Characteristics and Prognosis of Patients with Acute Heart Failure According to the Universal Ejection Fraction Classification

Michelle Bozko Collini,[1] Gustavo Sarot Pereira da Cunha,[1] Leonardo Henrique dos Santos de Melo,[1] Matheus Bissa Duarte Ferreira,[1] Jorge Tadashi Daikubara Neto,[1] Rafael Moretti,[1] Carolina Ruschel Senger,[1] Karoline Cordeiro Vercka,[1] Jessica Tamires Reichert,[1] Lucas Muller Prado,[1] Jamilly Giuriatti Anziliero,[1] Eduardo Leal Adam,[1] Raphael Henrique Déa Cirino,[1] Miguel Morita Fernandes-Silva[1]
Universidade Federal do Paraná,[1] Curitiba, PR – Brazil

Abstract

Background: The universal classification of heart failure (HF) defined four categories based on ejection fraction (EF). Although it has been shown these EF-based categories have distinct prognoses and responses to treatment, most of the data has been focused on chronic HF.

Objectives: We compared the prognosis and characteristics of patients with acute HF according to the universal EF classification.

Methods: We performed a prospective cohort study of patients admitted to a tertiary hospital for acute HF. Patients were classified into the four categories of the universal EF classification: reduced (HFrEF), mildly reduced (HFmrEF), preserved (HFpEF), and improved (HFimpEF), based on an echocardiogram conducted during the hospitalization. The primary outcome was all-cause death in six months of follow-up.

Results: 153 patients hospitalized for acute HF (67.2 ± 14.9 years, 50.3% female, EF = 43.8 ± 17.6%) were included, being 52% HFrEF, 35% HFpEF, 12% HFmrEF, and 1% HFimpEF. HFrEF patients were more likely to have an ischemic etiology (42.5%), while HFpEF patients were more likely female (67.3%), had hypertension (90.9%) and atrial fibrillation (49.1%). Six-month mortality was similar among HFrEF, HFpEF, and HFmrEF categories (15% vs 20% vs 11%, respectively, Log-rank p = 0.75), and change in EF from a previous echocardiogram was not associated with outcomes.

Conclusion: In patients with acute HF, the EF categories from the universal classification had similar mortality rates. The proportion of patients with improved EF was very small in patients with acute HF and improvement of EF was not associated with better outcomes.

Keywords: Heart Failure; Stroke Volume; Prognosis.

Introduction

Heart failure (HF) is a heterogeneous clinical syndrome with current or previous symptoms and signs caused by cardiac abnormalities and the rise of natriuretic peptides or objective evidence of congestion.[1] The prevalence of HF is estimated at around 1% to 2%, representing 26 million adults worldwide, rising to 10% in individuals older than 70 years.[2] HF is a major cause of hospitalization in Europe and the United States, with over one million admissions and representing 1% to 2% of all hospitalizations.[3]

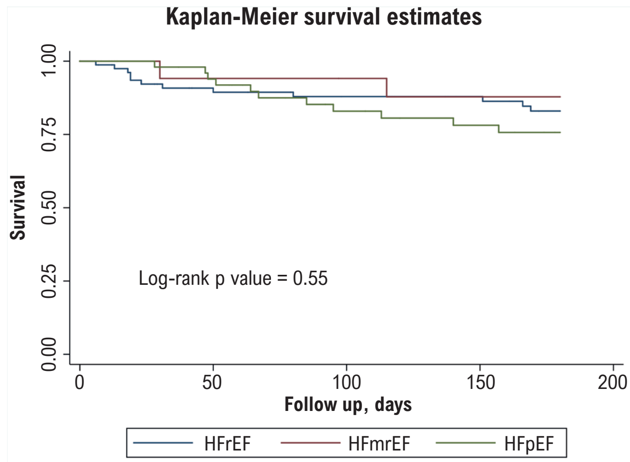
HF patients can be subcategorized in many ways, according to their functional classification from the New York Heart Association,[4] etiology,[5] stages,[1] and according to the Left Ventricle (LV) Ejection Fraction (EF). Recently, a position paper from the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, the Japanese Heart Failure Society, and the Writing Committee of the Universal Definition of Heart Failure proposed a universal classification, dividing the LVEF into four classes: HF with reduced EF (HFrEF), HF with mildly reduced EF (HFmrEF), HF with preserved EF (HFpEF) and HF with improved EF (HFimpEF).[1]

