STUDENTS' CORNER
LETTER TO THE EDITOR

Tirzepatide: A turning point in obesity related heart failure with preserved ejection fraction?

Rahemeen Goraya, Anfal Babar Saeed

Madam, Heart failure with preserved ejection fraction (HFpEF) is a prevailing health concern across the world. It is commonly defined as heart failure with an ejection fraction of 50% or above.[1] It presents as a major complication in people with diabetes and obesity (diabesity).[2] Over the years, obesity has been a major culprit in the development and progression of various complications such as diabetes, chronic kidney disease, atherosclerotic cardiovascular disease, coronary artery calcification, and heart failure.[2] Comprehensive research is required to explore its role in disease progression and to determine the interplay of diabetes, obesity, and heart failure (HF).

Unlike Heart failure with reduced ejection fraction (HFrEF), there has been little research on the treatment and management of HFpEF. The current treatment regimen for HFpEF includes drugs such as SGLT2 inhibitors, diuretics, renin–angiotensin–aldosterone system (RAAS) inhibitors, and beta blockers. However, none of these directly targets obesity. Tirzepatide, a glucose-dependent insulinotropic peptide (GIP) and glucagon-like peptide 1 (GLP-1) receptor agonist, has been widely used in the treatment of diabetes mellitus due to its significant weight-reducing effects along with regulation of blood glucose levels. Recent studies demonstrate the multi-organ therapeutic effect of tirzepatide due to the presence of GLP1-receptors in other organs such as the brain, heart, pancreas, stomach, and endometrium.[3] Its benefits in cardiovascular outcomes are an area of active investigation.

Ongoing clinical trials have shown that tirzepatide significantly reduces heart failure events and mortality in obesity-induced HFpEF by various mechanisms; reduction of left ventricular mass, pericardiac adipose tissue, cardiac compression, obesity-induced inflammation, concentric cardiac remodelling, and improving heart chambers' compliance and filling. This improves functional capacity, health-related quality of life, exercise tolerance, and reduces the need for multiple heart failure medications.[4] This offers a promising future for the control of obesity induced HFpEF in diabetic, non-diabetic, and chronic kidney disease (CKD) patients.

The US Food and Drug Administration (FDA) has approved this drug for the treatment of diabetes, chronic weight management and recently also for obstructive sleep apnoea.[5] Further clinical trials substantiating the efficacy of tirzepatide in reducing heart failure events may lead to its approval for use in HFpEF treatment. Additionally, long-term safety data are limited, and further research is crucial to determine its long-term effects. Clinicians and researchers worldwide should stay informed regarding the potential of this drug and outcomes of the ongoing trials.

Disclaimer: None.

Conflict of interest: None.

Funding disclosure: None.

DOI: https://doi.org/10.47391/JPMA.32630

References

1. Redfield MM, Borlaug BA. Heart failure with preserved ejection fraction. JAMA. 2023;329:827.DOI: 10.1001/jama.2023.2043
2. Ng AC, Delgado V, Borlaug BA, Bax JJ. Diabesity: the combined burden of obesity and diabetes on heart disease and the role of imaging. Nat Rev Cardiol. 2021;18:291–304.DOI: 10.1038/s41569-020-00476-4
3. Hammad BF, Zafar N, Ullah M, Faisal SJ, Iftikhar F, Waheed H, et al. Exploring the multifaceted roles of GLP-1 receptor agonists: a comprehensive review. Front Clin Diabetes Healthc. 2025;6:1590530. DOI: 10.3389/fcdhc.2025.1590530
4. Borlaug BA, Zile MR, Kramer CM, Ye W, Ou Y, Hurt K, et al. Impact of body mass index, central adiposity, and weight loss on the benefits of tirzepatide in HFpEF: the SUMMIT trial. J Am Coll Cardiol. 2025;86: 242–55.
5. Jastreboff AM, le Roux CW, Stefanski A, Aronne LJ, Halpern B, Wharton S, et al. Tirzepatide for obesity treatment and diabetes prevention. N Engl J Med. 2025;392:958–71.DOI: 10.1056/NEJMoa2410816

Fourth year MBBS Student, Allama Iqbal Medical College, Lahore, Pakistan.
Correspondence: Anfal Babar Saeed. e-mail: anfalbabar9@gmail.com
ORCID ID: 0009-0008-0619-2273

Submission completed: 17-09-2025 **1st Revision received:** 30-09-2025
Acceptance: 24-12-2025 **2nd Revision received:** 23-12-2025

Author Contribution:
RG: Concept, drafting, literature review and final approval.
ABS: Literature review, editing and adding references.