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REVIEW

Effects of Anti-Diabetic Drugs on Erectile Dysfunction: A Systematic Review and Meta-Analysis

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Background: Erectile dysfunction (ED) is considered one of the complications of diabetes mellitus (DM), affecting about 35–75% of diabetic patients. Studies suggest that anti-diabetic drugs could potentially alleviate ED in diabetics, yet the effects of different drug classes remain unknown.

Objective: Our study aims to investigate the influence of various anti-diabetic drugs on ED.

Materials and Methods: Adhering to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, a systematic review and meta-analysis were carried out, focusing on clinical research linking anti-diabetic drugs and ED. Relevant studies were sought from PubMed, Embase, and Cochrane Library databases. Review Manager 5.4.1 facilitated meta-analysis and subgroup analysis, while Stata 15.1 was employed for sensitivity analysis to ensure result robustness.

Results: An initial search yielded 3,906 articles across databases. After screening the titles and abstracts of 3,906 articles and performing a full-text review of 30 selected articles, we selected three studies for analysis ultimately. Our most significant finding is that glucagon-like peptide-1 receptor agonists (GLP-1RAs) show an advantage over metformin in improving erectile dysfunction in diabetic patients ($Z = 2.41$, $P = 0.02$), with a particularly notable effect observed in patients with higher BMI or obesity ($Z = 2.26$, $P = 0.02$). This suggests that GLP-1RAs may offer a promising therapeutic option for this patient population. Additionally, thiazolidinediones may enhance sexual function, although their safety and efficacy require further confirmation. Acarbose, insulin, and sodium-glucose cotransporter-2 inhibitors (SGLT-2i) also show potential for positively impacting ED, but more research is needed to establish their efficacy. Finally, the impact of metformin and sulfonylureas on ED remains uncertain, with mixed evidence from existing studies.

Conclusion: In conclusion, GLP-1RAs demonstrate an advantage over metformin in improving erectile dysfunction in diabetic patients. Other antidiabetic drugs also show potential for enhancing erectile function in this population, but further extensive clinical trials are needed to address knowledge gaps and safety concerns.

Keywords: anti-diabetic drugs, erectile dysfunction, obesity, glucagon-like peptide-1 receptor agonists, vascular endothelial function

Introduction

Erectile dysfunction (ED) refers to the inability of patients to achieve or maintain a sufficient erection for satisfactory sexual intercourse, lasting more than three months.[1] ED is one of the most common sexual function disorders in men, with an estimated 150 million males globally affected by varying degrees of ED. This number is projected to increase to 322 million by 2025.[2] The occurrence of ED is closely associated with peripheral neuropathy and vascular endothelial damage, often accompanying diseases such as diabetes, obesity, hyperlipidemia, and hypertension.[3,4] By reducing hyperglycemia and achieving weight loss, patients can improve their ED.[5] Diabetes Mellitus (DM) is an independent

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risk factor for ED, and some research suggests that ED may be a microvascular complication of DM.[6,7] The prevalence of ED among individuals with DM worldwide is approximately 67.4%.[8] Chronic hyperglycemia promotes the accumulation of advanced glycation end products (AGEs), which trigger inflammatory responses and oxidative stress. These processes can impair vascular function and induce peripheral neuropathy, ultimately resulting in ED. In treatment, phosphodiesterase type 5 inhibitors are still the first-line drugs for ED in DM.[9] Recently, some studies have shown that some anti-diabetic drugs may improve ED, but the effects for different types of anti-diabetic drugs are still controversial. For instance, research has demonstrated that glucagon-like peptide-1 receptor agonists (GLP-1RAs), thiazolidinediones, and sodium-glucose cotransporter-2 inhibitors (SGLT-2i) may enhance erectile function in individuals with diabetes. However, for other drugs such as metformin and sulfonylureas, while some studies suggest that these drugs might have the potential to improve ED, other research indicates that they may have no effect or could even impair erectile function in diabetic patients. Therefore, we conducted a systematic review and meta-analysis of published data to investigate the relationship between various anti-diabetic drugs and ED in patients with DM, aiming to provide insights for future research.