These classes have different characteristics, prognosis, and treatment response in patients with chronic HF. HFrEF patients are more likely to have ischemic etiology, coronary artery disease, and be male,[6] and it is the class with the highest rates of hospitalization and death.[7] On the other hand, HFpEF is a heterogenous group, being more prevalent in women and patients with obesity and hypertension. HFmrEF has intermediate characteristics between HFrEF and HFpEF and reduced mortality rates compared to these classes.[1,7,8] Additionally, the HFimpEF class is more prevalent in women, young, and nonischemic etiology, and is the class with the

Mailing Address: Miguel Morita Fernandes-Silva •
Universidade Federal do Paraná – Rua Gen. Carneiro, 181. Postal Code 80060-900, Alto da Glória, Curitiba, PR – Brazil
E-mail: miguelmorita@ufpr.br
Manuscript received June 19, 2024, revised manuscript July 27, 2024, accepted July 27, 2024
Editor responsible for the review: Luis Beck-da-Silva

DOI: https://doi.org/10.36660/abchf.20240035i

Central Illustration: Characteristics and Prognosis of Patients with Acute Heart Failure According to the Universal Ejection Fraction Classification



ABC Heart Fail Cardiomyop. 2024; 4(2):e20240035

Survival probability curve, according to the ejection fraction classification. HFmrEF: heart failure with mildly reduced ejection fraction; HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reduced ejection fraction.

best prognosis, fewer hospitalizations, and lower mortality rates among all the other EF categories.[9,10]

However, despite the LVEF universal classification being extensively studied in patients with chronic HF, the literature is scarce on patients hospitalized with acute HF, particularly for the HFimpEF category, and the impact of the improvement of the EF in these patients.

Objectives

The primary objective of this study was to compare the clinical characteristics and prognosis of hospitalized acute HF patients according to the universal EF classification. We also evaluated the association between the improvement of the EF with all-cause mortality in these patients.

Methods

Population

The patients included in this study were hospitalized in the Clinical Hospital of the Federal University of Paraná (HC-UFPR). We included patients with 18 years old or older, admitted in HC-UFPR with the primary diagnosis of acute HF from October 2019 to July 2021. The exclusion criteria were: patients with hospitalization for another diagnosis, even if previous HF history, and patients that were hospitalized for less than 24 hours.

After consenting, each patient was interviewed by a trained researcher, who also reviewed medical charts. Clinical, laboratory, and echocardiographic parameters were collected at the patient's admission and inserted in the database as previously described for the BPC program. Data on previous echocardiograms was also reviewed from medical charts.

Exposure variable

The patients were classified according to the new EF classification regarding the index hospitalization: HFrEF when the EF was below or equal to 40%, HFmrEF when the EF was 41-49%, HFpEF when the EF was above or equal to 50%, and HFimpEF with a baseline EF below or equal to 40%, a 10% or more increase from baseline EF and a second measurement of EF above 40%.

A sub-analysis was made independently from the universal EF classification, in which the patients were classified in Delta EF $\geq +10\%$ and Delta EF $< +10\%$ according to the EF variation in two echocardiograms. This variation was calculated by the EF from the echocardiogram made in the index hospitalization subtracted from the EF from a previous echocardiogram (if the patient had more than one EF record, the lowest value was used), being considered Delta EF $\geq +10\%$ of those who presented a 10% or higher EF raise. It should be noted that this sub-analysis differs from the universal classification, as it considers only the EF variation

Outcome and follow-up

Every patient was contacted by a phone call in 30 days and six months after discharge. The primary outcome was death from any cause.

