ORIGINAL ARTICLE

Efficacy and safety of semaglutide in obese patients with heart failure with preserved ejection fraction: a systematic review and meta-analysis

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ABSTRACT

Background: Heart failure with preserved ejection fraction (HFpEF) affects nearly half of heart failure patients, with over 80% being either overweight or obese. Obesity is strongly associated with the pathogenesis of HFpEF, exacerbating diastolic dysfunction. Despite available therapies, effective treatments are limited, particularly in obese individuals. This systematic review and meta-analysis aimed to evaluate the safety and efficacy of semaglutide in obese patients with HFpEF.

Methods: A comprehensive literature search was conducted in PubMed, Google Scholar, and the Cochrane Library, adhering to PRISMA guidelines. Three studies (2 RCTs and 1 observational study) with 1,463 patients (677 in the semaglutide group, 786 in placebo) were included. Outcomes included percentage change in body weight, 6-minute walk distance, heart failure hospitalizations, cardiovascular mortality, and quality of life improvements. A random effects model was used, and heterogeneity was assessed using I^2 statistics.

Results: The meta-analysis demonstrated that semaglutide significantly reduced body weight (MD = -6.68; P = 0.0006) and improved 6-minute walk distance (MD = 16.37; P < 0.00001). Semaglutide also substantially reduced the risk of heart failure hospitalizations (RR = 0.28; P = 0.0005). However, no statistically significant reduction was observed in cardiovascular mortality (RR = 0.27; P = 0.16). Additionally, patients experienced significant improvements in quality of life, as measured by the Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS) (RR = 0.30; P < 0.0001).

Conclusion: Semaglutide shows promising effects in improving clinical outcomes, particularly in reducing body weight, enhancing functional capacity, and lowering heart failure-related hospitalizations in obese HFpEF patients. However, its impact on cardiovascular mortality remains inconclusive, warranting further research.

Keywords: Semaglutide, heart failure, preserved ejection fraction, obesity, meta-analysis.

Introduction

Heart failure is a leading cause of death worldwide, affecting approximately 64 million people [1]. Among these, nearly 50% are classified as having heart failure with a preserved ejection fraction (HFpEF) [2], and over 80% of these patients are either obese or overweight [3]. HFpEF is characterized by diastolic dysfunction of the left ventricle, where the heart struggles to fill with adequate blood due to the stiffening of its walls [4]. The primary risk factors for developing HFpEF include advancing age, obesity, hypertension, and diabetes mellitus [5]. Many studies have reported a strong association between

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obesity and HFpEF, suggesting that obesity may play a central role in the pathogenesis of heart failure. One study claimed that increased body fat in obesity induces body fluid volume expansion and elevates left ventricular filling pressure[6]. Another study highlighted that the inflammatory NLRP3 pathway, activated by obesity, can contribute to the development of HFpEF [7]. Managing HFpEF is challenging due to its complex pathophysiological mechanisms, leading to ineffective therapies targeting the underlying causes [8].

The management of HFpEF includes non-pharmacological approaches, such as lifestyle

filling pressure[6]. Another study highlighted that the inflammatory NLRP3 pathway, activated by obesity, can contribute to the development of HFpEF [7]. Managing HFpEF is challenging due to its complex pathophysiological mechanisms, leading to ineffective therapies targeting the underlying causes [8].

The management of HFpEF includes non-pharmacological approaches, such as lifestyle modifications like salt and fluid restriction, increased physical activity, and weight loss [9]. The current drug therapy for HFpEF primarily includes beta-blockers, diuretics, and angiotensin receptor blockers (ARBs) [10], which focus on symptomatic relief and improving the quality of life. However, these medications are associated with several adverse effects. For example, beta-blockers may prolong the time required for diastolic filling of the left ventricle, potentially worsening the condition due to their negative chronotropic effect [11]. Similarly, the use of diuretics can exacerbate diastolic dysfunction by reducing preload, further decreasing cardiac output [12]. These negative effects underscore the need for safer and more effective alternative therapies.

Semaglutide, a glucagon-like peptide-1 receptor agonist (GLP-1 RA), is primarily used to manage type 2 diabetes by lowering glucose levels [13]. It has also shown promising results in weight loss, mainly due to its anorexiant properties and delayed gastric emptying [14]. Currently, trials are underway to evaluate the use of semaglutide in the treatment of heart failure with preserved ejection fraction (HFpEF) owing to its cardioprotective effects. These effects are largely attributed to its anti-inflammatory properties, particularly underlying the pathophysiology of heart failure with a preserved ejection fraction and its role in weight reduction [15].

This systematic review and meta-analysis aim to critically evaluate the safety and efficacy of semaglutide compared to placebo in obese patients with HFpEF. By combining data from various studies, we aim to comprehensively analyze the impact of semaglutide on improving clinical outcomes in HFpEF associated with obesity, thus advancing knowledge in cardiology.

Methods

The systematic review and meta-analysis will adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria [16]. Adhering to PRISMA criteria ensures our review is thorough, transparent, and methodologically sound, enhancing the reliability of our findings. Also, this meta-analysis was registered on PROSPERO (CRD42024592622).