Materials and Methods

This systematic review and meta-analysis were conducted according to the PRISMA guidelines.[10]

Search Strategy

In PubMed, Embase, and Cochrane library databases, search for relevant studies on anti-diabetic drugs and ED were published before October 5th, 2024. In this study, the following keywords are used: ("Insulin" OR "metformin" OR "sulfonylureas" OR "glinides" OR "thiazolidinediones" OR "α-glucosidase inhibitors" OR "sodium-glucose cotransporter-2 inhibitors" OR "Dipeptidyl- peptidase-4 inhibitors" OR "Glucagon-Like Peptide-1 Receptor Agonists" OR "Glucagon Like Peptide 1 Receptor Agonists" OR "GLP-1 Receptor Agonists" OR "GLP 1 Receptor Agonists" OR "Incretin Mimetics", "GLP-1 Analogs" OR "GLP 1 Analogs") AND ("Erectile Dysfunction" OR "Dysfunction, Erectile" OR "Impotence" OR "Male Impotence" OR "Impotence, Male" OR "Male Sexual Impotence" OR "Impotence, Male Sexual" OR "Sexual Impotence, Male").

The literature search for this study includes publications from all countries and ethnicities. The reference lists of selected articles are manually checked to ensure that relevant papers are not overlooked. The full texts of these articles are then reviewed to determine if they meet the inclusion criteria. This process is carried out independently by two authors, and any differences are resolved through discussion to reach a consensus opinion.

Inclusion and Exclusion Criteria

Inclusion Criteria: (1) The study subjects are adult male participants who simultaneously suffer from diabetes and ED; (2) At least one group of patients must use at least one type of anti-diabetic drugs, while another group must either use at least one type of anti-diabetic drugs or a placebo; (3) It is necessary to report the mean and standard deviation of the International Index of Erectile Function (IIEF) score[11] for each group; (4) The study types include randomized controlled trials, cohort studies, or case–control studies.

Exclusion Criteria: (1) Reviews, editorials, or preclinical studies; (2) Klinefelter syndrome or Idiopathic Hypogonadotropic Hypogonadism.

Data Extraction

Data were extracted by two authors based on the inclusion and exclusion criteria set forth from the retrieved literature. Discrepancies were resolved through discussion with a third author. The extracted data included: (1) Name of the first author, publication year, and country where the research was conducted; (2) Type of study design; (3) Characteristics of the participants, including average age, body mass index (BMI), sample size, treatment methods, follow-up time, and average IIEF scores in each group. For literature with missing data, the corresponding author of the paper was contacted to obtain the missing information.

Methodological Quality Assessment

Two authors independently assessed the methodological quality of the included cohort studies using the Newcastle-Ottawa Scale (NOS). Any disagreements were resolved through discussion. The NOS is a useful tool for assessing the risk of bias in non-randomized studies, and it mainly consists of three components: selection, comparability, and outcome (for cohort studies) or exposure (for case–control studies). The total score on the NOS can reach up to 9 points, with studies scoring above 5 considered to have high quality. The maximum scores for selection, comparability, and outcome (for cohort studies) or exposure (for case–control studies) are 4, 2, and 3 points respectively.[12,13]

Statistical Analysis

The IIEF scores extracted from the literature were pooled using a random-effects model. To analyze the effects of GLP-1RAs and metformin on diabetes with ED, statistical differences between the GLP-1RAs group and the metformin group were compared separately. An I^2 value of ≤25%, 25%–50%, 50%–75%, and >75% represents no, small, moderate, and high heterogeneity, respectively. Considering the presence of high heterogeneity (I2 > 50%), subgroup analyses were performed based on the following stratifications: BMI and treatment modality (whether combined with testosterone undecanoate use). Meta-analysis and subgroup analysis were conducted using Review Manager version 5.4.1 software, and sensitivity analysis was performed using Stata version 15.1 software to assess the stability of the results.

Results

Literature Research

By searching the databases of PubMed, Embase, and Cochrane, a total of 3,906 initial articles were identified. After screening titles and abstracts, 734 duplicate articles were removed, and 3,139 articles were excluded based on the established inclusion and exclusion criteria. Full text reading led to the exclusion of 30 studies, among which 16 studies involved only animal subjects, 12 studies did not include IIEF scores as an outcome measure, 1 study could not be included in the analysis because it did not present the IIEF scores of each group after drug intervention, and 1 study could not be included due to different grouping compared to the other included studies. According to the inclusion criteria, a final selection of 3 studies was made, and their relevant data were combined to assess the relationship between GLP-1RAs and erectile dysfunction in patients with diabetes. The above process is depicted in Figure 1.

