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Influence of sex and menopausal status on anthropometric and metabolic responses to tirzepatide in patients with obesity and without diabetes: a gender medicine perspective

Federica Barbagallo[1], Roberto Curto[1], Alessandra Chiarenza[1], Federica Lo Vasco[1], **Rosario Randazzo[1]**, Rossella Cannarella[1], Sandro LaVignera[1], Rosita A. Condorelli, Laura Cucinella[2], Rossella E. Nappi[2,3], Aldo E. Calogero[1]

1 Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy;
2 Research Center for Reproductive Medicine, Gynecological Endocrinology and Menopause, IRCCS San Matteo, Pavia
3 Department of Clinical, Surgical, Diagnostic and Pediatric Sciences, University of Pavia;

1 INTRODUCTION

Menopause represents a critical cardiometabolic transition characterized by weight gain and central adipose tissue redistribution, contributing to increased cardiovascular and metabolic risk.

Incretin-based therapies have substantially revolutionized obesity management. However, evidence regarding sex-specific differences and the influence of menopausal status on the anthropometric and metabolic response to tirzepatide remains scarce.

Objective: to evaluate sex-related differences in response to tirzepatide in patients with obesity and without diabetes mellitus, and to explore the influence of menopausal status in women.

2 METHODS

- **Design:** single-center retrospective longitudinal study
- **Patients:** 133 patients (65 men and 68 women: 28 premenopausal and 40 peri/post-menopausal)
- **Intervention:** treatment with tirzepatide in a real-world clinical setting
- **Primary outcomes** (baseline, 3 and 6 months): changes in body weight, body mass index (BMI), waist circumference (WC) and waist-to-height ratio (WHtR)
- **Secondary outcomes:** fasting glucose, fasting insulin, glycated hemoglobin (HbA1c), homeostasis model assessment for insulin resistance (HOMA-IR) and lipid profile

Study population

133 patients

65 Men

68 women

28 Pre-menopausal

40 Peri/post-menopausal

Assessments

Baseline → 3 months → 6 months

3 RESULTS

- Tirzepatide induced significant reductions in body weight, BMI, WC and WHtR across all groups at both 3 and 6 months (all p<0.001).
- Between-group differences did not reach statistical significance.
- After 6 months, ≥10% weight loss was achieved in 85.7% of men, in 94.3% of women overall, and in all premenopausal women.
- HOMA-IR significantly decreased in men at 3 months (p<0.001).
- In women, HOMA-IR also significantly decreased at 3 months (p=0.015), with a further significant reduction at 6 months compared with 3 months (p=0.008).

Mean body weight change at 6 months (%)

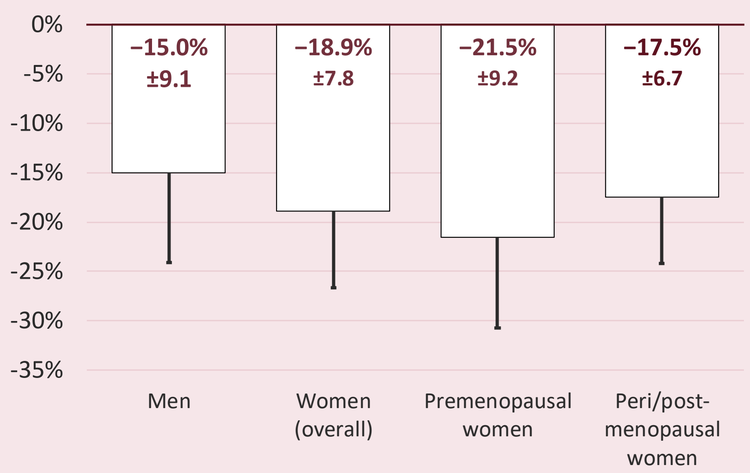


Figure 1. Mean percentage body weight change after 6 months of tirzepatide in men, women overall, premenopausal and peri/post-menopausal women (mean ± SD).

Patients achieving ≥10% weight loss at 6 months (%)

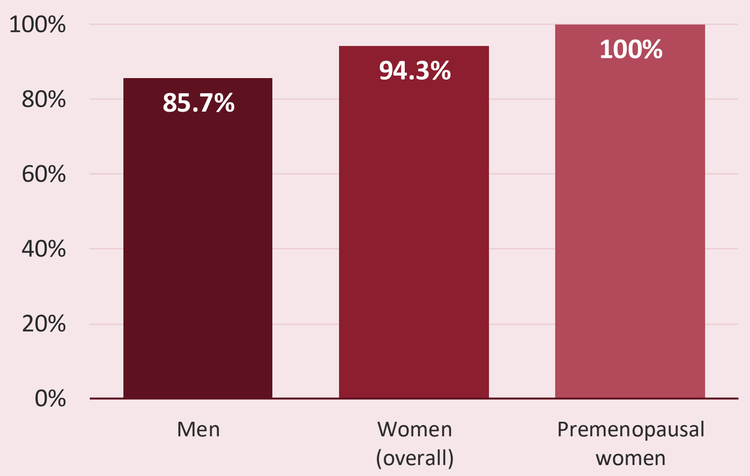


Figure 2. Proportion of patients with ≥10% weight loss after 6 months: 85.7% of men, 94.3% of women overall and all (100%) premenopausal women.

4 DISCUSSION

- Clinically relevant weight loss was observed even in peri-/post-menopausal women (−17.5±6.7% at 6 months), which is particularly relevant given the increased cardiometabolic burden of this life stage.
- Although between-group differences did not reach statistical significance, distinct weight-loss trajectories emerged according to sex and menopausal status, with a more sustained response over time in women, particularly in premenopausal women.
- In women, the further significant reduction in HOMA-IR from 3 to 6 months suggests a more progressive improvement in insulin sensitivity.

HOMA-IR (insulin resistance)

Men HOMA-IR decrease at 3 months	**p<0.001**
Women HOMA-IR decrease at 3 months	**p=0.015**
Women Further HOMA-IR decrease, 6 vs 3 months	**p=0.008**

5 CONCLUSION

Tirzepatide was effective in promoting significant weight loss and metabolic improvement across both sexes and all female reproductive stages.

These findings extend the existing evidence from pivotal clinical trials to a real-world setting.

Preliminary differences according to menopausal status suggest that sex and reproductive stage may influence treatment response, supporting the need for further investigation to enable more personalized, gender-informed approaches to obesity pharmacotherapy.

ABBREVIATIONS

BMI, body mass index; WC, waist circumference; WHtR, waist-to-height ratio; HbA1c, glycated hemoglobin; HOMA-IR, homeostasis model assessment for insulin resistance; SD, standard deviation.