Literature search strategy

A systematic search of the published literature across several databases, such as PubMed, Google Scholar, and the Cochrane Library, was conducted by two researchers. Using the keywords “Semaglutide,” “Heart failure with preserved ejection fraction,” and “Obesity,” we looked for publications that were published from inception till September 2024. A detailed search string containing all the relevant keywords used during the search is outlined in Supplementary Table 1.

Study selection

All articles found from the search were imported into EndNote X9 Reference Manager (Clarivate Analytics, Philadelphia, Pennsylvania), and duplicates were deleted. Two separate researchers reviewed the titles and abstracts of the remaining papers to assess their relevance. The full texts of the chosen papers were assessed for methodology, outcomes of interest, and the existence of appropriate intervention and control groups. Any disagreements were resolved with the agreement of a third author. Two randomized clinical trials [17,18] and one retrospective cohort study [19] that directly contrasted the effects of Semaglutide with a placebo in individuals with obesity and preserved ejection fraction for heart failure were shortlisted [17-19].

Inclusion criteria and exclusion criteria

All randomized controlled trials (RCTs) and retrospective cohort studies in which Semaglutide and placebo were administered to individuals with obesity and preserved ejection fraction who had heart failure were included. Studies with participants who were adults and at least 18 years old were considered. We did not include any single-arm studies or studies that did not directly compare Semaglutide with a placebo. Furthermore, case reports or series, abstracts, conference articles, narrative reviews, and research with patients younger than 18 years old were not included. Studies that did not report any relevant outcomes of interest were also omitted from this systematic review and meta-analysis.

Data extraction

Two reviewers used Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) to extract data from the included studies. Important information about the study, including the author’s name, the year, the sample size, the age of the participants, and baseline variables like male sex percentage and body mass index (BMI), was gathered. This systematic review and meta-analysis focused on the following key outcomes:(1) Percentage change in body weight; (2) Change in 6-minute walk distance; (3) Attainment of the anchor-based threshold for change in 6-minute walk distance; (4) Percentage reduction in body weight; (5) Hospitalization or urgent visit for heart failure; (6) Death from cardiovascular

causes; (7) Heart failure events; (8) Increase in Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS); (9) Attainment of the anchor-based threshold for change in KCCQ-CSS; (10) Change in KCCQ-CSS; (11) Change in Kansas City Cardiomyopathy Questionnaire overall summary score (KCCQ-OSS); (12) Change in systolic blood pressure; (13) Change in waist circumference; (14) Change in CRP level; (15) Change in NT-proBNP level; (16) Serious adverse event; (17) Adverse events leading to permanent discontinuation of the trial product, irrespective of seriousness; and (18) All-cause mortality, all of which were assessed at fifty-second weeks. The primary outcome is a percentage change in body weight from baseline to week 52.

Quality assessment

Using the risk of bias (RoB 2.0) tool, the quality of the included randomized-controlled trials (RCTs) was evaluated [20]. The included studies all show a low risk of bias. We used the Newcastle Ottawa quality assessment scale to assess the methodological quality of the retrospective cohort study [21]. A comprehensive evaluation of quality assessment can be found in Supplementary Table 2(a) and 2(b).

Statistical analysis

We used Review Manager (V.5.4.1 Cochrane Collaboration, London, United Kingdom) to perform the statistical analysis. Risk ratios (RR) were calculated for dichotomous outcomes and mean differences (MD) were calculated for continuous outcomes with 95% confidence intervals (CIs). A random effects model was used to evaluate all the outcomes. The heterogeneity across studies was assessed using Higgins I2 statistics [22]. A value of I^2=25%-50% was considered mild, 50%-75% as moderate, and greater than 75% as severe heterogeneity. The *p*-value of <0.05 was considered significant throughout our analysis.

Results

Study characteristics and baseline demographics

An extensive initial literature search identified 1,605 studies, from which 3 were selected for inclusion in this meta-analysis, comprising 2 randomized controlled trials (RCTs) and 1 observational study [17-19]. The selection process is illustrated in Figure 1, following the PRISMA flowchart guidelines. Outcome data were extracted and pooled from a total of 1,463 patients, with 677 assigned to receive semaglutide and 786 assigned to receive placebo. The mean age in both groups was 69.7 years. Further details regarding the study and baseline characteristics are provided in Tables 1 and 2.

Quality assessment

Both RCTs incorporated into this meta-analysis demonstrated a consistently low risk of bias across the board. A detailed individual assessment of bias risks is provided in Figures 2A and 2B. The observational study [19] scored 9/9 on the Newcastle-Ottawa Scale, with

Table 1. *General characteristics of included studies table.*

Study name	Study year	Study design	Clinical trial number	Total sample size	Patients		Primary outcome	Drug dose(mg)	Follow up duration (days)	Patient category
					Semaglutide	Placebo				
Kosiborod	2023	Randomized, double-blind study	NCT04788511	529	263	266	Percentage change in body weight from baseline to week 52	2.4mg	5 weeks	Heart Failure with Preserved Ejection Fraction
Kosiborod	2024	Randomized, double-blind study	NCT04916470	616	310	306	Percentage change in body weight from baseline to week 52	2.4mg	5 weeks	Heart Failure with Preserved Ejection Fraction
Rehman	2024	Retrospective cohort study	NA	318	104	214	Percentage change in body weight from baseline to week 52	2.4mg	NA	Heart Failure with Preserved Ejection Fraction