Other variables

We also collected data on sex, age, comorbidities (hypertension, diabetes, dyslipidemia, coronary artery disease, previous myocardial infarction, atrial flutter/atrial fibrillation, previous HF, chronic kidney disease, chronic obstructive pulmonary disease/asthma, valvar disease, and stroke/transient ischemic attack), previous cardiac procedures (percutaneous and surgical myocardial revascularization), HF etiology (ischemic, Chagas disease and others) and hemodynamic profile (dry-warm, wet-warm, dry-cold, wet-cold), according to medical notes of patient's admission. The patient was also interviewed for family income, in which low was defined by less than two minimal wages, and education level, low being characterized by illiteracy or incomplete elementary schooling. Each patient's weight and height measured at the admission was used to calculate the body mass index (BMI).

HF medications in use prior to the hospitalization were also collected: angiotensin-converting enzyme inhibitor (ACEI), angiotensin II receptor blockers (ARB), angiotensin receptor-neprilysin inhibitor (ARNi), beta blocker, spironolactone, hydralazine, nitrate, loop diuretics, digoxin, and anticoagulant.

The LVEF was obtained from the echocardiogram performed during the hospitalization. As for the previous echocardiogram, it was obtained in the patient's charts. An analysis of the subgroups Delta EF ≥ +10% and Delta EF < +10% was made for the following echocardiographic parameters: previous and hospitalization Left Atrium (LA) diameter, previous and hospitalization LV diastolic and systolic diameters and its variations, and the time difference between the echocardiograms.

Statistical analysis

The categorical variables were presented in proportions and the continuous in mean ± standard deviation or median and quartiles. The continuous variables were compared among the groups with ANOVA if normal distribution and Kruskal-Wallis if not normal. The categorical variables were compared with the use of the chi-square test. Kaplan-Meier curves were built for the survival analysis, being censured in 180 days and compared with the Log-rank test. Then, the association between the EF categories and the EF variation with the primary outcome were analyzed with the Cox regression adjusted for possible confusion factors. A p-value lower than 0.05 was considered statistically significant. The software used for analysis was the Stata v.15.1 (Stata Corp, College Station, TX).

Results

One hundred and fifty-three patients were hospitalized with acute HF in this period, of which only 77 had a previous echocardiogram, 52% were classified as HFrEF, 35% as HFpEF, 12% as HFmrEF and 1% as HFimpEF, representing only two patients (Figure 1). Due to the small number of patients in the HFimpEF category, we divided the patients into one of the other three categories and evaluated the Delta EF separately (see below). The mean age varied between 64 to 71 years (HFrEF 64.30 ± 14.14, HFmrEF 67.73 ± 12.83, and HFpEF 71.40 ± 14.37), and the women proportion also varied amongst the categories (HFrEF 33.8%, HFmrEF 55.6%, and HFpEF 67.3%).

For the EF variation analysis, the 77 previous echocardiograms were used (67 ± 14 years, 48% women, EF = 43 ± 18%). The median period between the previous echocardiogram and the hospitalization echocardiogram was 224 [114, 463] days.

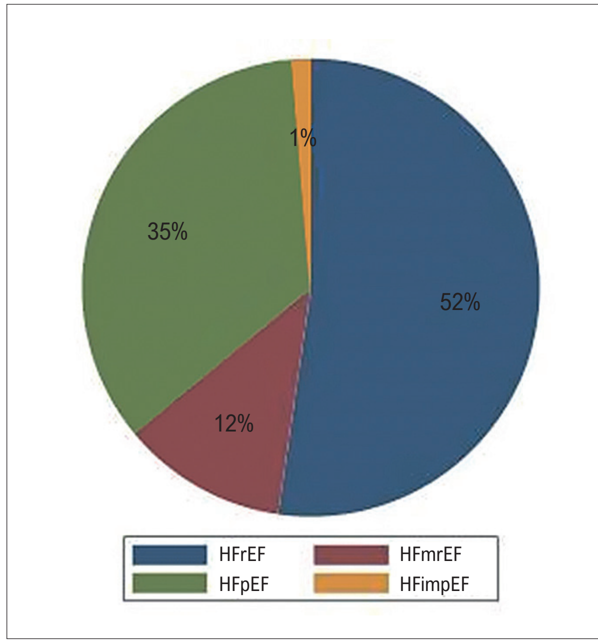


Figure 1 – *Proportion of patients in each ejection fraction category. EF: ejection fraction; HFimpEF: heart failure with improved ejection fraction; HFmrEF: heart failure with mildly reduced ejection fraction; HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reduced ejection fraction.*

Clinical characteristics

Most patients were overweight and had hypertension and previous HF. Also, more than a third had diabetes mellitus and dyslipidemia. The most common hemodynamic profile was the wet-warm, and more than half of the included patients had low family income and education level (Table 1).

