

# Clinical and echocardiographic characteristics of heart failure with improved ejection fraction patients: a single-centre prospective study

## Les caractéristiques cliniques et échocardiographiques des patients avec insuffisance cardiaque à fraction d'éjection améliorée : étude monocentrique prospective

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### SUMMARY

**Introduction :** A new subset of heart failure (HF) patients has been recently identified, representing patients with reduced LVEF who have demonstrated an improvement in systolic function

**Aim :** We sought by this study to describe clinical and echocardiographic characteristic.

**Patients and methods :** We conducted a monocentric survey including patients diagnosed with HF with reduced LVEF (<40%) followed up the cardiology department of Medenine. after a 12-month follow-up involving at least one echocardiography re-examination, we identified patients who had shown an improvement of the LVEF to reach a LVEF > 50%.

**RESULTS :** In all, 87 patients were enrolled in the study, based (mean age: 66.1; gender ratio: 1.55), 13.8% (12 patients) had shown an improvement of LVEF and then considered to have HFiEF and 86.2% (75 patients) had a persistent HFrEF. Patients with HFiEF were younger (mean age: 58.5 vs 67.7; p= 0.04), had more recent onset of heart failure (de Novo HF: 41.6% vs 22.9%; p=0.01) and less diabetes (25% vs 56%; 0.04). Prevalence of HTA and AF were similar (HTA: 41.7% vs 52%; 0.5; AF: 16.7% vs 28%; 0.4).

**Conclusion :** HFiEF is a distinct HF subgroup with particular clinical and echocardiographic characteristics.

### KEYWORDS

Echocardiography;  
heart failure ;  
improved ejection  
fraction

### RÉSUMÉ

**Introduction :** Une nouvelle sous-classe de patients atteints d'insuffisance cardiaque a été récemment identifiée correspondant aux patients dont la FEVG est réduite mais qui ont démontré une amélioration de leur fonction systolique.

**Objectif :** L'objectif de cette étude est de décrire les caractéristiques cliniques et échocardiographiques des patients avec IC et FEVG améliorée.

**Patients et méthodes :** Nous avons mené une étude monocentrique incluant des patients atteints d'IC avec une FEVG réduite (<40%) suivis au service de cardiologie de Medenine. Après un suivi de 12 mois comprenant au moins un réexamen échocardiographique, nous avons identifié les patients qui avaient montré une amélioration de la FEVG pour atteindre une FEVG > 50%.

**Résultats :** Au total, 87 patients ont été inclus dans l'étude, âge moyen : 66,1 ; rapport hommes/femmes : 1,55, 13,8 % (12 patients) avaient montré une amélioration de la FEVG et étaient alors considérés comme atteints d'HFipEF et 86,2 % (75 patients) avaient une HFrEF persistante. Les patients atteints d'HFipEF étaient plus jeunes (âge moyen : 58,5 vs 67,7 ; p= 0,04), avaient une insuffisance cardiaque d'apparition plus récente (HF de Novo : 41,6% vs 22,9% ; p=0,01) et moins de diabète (25% vs 56% ; 0,04). La prévalence de l'HTA et de la FA était similaire (HTA : 41,7% vs 52% ; 0,5 ; FA : 16,7% vs 28% ; 0,4).

**Conclusion :** L'HFipEF est un sous-groupe distinct de l'HF avec des caractéristiques cliniques et échocardiographiques particulières.

### MOTS-CLÉS

Echocardiographie;  
insuffisance  
cardiaque ;  
fraction d'éjection  
améliorée

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## INTRODUCTION

Heart failure (HF) is a common and devastating disease, it represents a major and growing public health issue due to its high morbidity and mortality rate and its burden on the health care system (1). The European Society of Cardiology (ESC) has divided heart failure into distinct phenotypes based on the measurement of left ventricular ejection fraction is based on the estimation of the left ventricular ejection fraction (LVEF) (2). Three types are identified: HF with reduced systolic function if LVEF  $\leq$  40%, HF with preserved systolic function if LVEF  $\geq$  50% and HF with moderately reduced ejection fraction if the LVEF is between 41% and 49% (3). Nevertheless, the echocardiographic parameters and especially the LVEF are dynamic so could worsen or, on the other side, get improved spontaneously when the cause is reversible or in response to a therapeutic intervention. Thus, a new subset of heart failure (HF) class has been recently identified, representing patients with reduced LVEF who have demonstrated an improvement in systolic function (4).