Table 2. *Patient baseline characteristics table.*

Study Name	Sample Size			Gender (Male/Female)		Age-yrs		BMI		Body Weight-kg	
	Total	Semaglutide	Placebo	Semaglutide	Placebo	Semaglutide	Placebo	Semaglutide	Placebo	Semaglutide	Placebo
Kosiborod 2023	529	263	266	114/149	118/148	70±9.63	69 ± 9.63	37.2 ± 5.33	36.9 ± 6.15	104.7 ± 20.52	105.3 ± 21.93
Kosiborod 2024	616	310	306	182/128	161/145	69 ± 8.89	70 ± 8.89	36.9 ± 5.85	36.9 ± 5.63	N/A	N/A
Rehman 2024	318	104	214	45/59	101/113	70 ± 3.25	69 ± 3.0	37.2 ± 1.8	36.9 ± 2.08	104.7 ± 6.93	105.3 ± 7.4

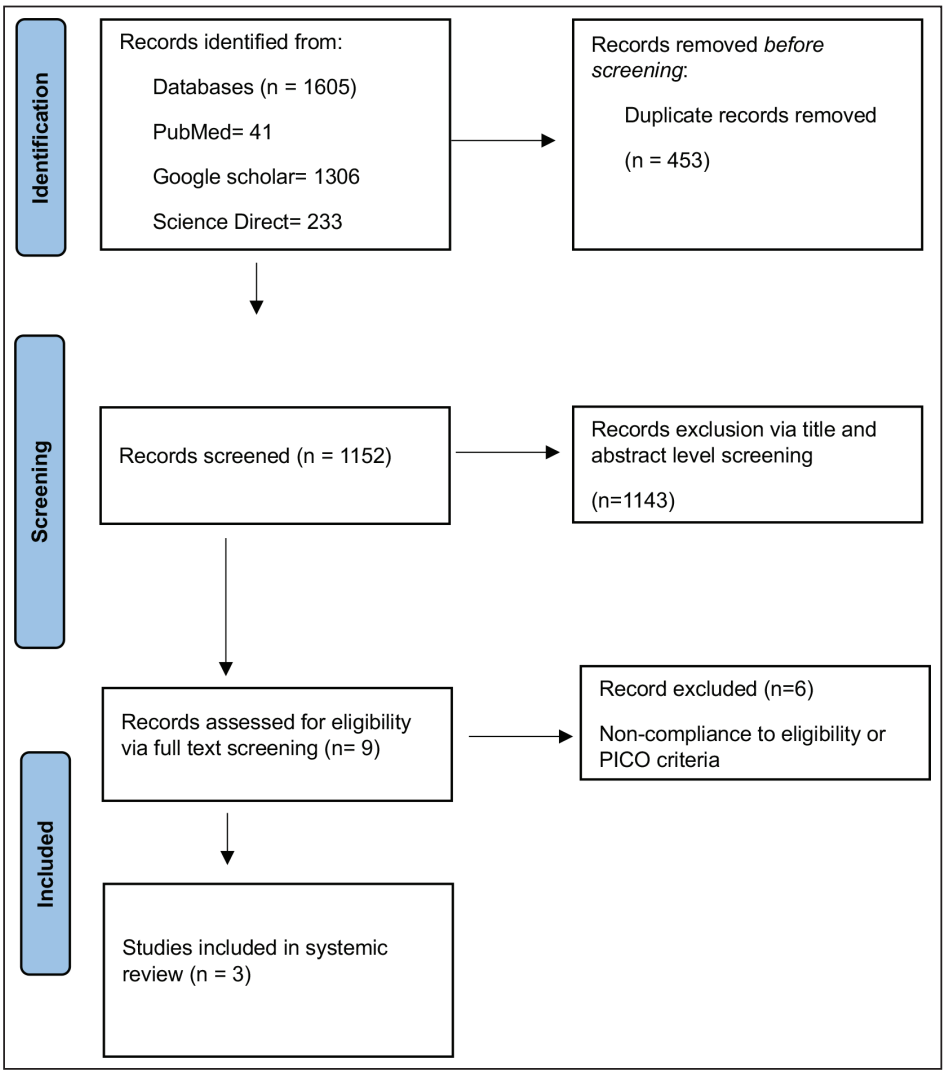

Figure 1. *PRISMA flow chart.*

full marks in selection, comparability, and outcome assessment categories.

Primary outcomes

Body weight reduction and physical function

In the study, semaglutide demonstrated a significant effect on the primary outcome, with a notable percentage reduction in body weight from baseline to week 52 compared to placebo (MD = -6.68; 95% CI: -10.51, -2.85; $P = 0.0006$; $I^2 = 91\%$) (Figure 3). In terms of key primary secondary outcomes, semaglutide significantly improved the 6-minute walk distance at week 52 (MD = 16.37; 95% CI: 13.26, 19.48; $P < 0.00001$; $I^2 = 84\%$) (Figure 4). Additionally, a higher proportion of patients in the semaglutide group achieved the anchor-based threshold for change in a 6-minute walk distance (RR = 1.34; 95% CI: 1.15, 1.56; $P = 0.0001$; $I^2 = 24\%$) (Figure 5).

