

Comparative Analysis of IDegLira versus Insulin Glargine in Short-Term Intensive Therapy for Overweight or Obese Patients with Type 2 Diabetes Mellitus

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Abstract

Purpose

To compare the efficacy of insulin degludec/liraglutide (IDegLira) versus insulin glargine, both combined with insulin aspart, for short-term intensive glycemic control in overweight or obese patients with type 2 diabetes mellitus (T2DM).

Method

Severely hyperglycemic overweight/obese T2DM patients were randomly assigned to receive either IDegLira plus insulin aspart (observation group) or insulin glargine plus insulin aspart (control group). Continuous glucose monitoring systems (CGMS) were used to assess glycemic control, insulin requirements, pancreatic β -cell function, and insulin resistance over a seven-day intensive therapy period.

Result

The observation group exhibited a higher time in range (TIR) compared with the control group ($P = 0.007$). Measures of glycemic variability, including time above range (TAR), mean of daily differences (MODD), mean glucose (MG), standard deviation (SD), and coefficient of variation (CV), were all significantly lower in the IDegLira group ($P < 0.01$). After seven days of treatment, the reduction in C-peptide-based homeostasis model assessment of insulin resistance (HOMA-IR-CP) was greater in the IDegLira group ($P = 0.001$), while the improvement in C-peptide-based homeostasis model assessment of β -cell function (HOMA islet-CPDM) was markedly greater ($P < 0.001$). The IDegLira group also required a lower total daily insulin dose at the end of treatment, achieved glycemic targets more rapidly, and demonstrated a higher rate of excellent glycemic control ($P = 0.001$).

Conclusion

IDegLira combined with insulin aspart provides superior short-term intensive glycemic control compared with insulin glargine plus insulin aspart in overweight or obese patients with T2DM, with faster target achievement, improved glycemic stability, reduced insulin requirements, and greater improvements in insulin resistance and β -cell function.

Introduction

The latest data from the International Diabetes Federation (IDF) indicate that 537 million adults worldwide currently have diabetes, and this number is projected to increase to 643 million by 2030.¹ Overweight and obesity are prominent features among individuals with T2DM globally, affecting

approximately 85% of patients.² Studies have shown that visceral fat accumulation is associated with insulin resistance and represents one of the major risk factors for the development of this disease.^{3,4} Overweight and obesity increase the difficulty of blood glucose control in diabetic patients and elevate the risk of cardiovascular disease, while early intensive glycemic control can reduce the metabolic memory effect of vascular complications.⁵ In overweight or obese patients with T2DM, treatment strategies should address not only glycemic control but also weight reduction and the improvement of insulin resistance.

Short-term intensive insulin therapy is an effective approach for patients with T2DM presenting with severe hyperglycemia.⁶ The current standard intensive insulin therapy typically involves either continuous subcutaneous insulin infusion with short-or rapid-acting insulin or a regimen of preprandial short-or rapid-acting insulin combined with insulin glargine; however, this approach is often less effective in overweight or obese patients with T2DM who exhibit marked insulin resistance.^{7,8} The 2022 American Diabetes Association (ADA) Standards of Care state that for patients with T2DM inadequately controlled on basal insulin and oral antihyperglycemic agents, a basal insulin–GLP-1 receptor agonist (GLP-1 RA) injection may be considered as a treatment option.⁹ In 2016, the U.S. Food and Drug Administration (FDA) approved the basal insulin GLP-1 receptor agonist injection—IDegLira—for the treatment of diabetes.¹⁰ This study aimed to evaluate the short-term intensive effects of IDegLira versus insulin glargine, each combined with insulin aspart, in overweight or obese patients with T2DM, with the goal of exploring novel strategies for short-term insulin-based glycemic management in this population.

Materials and Methods

Research subjects

A total of 126 eligible overweight or obese patients with T2DM hospitalized in the Endocrinology Department between October 2024 and June 2025 were randomly assigned in a 1:1 ratio to the control group (n = 63) or observation group (n = 63).