Study Characteristics

This study included a total of three cohort studies, two from Italy and one from Canada, involving 314 participants. Relevant data from 209 eligible participants were used for meta-analysis, with an average age from 52.7 to 64.1 years old. All studies utilized the IIEF questionnaire to assess patients' erectile function. Among the three studies, two studies showed that GLP-1RAs had a more beneficial effect on improving patients' erectile function compared to metformin.[14,15] However, it is noteworthy that the remaining study did not demonstrate this statistically significant difference.[16] Detailed information about the three studies analyzed can be found in Table 1.[14–16] According to the Newcastle-Ottawa Scale, the methodological quality of all three studies were high (scores ≥5 points), as shown in Table 1.[14–16] Detailed scores for each component of the NOS for individual studies can be found in Supplementary Table 1.[14–16]

Insulin

Insulin holds an irreplaceable position in the treatment for DM. Insulin can help diabetes by controlling blood sugar better and avoiding complications. However, the relationship between insulin treatment and ED remains unclear. Some studies suggest that insulin therapy combined with simvastatin or icariin II may improve erectile function in diabetic rats.[17,18] In clinical trials, Wessells et al found that type 1 diabetic patients (T1DM) with retinopathy or microalbuminuria who received intensive insulin therapy had a lower incidence of ED compared with conventional insulin therapy.[19] Moreover, a cohort study by Maiorino et al investigated the impact of multiple daily injections (MDI) and continuous subcutaneous insulin infusion (CSII) on ED in T1DM. The study found no statistically significant difference in the prevalence of ED or IIEF scores between the MDI and CSII groups.[20] However, Kesavadev et al explored that patients

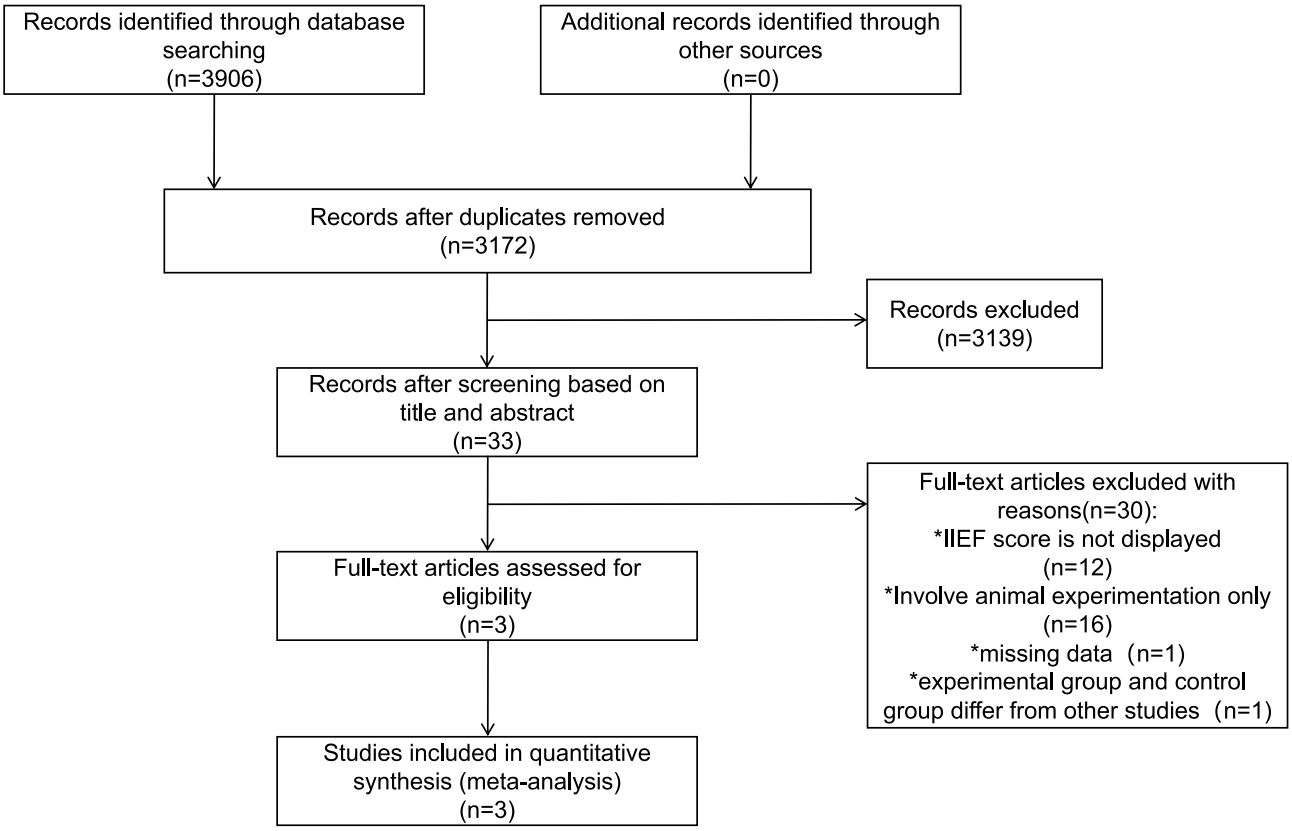

Figure 1 PRISMA flowchart describing the search and selection of relevant studies.
Abbreviations: n, number of records; IIEF, International Index of Erectile Function.

with type 2 diabetic patients (T2DM) who received continuous CSII treatment for 6 months showed an improvement in their IIEF scores, and severity of their ED compared to the MDI group.[21] In conclusion, insulin therapy may improve erectile function of DM by enhancing blood glucose control. However, the comparative efficacy of different insulin delivery methods (MDI vs CSII) remains inconclusive.

