

## Heart failure with midrange EF Do we have enough data ?

PROF.DR.SHERIF WAGDY AYAD  
Faculty of Medicine  
Alexandria university

- 
- Heart failure with midrange ejection fraction (HFmrEF) is a new category of heart failure (HF), inbetween HF with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF).



European Heart Journal (2016) 37, 2129–2200  
doi:10.1093/eurheartj/ehw128

ESC GUIDELINES



## 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

Developed with the special contribution of the Heart Failure Association (HFA) of the ESC

**Table 3.1** Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF) and reduced ejection fraction (HFrEF)

Type of HF	HFrEF	HFmrEF	HFpEF
<b>CRITERIA</b>	1	Symptoms ± Signs <sup>a</sup>	Symptoms ± Signs <sup>a</sup>
	2	LVEF <40%	LVEF 40–49%
	3	-	1. Elevated levels of natriuretic peptides <sup>b</sup> ; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).

## PREVALENCE

---

Based on recent studies, the percentage of the HF population that falls into the HFmrEF category is between 13% and 24% suggesting that approximately 1.6 million people in the United States have HFmrEF.

## CLINICAL CHARACTERISTICS

---

Analysis of more than 50000 patients with heart failure in OPTIMIZE-HF , ADHERE registry found that Patients with HFmrEF had clinical characteristics that were more similar to those of the HFpEF cohort .

---

These characteristics include **older age**, **female** sex, **comorbidities** (hypertension, chronic obstructive pulmonary disease [COPD]), and **diabetes mellitus** .

The characteristic in which the HFmrEF population was more similar to the HFrEF population was the comorbidity of **coronary artery disease**.

## **PATHOPHYSIOLOGY OF HFmrEF**

---

The underlying pathophysiology of HFmrEF is not entirely clear. The ESC guidelines suggest that patients with HFmrEF likely have mild systolic dysfunction as well as diastolic dysfunction

A critical question is whether HFmrEF is in itself a distinct clinical syndrome or whether patients with HFmrEF are “in transition” between HFrEF and HFpEF

## MORTALITY RISKS

---

Mortality rates are modestly higher among patients with HFrEF but similar between those with HFmrEF and HFpEF. In OPTIMIZEHF, the mortality rates were 3.9% for patients with HFrEF, 3.0% for HFmrEF, and 2.9% for HFpEF

---

A recent study of the Swedish Heart Failure registry observed that **chronic kidney disease** was more strongly predictive of mortality in patients with HFmrEF and HFrEF than in patients with HFpEF .

Meanwhile, in a separate study, **age > 85 years** and **COPD** were associated with a higher risk of mortality within 1 year after hospital discharge in the HFmrEF group compared with the other groups.

## MORBIDITY IN HFmrEF

---

Rates of cardiovascular readmission for patients with HFmrEF are higher than those seen in HFpEF and closer to those observed in patients with HFrEF.

HF-specific readmission rates are intermediate in HFmrEF compared to those seen in HFrEF and HFpEF

---

The main precipitants in HFmrEF for HF-specific readmissions were **respiratory** issues and uncontrolled **hypertension**.

These more closely resembled in HFpEF, with the exception of **coronary ischemia**, which resembled the contributions seen in HFrEF

## MANAGEMENT OF HFmrEF

---

The recommendations from the AHA/ACCF and the ESC guidelines for the HFmrEF population currently focus on managing **comorbidities** and **risk factors** .

In addition, **diuretic therapy** is recommended to help alleviate symptoms in patients who exhibit signs of congestion.

---

Otherwise, there are currently **no specific** guideline directed medical therapies that are Class I or Class IIa recommended to improve outcomes for patients with HFmrEF.