Inclusion, exclusion, and grouping criteria

Inclusion Criteria: (1) Met the diagnostic and classification criteria for T2DM; (2) Had glycated hemoglobin (HbA1c) $\geq 9.0\%$ or fasting plasma glucose (FPG) ≥ 11.1 mmol/L; (3) Had a body mass index (BMI) ≥ 24 kg/m² or a waist circumference > 90 cm in males and > 85 cm in females; (4) Were aged between 18 and 80 years; (5) The patient and family members were informed about the study and had signed the consent form.

Exclusion Criteria: (1) Had severe infection or acute complications of diabetes; (2) Had severe heart, liver, or kidney failure; (3) Were pregnant, breastfeeding, or trying to conceive; (4) Were allergic to the drugs used in this study; (5) Had sarcopenia, medullary thyroid carcinoma (including a personal or family

history), or multiple endocrine neoplasia type 2. (6) Patients with severe non-proliferative diabetic retinopathy (NPDR) or proliferative diabetic retinopathy (PDR) were excluded.

Treatment Methods

Eligible patients were randomly assigned to the control or observation group in a 1:1 ratio using a random number table, and intensive therapy was administered for 1 week.

Patients in the observation group received preprandial subcutaneous injections of insulin aspart (Novo Nordisk, 3 mL:300 U) combined with once-daily subcutaneous injections of IDegLira (Novo Nordisk, 3 mL containing 300 U insulin degludec and 10.8 mg liraglutide). Patients in the control group received preprandial subcutaneous injections of insulin aspart combined with once-daily subcutaneous injections of insulin glargine (Sanofi-Aventis Deutschland GmbH, 1.5 mL:450 U per prefilled pen, 300U/ml).

The initial total insulin dose in both the observation and control groups was 0.5 U/(kg·d). The starting dose of insulin glargine or IDegLira constituted 50% of the total dose, with the remaining 50% distributed equally among the three pre-meal doses of insulin aspart at a ratio of 1:1:1. The starting dose of IDegLira did not exceed 16 units in principle, with a maximum dose not exceeding 50 units. Dosage was adjusted based on fasting blood glucose (FBG) levels: when FBG was > 7.8 mmol/L, the dose was increased by 4 U; when $6.1 \text{ mmol/L} \leq \text{FBG} \leq 7.8 \text{ mmol/L}$, the dose was increased by 2 U; when $4.4 \text{ mmol/L} \leq \text{FBG} < 6.1 \text{ mmol/L}$, no adjustment was made; when FBG was < 4.4 mmol/L, the dose was reduced by 2 U. The method for adjusting the initial dose of insulin glargine in the control group was the same as described above. Pre-meal insulin doses were adjusted as needed based on pre-meal blood glucose levels before the next meal, with dose adjustments performed every 2–3 days.

All participants in both groups received the same standardized lifestyle management and education program, including dietary and exercise counseling. Both groups were equipped with the same continuous glucose monitoring system (manufacturer: Shenzhen Silicon-based Sensor Technology Co., Ltd.; model: GS1-10).

Data Collection

On the first day of hospitalization, clinical and laboratory data were collected, including age, sex, height, weight, BMI, duration of type 2 diabetes, FPG, glycated hemoglobin (HbA1c), fasting C-peptide (FCP), and adiponectin (APN). On day 7 of treatment, the achievement of the composite endpoint for high-quality glycemic control was assessed, which required patients to meet all three of the following criteria: (1) efficacy: TIR > 70%; (2) stability: CV < 36%; and (3) safety: no hypoglycemic events (3.0 mmol/L).

Hypoglycemia, gastrointestinal symptoms, and other adverse events were recorded, along with total daily insulin dose on the final day (U/kg/day), FCP, and APN levels. C-peptide–based indices of insulin resistance (HOMA-IR-CP) and β -cell function (HOMA islet-CPDM) were calculated before and after treatment using FCP, according to the following formulas:

$$\text{HOMA-IR-CP} = 1.5 + \text{FPG} \times \text{FCP} / 2800;$$

$$\text{HOMA islet-CPDM} = 0.27 \times \text{FCP} / (\text{FPG} - 3.5)^{11,12}$$

The CGMS sensor kit was used for a 7-day monitoring period. The glycemic target in the reports was set at 3.9–10.0 mmol/L. Observed indicators included TIR, TAR, time below range (TBR; 3.9 mmol/L or < 2.9 mmol/L), largest amplitude of glucose excursion (LAGE), mean amplitude of glycemic excursions (MAGE), MODD, MG, SD, and CV.