Metformin

Metformin is widely used for T2DM, it can also modulate lipid metabolism and improve vascular endothelial function. Research revealed that metformin could enhance erectile function in mice by improving vascular endothelial function and promoting relaxation of the corpus cavernosum in the penis.[22,23] In clinical studies, the combination of metformin and

Table 1 Main Characteristics of the Studies Included in the Meta Analysis

Author, Year	Country	Study Design	Age (y) †	BMI†	IIEF	Therapy	Follow Up	Quality Score
Defeudis,2022[16]	Italy	Cohort	62.3/64.1	29.3/28.1	GLP-1RAs group:16.7 ± 4.7; Met group:15.5 ± 5.7	Met group:Metformin; GLP-1RAs group:GLP-1RAs	4 years	7
Giagulli, 2015[14]	Canada	Cohort	52.7/55.0	35.2/32.5	GLP-1RAs group:19.9 ±2.0; Met group:14.3 ± 1.9	Met group:Metformin+testosterone; GLP-1RAs group:GLP-1RAs +testosterone +Metformin	2 years	6
Giuseppe, 2023[15]	Italy	Cohort	59/60	34/33.7	GLP-1RAs group:18.9 ± 1.2; Met group:16.7 ± 1.5	Met group:Metformin; GLP-1RAs group:GLP-1RAs+Metformin	1 year	8

Notes: †(GLP-1RAs group) / (Metformin group); Quality score, Newcastle-Ottawa Scale score.
Abbreviations: IIEF, International Index of Erectile Function; BMI, body mass index; y, years old; GLP-1 RAs, Glucagon-like peptide 1 receptor agonists; Met, Metformin.

sildenafil for 4 months significantly improved erectile function in patients compared to placebo and sildenafil treatments.[24] On the contrary, some studies suggest that metformin cannot improve erectile function and may even lead to ED.[25–27] Therefore, the relationship between metformin and ED in patients with diabetes remains uncertain. More large-scale clinical research is needed to clarify the potential effects of metformin on erectile function in DM.

Sulfonylureas and Glinides

Sulfonylureas are classic anti-diabetic agents. They act by inhibiting the activity of ATP-sensitive potassium channels in pancreatic β-cells, leading to membrane depolarization and promoting the secretion of insulin.[28,29] Research has found that glibenclamide can inhibit the relaxation of smooth muscle in the corpus cavernosum, induced by some vasodilators such as pinacidil, levodetirazil, prostaglandin, and lopram.[30] But it had no effect on the vasodilation induced by sildenafil.[31] In contrast, a case–control study revealed that diabetic patients scored lower in sexual function compared to non-diabetic patients. However, when compared to metformin, glibenclamide showed more benefit in enhancing erectile function among patients with T2DM.[32] Therefore, the relationship between sulfonylureas and ED in DM remains uncertain. Unfortunately, there is currently no relevant research reporting on the relationship between glinides and ED in diabetes.[29,33]

Thiazolidinediones

Thiazolidinediones can improve insulin sensitivity in peripheral tissues, thereby exerting a hypoglycemic effect.[34,35] Studies have shown that Pioglitazone can increase the production of Nitric Oxide (NO) and improve vascular endothelial function.[36–38] Furthermore, thiazolidinedione drugs can inhibit neuropathic pain by activating Peroxisome Proliferator-Activated Receptor Gamma (PPAR-γ) and suppressing oxidative stress.[39,40] In rat experiments, studies have shown that pioglitazone can enhance the synthesis of NO, modulate insulin-like growth factor 1 (IGF-1), suggesting that pioglitazone may have the potential to improve erectile function.[41–43] In a clinical study, a randomized controlled trial revealed that pioglitazone increased the response of diabetes patients to sildenafil, thereby improving their erectile function.[44] In summary, thiazolidinedione drugs may potentially improve erectile function in patients with diabetes-related ED.