### Recommendations for treatment of patients with heart failure with preserved ejection fraction and heart failure with mid-range ejection fraction

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>	Ref <sup>c</sup>
it is recommended to screen patients with HFpEF or HFmrEF for both cardiovascular and non-cardiovascular comorbidities, which, if present, should be treated provided safe and effective interventions exist to improve symptoms, well-being and/or prognosis.	I	C	
Diuretics are recommended in congested patients with HFpEF or HFmrEF in order to alleviate symptoms and signs.	I	B	178, 179

## MANAGEMENT OF COMORBIDITIES

Screening for and management of CAD is a reasonable approach that may help prevent further progression of left ventricular systolic dysfunction in patients with HFmrEF, as they have been shown to have a higher rate of transitioning to HFrEF compared with patients with HFpEF.

In light of the modest signals for reduced hospitalizations with **ARBs** or **aldosterone antagonist** therapy in patients with HFpEF, these agents may be reasonable to use in efforts to manage hypertension and reduce the risk of progressive decline in LVEF in the HFmrEF population.

**CENTRAL ILLUSTRATION** Characterization of HFpEF, HFmrEF, and HFrEF

	Characteristics			Outcomes		Guideline-Directed Medical Therapies				
	Older Age	Male Sex	CAD	Morbidity	Mortality	ACEI	ARB	ARNI	BB	MRA
HFpEF (LVEF>50%)	+++	+	++	++	++	X	✓ (IIB)	?	X	✓ (IIB)
HFmrEF (LVEF40-50%)	++	++	+++	++/+++	++	?	✓ (IIB)	?	?	✓ (IIB)
HFrEF (LVEF<40%)	+	+++	+++	+++	+++	✓ (I)	✓ (I)	✓ (I)	✓ (I)	✓ (I)

Hsu, J.J. et al. J Am Coll Cardiol HF. 2017;5(11):763-71.

## FUTURE DIRECTIONS

---

The next advances in the management of HFmrEF may involve advanced **imaging modalities** that may identify high-risk patients within the HFmrEF group.

Detection of late gadolinium enhancement on **cardiac magnetic resonance** imaging was found to be predictive of death or appropriate ICD in HF patients with LVEF >30%.

---

The use of an implantable **microelectromechanical** systems pressure sensor in the pulmonary artery to guide management of patients with HF was found to reduce hospitalizations for HF, including in those patients with LVEF over 40%.

## CONCLUSIONS

---

- The **percentage** of the HF population that falls into the HFmrEF category is between 13% and 24%.
- Patients with HFmrEF have **clinical characteristics** that are more similar to those of HFpEF than HFrEF.
- Clinical characteristics of patients with HFmrEF include older age, female gender, comorbidities (hypertension, COPD, and diabetes mellitus).

- 
- The HFmrEF population is more similar to the HFrEF population regarding the comorbidity of **CAD**.
  - In patients with HFmrEF, uncontrolled hypertension is more often the **precipitating factor** for HF hospitalization compared with the other HF groups.

- 
- The European Society of Cardiology (ESC) guidelines suggest that patients with HFmrEF likely have mild systolic dysfunction as well as diastolic dysfunction.
  - Recently they suggested that HFmrEF is in itself a distinct clinical syndrome or patients with HFmrEF are “in transition” between HFrEF and HFpEF.

- 
- **Mortality rates** are modestly higher among patients with HFrEF, but similar between those with HFmrEF and HFpEF.
  - Chronic kidney disease COPD and age  $\geq 85$  years are more **strong predictives** of mortality in patients with HFmrEF compared with the other two groups.

- 
- **No therapies** have conclusively been shown to improve outcomes in patients with HFmrEF. Therefore, the AHA/ACC and the ESC guidelines currently focus on management of **risk factors** and **comorbidities**.
  - **Diuretic** therapy is recommended to help alleviate symptoms in those who exhibit signs of congestion.

- 
- Screening for and management of **CAD** is an acceptable approach that may help prevent further progression of left ventricular systolic dysfunction in patients with HFmrEF, as they have been shown to have a higher rate of transitioning to HFrEF compared with patients with HFpEF. Also, management of **hypertension** is a reasonable approach.

**Thank You**