Statistical Methods

Statistical analysis was performed using SPSS version 26.0 (SPSS Inc., Chicago, IL, USA) and Prism software (GraphPad, version 10.6.0). Continuous variables with a normal distribution were expressed as mean±standard deviation (Mean ± SD) and analyzed using the t-test or analysis of variance (ANOVA). Non-normally distributed data were presented as median with interquartile range and compared using nonparametric tests (Mann-Whitney U). Categorical variables were expressed as frequency (n) and percentage and analyzed using the chi-square test. Paired t-tests were used to compare pre-and post-treatment parameters within groups. Fisher's exact test was applied when appropriate. Two-sided *P*-values < 0.05 were considered statistically significant.

Results

Comparison of Baseline Characteristics Between the Two Patient Groups

There were no significant differences between the two groups in baseline characteristics, including age, sex, BMI, HbA1c, and duration of type 2 diabetes, as well as metabolic and islet function parameters (*P* > 0.05) (Table 1).

Table 1
Baseline Characteristics of Randomized Participants

Clinical Data	Control group (n = 63)	Observation group (n = 63)	P-value
Gender (Male: Female)	33: 30	36: 27	0.591
Age(years)	58.48 ± 1.27	55.81 ± 1.34	0.15
Duration of illness (years)	4(3,6)	4(3,5)	0.739
BMI (kg/m ²)	28.57(25.95, 30.32)	27.99(25.97, 30.48)	0.610
HbA1c(%)	10.2(8.67,11.42)	10.1(8.9,11.2)	0.639
FPG(mmol/L)	10.6(8.1,13.4)	10.1(8.2,13.7)	0.874
FCP (pmol/L)	440.23(271.42,562.70)	486.57(347.55,662.00)	0.127
APN(mg/L)	7.79(4.4,9.8)	7.0(5.2,11.0)	0.857
HOMA-IR-CP	3.19(2.65,3.89)	3.47(2.75,4.04)	0.273
HOMAislet-CPDM	17.08(10.43,25.64)	21.28(13.11,29.38)	0.134
Note: BMI: Body mass index; FPG: Fasting Plasma Glucose; FCP: Fasting C-peptide; APN: Adiponectin; HOMA-IR-CP: C-peptide Insulin Resistance Index; HOMAislet-CPDM: C-peptide Islet Function Index			

Comparison of Post-treatment Metabolic and Islet Function Parameters Between the Two Groups

After 7 days of treatment, there were no significant differences between the two groups in APN, FCP, or their corresponding change values (Δ) ($P > 0.05$). In contrast, significant differences were observed between the two groups in FPG, HOMA-islet-CPDM, and their changes (Δ) ($P < 0.05$). Post-treatment FPG in the observation group was significantly lower than that in the control group [5.2(5.0-5.5) mmol/L vs. 7.5(6.6–8.4) mmol/L, $P < 0.001$], and the decrease in FPG (Δ FPG) was also markedly greater [4.7(3-8.7) mmol/L vs. 2.9(0.4–5.8) mmol/L, $P < 0.001$]. HOMA-islet-CPDM increased significantly in the observation group [73.28(44.05-100.09) vs. 25.08(15.79–38.73), $P < 0.001$], and its change value (Δ) was also higher than that in the control group ($P < 0.001$), indicating a more pronounced improvement in β -cell function. A significantly greater reduction in HOMA-IR-CP was observed in the observation group compared with the control group ($P = 0.005$), despite comparable post-treatment levels between groups, indicating a more pronounced improvement in insulin resistance (Table 2, Fig. 1).