α-Glucosidase Inhibitors

Alpha-glucosidase inhibitors are competitive inhibitors of enzymes that break down oligosaccharides into monosaccharides in the intestinal brush border epithelium. Their primary action is to lower postprandial blood glucose levels.[45,46] Currently, there are few studies investigating the relationship between α-glucosidase inhibitors and ED. It is known that the occurrence of ED in diabetic patients may be associated with vascular inflammation caused by advanced glycation end products, leading to vascular endothelial dysfunction.[47–49] Some studies have shown that acarbose can increase the level of NO in penile tissue of diabetes rats and improve the erectile function of diabetes rats.[50,51] However, there is a lack of strong clinical data supporting its effectiveness, which remains to be confirmed.

Sodium-Glucose Cotransporter-2 Inhibitors (SGLT-2i)

SGLT-2i is a new type of anti-diabetic drugs, which can improve vascular endothelial function and enhance vasodilation by reducing oxidative stress and the production of pro-inflammatory cytokines.[52] This indicates that SGLT-2i may be beneficial for improving erectile function in DM. Research has found that empagliflozin can improve erectile function by promoting corpus cavernosum relaxation mediated by NO.[53] However, the current number of related studies is limited.

Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RAs)

GLP-1RAs can promote insulin secretion, improve insulin resistance, and also possess functions such as appetite suppression, weight loss, anti-inflammatory effects, and anti-oxidation.[54,55] Some studies have found that lilalutide can improve the erectile function of diabetes rats and protect the endothelial cells of cavernous body by regulating the Ras Homolog Family Member A/Rho-Associated Coiled-Coil Containing Protein Kinase (RhoA/ROCK) pathway and Protein Kinase B/Endothelial Nitric Oxide Synthase (Akt/eNOS) signaling pathway, and improve autophagy induced by oxidative stress.[56] Additionally, a study by Dalaklioglu showed that exendin-4 might improve the relaxation function

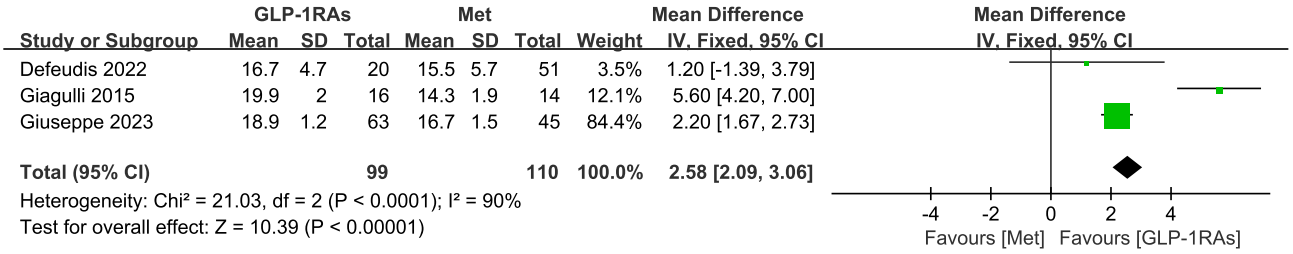

Figure 2 Forest plot of comparison of GLP-1 RAs and Metformin. Compared to Metformin, GLP-1 RAs is more conducive to the improvement of erectile function in diabetic patients.

Abbreviations: Fixed, Fixed Effect Model; GLP-1 RAs, Glucagon-like peptide 1 receptor agonists; Met, Metformin; SD, Standard Deviation; IV, Inverse Variance Method; CI, confidence interval.

of the corpus cavernosum by inhibiting Nicotinamide Adenine Dinucleotide Phosphate (NADPH) oxidase.[57] These studies suggest that GLP-1RAs may have potential in improving erectile function in DM.

This potential is further supported by an exploratory analysis of a randomized controlled trial, which indicated that long-term use of dulaglutide may reduce the incidence of ED in patients with type 2 diabetes compared to a placebo group (HR 0.92, 95% CI 0.85–0.99, p = 0.021).[58] However, the study only reported the prevalence of ED in each group and did not show the improvement in erectile function scores before and after treatment with GLP-1RAs.

Our meta-analysis results indicate that GLP-1RAs significantly improve erectile function in diabetic patients compared to metformin (Z = 2.41, P = 0.02); however, there was high heterogeneity among the three studies included in the meta-analysis (I^2= 90%) (Figure 2). To investigate the primary source of the observed heterogeneity between the three study results, we conducted subgroup analyses.

Subgroup Analysis for GLP-1RAs

In this study, we conducted a subgroup analysis based on the BMI of the participants included in the three studies for the meta-analysis. The results showed that GLP-1RAs had a more significant effect on improving erectile function in individuals with BMI >30 compared to those with BMI <30 (Z = 2.26, P = 0.02, I^2 = 95%) (Figure 3).