The percentage reduction in body weight was consistently higher in the semaglutide group, with a significantly larger proportion of patients achieving any reduction in body weight (RR = 9.96; 95% CI: 6.29, 15.78; $P < 0.00001$; $I^2 = 75\%$) as well as a ≥10% reduction compared

to placebo (RR = 6.73; 95% CI: 4.57, 9.91; $P < 0.00001$; $I^2 = 61\%$). This trend extended to higher thresholds, with more patients in the semaglutide group reaching ≥15% and ≥20% reductions in body weight (RR = 13.56; 95% CI: 4.91, 37.42; $P < 0.00001$; $I^2 = 80\%$) and (RR = 22.94; 95% CI: 2.51, 210.0; $P = 0.006$; $I^2 = 82\%$), respectively (Figure 6).

Secondary outcomes

Heart failure-related outcomes

Semaglutide showed a promising trend in improving heart failure-related outcomes compared to placebo. Notably, there was a significant reduction in hospitalizations or urgent visits for heart failure in the semaglutide group (RR = 0.28; 95% CI: 0.14, 0.58; $P = 0.0005$; $I^2 = 39\%$) (Figure 7). Moreover, the reduction in cardiovascular

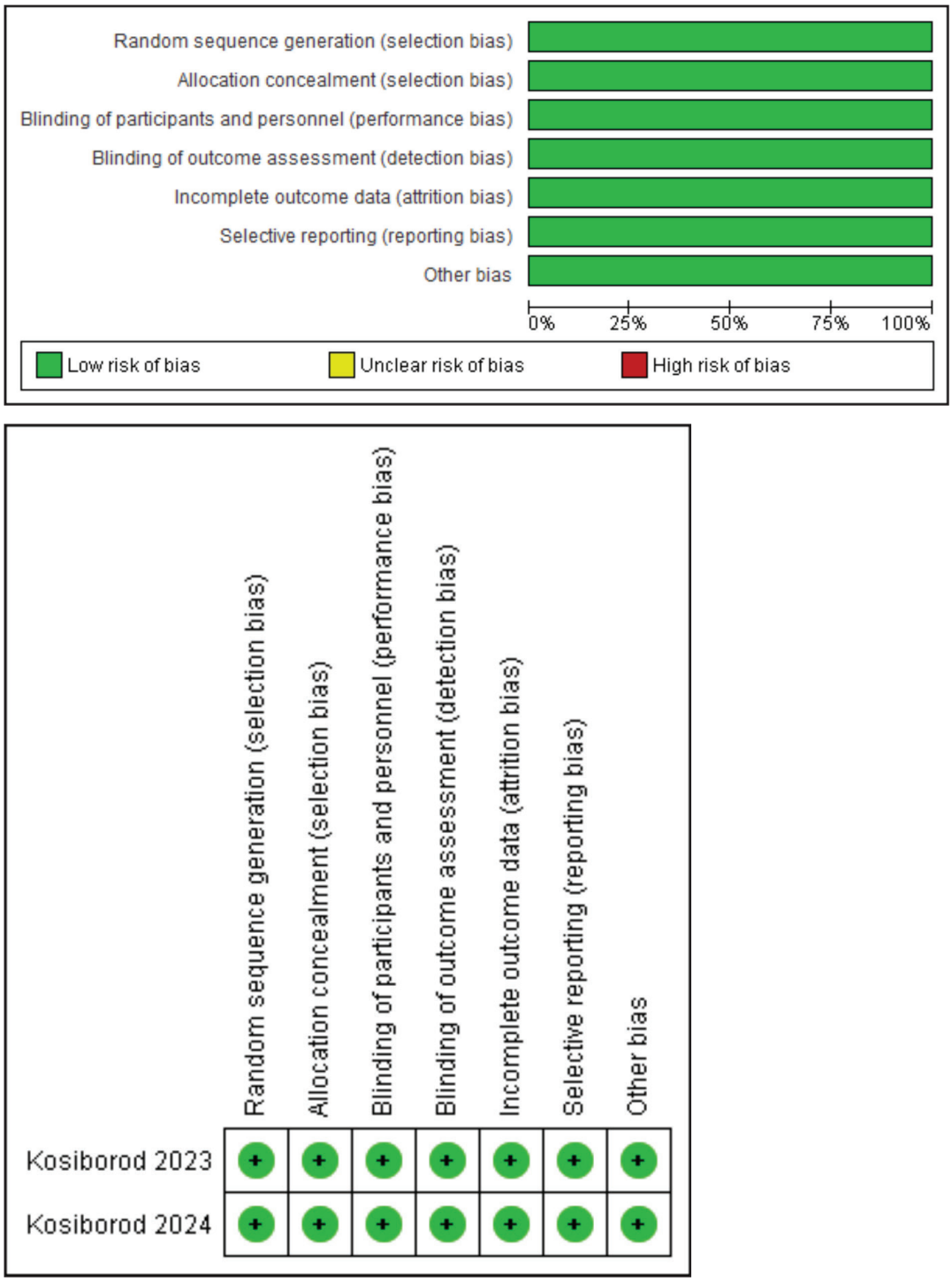

Figure 2. *(A) Risk of bias graph. (B). Risk of bias summary.*

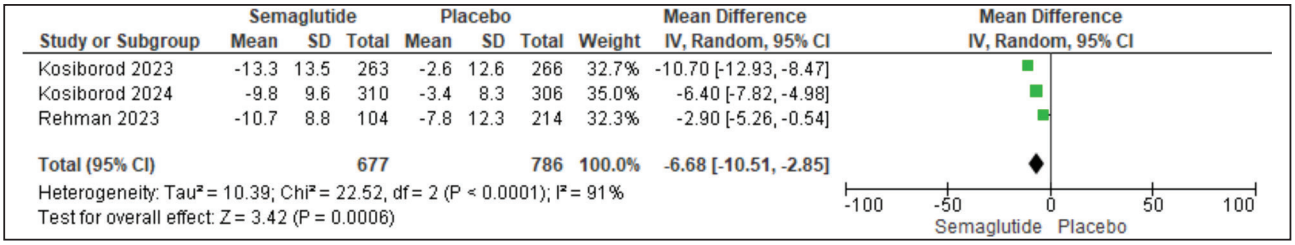

Figure 3. *Forest plot of Percentage change in body weight from baseline to week 52.*

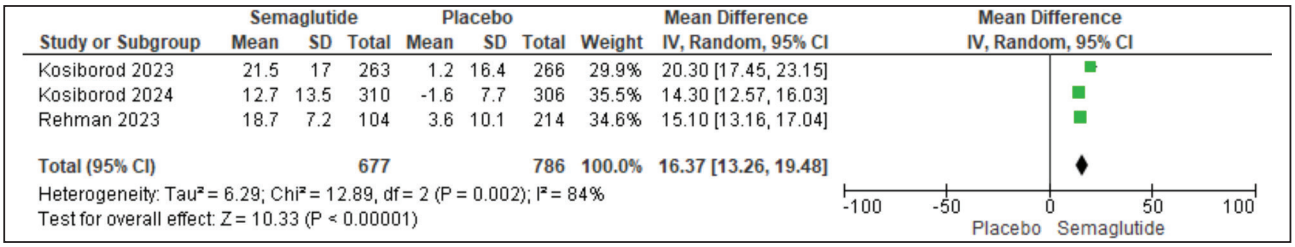

Figure 4. *Forest plot of Change from baseline to week 52 in 6-minute walk distance.*

mortality was significantly lower (RR = 0.27; 95% CI: 0.04, 1.66; $P = 0.16$; $I^2 = 0\%$) (Supplementary Figure 1). Despite this, semaglutide was associated with a lower overall burden of heart failure events, including both hospitalizations and heart failure-related deaths, compared to placebo (RR = 0.18; 95% CI: 0.11, 0.31; $P < 0.00001$; $I^2 = 0\%$) (Supplementary Figure 2).

Quality of life improvements