Table 2

Comparison of Post-treatment Metabolic and Islet Function Parameters Between the Two Groups

Clinical Data	Control group (n = 63)	Observation group (n = 63)	P-value
FPG (mmol/L)			
Post-treatment	7.5(6.6,8.4)	5.2(5.0,5.5)	<0.001 ^b
--△Change	2.9(0.4,5.8)	4.7(3,8.7)	<0.001
APN (mg/L)			
Post-treatment	7.4(4.7,10.0)	7.3(5.2,10.61)	0.547
--△Change	-0.05(-0.6,0.67)	-0.1(-0.7,0.6)	0.914
FCP (pmol/L)			
Post-treatment	364.10(231.70,589.18)	446.85(258.18,628.90)	0.162
--△Change	36.41(-72.82,139.02)	23.17(-86.06,175.43)	1.000
HOMA-IR-CP			
Post-treatment	2.51(2.08,3.08)	2.36(1.96, 2.75)	0.104
--△Change	0.60(-0.05,1.35)	0.98(0.41,1.60)	0.005
HOMA islet-CPDM			
Post-treatment	25.08(15.79,38.73)	73.28(44.05,100.09)	<0.001
--△Change	7.18(-1.79,16.94)	46.98(27.73,77.72)	<0.001
Note: FPG: Fasting Plasma Glucose; FCP: Fasting C-peptide; APN: Adiponectin; HOMA-IR-CP: C-peptide Insulin Resistance Index; HOMAislet-CPDM: C-peptide Islet Function Index			

Comparison of CGMS Metrics Between the Two Groups

The observation group showed significantly improved overall glycemic control compared with the control group, as reflected by CGMS-derived metrics.. TIR was higher, and TAR was lower in the observation group ($P = 0.007$ and $P = 0.005$, respectively), whereas no significant difference was observed in TBR. Glycemic variability was reduced, as indicated by significantly lower MODD, MG, SD, and CV (all $P \leq 0.003$), while LAGE and MAGE did not differ significantly between groups. The time to achieve target blood glucose levels was significantly shorter, and the total daily insulin dose at the end of treatment was lower in the observation group ($P < 0.001$ and $P = 0.03$, respectively). In addition, the rate of achieving good glycemic control was significantly higher in the observation group ($P = 0.001$). Although the incidences of mild and severe hypoglycemia were numerically lower in the observation group, these

differences were not statistically significant, and no significant difference in adverse events was observed between groups. (Table 3)(Fig. 2).

Table 3
Glycemic excursion parameters, insulin dosage, and adverse reactions at the end of the two treatment groups

Clinical Features	Control group (n = 63)	Observation group (n = 63)	P-value
TIR(%)	74.67 ± 22.03	84.03 ± 15.36	0.007
TAR(%)	22.14 ± 20.86	13.59 ± 11.32	0.005
TBR(%)	1.59 ± 2.84	0.98 ± 2.26	0.187
LAGE (mmol/L)	8.78 ± 2.84	8.17 ± 2.20	0.185
MAGE (mmol/L)	5.41 ± 2.05	5.04 ± 1.69	0.277
MODD (mmol/L)	2.47 ± 0.88	1.84 ± 0.74	<0.001
MG (mmol/L)	9.74 ± 1.77	8.26 ± 1.41	<0.001
SD (mmol/L)	3.47 ± 0.74	2.74 ± 0.72	<0.001
CV(%)	35.62 ± 5.83	32.42 ± 6.08	0.003
Time to Achieve Target Blood Glucose Level(days)	5.0 ± 1.8	3.1 ± 1.7	<0.001
Total insulin dose at end of treatment(U/kg/day)	41.59 ± 9.45	37.95 ± 9.13	0.03
Mild hypoglycemia (≤ 3.9 mmol/L)	28(44.4%)	19(30.2%)	0.097
Severe hypoglycemia (≤ 3.0 mmol/L)	9(14.3%)	3(4.8%)	0.069
Rate of Achieving Good Glycemic Control(%)	23(36.5%)	41(65.1%)	0.001
Gastrointestinal reactions and other adverse events (n)	3(37.5%)	5(62.5%)	0.359
Note: TIR: Time in Range for glucose; TAR: Time Above Range; TBR: Time Below Range; LAGE: Maximum Amplitude of Glucose Excursion; MAGE: Mean Amplitude of Glucose Excursion; MODD: Mean Daily Glucose Deviation; MG: Mean Glucose; SD: Standard Deviation of Glucose; CV: Coefficient of Variation			

Discussion

Currently, the duration of intensive insulin therapy for severe hyperglycemia has gradually evolved from the initial 3-month period to shorter intervals (2 weeks to 3 months). However, within China's Diagnosis-Related Groups (DRG) framework, exploring a 1-week intensive insulin therapy regimen holds practical

significance. This study compared the efficacy differences between intensive hypoglycemic therapy with IDegLira combined with insulin aspart versus insulin glargine combined with insulin aspart over a 1-week period in overweight/obese patients with T2DM. Research findings indicate that IDegLira, combined with aspart insulin, achieves high-quality glycemic control more rapidly than glargine insulin combined with aspart insulin. It demonstrates significant advantages in glycemic stability, improvement of pancreatic function, and insulin dose savings, suggesting its important clinical application value in short-term intensive therapy.

