Original Article

The Clinical Characteristics of Acute Heart Failure Patients with Mid-Range Ejection Fraction in Turkey: A Subgroup Analysis from Journey HF-TR Study

Umit Yasar Sinan, Dogac Caglar Gurbuz[1], Oguzhan Celik[2], Huseyin Altug Cakmak[3], Salih Kilic[4], Sinan Inci[5], Gulay Gok[6], Mehmet Serdar Kucukokglu, Mehdi Zoghi[7]

Department of Cardiology, Istanbul University Cerrahpasa Institute of Cardiology, Istanbul, [1]Department of Cardiology, Izmir Katip Celebi University Ataturk Training and Research Hospital, Izmir, [2]Department of Cardiology, Hitit University School of Medicine, Corum, [3]Department of Cardiology, Mustafakemalpasa State Hospital, Bursa, [4]Department of Cardiology, Gaziantep Doctor Ersin Arslan Training and Research Hospital, Gaziantep, [5]Department of Cardiology, Aksaray State Hospital, Aksaray, [6]Department of Cardiology, Mardin State Hospital, Mardin, [7]Department of Cardiology, Ege University School of Medicine, Izmir, Turkey

ORCID:
Umit Yasar Sinan: https://orcid.org/0000-0002-4837-7099
Dogac Caglar Gurbuz: https://orcid.org/0000-0002-0517-8612
Oguzhan Celik: https://orcid.org/0000-0002-0716-8602
Huseyin Altug Cakmak: https://orcid.org/0000-0002-5101-1928
Salih Kilic: https://orcid.org/0000-0002-5138-744X
Sinan Inci: https://orcid.org/0000-0002-4576-128X
Gulay Gok: https://orcid.org/0000-0003-0205-1138
Mehmet Serdar Kucukoglu: https://orcid.org/0000-0002-3145-6209
Mehdi Zoghi: https://orcid.org/0000-0002-8156-2675

Abstract

Background: Heart failure (HF) is a clinical syndrome characterized with a wide spectrum of left ventricular (LV) structural and functional abnormalities. LV ejection fraction (EF) is considered important with respect to classifying HF patients because of differing patient demographics and prognosis; as well as the response to HF therapies. We aimed to investigate the clinical characteristics, demographics, in-hospital management and in-hospital outcome of HF patients with mid-range EF (HFmrEF) in comparison with those with HF patients with reduced EF (HFrEF) or HF patients with preserved EF (HFpEF) in a large acute HF (AHF) cohort. **Materials-Methods and Results:** The Journey HF-TR study is a multicenter, and observational registry. One thousand six hundred and six patients who were diagnosed with AHF were enrolled in this study. The mean age was 67.8 ± 13.0 years and 57.2% of the study population was male. Patients were classified as HFrEF (n = 1028, 64%), HFmrEF (n = 305, 19%), and HFpEF (n = 273, 17%) according to LVEF. HFmrEF patients were elder than HFrEF patients but younger than HFpEF patients and the female proportion was the highest in HFpEF group followed by HFmrEF and HFrEF groups ($P < 0.001$ and $P = 0.03$, respectively). The prevalence of coronary artery disease was 56.7% in HFmrEF patients. It was lower than HFrEF patients (65.2%) and higher than HFpEF patients (41.4%) ($P < 0.001$). The prescription of evidence-based HF drugs (Renin-Angiotensin-System blocker, beta-blocker, mineralocorticoid receptor antagonist) was similar in HFrEF and HFmrEF patients and higher than HFpEF patients. The in-hospital mortality rate was the lowest in patients with HFmrEF (1.8%, 7.3%, and 7.5%, respectively for HFmrEF, HFrEF, and HFpEF patients) ($P < 0.001$). **Conclusion:** Patients with HFmrEF has unique clinical, echocardiographic, hemodynamic, and biomarker features compared with HFrEF and HFpEF. However, patients with HFmrEF seem to be more similar to HFrEF, in terms of etiology and use of guideline recommended medical therapy.