Semaglutide demonstrated significant improvements in quality of life, particularly in the Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS) (RR = 1.30; 95% CI: 1.22, 1.38; $P < 0.00001$; $I^2 = 0\%$) (Supplementary Figure 3). A 5-point increase in the KCCQ-CSS was observed more frequently in the semaglutide group compared to placebo (RR = 1.25; 95% CI: 1.12, 1.40; $P < 0.0001$; $I^2 = 44\%$) (Supplementary Figure 3). Further improvements were seen with a 10-point increase (RR = 1.34; 95% CI: 1.20, 1.49; $P < 0.00001$; $I^2 = 0\%$) and a 15-point increase (RR = 1.41; 95% CI: 1.21, 1.63; $P < 0.00001$; $I^2 = 0\%$) (Supplementary Figure 3). Additionally, a larger proportion of patients in the semaglutide group reached the anchor-based threshold for meaningful change in the KCCQ-CSS (RR = 1.37; 95% CI: 1.18, 1.60; $P < 0.0001$; $I^2 = 0\%$) (Supplementary Figure 4). The change in KCCQ-CSS from baseline to week 52 was significantly higher in the semaglutide group (MD = 7.55; 95% CI: 6.09, 9.01; $P < 0.00001$; $I^2 = 0\%$) (Supplementary Figure 5), and the KCCQ-OSS change was similarly greater (MD = 7.42; 95% CI: 6.35, 8.50; $P < 0.00001$; $I^2 = 0\%$) (Supplementary Figure 6).

Clinical and biomarker changes

Semaglutide resulted in significant improvements in both clinical and biomarker outcomes compared to placebo. Patients treated with semaglutide experienced greater reductions in systolic blood pressure (MD = -2.53; 95% CI: -3.06, -2.01; $P < 0.00001$; $I^2 = 0\%$) (Supplementary Figure 7) and waist circumference (MD = -7.45; 95% CI: -9.25, -5.64; $P < 0.00001$; $I^2 = 76\%$) (Supplementary Figure 8). Additionally, inflammatory markers, such as C-reactive protein (CRP), were significantly lower in the semaglutide group (MD = -29.16; 95% CI: -34.10, -24.21; $P < 0.00001$; $I^2 = 18\%$) (Supplementary Figure 9), indicating reduced systemic inflammation. Moreover, NT-proBNP levels also showed a more substantial decrease in the semaglutide group (MD = -14.24; 95% CI: -20.59, -7.90; $P < 0.0001$; $I^2 = 84\%$) (Supplementary Figure 10), suggesting improved cardiac function.

