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Changes in metabolic and cardiorenal parameters in patients with heart failure with reduced ejection fraction receiving incretin-based therapy: a retrospective observational study

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RECEIVED: October 25, 2026
UPDATED: November 4, 2026

KEYWORDS: heart failure with reduced ejection fraction, incretin-based therapy, tirzepatide, cardiorenal outcomes.

CITATION: Cardiol Croat. 2026;21(11-12):252-3. | https://doi.org/10.15836/ccar2026.252

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Introduction: Evidence on incretin-based therapies in patients with heart failure with reduced ejection fraction (HFrEF) receiving foundational medical therapy (FMT) remains limited, particularly in real-world clinical practice. While some concerns regarding the safety of use of older-generation drugs have been raised, safer signals have been noted with the newer ones.[1,2] We describe treatment patterns, changes in metabolic and cardiorenal parameters, and heart failure-related outcomes in patients with HFrEF receiving incretin-based therapy at our centre.

Patients and methods: This retrospective observational cohort included 34 patients with HFrEF (left ventricular ejection fraction [LVEF] <50%) receiving incretin-based therapy. Changes in heart rate, body weight, body mass index (BMI), glycated hemoglobin (HbA1c), N-terminal pro-B-type natriuretic peptide (NT-proBNP) and estimated glomerular filtration rate (eGFR) rate were assessed between baseline and a follow-up visit occurring between 6 and 9 months. Heart failure hospitalizations (HFH) and ICD activation related hospitalization were recorded during follow-up.

Results: A total of 34 patients were included (mean age, 52 ± 13 years; 27 [79%] male), of whom eight (24%) had type 2 diabetes. Tirzepatide was prescribed to 29 patients (85%), while five (15%) received semaglutide. Treatment was initiated primarily for weight loss (88%), while 12% were treated with the aim of heart transplantation eligibility. All four pillars of FMT were used in 31 patients (91%). An implantable cardioverter-defibrillator (ICD) or cardiac resynchronization therapy defibrillator (CRT-D) was present in 26 patients (76%). Treatment dosing and titration, as well as changes in clinical and laboratory parameters during follow-up, are summarized in **Table 1**. Over a median follow-up of 239 days, significant reductions in body weight, BMI, HbA1c, and eGFR were observed (all p≤0.05). Changes in NT-proBNP, and heart rate were not statistically significant. During follow-up, a single HFH occurred in three patients, while three patients had a total of four ICD activation related hospitalizations, all of which occurred on tirzepatide treatment.

TABLE 1. Incretin-based therapy dosing and changes in clinical and laboratory parameters during follow-up.

A. Treatment dosing and titration

Drug	Baseline	Follow-up
Tirzepatide 2.5 mg, n (%)	29 (100)	-
Tirzepatide 5 mg, n (%)	-	19 (66)
Tirzepatide 7.5 mg, n (%)	-	5 (17)
Tirzepatide 10 mg, n (%)	-	5 (17)
Semaglutide 0.25 mg, n (%)	4 (80)	-
Semaglutide 1 mg, n (%)	1 (20)	-
Semaglutide 2.4 mg, n (%)	-	5 (100)

B. Clinical and laboratory parameters

Parameter	Baseline	Follow-up	Change from baseline	p- value
Heart rate, bpm	73.18±9.62	74.26±7.89	1.09±9.87	0.525
Body weight, kg	121.76 ± 19.56	108.32±17.72	-13.44±7.56	<0.001
BMI, kg/m²	38.17±4.52	33.98±4.29	-4.19±2.19	<0.001
NT-proBNP, ng/L	801 (342.5-2166.5)	829.5 (297.75-1772.75)	-16.30% (95% CI: -38.40% to 13.72%)	0.245
eGFR, mL/min/1.73 m²	76.03±20.37	67.03±22.62	-9.00±12.79	<0.001
HbA1c, %	5.94±0.90	5.62±0.65	-0.32±0.41	<0.001

body mass index (BMI); glycated hemoglobin (HbA1c); N-terminal pro-B-type natriuretic peptide (NT-proBNP); estimated glomerular filtration rate (eGFR)

Mean±SD, paired t-tests; NT-proBNP: median/IQR, log-transformed percentage change (95%CI).

Conclusion: In this small, retrospective real-world cohort of patients with HFrEF, incretin-based therapy was associated with reductions in body weight, BMI, and HbA1c. NT-proBNP levels and heart rate remained comparable during follow-up, while eGFR decreased. HFH and hospitalizations related to ICD activation were observed; however, their clinical significance and relation to certain drug remains uncertain. Given the retrospective design and small sample size, these findings should be interpreted cautiously and require confirmation in larger prospective studies.

LITERATURE

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