Keywords: Acute heart failure, clinical characteristics, demographics, heart failure with mid-range ejection fraction

Address for correspondence: Dr. Umit Yasar Sinan, Department of Cardiology, Istanbul University Cerrahpasa, Institute of Cardiology, Fatih, Istanbul, Turkey.
E-mail: drumityasar@hotmail.com

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Introduction

Heart failure (HF) is a clinical syndrome characterized by a wide spectrum of factors, including left ventricular (LV) structural and functional abnormalities ranging from preserved LV ejection fraction (LVEF) with normal LV size to severely reduced LVEF with marked dilatation of the left ventricle.[1] LVEF is considered important for classifying HF patients because of differing patient demographics, prognosis, as well as response to HF therapies.

The 2016 European Society of Cardiology HF guideline recognized HF with mid-range EF (HFmrEF, EF 40%–49%) as an entity distinct from HF with reduced EF (HFrEF, EF <40%) and preserved EF (HFpEF, EF ≥50%).[2] In this guideline, HFmrEF was defined as HF with an EF between 40% and 49%, along with symptoms and/or signs of HF, elevated levels of natriuretic peptides and evidence of other cardiac functional or structural alterations such as left atrial enlargement, LV hypertrophy or diastolic dysfunction.[2] Clinical characteristics and clinical outcomes of HFmrEF patients are described in various cohorts.[3-8] Especially Organized Program to Initiate Life-saving Treatment in Hospitalized Patients with HF (OPTIMIZE-HF) and Acute Decompensated HF National Registry (ADHERE) studies lead other studies to explore the characteristics, treatment patterns, and outcomes of patients with mildly reduced LVEF.[9,10]

The percentage of HFmrEF patients is reported to be between 13% and 24%.[4,7,11] GWTG-HF registry has found that although the percentage of patients with HFpEF increased (from 33% to 39%) and the percentage HFrEF decreased (from 52% to 47%) from 2005 to 2010, the percentage of patients with HFmrEF has remained relatively steady (between 13% and 15%) over this period.[12] Often considered a "gray" area or the "middle child" in HF, HFmrEF is gaining increasing attention in recent studies.[5]

In this analysis, we aimed to investigate the clinical characteristics, demographics, in-hospital management, and in-hospital outcomes of patients with HFmrEF and compare them to those with HFrEF and HFpEF in a large acute HF (AHF) cohort.

Materials and Methods

The Journey HF-TR study is a cross-sectional, multicenter, noninterventional, and observational registry.[13] The patients who were hospitalized with AHF in the intensive/coronary care units and cardiology wards of participating centers between September 2015 and September 2016 were included in our study. We enrolled a total of 1606 patients in 37 centers, in seven geographical regions of Turkey. Study centers were designed to represent the 12 territorial units of Turkey, accepted by the National Statistics Unit (NUTS 1). The inclusion criteria were being older than 18-year-old, hospitalization with AHF and accepting to give informed consent to participate in this study. The patients were diagnosed with AHF at first hospital admission by attending cardiologists and were classified according to ESC HF Guideline in 2016. Patients' demographic and clinical characteristics, clinical histories, symptoms and signs and their progress in hospital (diagnostic tests, laboratory findings, medications, length of stay, and mortality) were evaluated and recorded.

We selected patients with documented LVEF and we compared baseline demographic and clinical characteristics, clinical presentation, in-hospital intravenous and oral therapies, and in-hospital mortality among patients with HFrEF, HFmrEF, and HFpEF. HFrEF was defined as an LVEF lower than 40%, typical symptoms and or signs of HF; HFmrEF was defined as an LVEF ranging between 40% and 49%, typical symptoms and or signs of HF, elevated natriuretic peptides and relevant structural heart disease or diastolic dysfunction; and HFpEF was defined as an LVEF equal to or higher than 50%, typical symptoms and/or signs of HF, elevated natriuretic peptides and relevant structural heart disease or diastolic dysfunction. Demographic and clinical data were recorded at or close to patient discharge, based on medical records. In-hospital mortality rates were also recorded.