Safety and mortality outcomes

Serious adverse events were significantly lower in the semaglutide group compared to the placebo group (RR = 0.54; 95% CI: 0.43, 0.66; $P < 0.00001$; $I^2 = 32\%$) (Supplementary Figure 11). Additionally, there was no significant difference in treatment discontinuation due to adverse events between the groups (RR = 1.58; 95% CI: 0.83, 3.01; $P = 0.16$; $I^2 = 72\%$) (Supplementary Figure 12). Moreover, no significant differences were observed in all-cause mortality between the treatment groups (RR = 0.64; 95% CI: 0.28, 1.47; $P = 0.29$; $I^2 = 0\%$) (Supplementary Figure 13).

Discussion

Our comprehensive meta-analysis, which incorporated data from three studies involving 1,463 patients, sought to evaluate the safety and efficacy of semaglutide in patients with obesity and HfpEF [17-19]. Our findings reveal that semaglutide has a significant positive impact on weight reduction and health outcomes for individuals with heart failure. The results demonstrated that individuals treated with semaglutide experienced a substantial mean weight loss of −6.68 kg compared to those who received a placebo, with a greater proportion achieving ≥10%, ≥15%, and ≥20% reductions. Additionally, semaglutide

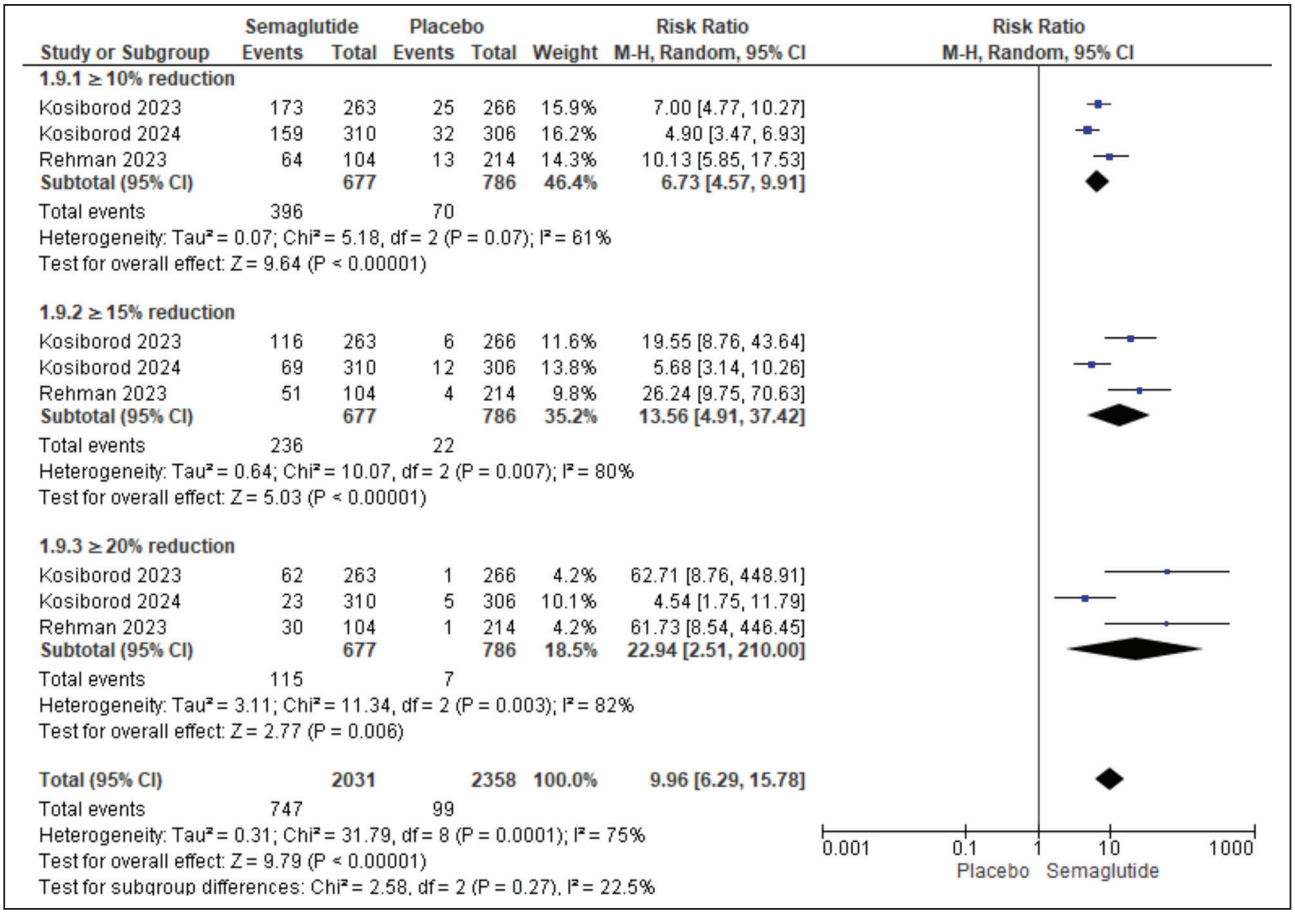

Figure 5. *Forest plot of Percentage reduction in body weight at week 52.*

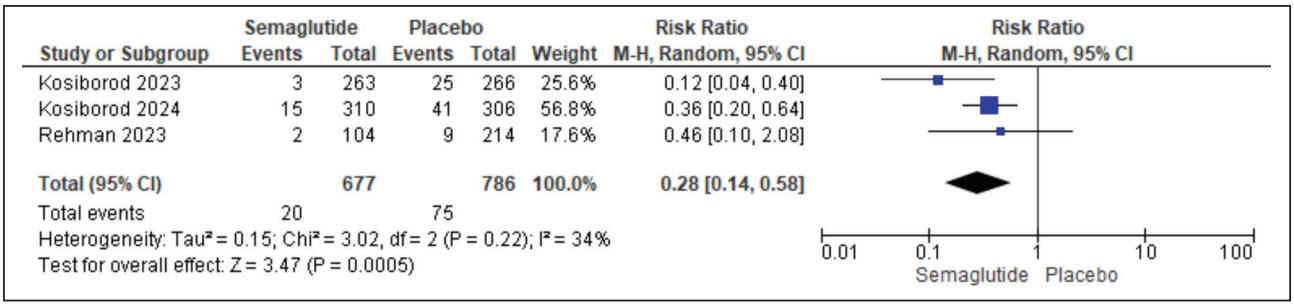

Figure 6. *Forest plot of Attainment of anchor-based threshold for change in 6-minute walk distance.*

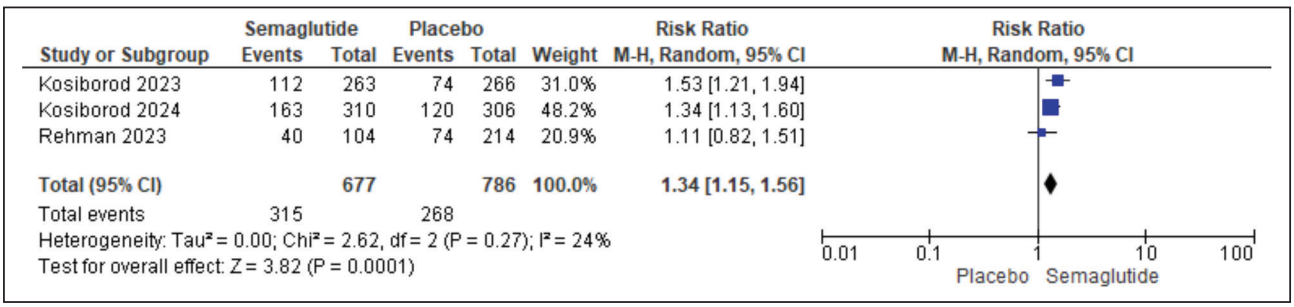

Figure 7. *Forest plot of Hospitalization or urgent visit for heart failure.*

was linked to a reduction in hospitalizations for heart failure, a diminished overall burden of heart failure events, and a decrease in cardiovascular mortality. The improvements in quality of life were remarkable, as evidenced by significant enhancements in the Kansas City Cardiomyopathy Questionnaire scores. Furthermore, semaglutide led to noteworthy reductions in systolic blood pressure, waist circumference, inflammatory markers, and NT-proBNP levels, indicating enhanced cardiac function and reduced systemic inflammation. In addition, Serious adverse events were significantly lower in the semaglutide group. Overall, these results provide strong support for the efficacy and safety of semaglutide in the management of obesity and the enhancement of heart failure outcomes.