Myocardial ischemia, coronary artery disease, previous myocardial infarction, myocardial revascularization, and ischemic HF etiology were more prevalent in the HFrEF group. The HFpEF group presented higher age, more frequently female sex, and higher rates of chronic obstructive pulmonary disease/asthma, valvar disease, and hypertension. The HFmrEF group presented intermediate characteristics between the HFrEF and HFpEF groups concerning: age, sex, hypertension, BMI, coronary artery disease, previous myocardial infarction, percutaneous revascularization, and valvar disease. However, the flutter/atrial fibrillation rates were similar between the HFmrEF and HFpEF groups, being higher when compared to HFrEF (Table 1).

There was no statistically significant difference between the analyzed EF categories and the use of HF medications previous to the index hospitalization (Table 2).

Echocardiographic variables

There was no statistically significant difference when comparing the following echocardiographic parameters between the subgroups Delta EF ≥ +10% e Delta EF < +10%: previous and hospitalization LA diameter, previous

Table 1 – Clinical and demographic characteristics according to the ejection fraction classification

	HFrEF n = 80	HFmrEF n = 18	HFpEF n = 55	p-value
Age, years	64.30 ± 14.14	67.73 ± 12.83	71.40 ± 14.37	0.017
Female, n (%)	27 (33.8%)	10 (55.6%)	37 (67.3%)	< 0.001
BMI, kg/m²	27.93 ± 6.04	29.16 ± 5.88	30.01 ± 8.41	0.23
Hypertension, n (%)	57 (71.2%)	15 (83.3%)	50 (90.9%)	0.019
Diabetes, n (%)	32 (40.0%)	6 (33.3%)	20 (36.4%)	0.83
Dyslipidemia, n (%)	24 (30.0%)	9 (50.0%)	16 (29.1%)	0.22
Coronary Artery Disease, n (%)	33 (41.2%)	5 (27.8%)	8 (14.5%)	0.004
Myocardial infarction, n (%)	18 (22.5%)	3 (16.7%)	3 (5.5%)	0.028
PCI, n (%)	20 (25.0%)	2 (11.1%)	3 (5.5%)	0.009
CABG Surgery, n (%)	8 (10.0%)	1 (5.6%)	3 (5.5%)	0.58
Atrial Fibrillation/Flutter, n (%)	23 (28.7%)	9 (50.0%)	27 (49.1%)	0.033
Previous Heart Failure, n (%)	57 (71.2%)	13 (72.2%)	36 (65.5%)	0.74
Chronic kidney disease (Cr >2.0), n (%)	18 (22.5%)	2 (11.1%)	6 (10.9%)	0.16
COPD/Asthma, n (%)	11 (13.8%)	2 (11.1%)	17 (30.9%)	0.030
Valvar Disease, n (%)	14 (17.5%)	5 (27.8%)	24 (43.6%)	0.004
Stroke/Transient Ischemic Attack, n (%)	17 (21.2%)	0 (0.0%)	7 (12.7%)	0.06
Etiology, n (%)				< 0.001
Ischemic	34 (42.5%)	4 (22.2%)	6 (10.9%)	
Chagas Disease	3 (3.8%)	0 (0.0%)	0 (0.0%)	
Other	43 (53.8%)	14 (77.8%)	49 (89.1%)	
Hemodynamic Profile, n (%)				0.54
Dry-warm	3 (3.8%)	0 (0.0%)	2 (3.6%)	
Wet-warm	70 (88.6%)	17 (94.4%)	48 (87.3%)	
Wet-cold	3 (3.8%)	1 (5.6%)	5 (9.1%)	
Dry-cold	3 (3.8%)	0 (0.0%)	0 (0.0%)	
Low Level of Education, n (%)	52 (65.0%)	11 (61.1%)	39 (70.9%)	0.67
Low Family Income, n (%)	42 (53.2%)	12 (66.7%)	32 (58.2%)	0.55