## AIM

We sought by this study to determine the prevalence of patients with HF with improved EF (HFipEF), as well as to describe clinical and echocardiographic characteristics of these patients.

## PATIENTS AND METHODS

We conducted a cross-sectional monocentric study including patients aged 18 years and older diagnosed with HF with reduced LVEF (HFrEF) ( $<40\%$ ). After a 1-year follow-up involving at least one echocardiography re-examination, we identified patients who had shown an improvement of the LVEF to reach a LVEF  $> 50\%$ .

The trans-thoracic echocardiography (TTE) was performed by a GE (General Electric) ultrasound machine model Vivid S6 with a 5 MHz cardiac probe in our cardiology department. All measurements were performed in conformity with the joint recommendations of the of the American Society of Ultrasound (ASE) and the European Association of Cardiovascular Imaging (EACVI) (5). Demographic, clinical and echocardiographic data were collected for all patients. Patients who died or lost their follow up or did not have a second TTE within 12 months of follow-up were excluded.

## STATISTICAL ANALYSIS

Distributions of continuous variables are described using means and SDs and categorical variables as proportions expressed as percentages. Baseline characteristics were compared using a t test, Rank-sum test or chi two test as appropriate for the level of measurement and distribution of the variable.

## RESULTS

In all, 87 patients were enrolled in the study. The time period between enrolment and the control TTE was on average 8 months with extremes of 4 and 12 months. Patients had shown an improvement of LVEF were 13.8% (12 patients) and 86.2% (75 patients) had a persistent HFrEF.

### Baseline Clinical Characteristics

The mean age was 66.1 years and the gender ratio was 1.55. Hypertension (HTN) was the most common comorbidity (39.7%, n=39) followed by diabetes (33.3%, n=29). Patients with HFipEF were younger (mean age: 58.5 years vs 67.7 years; p= 0.04), had more recent onset of heart failure (de Novo HF: 41.6% vs 22.9%; p=0.01) and less diabetes (25% vs 56%; 0.04). Prevalence of HTN and atrial fibrillation (AF) were similar (HTN: 41.7% vs 52%; p=0.5; AF: 16.7% vs 28%; p=0.4). For the etiology of HF, ischemic cardiomyopathy was the most prevalent etiology for both groups followed by hypertensive cardiomyopathy in HFipEF and valvular cardiomyopathy for patient with persistent HFrEF. Table 1 summarize the demographic and clinic characteristics.

**Table 1.** Demographic and clinical characteristics

	Over all (n=87)	HFrEF (n=75)	HFipEF (n=12)	P
Age years $\pm$ SD	66.1 $\pm$ 11	67.7 $\pm$ 8	58.5 $\pm$ 9	0.04
Gender ratio	1.55	1.42	1.57	0.09
BMI, Kg/m <sup>2</sup> $\pm$ SD	27.5 $\pm$ 2.9	26.4 $\pm$ 3	27.1 $\pm$ 3	0.12
Hypertension (%)	39.7	52	41.7	0.5
Diabetes (%)	33.3	56	25	0.04
Dyslipidaemia (%)	49.4	57.7	41.6	0.2
Chronic renal disease (%)	12.6	12	16.6	0.55
Coronary artery disease (%)	31	30.6	33.3	0.72
Valvular heart disease (%)	21.8	22.6	16.6	0.23
Cerebral vascular accident (%)	11.4	12	8.3	0.12
Atrial fibrillation (%)	26.4	28	16.7	0.4
Current smoking (%)	8	9.3	8.3	0.66
Heart rate $\pm$ SD	73 $\pm$ 12	77 $\pm$ 9	75 $\pm$ 8	0.72