HFpEF represents the largest proportion of heart failure cases in the community, and its incidence is rising with an aging population. Individuals with HFpEF often face significant challenges due to severe symptoms and limitations in their physical abilities [23,24]. The primary goals in managing this condition are to relieve symptoms, enhance quality of life, prevent disease progression, reduce hospitalizations, and manage comorbidities [25]. There remains a notable lack of effective treatments targeting these essential outcomes, like improvement in physical function, underscoring a significant unmet need in this patient population. Although the condition is underrecognized [26], especially in patients with obesity, epidemiologic data indicate that the majority of patients with HFpEF have obesity, and growing evidence suggests that adipose tissue may play a pivotal role in the development, progression, and adverse outcomes of heart failure with preserved ejection fraction [27,28]. The presence of visceral adiposity is associated with increased inflammation, left ventricular hypertrophy, insulin resistance, and diastolic and systolic left ventricular dysfunction, as well as with arterial, skeletal muscle, and physical dysfunction[29]. Obesity is a major risk factor for HFpEF, particularly driving a distinct obese phenotype of the disease. Obese HFpEF patients often exhibit characteristics such as greater plasma volume expansion, adverse right ventricular-pulmonary arterial interactions, and enhanced pericardial restraint, which contribute to increased central venous pressure (CVP) and stressed blood volume (SBV) [30-33]. Visceral adiposity plays a critical role in this process by raising intra-abdominal pressure, leading to reduced venous compliance and venous capacitance, and subsequently requiring a higher SBV to maintain adequate perfusion[34,35]. Obesity also results in natriuretic peptide deficiency as a consequence of decreased production and increased clearance, which leads to a reduced capacity for vasodilation and natriuresis [36]. Despite established relationships among obesity, excess adiposity, and worse health outcomes, as well as previous evidence indicating that health status and exercise function improve with lifestyle modification-mediated weight loss in patients with heart failure with HFpEF and obesity, there remains a notable lack of evidence evaluating semaglutide for the obesity phenotype of this condition. To the best of our knowledge, this is the first meta-analysis covering semaglutide in patients with HFpEF and obesity.