Chronic kidney disease (CKD) is defined as kidney damage or glomerular filtration rate <60 mL/min/1.73 m^2 for 3 months or more, irrespective of cause. Dyslipidemia is defined as increased total or low-density lipoprotein cholesterol or being on lipid-lowering therapy. Patients whose office blood pressure (BP) is out of target range (systolic BP higher than 140 mmHg and diastolic BP higher than 90 mmHg) are defined as patients with uncontrolled HT. Anemia is defined as Hb <13.0 g/dl for males and Hb <12.0 g/dl for females using the WHO definition. Cardiorenal syndrome is defined as the disorder of the heart and kidneys, where acute or chronic dysfunction in one organ may induce acute or chronic dysfunction of the other. We accepted infection as the cause of worsening of HF if there were signs of infection (fever, high C-reactive protein, leukocytosis, and nidus. New-onset ("*de novo*") HF may present acutely as a consequence of acute myocardial infarction, or in a subacute (gradual) fashion in patients with dilated cardiomyopathy who often have symptoms for weeks or months before the diagnosis becomes apparent.[2] If patients with AHF present with elevated systolic BP (>140 mmHg), it is defined as hypertensive AHF.[2]

Statistical analysis

For baseline characteristics, categorical variables were described as numbers and percentages and continuous variables as mean ± standard deviation, or as median with inter-quartile range if skewed. Categorical variables were compared using a Chi-square test or Fisher's exact test if any expected cell count was <5. One-sample Kolmogorov–Smirnov test was used to identify whether the distribution of variable was normal or not. Differences in characteristics across the three EF groups were compared with analysis of variance test for continuous variables. A value of $P < 0.05$ was considered statically significant. All tests were two-sided. Analyses were performed using the Statistical Package for the Social Sciences (SPSS) software for windows, version 22.0 (IBM Corp., Armonk, NY, USA).

Results

One thousand six hundred and six patients who were diagnosed with AHF in 37 centers, in seven geographical regions of Turkey were enrolled in this study. The mean age was 67.8 ± 13.0 years and 57.2% of the study population was male. Most of the patients had the New York Heart Association functional capacity III or IV. The mean EF of the whole group was 32.7 ± 14.1%. Patients were classified as HFrEF (n = 1028, 64%), HFmrEF (n = 305, 19%), and HFpEF (n = 273, 17%) according to LVEF.

The number of female and male patients was almost the same in HFmrEF patients (51.1% and 48.9%). The mean age of HFmrEF patients was higher than HFrEF patients but lower than HFpEF patients. The female proportion was the highest in HFpEF group followed by HFmrEF and HFrEF groups (respectively, $P < 0.001$ and $P = 0.03$). The prevalence of coronary artery disease (CAD) was 56.7% in HFmrEF patients, lower than the prevalence in HFrEF patients (65.2%) and higher than HFpEF patients (41.4%) ($P < 0.001$). Atrial fibrillation (AF) was less prevalent in HFmrEF patients (41.8%) than the other two groups (52% in HFrEF patients and 56.3% in HFpEF patients, $P < 0.001$). Compared to HFrEF, not only HFmrEF patients but also HFpEF patients had higher prevalence of anemia ($P < 0.001$) and hypertension ($P < 0.001$). The other comorbidities (diabetes mellitus [DM], dyslipidemia, CKD, previous history of transient ischemic attack (TIA), or cerebrovascular attack (CVA) were similar between three groups.

Acute decompensation of chronic HF was the leading cause of hospitalization in all groups (74.3%, 52.8%, and 44.4% in HFrEF, HFmrEF, and HFpEF patients, respectively). *De novo* AHF was more common among HFmrEF patients. Fourteen percent of HFrEF patients, 23.0% of HFmrEF patients, and 20.1% of HFpEF patients were hospitalized with *de novo* HF diagnosis ($P = 0.02$). The main causes for hospitalization in HFmrEF patients were acute coronary syndrome (ACS) 30.5%, arrhythmias 24.8%, uncontrolled HT 24.2%, cardio-renal syndrome 8.4%, lack of compliance to therapy 8.0%, and infection 4.1%. HFmrEF patients had a higher prevalence of ACS as the precipitating factor compared to the other two groups (30.5% and 19.4% for HFrEF and 12.3% for HFpEF; $P < 0.01$). Hypertensive

Table 1: Demographics, etiologies, precipitants, clinical risk factors of heart failure groups which was classified according to left ventricular ejection fraction