The effectiveness and stability of blood glucose control are key objectives in the management of T2DM. Significant fluctuations in blood glucose levels among overweight/obese patients can further exacerbate insulin resistance, impair vascular endothelial function, and increase the risk of long-term cardiovascular events.^{4,5,13} TIR is considered a key indicator reflecting the quality of glycemic control and shows a significant negative correlation with the risk of diabetic microvascular complications.^{14,15} This study demonstrated that the TIR rate in the IDegLira group reached 84.03%, significantly higher than the 74.67% observed in the insulin glargine group ($P < 0.05$). Simultaneously, the TAR, MODD, CV, and SD values in the IDegLira group showed significant reductions, indicating that this regimen not only offers superior overall glycemic control but also markedly reduces intraday and diurnal blood glucose fluctuations, thereby achieving more stable glycemic management. Malighetti et al.¹⁶ demonstrated in the TiREX study that IDegLira significantly increased TIR (56.8%→81.3%) and markedly reduced TAR (42.3%→17.1%) in the short term, suggesting dual benefits in improving hyperglycemic exposure and enhancing target achievement rates. Philis-Tsimikas et al.¹⁷ further demonstrated that IDegLira significantly outperformed insulin glargine U100 in improving TIR. This advantage in TIR may be related to the ultra-long and stable basal insulin profile of IDegLira. Insulin degludec ensures sustained 24-hour basal glucose control with minimal intraday variability, thereby reducing periods of hyperglycemic exposure. In contrast, the pharmacodynamic profile of insulin glargine is associated with relatively greater post-injection fluctuations, which may compromise the stability of fasting and early morning glycemic control.¹⁸ In contrast, glargine insulin primarily acts on basal blood glucose levels and has limited capacity to regulate postprandial fluctuations.¹⁹ Furthermore, the study demonstrated that the MG level in the IDegLira group was significantly lower than that in the control group (8.26 vs 9.74 mmol/L, $P < 0.05$), further confirming its ability to enhance glycemic control while better maintaining glucose homeostasis. The findings of this study not only align with the ADA guidelines principle that "glycemic management requires balancing target achievement with stability",²⁰ but also support that the combination of GLP-1RA with basal insulin reduces glycemic variability, potentially offering cardiovascular and metabolic protective effects.²¹ Impaired pancreatic β -cell function and insulin resistance constitute the core pathological basis in overweight/obese T2DM patients. Therefore, improving pancreatic function and alleviating insulin resistance are crucial for optimizing long-term prognosis.^{3,22} A treatment study in elderly patients with T2DM demonstrated a significant reduction in the insulin resistance index after 6 months of treatment with IDegLira (from 42.39 to 32.84, $P < 0.0001$).²³ In this study, the IDegLira group demonstrated a reduction in HOMA-IR-CP after one week of

treatment, with levels falling below those of the control group, consistent with previous reports.²⁴ In a 26-week open-label trial, Holst et al. demonstrated that IDegLira enhances endogenous insulin secretion and improves β -cell function.²⁵ Our findings also indicate that the IDegLira group demonstrated an improvement in HOMA-islet-CPDM in the short term. This early improvement may be primarily attributable to liraglutide-induced glucose-dependent insulin secretion enhancement and glucagon release inhibition, along with reduced hepatic glucose output and improved peripheral insulin sensitivity, rather than long-term structural changes in β -cell mass or differentiation. In contrast, glargine insulin primarily supplements basal insulin and lacks direct protective effects on pancreatic function.^{26–28} Furthermore, several previous studies have demonstrated that IDegLira reduces insulin dosage compared with IGLar U100 or degludec insulin.^{26,29,30} This study found that the daily total insulin dose was lower in the IDegLira group (37.95 U/d vs 41.59 U/d). This outcome demonstrates that Ideglirase not only exhibits superior glycemic control efficacy but also helps mitigate the risk of weight gain associated with increased insulin dosing, aligning with the clinical strategy of "coordinated management of glycemic control and body weight".³¹ Therefore, for individuals with severe hyperglycemia and overweight/obesity in T2DM, selecting IDegLira over glargine insulin combined with rapid-acting insulin for short-term intensive insulin therapy can reduce blood glucose levels while also alleviating insulin resistance and improving pancreatic function.