The substantial reduction in body weight and improvements in exercise capacity observed in our meta-analysis provide meaningful insights into the management of obesity in patients with HFpEF. These findings address the controversy surrounding weight loss in heart failure, where higher BMI has traditionally been linked with better outcomes in what is termed the "obesity paradox"[37]. The distinction between unintentional weight loss, typically linked to poor outcomes due to cardiac cachexia, and intentional weight loss achieved through lifestyle modifications, medications, or surgical interventions has not been established in the existing literature [38]. Our results align with previous studies that demonstrate Intentional weight loss in HFpEF has been shown to improve symptoms, quality of life, and potentially left ventricular function [38]. The magnitude of the reductions in symptoms and physical limitations observed with semaglutide in our meta-analysis was substantial, with a mean increase in the KCCQ-CSS of nearly 8 points in favour of semaglutide. For context, previous global clinical trial programs involving medications such as SGLT2 inhibitors, sacubitril–valsartan, and spironolactone for heart failure with preserved ejection fraction demonstrated only minimal changes in KCCQ scores, ranging from 0.5 to 2.3 points [39-42]. Furthermore, all responder analyses in our trial, including those evaluating substantial improvements (≥15 points) in the KCCQ-CSS, consistently demonstrated the superiority of semaglutide over placebo. Participants who received semaglutide had more than double the odds of experiencing these significant improvements compared to those who received placebo. The improvement in the 6-minute walk distance that we observed in the meta is also clinically relevant. Even when patients have well-compensated HFpEF and are in stable condition, they have markedly impaired objectively measured physical function [43]. An increase in 6MWD signifies enhanced functional capacity and exercise tolerance, crucial outcomes in both HFpEF and obesity management. Clinically, this reflects improvements in a patient's ability to perform daily activities, enhancing their quality of life and potentially reducing hospitalizations. Additionally, in HFpEF, where few treatments can improve exercise ability, this finding suggests that interventions that increase 6MWD, whether through medications or weight management, could offer important benefits to patients [44]. Several key mechanisms may be responsible for the treatment benefits observed with semaglutide in this group of patients. The trajectory of reductions in symptoms and physical limitations and improvements in exercise function suggest that weight loss, with its attendant decrease in visceral adipose tissue, is likely to be an important contributor to these benefits. Decreases in the CRP level, systolic blood pressure, and NT-proBNP level were also greater in the semaglutide group than in the placebo group, which indicates that semaglutide may have favourable anti-inflammatory and hemodynamic effects in line with previous studies [45]. The extent to which the benefits of semaglutide are driven by weight loss, other direct mechanisms, or a combination of both remains uncertain and warrants further investigation. Nonetheless, semaglutide demonstrates a promising trend in improving heart failure-related outcomes compared

to placebo. Its multifaceted benefits—including weight loss, improved metabolic health, anti-inflammatory effects, and enhanced physical function—collectively contribute to its potential efficacy in reducing heart failure-related complications. These mechanisms underscore the importance of addressing obesity and metabolic dysfunction in heart failure management, particularly for patients with HFpEF, who often face significant challenges related to their weight and overall health. Thus, understanding the specific contributions of these factors to semaglutide's effectiveness could inform more targeted approaches in the management of HFpEF and related conditions.

Our meta-analysis has several limitations that deserve careful consideration. Firstly, the trials included in our review were predominantly conducted in Western settings, which may restrict the generalizability of our findings to more diverse populations. Furthermore, the follow-up periods in the included studies were relatively short, typically around 52 weeks. This limitation raises concerns about the long-term effects of semaglutide on weight reduction, cardiovascular outcomes, and quality of life in patients with heart failure with preserved ejection fraction (HFpEF) and obesity. Additionally, we observed high heterogeneity in several key outcomes, such as weight loss and the 6-minute walk distance. This variability is likely attributed to differences in baseline characteristics, study designs, and treatment adherence across the trials. Such heterogeneity affects the precision of our conclusions, highlighting the need for further research with more uniform protocols and extended follow-up periods.

Conclusion

In summary, this meta-analysis demonstrates that semaglutide is an effective treatment for patients with obesity and HFpEF. Over 52 weeks, semaglutide significantly reduced body weight and improved key health outcomes, including exercise capacity and quality of life, while also decreasing hospitalizations for heart failure. Although the reduction in cardiovascular mortality was not statistically significant, the observed benefits suggest that semaglutide addresses critical needs in managing obesity related HFpEF. Given the limitations related to study demographics and follow-up duration, further research is essential to validate these findings and explore the long-term impacts of semaglutide in diverse populations.

Ethics approval

As this study was based solely on publicly accessible, de-identified data from the CDC WONDER database, it did not involve human subjects directly and thus did not require institutional review board approval or informed consent.

Consent for publication

No individual-level or personally identifiable information is included, rendering publication consent irrelevant.

Conflict of Interest

The authors declare the absence of any financial, personal, or academic conflicts that might have influenced the conduct or outcomes of this study.

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Supplementary content (If any) is available online.

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