We also performed a subgroup analysis based on whether the participants were co-administered with testosterone undecanoate. The results indicated that the heterogeneity between the two studies without the use of testosterone undecanoate significantly decreased (I^2 = 0), and the pooled effect size of these two studies still supported that GLP-1RAs were beneficial for improving erectile function in DM (pooled MD 2.16, 95% CI 1.64–2.68; Z = 8.17, P < 0.00001) (Figure 3). Testosterone plays an important role in the neural and vascular regulation of erectile function and testosterone replacement therapy is beneficial for improving patients' erectile function.[59–62] Therefore, we believe that the high heterogeneity among the three studies included in this analysis may stem from this factor.

Sensitivity Analysis

In the sensitivity analysis, removing any one of the three studies did not fundamentally alter the overall results (Figure 4).

Discussion

Diabetes not only leads to disturbances in glucose metabolism but also often accompanies dyslipidemia, excessive inflammatory responses, and oxidative stress, among other risk factors.[63] Under the long-term combined influence of these factors, patients may experience impaired vascular endothelial function and reduced levels of NO, leading to various microvascular and neurological complications, including ED.[64,65]

In terms of lipid metabolism, adipose tissue can secrete a series of cytokines, such as Tumor Necrosis Factor Alpha (TNF-α), Interleukin-6 (IL-6), and adiponectin, which have pro-inflammatory or anti-inflammatory effects on vascular endothelial cells and maintain a balance. Adiponectin, in particular, has multiple functions, including insulin sensitization, anti-inflammation, and increasing the level of phosphorylated Endothelial Nitric Oxide Synthase (p-eNOS) in endothelial cells.[66–68] However, in the state of obesity, this balance is disrupted, with a significant decrease in the level of adiponectin, which has anti-inflammatory properties. Meanwhile, the expression of pro-inflammatory factors such as