BMI: body mass index; CABG: Coronary artery bypass graft surgery; COPD: chronic obstructive pulmonary disease; HFmrEF: heart failure with mildly reduced ejection fraction; HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reduced ejection fraction; n: number of patients; PCI: percutaneous coronary intervention.

and hospitalization LV diastolic diameter and its variations, previous and hospitalization LV systolic diameter and the time difference between the echocardiograms.

As for the LV systolic diameter variation, there was a difference between the groups, with higher values in the Delta EF < +10% group (2.49 ± 5.02 vs -5.33 ± 3.01, $p < 0.001$) (Table 3).

Outcome

From the 153 patients analyzed, 25 (16.3%) died during the follow-up. There were no statistically significant differences in the outcome of death by all causes according to the EF classes (HFrEF 15% vs HFpEF 20% vs HFmrEF 11%, Log-rank $p = 0.55$) (Central Illustration).

Table 2 – Medications that were used previously to index hospitalization according to the ejection fraction categories

	HFrEF n = 80	HFmrEF n = 18	HFpEF n = 55	p-value
ACEI/ARB/ARNI	60.0%	72.2%	56.4%	0.49
Beta-Blockers	53.8%	61.1%	43.6%	0.34
Spironolactone	28.7%	33.3%	16.4%	0.18
Hydralazine	10.0%	5.6%	0.0%	0.053
Nitrate	6.2%	11.1%	1.8%	0.26
Loop Diuretics	40.0%	55.6%	41.8%	0.48
Digoxin	2.5%	0.0%	7.3%	0.25
Anticoagulant	2.5%	0.0%	7.3%	0.25

ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blockers; ARNI: angiotensin receptor-neprilysin inhibitor; HFmrEF: heart failure with mildly reduced ejection fraction; HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reduced ejection fraction.

Table 3 – Echocardiographic variables according to the ejection fraction variation

	Delta EF < +10 n = 71	Delta EF ≥ +10 n = 6	p-value
LA Diameter, mm			
Previous	46.3 ± 7.3	47.8 ± 3.7	0.61
Hospitalization	47.4 ± 6.8	51.7 ± 7.1	0.15
LV Diastolic Diameter, mm			
Previous	54.0 ± 9.6	52.5 ± 8.4	0.72
Hospitalization	54.6 ± 9.6	52.7 ± 8.9	0.64
LV Systolic Diameter, mm			
Previous	40.4 ± 12.4	41.7 ± 11.8	0.82
Hospitalization	42.3 ± 11.7	36.3 ± 11.1	0.23
LA Diameter Variation, mm	1.1 ± 5.5	3.8 ± 5.2	0.25
LV Diastolic Diameter Variation, mm	0.8 ± 5.1	0.2 ± 3.7	0.76
LV Systolic Diameter Variation, mm	2.5 ± 5.0	-5.3 ± 3.0	< 0.001
The time between Echocardiograms, days	220 [87; 463]	423 [133; 592]	0,46

EF: ejection fraction; LA: left atrium; LV: left ventricle.

As for the analysis according to the EF variation, in the 180 days survival analysis, there was no association between the improvement of EF (Delta > 10%) and mortality (hazard ratio [HR] =2.22; confidence interval [CI] 95% 0.49 - 10.03; p = 0.30), even after adjustment for age, sex, current EF and period between the EF measurements (adjusted HR = 2.40; CI 95% = 0.45 - 12.9; p = 0.31). The EF variation as a continuous variable showed an apparent "U" shaped association with mortality in 180 days, but was not statistically significant (p = 0.32; Figure 2).