Notably, the observation group achieved glycemic control significantly faster (3.1 ± 1.7 days vs. 5.0 ± 1.8 days, $P < 0.001$), and the rate of achieving the composite primary endpoint was nearly double that of the control group (65.1% vs. 36.5%). Against the backdrop of current DIP/DRG cost containment and efforts to shorten hospital stays, achieving rapid, safe, and high-quality compliance within a short timeframe holds significant clinical importance.³² CGMS ensured the accuracy of glucose fluctuation assessment in this study, overcoming the limitations of traditional fingerstick glucose monitoring in capturing the full dynamics of blood glucose changes during short-term treatment.³³ This also provides an objective basis for evaluating future short-term intensive insulin therapy regimens.

This study has certain limitations that require refinement in subsequent research: First, the sample was limited to a single center. Future studies could conduct multicenter collaborative research, incorporating patients from different regions and hospitals to enhance sample representativeness. Second, the observation period was only 7 days; a follow-up study lasting 2 weeks to 3 months could be designed to further validate the efficacy of the protocol. Third, no subgroup analysis was conducted for different BMI strata (e.g., BMI 24–28 kg/m², BMI ≥ 28 kg/m²). Future studies should refine stratification to explore individualized intensive glucose-lowering strategies.

In summary, the combination of IDegLira with aspart insulin for overweight/obese patients with T2DM enables faster and more stable glycemic control. This approach reduces insulin dosage while effectively improving pancreatic function, and overweight/obese T2DM patients enables faster and smoother glycemic control. It effectively improves pancreatic function and reduces insulin resistance while decreasing insulin dosage, with a favorable safety profile. This regimen demonstrates superiority over

the traditional insulin glargine combination therapy and is recommended as the preferred short-term intensive treatment option for this patient population.

Declarations

Funding

This study received no funding support.

Competing Interests

The authors claim no conflict of interest in this study

Author Contributions

Yaping Sun and Liwu Xu jointly designed the study and developed the protocol. Yaping Sun collected and analyzed the data and drafted the initial manuscript. Xiaolei Li assisted with statistical analysis and the preparation of figures and tables. Liwu Xu provided critical revisions to multiple versions of the manuscript. As the corresponding author, Liwu Xu assumes full responsibility for the integrity of the data, the accuracy of the analysis, and the work as a whole.

Ethics Review and Institutional Affiliation

The study was approved by the Medical Ethics Committee of the First Hospital of Anhui University of Science and Technology (Ethics Approval No.2025-KY-Y026-001) and is in accordance with the Declaration of Helsinki and registered with the China Clinical Trial Center.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