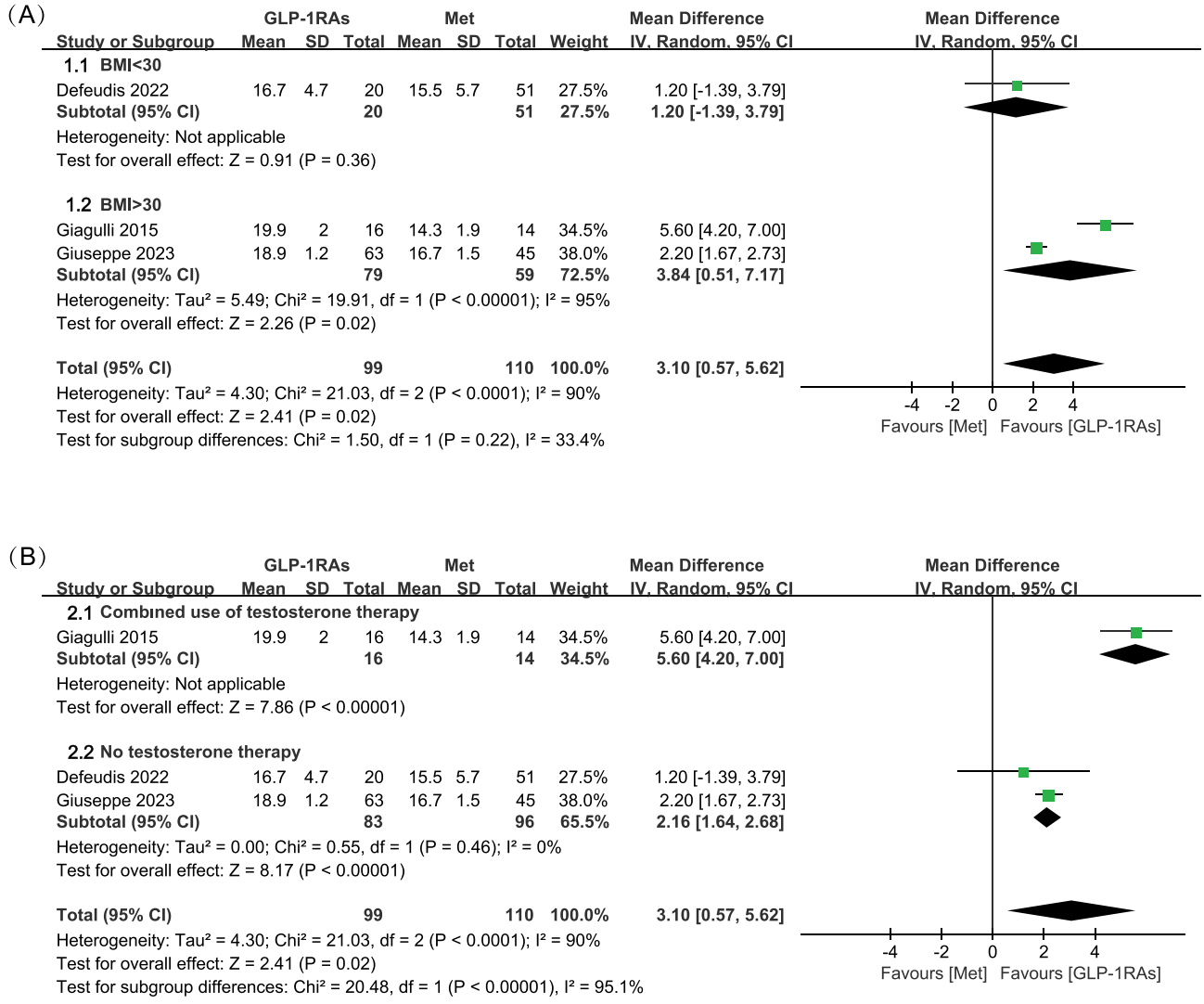

Figure 3 Subgroup Analysis of the Impact of GLP-1 RAs on Erectile Function in Diabetic Patients. Subfigure (**A**): A Subgroup Analysis based on the BMI of patients. The effect of GLP-1 RAs on the improvement of erectile function in diabetic patients is more pronounced in the subgroup with a BMI greater than 30. Subfigure (**B**): A Subgroup Analysis based on whether testosterone was co-administered. The heterogeneity among the three studies included in the analysis primarily stems from whether the participants were concurrently using testosterone.

Abbreviations: GLP-1 RAs, Glucagon-like peptide 1 receptor agonists; Met, Metformin; SD, Standard Deviation; IV, Inverse Variance Method; Random, Effect Model; CI, confidence interval; BMI, body mass index.

TNF-α and IL-6 increases.[69] This may suppress the expression of eNOS in endothelial cells, resulting in a reduction of NO levels, thereby affecting the patient's erectile function.

In terms of oxidative stress, the chronic hyperglycemic state in diabetic patients can activate various inflammatory pathways and stimulate oxidative stress, generating large amounts of reactive oxygen species and inflammatory factors.[70,71] These reactive oxygen species and inflammatory factors may inhibit the expression of endothelial eNOS, thereby reducing the level of NO and promoting the contraction of the corpus cavernosum in the penis, which mediates ED.[72]

In addition to disorders in glucose and lipid metabolism and excessive oxidative stress, insulin resistance may also play a significant role in the development of ED in diabetic patients. Research conducted by El Assar et al found that vascular endothelial dysfunction was observed only in human morbid obesity accompanied by insulin resistance.[73] Subsequent animal experiments showed that insulin resistance might mediate vascular endothelial dysfunction by

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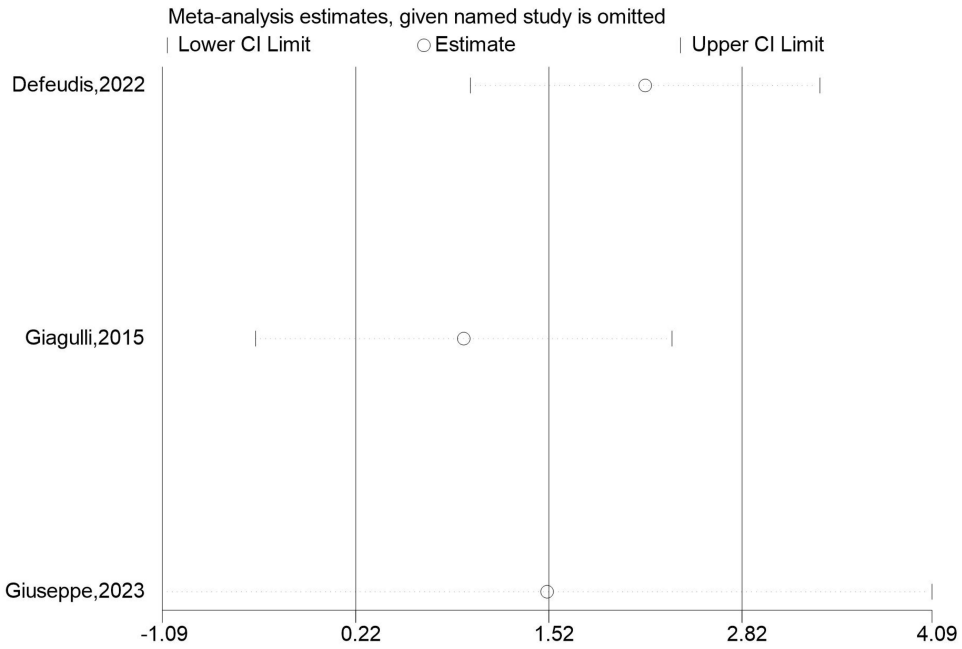

Figure 4 Sensitivity analysis showing that the results of the meta-analysis are relatively reliable.
Abbreviation: CI, 95% confidence interval.

increasing the expression of asymmetric dimethylarginine (ADMA) and arginase.[74] Their findings suggest that insulin resistance may be one of the important factors contributing to the occurrence of ED in patients with T2DM.

