Is heart failure with mid-range or mildly reduced ejection fraction only a transitional stage? Real-world experience

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Background: Heart failure (HF) societies classify LVEFs of 41–49% as mildly reduced ejection fraction (HFmrEF)[1,2]. HFmrEF is an intermediate HF type between HF with preserved EF (HFpEF) and HF with reduced EF (HFrEF), as it shares characteristics from both ends of the spectrum. HFmrEF is controversial due to LVEF changes and inter-rater variability[3,4]. Studies on HFmrEF are inconsistent and it is not clear whether HFmrEF is a transition or an independent clinical entity. No prospective studies have assessed the effect of therapy in patients with HFmrEF. Current evidence in patients with HFmrEF is based on post-hoc analyses of studies[3].

Patients and Methods: This was a prospective observational study conducted at University Hospital Dubrava, Zagreb. We recruited patients presenting with HF symptoms from May 2021 to August 2023. We collected data on gender, age, drugs and adherence, comorbidities, NT-proBNP and HbA1c levels and EF. Categorical variables are presented as frequencies and percentages and continuous variables are presented as medians and interquartile ranges. P value < 0.05 was considered as significant. Statistical analysis was performed using JASP software.

Results: We collected data from 850 participants. HFmrEF was diagnosed in 129 patients (15.1%). 76 (58.9%) participants had coronary artery disease and 59 participants (46%) had atrial fibrillation. Dapagliflozin was initiated in 60 (47%) and empagliflozin in 68 (53%) participants. Only 8 participants had optimal medical therapy prior to SGLT-2 initiation. Adherence was evaluated in 87 participants, and it was high in 48, moderate in 21 and low in 18 participants. EF at 12 months was assessed in 51 participants. Median EF was 44.6% (95% CI 44.2%-45%) at initiation and 49% at 12 months (95% CI 47%-51%) (p=0.0001). EF has improved to >50% in 21 and decreased to <40% in 4 participants. EF has not changed in 26 participants. Level of NT-proBNP was 1.834pg/mL (95% CI 66-32,127) during initial visit and 651pg/mL (95% CI 44-12,555) at 12 months (p<0.001). HbA1c levels decreased from 6.3% (95% CI 5.3-10.9) at the initial visit to 5,85% (95% CI 4.9-8.3) at 12 months (p<0.001).

Conclusion: HFmrEF remains a mystery. Optimal medical treatment might improve EF or prevent it from deteriorating further in some patients, but long-term real-world data is needed.

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