

## CLINICAL TRIAL

# Clinical and Laboratory Features of Patients with Heart Failure (HFrEF vs. HFmrEF): a Retrospective Evaluation

Z.K. Rakhmanov, A.B. Hajiyev, G.M. Dadashova, S.A. Alieva, G.I. Mammadova, Gurbanova Jahan

*Scientific Research institute of cardiology named by acad. D. Abdullayev*

### Introduction

Heart failure (HF) is one of the most frequent and fatal outcomes of cardiovascular disease (CVD), and worldwide, HF is one of the leading causes of mortality [1]. It is a condition in which the heart is unable to pump sufficient oxygen and nutrients to the body [2]. The clinical characteristics of patients and treatment strategies often differ depending on the ejection fraction (EF) [3]. EF refers to the volume of blood pumped out by the heart during each contraction as a percentage. Depending on EF, patients with HF with reduced myocardial systolic function are classified into two types: HF with reduced EF (HFrEF), with EF values  $\leq 40\%$ , and HF with mild reduced EF (HFmrEF), with EF values ranging from 41-49%. There are both differences and similarities between patients with HFrEF and HFmrEF. In both cases, the pumping function of the heart is impaired, but this impairment is more pronounced in HFrEF. HFmrEF is considered intermediate and requires special attention in terms of diagnosis and treatment approaches [4]. Although treatment strategies for both types are almost the same, an individualized approach is important. Treatment approaches for HFmrEF are still a subject of research [5, 6]. Currently, in the treatment of HF with HFmrEF, renin-angiotensin-aldosterone system (RAAS) blockers (angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), neprilysin receptor inhibitors in combination with sartans (ARNI)), beta-blockers, mineralocorticoid receptor antagonists (MRAs), sodium-glucose co-transporter inhibitors (SGCTI) and diuretics [7]. However, there are no guidelines for the treatment of patients with HFmrEF. There is disagreement as to whether HFmrEF should be considered a separate group or considered part of patients with HFrEF. At the same time, the causes of onset, clinical course and approaches to the treatment of HF in these groups of patients are somewhat

different, which requires a more detailed study of their features in perspective.

In light of the above, the present study analyzed the clinical features, etiology, complications, laboratory and instrumental data in the compared groups of patients, and also the approaches and criteria of drug therapy in both groups.

### Purpose

The aim of this study was to compare clinical, laboratory data in patients with HFrEF and HFmrEF, with evaluation of possibilities of optimization and differentiation of treatment approaches in the compared groups of patients.

### Materials and Methods

A retrospective study was conducted in 1123 patients with chronic HF admitted for inpatient treatment at the Research Institute of Cardiology in the period from September 2022 to September 2024. All examined patients were divided into two groups: HFrEF (n=794) and HFmrEF (n=329). Clinical characteristics, complications, comorbidities, laboratory data (NT-proBNP, cholesterol, creatinine), systolic (SBP), diastolic blood pressure (DBP) indices, therapy received (angiotensin-converting enzyme inhibitors (ACEIs), sartans, sacubitril/valsartan, beta-blockers, mineralocorticoid receptor antagonists (MCRAs), glyflosins, diuretics) were compared between the two groups. Statistical analyses were performed using the SPSS 21.0 statistical software package, with significant differences noted at  $p < 0.05$ .

### Results

No significant differences were found between the two groups in terms of age and gender ( $p > 0.05$ ). The proportion of elderly patients ( $>70$  years) was about the same in both groups, which was consistent with the overall distribution.

**Table 1:** Anthropological and etiological differences between HF<sub>r</sub>EF and HF<sub>m</sub>rEF patient groups

Characteristics	HF <sub>r</sub> EF (n=794) AF ≤40%	HF <sub>m</sub> rEF (n=329) AF 41–49%	p-value
Age, M±S	58.86 ± 10.57	60.17 ± 9.05	p>0.05
Age > 70 years, %	13.22	12.76	p>0.05
Male, %	85.01	82.98	p>0.05
Age, M±S (Male)	58.31 ± 10.66	60.38 ± 8.74	p>0.05
Female, %	14.99	17.02	p>0.05
Age, M±S (Female)	61.90 ± 9.88	59.11 ± 10.45	p>0.05
<b>Etiology</b>			
Ischemic (IHD), %	75.19	85.11	P<0.001
Hypertensive (HTN), %	2.64	4.25	P<0.001
Idiopathic (DCM), %	21.28	10.64	P<0.001