Etiologies	HFrEF (n=1028)	HFmrEF (n=305)	HFpEF (n=273)	*P*
De novo, *n* (%)	149 (14.5)	70 (23)	55 (20.1)	<0.001
Acute decompensated chronic HF, *n* (%)	879 (85.5)	235 (77)	218 (79.9)	<0.001
Clinical presentation				
Decompensation of CHF, *n* (%)	653 (74.3)	120 (52.8)	97 (44.4)	<0.001
Pulmonary edema, *n* (%)	85 (9.7)	50 (22)	68 (31.3)	<0.001
Cardiogenic shock, *n* (%)	40 (4.6)	5 (2.1)	5 (2.2)	0.07
HT HF, *n* (%)	89 (10.1)	50 (22)	38 (17.5)	<0.001
RV HF, *n* (%)	12 (1.3)	3 (1.1)	10 (4.6)	<0.001
Precipitants				
ACS, *n* (%)	200 (19.4)	30.5 (93)	12.3 (34)	<0.001
Infection, *n* (%)	205 (20.0)	13 (4.1)	55 (20.0)	<0.001
Arrhythmia, *n* (%)	230 (22.4)	75 (24.8)	85 (31.3)	0.005
Uncontrolled HT, *n* (%)	148 (14.4)	74 (24.2)	70 (25.7)	<0.001
Cardio-renal syndrome, *n* (%)	28 (2.7)	26 (8.4)	17 (6.4)	0.01
Medical in-adherence, *n* (%)	217 (21.1)	24 (8.0)	12 (4.3)	<0.001
Age (years old)	66.9±13.3	68.6±12.6	71.5±11.5	<0.001
Male sex, *n* (%)	664 (64.6)	149 (48.9)	105 (38.4)	<0.001
CAD, *n* (%)	670 (65.2)	173 (56.7)	113 (41.4)	<0.001
HT, *n* (%)	639 (62.2)	240 (78.7)	200 (73.1)	<0.001
DM Type 2, *n* (%)	432 (42)	137 (45)	101 (37)	0.148
Smoking, *n* (%)	293 (28.5)	83 (27.3)	43 (15.7)	<0.001
AF, *n* (%)	535 (52)	127 (41.8)	154 (56.3)	<0.001
HL, *n* (%)	292 (28.4)	93 (30.5)	72 (26.5)	0.580
TIA/CVA, *n* (%)	123 (12)	27 (8.9)	22 (8.2)	0.197
CKD, *n* (%)	306 (29.8)	78 (25.5)	68 (25)	0.167
Anemia, *n* (%)	421 (41)	189 (62)	172 (63)	<0.001
PAD, *n* (%)	81 (7.9)	119 (3.9)	10 (3.7)	0.02

ACS: Acute coronary syndrome, AF: Atrial fibrillation, CAD: Coronary artery disease, CHF: Chronic heart failure, CKD: Chronic kidney disease, CVA: Cerebrovascular accident, DM: Diabetes mellitus, HF: Heart failure, HFmrEF: Heart failure mid-range ejection fraction, HFpEF: Heart failure with preserved ejection fraction, HFrEF: Heart failure with reduced ejection fraction, HL: Hyperlipidemia, HT: Hypertension, LVEF: Left ventricular ejection fraction, PAD: Peripheral artery disease, RV: Right ventricle, TIA: Transient ischemic attack

HF was also more common in HFmrEF patients (22%). While uncontrolled hypertension and cardio-renal syndrome were much more seen in HFmrEF (24.2% and 8.2%) and HFpEF (25.7% and 6.4%) patients compared to HFrEF (14.4% and 2.7%) patients ($P < 0.01$ and $P = 0.01$), lack of compliance to therapy was seen much more in HFrEF patients (21.1% and 8.0 for HFmrEF and 4.3% for HFpEF; $P < 0.01$). Infection was the least precipitating factor for hospitalization in HFmrEF patients (4.1%; $P < 0.01$) [Table 1].

Vital signs of the three groups are compared in Table 2. The mean N-terminal pro-brain natriuretic peptide level was 8902 pg/ml (7923–9932) in HFrEF patients, 6030 pg/ml (4317-7742) in HFmrEF, and 4406 pg/ml (3334-5479) in HFpEF patients ($P < 0.001$) [Table 2]. At discharge, the natriuretic peptide levels of the three groups were similar.