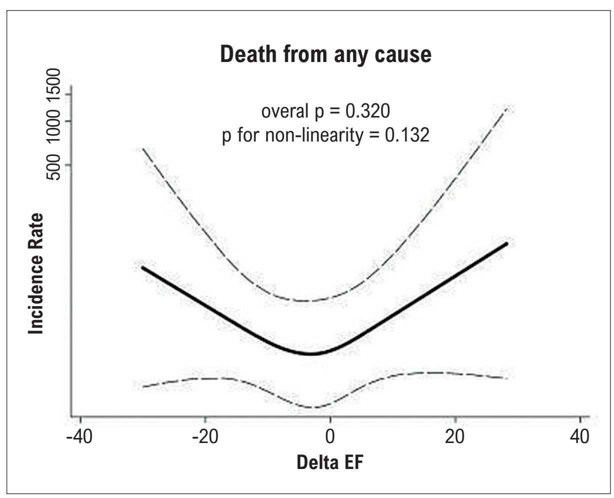


Figure 2 – *Mortality according to the ejection fraction variation as a continuous variable. EF: ejection fraction.*

Discussion

In this cohort of patients with acute HF, we found that the clinical characteristics differed among the EF classes according to the universal definition, similar to what has been found in patients with chronic HF. Nevertheless, the mortality was similar across the EF classes, which is the opposite of what is known for patients with chronic HF, where HFrEF patients display the lowest survival rates,[7] while HFimpEF patients have the highest survival rates.[8-10] Noteworthy, the proportion of patients with HFimpEF in our study was very small, and we did not find a significant association between improvement of EF and mortality. This suggests that the EF and its categories appear to have a different role in patients with acute HF, who have a more severe presentation of the disease even if they have had improvement of EF.

There are divergences in the literature about the relationship between EF and outcomes in patients with acute HF. A previous study from Brazil described similar survival rates in acute HF patients according to EF categories, although they did not evaluate the improvement in EF and outcomes.[11] Another study evaluated patients with HFmrEF and subdivided them into improved (if the EF improved at least 5 points and was > 50% in a posterior measurement), worsened (EF change of at least 5 points and EF < 40%), or no change, and they found that improved EF was associated with better survival.[12] It has also been suggested that the association between EF and outcomes may attenuate in patients with the first acute HF episode, so-called *de novo* (again) acute HF. While EF was not associated with outcomes in patients with *de novo* acute HF, the HFrEF category displayed worse survival compared with HFmrEF and HFpEF ones among patients with chronic decompensated HF.[12] These divergences demonstrate the need for more data on the impact of LVEF on cardiovascular outcomes among patients with acute HF. Our study agrees with previous data that suggested no association between EF and outcomes in patients with acute HF and further provides data on previous EF changes in an acute scenario.

The distribution of HF categories was similar to what had been published before.[13,14] Nevertheless, we found a very low number of patients with HFimpEF, which may be related to a low hospitalization rate among patients with chronic HF in this category.[9,10,15-17] Characteristics of patients across categories in our study followed what has been described in chronic patients: while HFrEF patients had a higher prevalence of coronary artery disease, previous myocardial infarction, and ischemic HF etiology, HFpEF patients were older, more frequently women had a higher prevalence of hypertension and atrial flutter/atrial fibrillation.[2,14,18] The HFmrEF patients presented intermediate characteristics between HFrEF and HfpEF.[19]

Acute HF is a pathophysiological entity less known when compared to chronic HF. It is characterized as a quick installation or a gradual worsening of HF signs and symptoms, severe enough to make the patient seek urgent medical assistance. Mortality rates in one year after discharge vary from 25% to 30%, and rehospitalization rates reach up to 45%.[20] Clinical risk scores have been validated to predict the risk of in-hospital mortality in decompensated acute HF patients, such as the ADHERE and the GWTG scores,[21] and they do not incorporate EF as predictors of mortality. Instead, they include age, race, comorbidities, systolic blood pressure, sodium levels, and kidney function. This indicates that the short-term prognosis of acute HF is better evaluated by parameters that reflect acute hemodynamic abnormalities, which are not captured by EF. The EF measured during hospitalization is a lumped parameter that reflects both chronic and acute hemodynamic abnormalities. Acute changes in EF are associated with variations in stroke volume, preload, afterload, and myocardial contractility, but measuring them is unfeasible since they would need to be assessed in a short period, with previous EF measured days or weeks before hospitalization. With the data available so far, the one-point measurement of EF during hospitalization does not appear to predict in-hospital mortality. Our study adds by further studying the EF fluctuations over a long period, which was not associated with mortality during hospitalization or in the six months afterward.