HFrEF : Heart failure reduced ejection fraction ; HFipEF : Heart failure with improved ejection fraction, BMI : body mass index

## Echocardiographic characteristics

Overall, the average LVEF was  $31.2 \pm 6.5\%$ , the group with HFipEF had features of higher baseline LVEF ( $36.2 \pm 3.7\%$  vs  $30.5 \pm 4.7\%$ ,  $p=0.03$ ) and lower baseline left ventricular end diastolic diameter (LVEDD) ( $6.3 \pm 2.4$  mm vs  $5.9 \pm 3.2$  mm,  $p=0.05$ ). Change of LVEF from first TTE to follow-up TTE was  $12.7 \pm 13.1\%$  in all,  $3.8 \pm 9.6\%$  in persistent HFrEF, and  $25.7 \pm 11.6\%$  in HFipEF. Severe mitral regurgitation was significantly more common among patient with persistent HFrEF ( $8.3\%$  vs  $16\%$ ,  $p=0.02$ ). Table 2 summarize the echocardiographic characteristics.

**Table 2.** Echocardiographic characteristics

Patients number	Over all (n=87)	HFrEF (n=75)	HFipEF (n=12)	P
LVEF (% $\pm$ SD)	$31.2 \pm 6.5$	$30.5 \pm 4.7$	$36.2 \pm 3.7$	0.03
LVEF variation	$12.7 \pm 13.1$	$3.8 \pm 9.6$	$28.7 \pm 11.6$	0.01
LVEDd	$6.2 \pm 3$	$6.3 \pm 2.4$	$5.9 \pm 3.2$	0.05
LVESd (mm $\pm$ SD)	$55 \pm 2.4$	$57 \pm 3.2$	$54 \pm 1.1$	0.63
LAD (mm $\pm$ SD)	$48 \pm 6$	$48.6 \pm 5$	$43.4 \pm 7$	0.45
LA area (cm <sup>2</sup> $\pm$ SD)	$26 \pm 7$	$27.3 \pm 5$	$25 \pm 4$	0.73
Severe MR (%)	14.9	16	8.3	0.02
E/E' mean $\pm$ SD	$13.8 \pm 5$	$15.3 \pm 4$	$11 \pm 7$	0.23
PASP mmHg	$37.5 \pm 11$	$39 \pm 14$	$35 \pm 10$	0.33
TAPSE	$14 \pm 7$	$13.5 \pm 9$	$15.2 \pm 7$	0.45

**HFrEF:** Heart failure reduced ejection fraction; **HFipEF:** Heart failure with improved ejection fraction; **LVEF:** left ventricular ejection fraction; **LVEDd:** left ventricular end diastolic diameter; **LVESd:** left ventricular end systolic diameter; **LAD:** left atrial diameter; **LA:** left atrial; **MR:** mitral regurgitation; **PAPS:** pulmonary artery systolic pressure; **TAPSE:** tricuspid annular plane systolic excursion

## DISCUSSION

In this cross-sectional study about HFipEF, we investigated the clinical characteristics of patients with HFipEF in comparison with persistent HFrEF. Younger age, de novo onset and the absence of diabetes were associated with ejection fraction improvement. However, HTN and AF were negative independent predictors of EF improvement among patients with HFrEF at initial TTE. A published meta-analysis conducted by Florea et al. (6) reported similar results, comparing HFipEF patients to HFrEF patients and/or those with heart failure with preserved ejection fraction. In this study, patients with HFipEF were younger, had shorter duration of HF, de novo onset of HF and less adverse myocardial remodeling at initial evaluation. HFipEF patients also had normal global longitudinal strain (GLS > 16), smaller LV end diastolic or systolic diameter

(LVEDD or LVESD) (7). A similar study published by Punnoose et al. (8) had shown that patients with HFipEF were younger with less AF, HTN, and diabetes. Many studies had also shown that HFipEF patients had better long-term outcomes than ones with HFrEF (9, 10). In fact, a study by Cintron et al. had shown that any substantial improvement in EF was associated with an improvement in survival (10).