Regarding medical management, diuretic therapy was more frequently used in HFrEF and HFmrEF patients than in HFpEF patients at admission [Table 3]. Compared to HFmrEF and HFpEF patients, HFrEF patients were characterized by higher use of mineralocorticoid-receptor antagonists (MRAs) ($P = 0.001$). There was a significantly larger number of patients with a history of cardiac device implantation (implantable cardioverter-defibrillator or cardiac resynchronization therapy) in HFrEF group. At hospital discharge, guideline-recommended medical therapy prescription was done more efficiently than first admission in all groups [Table 3]. The prescription of evidence-based HF drugs (RAAS blocker, beta-blocker, MRA) was similar in HFrEF and HFmrEF groups, which was higher than HFpEF group.

In-hospital mortality rate was least in HFmrEF patients (1.8%, 7.3%, and 7.5%, respectively, for HFmrEF, HFrEF, and HFpEF patients) ($P < 0.001$).

Table 2: Physical examination findings, laboratories, and QRS duration of heart failure subgroups

Physical examination	HFrEF	HFmrEF	HFpEF	*P*
SBP at admission (mmHg)	123±28	135±32	139±39	<0.001
HR at admission (bpm)	93±23	93±24	98±26	0.04
QRS duration (msn)	110±41	99±28	100±19	<0.001
EF (%)	27.1±7	42.5±4.2	55.2±4.8	<0.001
GFR at admission (ml/min)	50.4±29	47.6±33.5	49.6±30.5	0.398
NT-proBNP at admission (pg/ml)	8902 (7923-9932)	6030 (4317-7742)	4406 (3334-5479)	<0.001
HR at discharge (bpm)	73.1±20.7	64.6±30	72.8±24.5	<0.001
SBP at discharge (mmHg)	107±31.1	97.7±47.5	110.8±33.3	<0.001
NT-proBNP at discharge (pg/ml)	3817 (2875-4759)	2306 (1527-3086)	2028 (605-3451)	0.248

EF: Ejection fraction, GFR: Glomerular filtration rate, HF: Heart failure, HFmrEF: Heart failure mid-range ejection fraction, HFpEF: Heart failure with preserved ejection fraction, HFrEF: Heart failure with reduced ejection fraction, HR: Heart rate, NT-proBNP: N-terminal pro B-type natriuretic peptide, SBP: Systolic blood pressure

Table 3: Medications of heart failure subgroups at admission and hospital discharge and length of stay, in-hospital mortality rate

	HFrEF (*n*=1028)	HFmrEF (*n*=305)	HFpEF (*n*=273)	*P*
Medication at admission				
ACEIs/ARBs, *n* (%)	672 (65.4)	192 (63.1)	127 (46.4)	<0.001
BB, *n* (%)	781 (76)	203 (66.6)	153 (55.9)	<0.001
Diuretics, *n* (%)	763 (74.2)	207 (68)	168 (61.6)	<0.001
MRAs, *n* (%)	441 (42.9)	97 (31.9)	81 (29.8)	0.001
CCBs, *n* (%)	43 (4.2)	30 (9.9)	40 (14.5)	<0.001
Digoksin, *n* (%)	220 (21.4)	68 (22.3)	45 (16.4)	0.238
CRT/ICD, *n* (%)	221 (21.5)	24 (7.8)	14 (4.4)	<0.001
Medication at discharge				
ACEIs/ARBs, *n* (%)	828 (80.5)	269 (88.3)	167 (61.2)	<0.001
BB, *n* (%)	923 (89.8)	267 (87.6)	203 (74.3)	<0.001
Diuretics, *n* (%)	874 (85)	216 (70.9)	222 (81.3)	<0.001
MRA, *n* (%)	642 (62.5)	186 (61)	98 (35.8)	<0.001
CCB, *n* (%)	43 (4.2)	30 (9.9)	40 (14.5)	<0.001
Digoksin, *n* (%)	240 (23.3)	64 (20.9)	67 (24.6)	0.07
LOS (days)	11.7	22.5	10	<0.001
Mortality, *n* (%)	75 (7.3)	5 (1.8)	20 (7.5)	0.01

