32% did not use furosemide. Furosemide is used in HFrEF patients to manage fluid overload. It plays a crucial role in relieving congestion and symptoms caused by fluid overload; however, this drug does not modify disease progression nor reduce mortality. Unlike the four foundational therapy classes in GDMT, furosemide does not provide proven benefits in lowering mortality or morbidity. In addition, the use of high-dose loop diuretics can limit a clinician's ability to uptitrate ACE inhibitors or other GDMT drugs, thereby potentially hindering therapy optimization. Therefore, furosemide should be used at the lowest effective dose to maintain euvolemia, while the main priority remains on optimizing GDMT to improve long-term outcomes. In several studies, the majority of HFrEF patients receive furosemide therapy, with usage rates generally ranging from 68% to 92% [30]. In a Dutch cohort study involving over 10,000 chronic heart failure patients, 81.1% of HFrEF patients were recorded as receiving loop diuretics, primarily furosemide [30,31]. Another study also reported a similar usage rate, with up to 92.4% of HFrEF patients using loop diuretics [32]. A small minority of patients (around 8–32%) do not receive furosemide, typically due to milder symptoms, adequate volume status, or intolerance to diuretic therapy [30,31]

The majority of HFrEF patients used beta-blockers, amounting to 96%, while only 4% of patients did not use beta-blockers. Beta-blockers increases survival rates, reduce hospitalization rates, and improve patients' quality of life [33]. In HFrEF, chronic activation of the sympathetic nervous system worsens cardiac function and increases mortality. Beta-blockers work by inhibiting these effects, lowering the heart rate,

reducing arrhythmias, and suppressing cardiac remodeling [34]. These drugs help reverse left ventricular changes, increase the ejection fraction, and alleviate symptoms such as fatigue and shortness of breath [35]. Recent studies show that beta-blocker use in HFrEF ranges from 70% to 96%, with the highest rates found in groups with high adherence to treatment guidelines [36]. Most patients receive beta-blockers such as bisoprolol, metoprolol succinate, or carvedilol [37]. Bradycardia (heart rate <65 bpm) is the main reason for the discontinuation or delay of beta-blocker administration and serves as the primary factor in the small subset of patients (around 4–15%) who do not receive this therapy [38].

Our study results also showed that patients had several comorbidities, such as diabetes mellitus (DM), which was found in 32% of participants, while hypertension was found in 54%. On the other hand, 31.86% of the participants were active smokers. DM, hypertension, and smoking habits are very commonly found conditions in HFrEF patients and are modifiable risk factors that play an important role in the development and progression of this disease. DM is found in approximately 20–36% of HFrEF patients, which aligns with the 32% finding in this study [39]. DM is an independent factor associated with the occurrence of HFrEF and worsens cardiac function, especially when accompanied by hypertension. A longer duration of DM contributes to a more severe reduction in ejection fraction and increases the incidence of poor outcome [39,40]. Chronic hyperglycemia and insulin resistance in DM trigger signals of nutrient excess, mitochondrial dysfunction, and oxidative stress in cardiac muscle cells, thereby disrupting cell function and survival. DM also elevates pro-inflammatory cytokine levels and promotes myocardial fibrosis, which causes the heart to become stiff and progressively worsens contractility. In addition, DM affects sodium regulation in the kidneys, leading to fluid retention and an increased cardiac workload [41].

Hypertension is also found in 54–78% of HFrEF patients and is the strongest single risk factor, accounting for up to 30% of the attributable risk in men and 46% in women [42]. Hypertension accelerates cardiac remodeling and dysfunction, particularly when accompanied by diabetes mellitus. Chronic high blood pressure increases afterload, forcing the heart to work harder, which causes left ventricular hypertrophy that eventually progresses to dilatation and systolic dysfunction. Hypertension also triggers maladaptive changes in the cardiac muscle and blood vessels, including fibrosis and inflammation, which reduce the efficiency of the heart's pumping mechanism. Furthermore, hypertension shares similar pro-inflammatory mechanisms with HFrEF, thereby further exacerbating cardiac injury and damage [39]. Smoking is found in approximately 32% of HFrEF patients and is a significant risk factor, especially in men [40]. Smoking habits, alongside hypertension and diabetes mellitus, substantially increase the lifetime risk of developing HfrEF [43]. Smoking causes oxidative stress, inflammation, and endothelial dysfunction, which directly damage the cardiac muscle and blood vessels. Smokers have a greater left ventricular mass and cardiac wall thickness, accompanied by a decrease in systolic function, with a clear dose-response relationship between the amount of smoke exposure and the degree of cardiac damage. Even after smoking cessation, the risk of heart failure remains elevated for years, demonstrating the massive long-term impact of smoking on cardiovascular health [26,38,39].

Our present study has several important limitations. Firstly, although the study met the predetermined sample size requirement for the primary analysis, the relatively modest sample size and single-center design may have limited the precision of subgroup analyses and the generalizability of the findings. Secondly, the cross-sectional design inherently carries a potential for bias and prevents any causal inferences or evaluations of longitudinal clinical outcomes, such as mortality or rehospitalization rates. Future multicenter, prospective studies with larger cohorts and long-term follow-up are necessary to fully elucidate the real-world utilization and impact of these therapies.

CONCLUSION

In conclusion, the present study characterizes a typical HFrEF population that is predominantly middle-aged, male, and primarily driven by ischemic heart disease as the underlying etiology. The high male predominance aligns with pathophysiological differences in cardiac remodeling and the absence of estrogen-mediated cardioprotection, which traditionally shields premenopausal women from HFrEF and directs them more toward HFpEF post-menopause. The patients' mean systolic blood pressure falls below the optimal therapeutic range, highlighting a critical clinical concern given the established J-shaped curve that links lower systolic blood pressure to increased mortality and rehospitalization in HFrEF. Furthermore, the cohort exhibits a substantial burden of modifiable risk factors—including hypertension, diabetes mellitus, and active smoking—which synergistically accelerate myocardial fibrosis, oxidative stress, and adverse cardiac

remodeling, ultimately worsening systolic dysfunction. Regarding management, there is a commendable adherence to guideline-directed medical therapy, as evidenced by the high utilization of beta-blockers, though the concurrent high rate of furosemide use underscores the persistent symptomatic congestion in this population and the need to carefully balance symptom relief with the optimization of disease-modifying therapies. Ultimately, while these baseline findings successfully contextualize the demographic and clinical profile of HFrEF patients within existing literature, the cross-sectional and single-center design of the study limits causal inferences and broad generalizability, highlighting the necessity for future multicenter, prospective studies to accurately assess the long-term impact of these characteristics on mortality and rehospitalization outcomes.

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Conflict of Interest Statement
The author declares that there is no conflict of interest related to this study.

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