Limitations

Our study has limitations that should be considered. First, the relatively small sample size limited the power to detect differences in mortality. Second, the very small number of patients with HFimpEF precluded an analysis that included this category. Third, change in EF was calculated using an available previous echocardiogram that was usually performed by another observer and equipment with varied times between the previous and current echocardiograms, which inserted additional variability to the EF measurement. We adjusted for the time between the EF measurements, but we could not address other factors that may contribute to changes in EF, including medical treatment optimization, HF etiology, changes in volume status, and inter-observer variability.

Conclusions

In patients hospitalized for acute HF, EF categories represented distinct HF phenotypes, but they were not associated with mortality. The prevalence of HFimpEF was low in the acute setting, likely reflecting a lower risk of hospitalization in this category.

Author Contributions

Conception and design of the research and Critical revision of the manuscript for content: Collini MB, Cunha GSP, Melo LHS, Duarte MB, Daikubara Neto JT, Moretti R, Senger CR, Vercka KC, Reichert JT, Prado LM, Anziliero JG, Adam EL, Cirino RHD, Fernandes-Silva MM; Acquisition of data: Collini MB, Cunha GSP, Melo LHS, Duarte MB, Daikubara Neto JT, Moretti R, Senger CR, Vercka KC, Reichert JT, Prado LM, Anziliero JG, Fernandes-Silva MM; Analysis and interpretation of the data: Collini MB, Cunha GSP, Adam EL, Cirino RHD, Fernandes-Silva MM; Statistical analysis and Writing of the manuscript: Collini MB, Fernandes-Silva MM.

Potential conflict of interest

Miguel Morita Fernandes-Silva - Received lecture fees from Boehringer and Bayer.

Sources of funding

There were no external funding sources for this study.

Study association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Universidade Federal do Paraná under the protocol number CAEE 48561715.5.2021.0096. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

References

1. Bozkurt B, Coats AJS, Tsutsui H, Abdelhamid CM, Adamopoulos S, Albert N, et al. Universal Definition and Classification of Heart Failure: A Report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure: Endorsed by the Canadian Heart Failure Society, Heart Failure Association of India, Cardiac Society of Australia and New Zealand, and Chinese Heart Failure Association. Eur J Heart Fail. 2021;23(3):352-80. doi: 10.1002/ejhf.2115.
2. Vaduganathan M, Fonarow GC. Epidemiology of Hospitalized Heart Failure: Differences and Similarities between Patients with Reduced versus Preserved Ejection Fraction. Heart Fail Clin. 2013;9(3):271-6, v. doi: 10.1016/j.hfc.2013.04.001.

3. Ambrosy AP, Fonarow GC, Butler J, Chioncel O, Greene SJ, Vaduganathan M, et al. The Global Health and Economic Burden of Hospitalizations for Heart Failure: Lessons Learned from Hospitalized Heart Failure Registries. J Am Coll Cardiol. 2014;63(12):1123-33. doi: 10.1016/j.jacc.2013.11.053.

4. White PD, Myers MM. The Classification of Cardiac Diagnosis, with Especial Reference to Etiology. Am Heart J. 1925;1(1):87–95. doi:10.1016/S0002-8703(25)90008-7.

5. Udelson JE. Is Heart Failure Etiology Destiny?: Outcome and Therapeutic Implications. JACC Heart Fail. 2019;7(6):466-8. doi: 10.1016/j.jchf.2019.03.014.

6. Mann DL, Zipes DP, Libby P, Bonow RO. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. 10th ed. Philadelphia: Elsevier; 2014.

7. Lauritsen J, Gustafsson F, Abdulla J. Characteristics and Long-term Prognosis of Patients with Heart Failure and Mid-range Ejection Fraction Compared with Reduced and Preserved Ejection Fraction: A Systematic Review and Meta-analysis. ESC Heart Fail. 2018;5(4):685-94. doi: 10.1002/ehf2.12283.