ACEIs: Angiotensin converting enzyme inhibitors, ARBs: Angiotensin receptor blockers, BB: Beta blocker, CCB: Calcium channel blockers, CRT: Cardiac resynchronization therapy, HF: Heart failure, LOS: Length of hospital stay, Heart failure mid-range ejection fraction, HFpEF: Heart failure with preserved ejection fraction, HFrEF: Heart failure with reduced ejection fraction, ICD: Implantable cardiovertor defibrillator MRAs: Mineralocorticoid receptor blockers

Discussion

In this subgroup analysis of the Journey HF-TR registry, it has been shown that nearly one-fifth of patients (19%) who were hospitalized with a diagnosis of AHF had HFmrEF. In GTWG-HF registry, which was performed in >40,000 Medicare patients, 14% of patients fell into HFmrEF category.[12] The percentage of HFmrEF patients ranges between 13% and 24% in various cohorts.[4,7,11] In our study, 36% of patients had either mid-range or preserved LVEF. This prevalence is lower than the two largest AHF registries from US, ADHERE, OPTIMIZE-HF, and European Euro-HF Survey I, in which the prevalence of LVEF ≥40% ranged from 40% to 55%.[9,14,15] However, the prevalence was higher than Turkish HF registry (SELFIE-TR).[16] The total number of patients HFrEF, HFmrEF, and HFpEF was 801 (75%), 176 (16.7%), and 77 (7.3%), respectively, in SELFIE-TR.[16]

The prevalence of HF in Turkey was reported as 6.9% in the HAPPY trial[17] and the population older than 35 years in Turkey was reported as 29.6 million according to 2010 records.[18] The percentage of the patients with HFmrEF is 19%, suggesting that approximately 460,560 individuals in Turkey have HFmrEF.

Given the differences in demography, clinical presentation, etiology, and prognosis in the three groups, some authors suggest that HFmrEF has a phenotype closer to HFpEF, whereas others consider it to be closer to HFrEF. An analysis of 41,267 patients in OPTIMIZE-HF analyzed patients hospitalized with HF according to LVEF group showed that patients with LVEF between 40% and 50% were more similar to patients with HFpEF.[9] Moreover, in GTWG-HF registry, patients with HFmrEF had clinical characteristics (older age, female sex, comorbidities as HT, chronic obstructive pulmonary disease (COPD), DM, laboratory values as creatinine, BNP, troponin and medication use as beta-blockers, RAAS blockers) more similar to those of HFpEF cohorts.[12] On the other hand, CAD was the morbidity which was more similar between HFmrEF and HFrEF patients.[12] In conclusion, HFmrEF may resemble HFpEF with an exceptional etiology of ischemia, where it resembles HFrEF more.[12] Contrarily, in a paper by Nauta *et al*. evaluating what we learned about HFmrEF 1 year after its introduction, it was concluded that although HFmrEF patients are considered to be the "middle child," it seems to be more similar to HFrEF, in terms of ischemic etiology, biomarker profile, and response to treatment.[19]

In our study, patients with HFmrEF were younger and more predominantly male compared to those with HFpEF. This was compatible with other studies.[5,11,20-23] Several CV risk factors (DM, CKD, dyslipidemia, TIA, CVA) were shared among HFmrEF, HFrEF, and HFpEF, but patients with HFmrEF were more likely to have HT (78%) and *de novo* AHF (23%) compared to those with HFrEF and HFpEF. The HT prevalence in patients with HFmrEF was higher than other registries (between 60% and 77%).[5] Of note, patients with HFmrEF were more likely to have ischemic heart disease (57%) compared with those with HFpEF (41%) The ratio of patients who had ischemic heart disease in HFmrEF and HFrEF (65%) groups were similar. In the Sweedish HF registry, the percentages of IHD were 60% for HFrEF, 61% for HFmrEF, and 52% for HFpEF.[24] In ESC HF Long-Term Registry, the etiology was ischemia for 48.6% of HFrEF patients, 41.8% for HFmrEF patients, but only in 23.7% for HFpEF patients.[25] An extensive *post hoc* analysis of the TIME-CHF trial showed ischemic etiology was 58.2%, 56.5%, 31.3% for HFrEF, HFmrEF, and HFpEF, respectively.[21] Therefore, in terms of etiology HFmrEF is more like HFrEF than HFpEF. The AF prevalence is lower in patients with HFmrEF (42%) compared to those with HFrEF (52%) and HFpEF (56%). The prevalence of AF in Sweedish HF registry was 65%, 60%, and 53% in HFpEF, HFmrEF, and HFrEF, respectively.[24] In accordance with our study, Löfman *et al*. found that CKD was associated with similar covariates regardless of EF along the EF spectrum in the Swedish HF registry.[22] Chioncel *et al*.[25] showed that COPD, liver disease, and CKD were more common in HFrEF, but in Rickenbacher's study three EF strata had a comparably high burden of comorbidities.[21]