The precise mechanisms underlying HFipEF remains yet unclear but available evidence suggests the involvement of neurohormonal and electrical aberrations (11). During the process of reverse remodelling, several studies have showed that changes does accure within cardiac myocytes, extracellular matrix along with a reverse in genetic and proteomic alterations (12). Understanding the mechanisms underlying LVEF improvement may improve the HF patient's prognosis.

## LIMITATION

The main limitation of our study is the relatively small number of participants explained by the monocentric aspect, then the missing of several parameters in the echocardiographic examination such as strain study is an obvious limitation, due mainly to a technical issue.

## CONCLUSION

HFipEF is a relatively recent description of a subset of HF patients, characterised in our study by a younger age, more common de novo HF and less echocardiographic parameters deteriorations.

## REFERENCES

- Ziaeeian B, Fonarow GC. Epidemiology and aetiology of heart failure. *Nat Rev Cardiol* 2016;13(6):368-78. DOI: 10.1038/nrcardio.2016.25.
- 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.
- Bozkurt B, Coats AJ, Tsutsui H, Abdelhamid M, 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. *J*

Card Fail 2021. DOI: 10.1016/j.cardfail.2021.01.022.

4. Nauta JF, Santema BT, van der Wal MHL, Koops A, Warink-Riemersma J, van Dijk K, et al. Improvement in left ventricular ejection fraction after pharmacological up-titration in new-onset heart failure with reduced ejection fraction. *Neth Heart J* 2021;29(7-8):383-93. DOI: 10.1007/s12471-021-01591-6.
5. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *European Heart Journal - Cardiovascular Imaging* 2015;16(3):233-71. DOI: 10.1093/ehjci/jev014 %J European Heart Journal - Cardiovascular Imaging.
6. Florea VG, Rector TS, Anand IS, Cohn JN. Heart Failure With Improved Ejection Fraction: Clinical Characteristics, Correlates of Recovery, and Survival: Results From the Valsartan Heart Failure Trial. *Circ Heart Fail* 2016;9(7). DOI: 10.1161/circheartfailure.116.003123.
7. Stevenson LW. Heart failure with better ejection fraction: a modern diagnosis. *Circulation* 2014;129(23):2364-7. DOI: 10.1161/circulationaha.114.010194.
8. Punnoose LR, Givertz MM, Lewis EF, Pratibhu P, Stevenson LW, Desai AS. Heart failure with recovered ejection fraction: a distinct clinical entity. *J Card Fail* 2011;17(7):527-32. DOI: 10.1016/j.cardfail.2011.03.005.
9. Basuray A, French B, Ky B, Vorovich E, Olt C, Sweitzer NK, et al. Heart failure with recovered ejection fraction: clinical description, biomarkers, and outcomes. *Circulation* 2014;129(23):2380-7. DOI: 10.1161/circulationaha.113.006855.
10. Cintron G, Johnson G, Francis G, Cobb F, Cohn JN. Prognostic significance of serial changes in left ventricular ejection fraction in patients with congestive heart failure. The V-HeFT VA Cooperative Studies Group. *Circulation* 1993;87(6 Suppl):Vi17-23.
11. Rigolli M, Cicoira M, Bergamini C, Chiampan A, Rossi A, Vassanelli C. Progression of Left Ventricular Dysfunction and Remodelling under Optimal Medical Therapy in CHF Patients: Role of Individual Genetic Background. *Cardiol Res Pract* 2011;2011:798658. DOI: 10.4061/2011/798658.
12. Mann DL, Barger PM, Burkhoff D. Myocardial recovery and the failing heart: myth, magic, or molecular target? *J Am Coll Cardiol* 2012;60(24):2465-72. DOI: 10.1016/j.jacc.2012.06.062.