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EDITORIAL

Monitoring Changes in Ejection Fraction in Patients With Heart Failure and Mid-Range Ejection Fraction

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Since we started our cardiology residency, we have been measuring left ventricular ejection fraction (LVEF) to evaluate patients' cardiac function. Although LVEF is not an ideal parameter to stratify patients with heart failure (HF), many clinical trials that have set LVEF as an entry criterion clearly showed its utility in determining the outcome of HF therapies. Therefore, we decided to use LVEF as a convenient and useful parameter to make decisions on the therapeutic strategy of HF.

Previous studies of patients with HF and an EF ranging from 35% to 50% have mentioned that this range is a borderline or gray area.[1–3] Recently, the 2016 European Society of Cardiology guidelines proposed a new HF phenotype, termed HF with mid-range LVEF (HFmrEF), for patients with HF and an LVEF of 40–49%.[4] Since this guideline was released, several clinical registry trials have reported the clinical characteristics and mortality rates in patients with HFmrEF. According to those trials, patients with HFmrEF are more likely to show ischemic, diabetic, and hypertensive characteristics than patients with other types of HF.[5–9] Additionally, responses to HF therapy and prognosis are intermediate between patients with HFrEF and those with HFpEF.

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However, little is known about the association between changes in EF and prognosis in patients with HFmrEF. In this issue of the Journal, Gwag et al[10] report on selected follow-up data on LVEF from the Korean Acute Heart Failure (KoAHF) registry[11] and they investigate the

Table. Clinical Characteristics of Patients Hospitalized With Acute Heart Failure Syndrome in Korea Compared With Other Registries

	KorAHF	ATTEND	ADHERE	OPTIMIZE-HF	EHFS II
Region	Korea	Japan	USA	USA	Europe
Demographics					
Age, mean (SD), years	69 (14)	73 (14)	72 (14)	73 (14)	70 (13)
Male (%)	55	59	48	48	61
Comorbidities (%)					
Hypertension	59	71	74	71	63
Diabetes	36	34	44	42	33
Etiology (%)					
Ischemic	38	33	58	46	54
Hypertensive	6	18	NA	23	11
Clinical status on admission					
SBP, mean (SD), mmHg	136 (31)	147 (38)	144 (33)	143 (33)	Median 135
LVEF <40% (%)	56	57	51	49	66 (EF <45%)
Management (%)					
ACEI/ARB	65	NA	83	NA	80
β-blockers	44	NA	80	NA	61

ACEI, angiotensin-converting enzyme inhibitor; ADHERE, Acute Decompensated Heart Failure National Registry; ATTEND, Acute Decompensated Heart Failure Syndrome; EHFS II, EuroHeart Failure Survey II; KorAHF, Korean Acute Heart Failure; LVEF, left ventricular ejection fraction; NA, not available; OPTIMIZE-HF, Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure; SBP, systolic blood pressure; SD, standard deviation. (Cited with permission from Lee SE, et al.[11])

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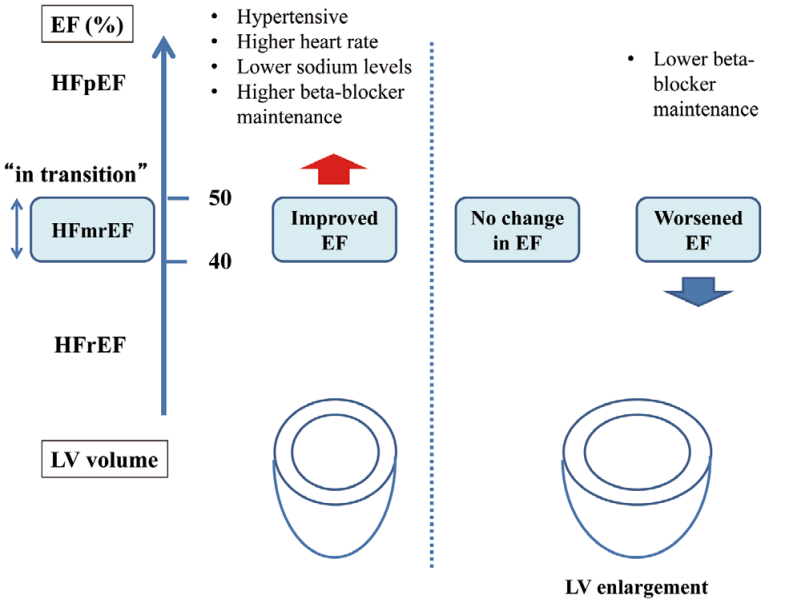

Figure. Clinical characteristics and changes in ejection fraction (EF) in patients with heart failure (HF). HFpEF, HF with preserved EF; HFmrEF, HF with mid-range EF; HFrEF, HF with reduced EF. Improved EF: patients with HFmrEF who have hypertension, a higher heart rate, lower sodium levels, and higher maintenance with β-blockers. Left ventricular (LV) volume is smaller than in the other groups. Worsened EF: patients with HFmrEF who have a tendency for low β-blocker maintenance. Red arrow: improved prognosis; blue arrow: worse prognosis. (Reproduced with permission from Gwag HB, et al[10] of copyright holder.)

association between improvement in LVEF and death in patients with acute HF who showed HFmrEF. The clinical characteristics of the patients who were hospitalized with acute HF in the KoAHF registry compared with other registries are shown in the **Table**.

Gwag et al defined the improved group as ≥5% change in LVEF and ≥50% in follow-up LVEF. The worsened group was defined as ≥5% change in LVEF and <40% in follow-up LVEF. As a result, the clinical characteristics associated with improved LVEF were hypertension, higher heart rate, lower sodium levels, and maintenance therapy with β-blockers (**Figure**). Dunlay et al[12] also focused on the association between changes in EF and clinical characteristics in patients with HF. They found a greater decrease in EF in patients with HF with preserved EF (HFpEF) who were older and had coronary artery disease, while there was a greater improvement in EF in patients with HF with reduced EF (HFrEF) who had nonischemic dilated cardiomyopathy.

With regard to response to HF therapies, several studies have reported that mortality and hospitalization rates of patients with HFmrEF are intermediate between those for patients with HFrEF and HFpEF.[5–9] Therefore, guidelines recommend that patients with HFmrEF should be treated similarly to those with HFrEF or therapy should be chosen according to each pathophysiology. Gwag et al describe young age and maintenance of renin-angiotensin system blockers or aldosterone antagonists as significantly associated with better survival in patients with HFmrEF.[10] Patients with HFmrEF are likely to be more hypertensive than those with other HF phenotypes, which may be one of the reasons why renin-angiotensin system blockers contribute to better survival in patients with HFmrEF. In contrast, Tsuji et al reported that use of renin-angiotensin system blockers or aldosterone antagonists was not associated with better prognosis in this HF population.[9] Further studies are required to determine this issue.

Although there is an association between changes in EF and clinical characteristics or prognosis, measurement of EF by echocardiography can vary. Interobserver variability of EF measurement by Simpson's method has been reported to range from 8% to 21%.[13] Therefore, care should be taken to interpret the transient status of patients who belong to this narrow 10% range of EF. According to Gwag et al,[10] LV volume in the improved EF group was smaller than that in the other groups (**Figure**). Zile et al reported that combined assessment of LV volume, mass, and geometry provided incremental prognostic information regarding cardiac events and death in patients with HF.[14] This combined assessment may potentially be another parameter for predicting the prognosis of patients with HF.

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Conflicts of Interest

None.

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