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GLP-1 Receptor Agonists in Heart Failure with Preserved Ejection Fraction and Obesity: A Systematic Review and Meta-Analysis

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Introduction: Heart failure with preserved ejection fraction (HFpEF) accounts for approximately half of all heart failure cases and is associated with high symptom burden and functional impairment, particularly in individuals with obesity. The efficacy and safety of GLP-1 receptor agonists (GLP-1 RAs) in patients with HFpEF and obesity remain uncertain.

Objective: To evaluate the efficacy and safety of GLP-1 RAs in improving functional capacity, quality of life, weight reduction, and inflammatory markers in patients with HFpEF and obesity.

Material and Methods: A systematic search was conducted in PubMed, Embase, and Cochrane for randomized controlled trials (RCTs) comparing GLP-1 RAs with placebo in patients with HFpEF and obesity. Primary outcomes included: change in 6-minute walk distance (from baseline to week 52), Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS), percent change in body weight (baseline to week 52), and C-reactive protein (CRP) levels (baseline to week 52). Statistical analyses were performed using RevMan 5.4.1, with heterogeneity assessed via Cochran's Q test and I^2 statistic. Mean differences (MD) with 95% confidence intervals (CI) were estimated using a random-effects model.

Results: Two RCTs (n = 132) were identified comparing the efficacy and safety of GLP-1 RAs versus placebo in patients with HFpEF and overweight/obesity. GLP-1 RA treatment showed significant benefits across multiple outcomes: 6-minute walk distance: MD = 15.91 m (95% CI: 15.35 to 16.47; $p < 0.0001$; $I^2 = 0\%$); KCCQ-CSS improvement: MD = 6.90 points (95% CI: 6.72 to 7.08; $p < 0.0001$; $I^2 = 0\%$); Percent change in body weight: MD = 11.83% (95% CI: 10.42 to 13.23; $p < 0.0001$; $I^2 = 6\%$); Reduction in CRP levels: MD =

–32.90% (95% CI: –33.61 to –32.19; $p < 0.0001$; $I^2 = 0\%$).

Conclusion: Use of GLP-1 receptor agonists in patients with HFpEF and overweight/obesity was associated with significant improvements in functional capacity, quality of life, weight reduction, and inflammatory marker reduction, suggesting a favorable efficacy and safety profile.

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