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Figures

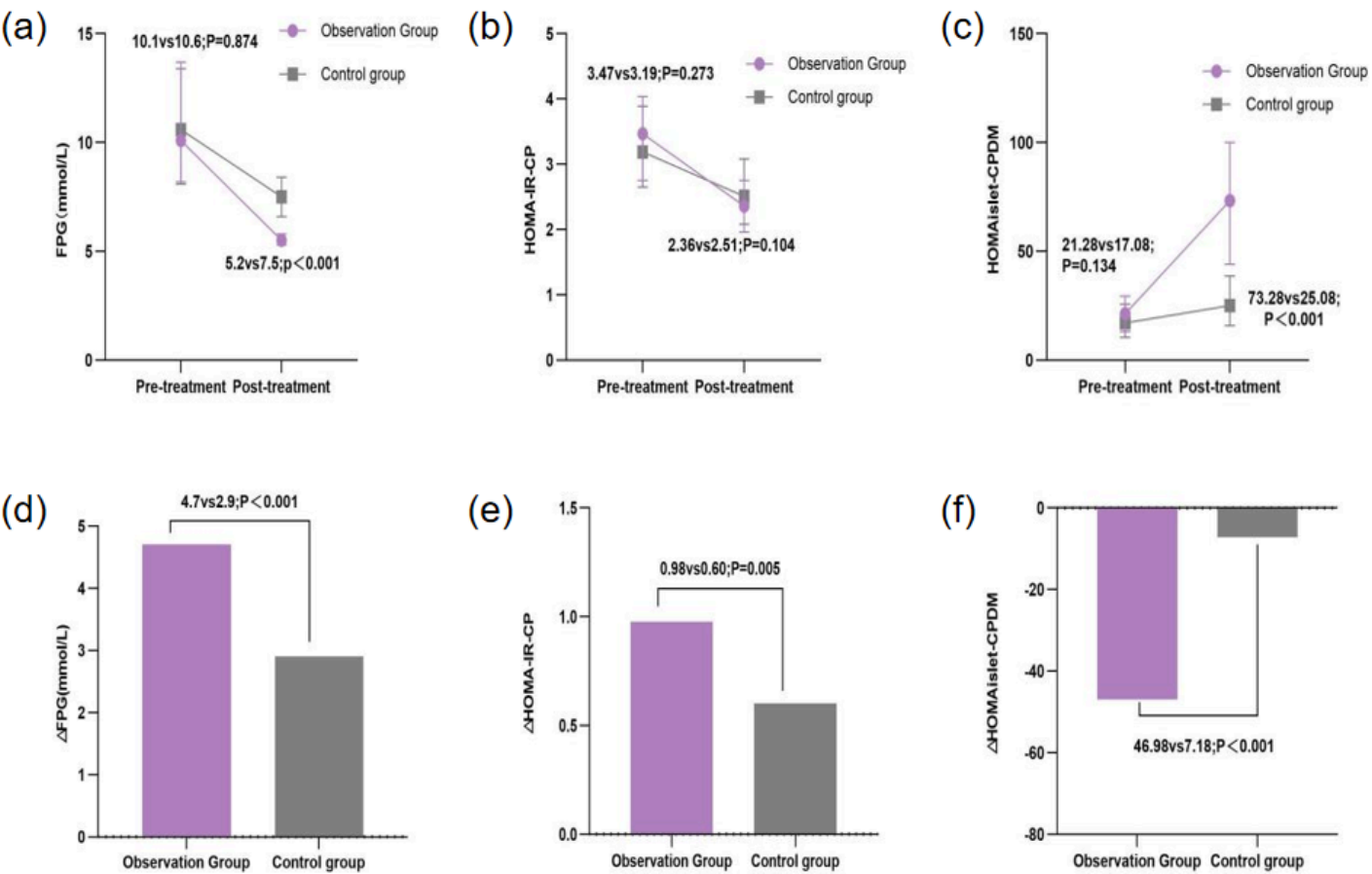


Figure 1

Comparison of FPG, HOMA-IR, and HOMA-islet-CPDM Levels and Their Changes Before and After Treatment Between the Two Groups. (a) Changes in FPG from baseline to post-treatment in both groups. (b) Changes in HOMA-IR from baseline to post-treatment in both groups. (c) Changes in HOMA-islet-CPDM from baseline to post-treatment in both groups. (d) Between-group comparison of Δ FPG. (e) Between-group comparison of Δ HOMA-IR. (f) Between-group comparison of Δ HOMA-islet-CPDM. FPG: Fasting Plasma Glucose; HOMA-IR-CP: C-peptide Insulin Resistance Index; HOMAislet-CPDM: C-peptide Islet Function Index