**Table 2:** Laboratory and instrumental differences between HF<sub>r</sub>EF and HF<sub>m</sub>rEF patient groups

Laboratory and Instrumental Results	HF <sub>r</sub> EF (n=794) AF ≤40%	HF <sub>m</sub> rEF (n=329) AF 41–49%	p-value
SBP, M±S (mmHg)	132.99 ± 25.58	140.9 ± 36.08	p<0.001
DBP, M±S (mmHg)	81.99 ± 13.87	84.67 ± 13.05	p<0.005
LVEF, M±S (%)	28.21 ± 6.82	44.76 ± 2.97	p<0.001
NT-proBNP, M±S (pg/mL)	3822.84 ± 6097.84	2973.67 ± 5783.23	P<0.05
Hemoglobin <12 g/dL, M±S	10.74 ± 1.04	10.57 ± 1.20	p>0.05
Cholesterol, M±S (mg/dL)	176.06 ± 53.78	174.51 ± 57.07	p>0.05
Potassium (K <sup>+</sup> ), M±S (mmol/L)	4.40 ± 0.62	4.37 ± 0.54	p>0.05
GFR (CKD-EPI), M±S (mL/min/1.73m <sup>2</sup> )	73.29 ± 22.55	72.81 ± 23.26	p>0.05

The proportion of men was slightly higher in both groups, reflecting the prevalence of HF among men, which was probably due to a higher frequency of cardiovascular risk factors (bad habits, higher frequency of stress, etc.).

Significant intergroup differences were observed in terms of etiological factors, results are shown in Table 1. While ischaemic and hypertensive aetiology of HF occurrence was comparatively more frequent in the group with HF<sub>m</sub>rEF than in the group with HF<sub>r</sub>EF (85.1% and 4.2% vs. 75.2% and 2.6%, respectively, p<0.001), idiopathic aetiology prevailed in the group with HF<sub>r</sub>EF (21.3% vs. 10.6%, p<0.001). Myocardial infarction and AH were more frequent in the group with HF<sub>m</sub>rEF (72.3% and 65.6% vs. 60.9% and 53.6%, respectively, p<0.001). At the same time, the number of patients with ischaemic AMI and pulmonary hypertension in the group with HF<sub>r</sub>EF was 3.1% (p<0.05) and 19.9% (p<0.001) higher than in the group of patients with HF<sub>m</sub>rEF, respectively.

The prevalence of conditions such as atrial fibrillation, diabetes mellitus, cerebrovascular disease, renal dysfunction and anaemia in both observed groups was approximately similar (p>0.05) (Figure 1). Results are shown in Table 2 that, laboratory analysis showed significant differences in NT-proBNP levels with predominance in the HF<sub>r</sub>EF group (3822.84 ± 6097.84 pg/ml vs. 2973.67 ± 5783.23 pg/ml,

p<0.05). In addition, SBP and DBP values were higher in the HF<sub>m</sub>rEF group (p<0.001 and p<0.005, respectively).

## Conclusion

The results of the study showed that in the treatment of patients in both groups, drugs from the group of AMCR and diuretics were most frequently used. To assess the severity and prognosis of HF, as well as to control the effectiveness of the conducted treatment it is reasonable to use NT-proBNP as a diagnostic biomarker. IAPP or BPA group drugs were used in approximately 30% of patients, and BAB group drugs – in 59% of patients in both groups, which, most likely, was associated with low blood pressure indices. It should be noted that, despite the generally accepted recommendations, ARNIs and glyflosins were used in only 30% and 26% of patients in the compared groups, which was apparently mediated by the fact that these drugs were not covered by insurance for the period of time in question.

## References

1. Статистика ВОЗ о ведущих причинах смертности и инвалидности во всём мире за период 2000-2019 год. Пресс-релиз. <https://www.who.int/ru/news/item/09-12-2020-who-reveals-leading-causes-of-death-and-disability-worldwide-2000-2019>
2. B. Bozkurt, A.J.S. Coats, H. Tsutsui 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 // *European Journal of Heart Failure*, 2021, Volume 23, p. 352-380, doi: 10.1002/ehf.2115. Epub 2021 Mar 3.
3. H.-P. Brunner-La Rocca, G.C. Linssen, F.J. Smeele et al. Contemporary Drug Treatment of Chronic Heart Failure with Reduced Ejection Fraction // *JACC: Heart Failure*, 2019-01-01, Volume 7, Issue 1, Pages 13-21, DOI: 10.1016/j.jchf.2018.10.010
  4. J.J. Hsu, B. Ziaeeian, G.C. Fonarow et al. Heart Failure with Mid-Range (Borderline) Ejection Fraction: Clinical Implications and Future Directions // *JACC: Heart Failure*, 2017, Volume 5, Issue 11, Pages 763-771, doi.org/10.1016/j.jchf.2017.06.013
  5. N.E. Ibrahim, Y. Song, C.P. Cannon et al. Heart failure with mid-range ejection fraction: characterization of patients from the PINNACLE Registry // *ESC Heart Failure* 2019; 6: 784–792. DOI: 10.1002/ehf2.12455 DOI: 10.1002/ehf2.12455
  6. Schwinger R.H.G. Pathophysiology of heart failure // *Cardiovasc Diagn Ther* 2021;11(1):263-276. doi: 10.21037/cdt-20-302
  7. Ларина В.Н., Скиба И.К., Скиба А.С. Краткий обзор обновлений клинических рекомендаций по хронической сердечной недостаточности Европейского общества кардиологов 2021 года // *Российский кардиологический журнал*, 2022, 27(2): 4820, с. 97-105, doi:10.15829/1560407120224820