8. Liang M, Bian B, Yang Q. Characteristics and Long-term Prognosis of Patients with Reduced, Mid-range, and Preserved Ejection Fraction: A Systemic Review and Meta-analysis. Clin Cardiol. 2022;45(1):5-17. doi: 10.1002/clc.23754.

9. Gulati G, Udelson JE. Heart Failure with Improved Ejection Fraction: Is it Possible to Escape One's Past? JACC Heart Fail. 2018;6(9):725-33. doi: 10.1016/j.jchf.2018.05.004.

10. Park CS, Park JJ, Mebazaa A, Oh IY, Park HA, Cho HJ, et al. Characteristics, Outcomes, and Treatment of Heart Failure with Improved Ejection Fraction. J Am Heart Assoc. 2019;8(6):e011077. doi: 10.1161/JAHA.118.011077.

11. Petersen LC, Danzmann LC, Bartholomay E, Bodanese LC, Donay BG, Magedanz EH, et al. Survival of Patients with Acute Heart Failure and Mid-range Ejection Fraction in a Developing Country - A Cohort Study in South Brazil. Arq Bras Cardiol. 2021;116(1):14-23. doi: 10.36660/abc.20190427.

12. Choi KH, Lee GY, Choi JO, Jeon ES, Lee HY, Cho HJ, et al. Outcomes of de Novo and Acute Decompensated Heart Failure Patients According to Ejection Fraction. Heart. 2018;104(6):525-32. doi: 10.1136/heartjnl-2017-311813.

13. Kapłon-Cieślicka A, Benson L, Chioncel O, Crespo-Leiro MG, Coats AJS, Anker SD, et al. A Comprehensive Characterization of Acute Heart Failure with Preserved versus Mildly Reduced versus Reduced Ejection Fraction - Insights from the ESC-HFA EORP Heart Failure Long-Term Registry. Eur J Heart Fail. 2022;24(2):335-50. doi: 10.1002/ejhf.2408.

14. Murphy SP, Ibrahim NE, Januzzi JL Jr. Heart Failure with Reduced Ejection Fraction: A Review. JAMA. 2020;324(5):488-504. doi: 10.1001/jama.2020.10262.

15. Tanabe K, Sakamoto T. Heart Failure with Recovered Ejection Fraction. J Echocardiogr. 2019;17(1):5-9. doi: 10.1007/s12574-018-0396-2.

16. Kalogeropoulos AP, Fonarow GC, Georgiopoulou V, Burkman G, Siwamogsatham S, Patel A, et al. Characteristics and Outcomes of Adult Outpatients with Heart Failure and Improved or Recovered Ejection Fraction. JAMA Cardiol. 2016;1(5):510-8. doi: 10.1001/jamacardio.2016.1325.

17. Jørgensen ME, Andersson C, Vasan RS, Køber L, Abdulla J. Characteristics and Prognosis of Heart Failure with Improved Compared with Persistently Reduced Ejection Fraction: A Systematic Review and Meta-analyses. Eur J Prev Cardiol. 2018;25(4):366-76. doi: 10.1177/2047487317750437.

18. Bloom MW, Greenberg B, Jaarsma T, Januzzi JL, Lam CSP, Maggioni AP, et al. Heart Failure with Reduced Ejection Fraction. Nat Rev Dis Primers. 2017;3:17058. doi: 10.1038/nrdp.2017.58.

19. Savarese G, Stolfo D, Sinagra G, Lund LH. Heart Failure with Mid-range or Mildly Reduced Ejection Fraction. Nat Rev Cardiol. 2022;19(2):100-16. doi: 10.1038/s41569-021-00605-5.

20. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure. Eur Heart J. 2021;42(36):3599-726. doi: 10.1093/eurheartj/ehab368.

21. Fonarow GC, Adams KF Jr, Abraham WT, Yancy CW, Boscardin WJ; ADHERE Scientific Advisory Committee, Study Group, and Investigators. Risk Stratification for In-hospital Mortality in Acutely Decompensated Heart Failure: Classification and Regression Tree Analysis. JAMA. 2005;293(5):572-80. doi: 10.1001/jama.293.5.572.