In patients with HFmrEF, ACS, arrhythmias, and uncontrolled HT were more often precipitating factors for HF hospitalization compared with other HF groups. Infection was the least precipitating factor in these patients. Systolic BP and natriuretic peptide levels of patients with HFmrEF also fell in between those of HFrEF and HFpEF.

The ESC HF Long-Term Registry gives precise information in the current practice regarding HF medication. The use of beta-blockers and ACE inhibitors was around 90% in both HFrEF and HFmrEF, compared to approximately 75% in patients with HFpEF.[25] Percentages in Swedish HF registry were comparable.[24] Use of MRAs was higher in the ESC HF Long-Term Registry: 70% in HFrEF, 55% in HFmrEF, and 35% in HFpEF compared to Swedish HF Registry.[24,25] In our study, use of RAAS blockers, beta-blockers, and MRAs was similar in those with HFrEF and HFmrEF, higher than the use of these medications in patients with HFpEF. At discharge, guideline-recommended medical therapy prescription was higher than first admission in all groups. Interestingly, prescription of diuretic was the lowest in patients with HFmrEF at discharge. As you can see in Table 1, the AF prevalence is the highest in HFpEF patients and it is followed by HFrEF and HFmrEF patients. Hence, digoksin may be used higher than expected in HFpEF and HFmrEF patients due to heart rate-limiting effect.

Among patients in ADHERE, in-hospital mortality was 4.7% in patients with LVEF <25%, 3.4% in patients with LVEF between 25% and 40%, 3.2% in those with LVEF between 41% and 54% and 3.0% in those with LVEF ≥55%.[10] Kapoor *et al*. found in hospital mortality of 3.2% for HFrEF, 2.6% for HFmrEF, and 3.0% for HFpEF in the GTWG-HF Registry, which included 98,825 adult patients hospitalized for new or worsening HF.[23] The in-hospital mortality rate of those with

HFrEF (7.3%) and HFpEF (7.5%) was higher in our study than ADHERE and GTWG-HF registry. However, patients with HFmrEF in our study had lower in hospital mortality rate (1.8%) than these two registry cohorts.

Although there are numerous studies that investigated the clinical characteristics, demographics, compliance with guideline-recommended medical therapy, and the prognosis of stable HFmrEF patients, only a few studies considered the features of HFmrEF patients in AHF population.[3,4,7,11,23,26,27] The study is unique in the sense that it investigates the characteristics of HFmrEF in the setting of AHF compared to HFrEF and HFmrEF in Turkey.

Study limitation

The registry data were based on documentation of medical history only. Information about management during hospitalization and follow-up was not obtained. Therefore, readmission rate of patients after discharge is unknown. Laboratory parameters, biomarkers, dosage, and the duration of HF medications should be standardized. In addition, medication dosage was not recorded, and hence, we were not sure if the patients were taking appropriate doses of HF medications. The last but not the least limitation of our study was the lack of natriuretic peptide levels in 60% of the study population due to limited local resources.

Conclusion

After the introduction of HFmrEF as a separate category, several registries were conducted to define these patients' characteristics, demographics, and prognosis. Several interesting insights have been yielded. In conclusion, patients with HFmrEF have unique clinical, echocardiographic, hemodynamic, and biomarker features compared to patients with HFrEF and HFpEF. However, patients with HFmrEF seem to be more similar to HFrEF, in terms of (ischemic) etiology and the use of guideline-recommended medical therapy.

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Conflicts of interest

There are no conflicts of interest.

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