Anti-diabetic drugs often have the effect of reducing these risk factors. However, the relationship between anti-diabetic drugs and ED remains unclear. Therefore, this paper reviews existing studies to comprehensively analyze the effects of various anti-diabetic drugs in improving erectile function. First, in terms of their impact on erectile function, the effects of insulin, metformin, and sulfonylureas remain highly contentious. More large-scale clinical studies are needed to clarify their relationship with ED. Second, thiazolidinediones may be beneficial for improving the erectile function of diabetic patients, but due to their significant cardiovascular risks, further confirmation of their effectiveness and safety is required. In addition, acarbose, SGLT-2i may have anti-inflammatory and oxidative stress inhibitory effects, thus improving vascular endothelial function, and therefore may have a positive impact on erectile function. However, research on these three types of drugs concerning ED is scarce, especially lacking clinical study data support, so their effectiveness also needs further verification. Finally, current research almost unanimously supports the beneficial effects of GLP-1RAs on erectile function.

Consistent with the findings of previous studies, our analysis suggests that GLP-1RAs are beneficial in improving erectile function in patients with diabetes. Furthermore, the results of subgroup analyses indicate that the positive effect of GLP-1RAs on erectile function is more pronounced in individuals with higher BMI. This may be due to the fact that the occurrence of ED is closely related to factors such as patient age, autonomic nervous system function, vascular endothelial function, and individual hormonal environment.[75–77] GLP-1RAs not only assist diabetic patients in achieving better blood glucose control by enhancing insulin secretion and improving insulin resistance,[78] but they also exhibit a variety of biological functions, such as suppressing appetite, reducing body weight, regulating lipid metabolism, exerting anti-inflammatory effects, acting as antioxidants, protecting nerves, and preserving vascular endothelial cells.[54,55,79–82] Therefore, we hypothesize that GLP-1RAs may protect peripheral nerves and cavernous endothelial cells of the penis by modulating patients' blood glucose and lipid metabolism, and by exerting anti-inflammatory and antioxidant effects, ultimately leading to an improvement in erectile function among diabetic patients. Additionally, it is possible that for individuals with a higher BMI, factors such as dysregulated lipid metabolism and decreased testosterone

levels have a greater impact on erectile function. Consequently, the effect of GLP-1RAs in improving erectile function through weight reduction and lipid metabolism regulation is more pronounced in these individuals.

Our findings may provide insights for future in-depth research into the relationship between GLP-1RAs and male erectile function. However, the limitation of this meta-analysis is that it includes too few studies, all of which are observational. Therefore, further research with larger sample sizes is needed to confirm the effects of GLP-1RAs on erectile function in patients with diabetes.

Conclusion

In summary, GLP-1RAs have demonstrated significant improvements in erectile function among diabetic patients compared to metformin, as supported by meta-analysis results. However, the high heterogeneity observed across studies, likely influenced by factors such as participant BMI and the co-administration of testosterone, complicates the interpretation of these findings. Moreover, insulin therapies have shown potential benefits for ED, although the comparative efficacy of different delivery methods (MDI versus CSII) remains inconclusive. Additionally, other anti-diabetic drugs, including thiazolidinediones, α-glucosidase inhibitors, and SGLT-2 inhibitors, have revealed promising mechanisms but lack robust clinical validation regarding their impact on ED. Finally, Metformin and sulfonylureas have exhibited both positive and negative effects on erectile function. The efficacy and safety of these drugs for treating erectile dysfunction in patients with diabetes require further validation through larger, more rigorous, and well-designed clinical trials.

Data Sharing Statement

All data used in this meta-analysis were derived from the corresponding published articles of the included studies. The review protocol was registered in PROSPERO (International Prospective Register of Systematic Reviews) under the registration number CRD42024599203 and is available at https://www.crd.york.ac.uk/PROSPERO/#myprospero.

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Author Contributions

All authors contributed significantly to the work reported, including the conception, study design, execution, acquisition of data, analysis and interpretation. They participated in drafting, revising, or critically reviewing the article, gave final approval of the version to be published, agreed on the journal to which the article has been submitted, and agree to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Disclosure

The authors declare no competing interests in this work.

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