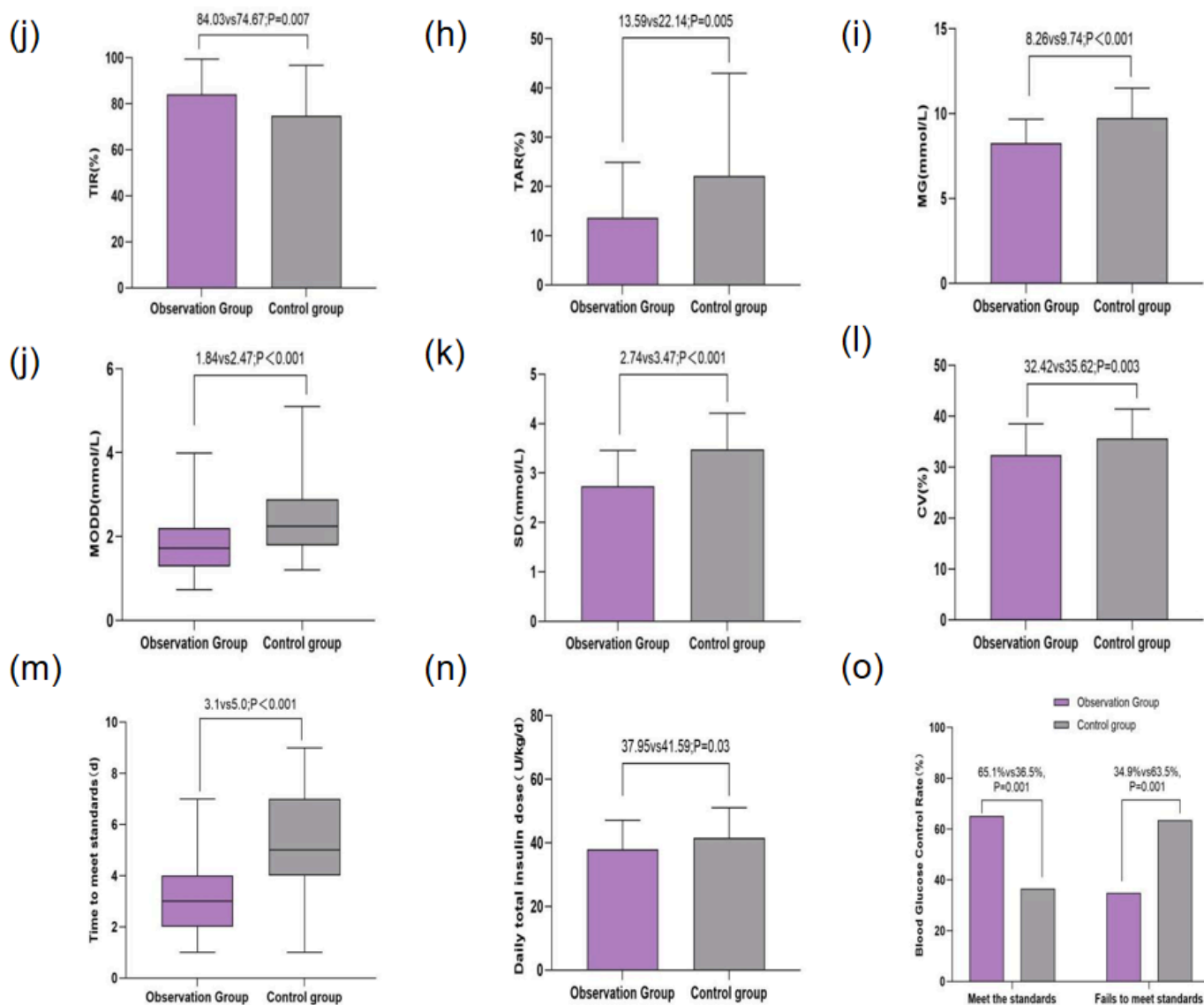


Figure 2

Comparison of glycemic control, variability, and treatment efficiency between the two treatment groups. (h) Comparison of TAR between the two groups. (i) Comparison of MG between the two groups. (j) Comparison of TIR between the two groups. (k) Comparison of SD between the two groups. (l) Comparison of CV between the two groups. (m) Comparison of time to achieve glycemic targets between the two groups. (n) Comparison of daily total insulin dose between the two groups. (o) Comparison of the proportions of patients meeting and not meeting glycemic targets between the two groups. TIR: Time in Range for glucose; TAR: Time Above Range; MODD: Mean Daily Glucose Deviation; MG: Mean Glucose; SD: Standard Deviation of Glucose; CV: Coefficient of Variation