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Effects of resistance exercise combined with metformin on glycemic stability and sleep quality in elderly patients with type 2 diabetes mellitus with sleep disorders

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Abstract: Sleep disorders in elderly type 2 diabetes mellitus (T2DM) patients worsen metabolic dysfunction. This study assessed resistance exercise plus metformin on glycemic stability and sleep quality in 180 elderly T2DM patients with sleep disturbances, divided into metformin alone (control) or metformin plus resistance exercise (intervention) for 12 weeks. Primary outcomes [fasting blood glucose (FBG), 2-hour postprandial glucose (2hPG), glycosylated hemoglobin (HbA1c), pittsburgh sleep quality index (PSQI) scores, electroencephalogram (EEG)-measured sleep architecture] and secondary outcomes [fasting insulin, homeostasis model assessment of insulin resistance (HOMA-IR), melatonin levels] were evaluated at baseline, 6 and 12 weeks. Baseline characteristics were similar (P>0.05). The intervention group showed greater reductions in FBG, 2hPG and HbA1c (P<0.05), along with significant PSQI score improvements (P<0.05) and better sleep architecture (P<0.05). Fasting insulin and HOMA-IR decreased in both groups but were lower in the intervention group (P<0.05). Melatonin increased only in the intervention group (P<0.05). No major adverse effects were observed. Resistance exercise combined with metformin enhances glycemic control and sleep quality in elderly T2DM patients, supporting nonpharmacologic interventions as valuable adjuncts in diabetes management.

Keywords: Blood glucose level; Metformin; Resistance exercise; Sleep quality; Sleep disorders; Type 2 diabetes

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INTRODUCTION

The prevalence of diabetes mellitus has been rising steadily worldwide, with type 2 diabetes mellitus (T2DM) representing the predominant form of the disease. This trend is particularly pronounced among older adults, who face a substantially higher likelihood of developing severe complications. Such progression not only compromises patients' physiological well-being but also markedly diminishes their overall life quality (Yan *et al.*, 2022). Among elderly T2DM patients, in addition to typical T2DM symptoms (such as polydipsia, polyuria, decreased body mass, hypertension, dyslipidemia, etc.), there is a significant bidirectional relationship with sleep disorders, which implies that T2DM may lead to or exacerbate sleep disorders and vice versa, disrupted sleep patterns have been associated with an elevated risk of T2DM onset and may also exacerbate disease progression (Antza *et al.*, 2021). Research shows that the prevalence of insomnia symptoms is relatively high among patients aged 60 and above with T2DM and it is associated with poor glycemic control (Koopman *et al.*, 2020). On the one hand, chronic hyperglycemia damages pineal cells through oxidative stress, affecting their ability to synthesize and secrete melatonin (Wajid *et al.*, 2020). On the other hand, sleep fragmentation increases upregulation of cortisol occurs following HPA axis activation, interfering with the insulin signaling pathway and exacerbating insulin resistance (Janssen, 2022). Notably, this bi-directional negative effect is more pronounced in elderly patients due to age-proliferative changes, leading to often unsatisfactory results of conventional monotherapy.

In contemporary clinical practice, metformin remains the cornerstone pharmacological intervention for T2DM management, owing to its extensive clinical applicability, well-documented therapeutic profile and favorable safety spectrum. As a first-line therapeutic agent endorsed by major international guidelines including the ADA/EASD consensus, metformin demonstrates multifaceted clinical benefits extending beyond glycemic control. Multiple investigations have substantiated the therapeutic efficacy of metformin in improving glycemic control in patients with T2DM (Al-Kuraishy *et al.*, 2023; Lee *et al.*, 2021; Singh *et al.*, 2025). In addition, regular resistance exercise has a synergistic effect on glucose metabolism and sleep regulation. The study by You *et al*. (You *et al.*, 2024) utilized data from the National Health and Nutrition Examination Survey (NHANES) conducted from 2007 to 2018 to investigate the association between physical exercise and diabetes mellitus (DM) in individuals with short sleep duration (≤7 hours per night). Weighted logistic regression analysis revealed a negative correlation between physical exercise and DM, with sufficient exercise (>600 metabolic equivalent minutes per week) significantly

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reducing the risk of developing diabetes. Furthermore, Wilson *et al*. (Wilson *et al.*, 2023) are planning to conduct a 52-week double-blind randomized controlled trial (RCT) aimed at investigating the efficacy of metformin pharmacotherapy as an adjunct to a healthy lifestyle behavioral intervention in improving cardiometabolic outcomes, as well as depressive, anxiety and psychotic symptoms, in young patients with clinically diagnosed major mood syndromes. Amiri *et al*. (Amiri *et al.*, 2024) conducted a clinical trial in which 62 children with type 1 diabetes participated and were divided into an intervention group and a control group, with 31 children in each group. The Children's Sleep Habits Questionnaire was used to measure sleep habits. The intervention group received an 8-week regular exercise program presented in the form of educational videos. The results revealed a significant difference in the average sleep habit scores between the intervention group and the control group, indicating that exercise, as a non-pharmacological treatment, can effectively improve the sleep quality of children with diabetes. These studies collectively highlight the critical role of exercise in diabetes management, particularly in improving metabolic health and sleep quality across different age groups.

Sleep quality correlates with blood glucose levels and duration of hyperglycemia, individuals experiencing sleep fragmentation tend to show worse metabolic control and an increased risk of diabetes (Tsereteli *et al.*, 2022). Sleep disorders are also associated with the progression of T2DM and individuals with sleep disorders may have increased endocrine disruption, as well as an increased prevalence of vascular complications (Eleftheriou *et al.*, 2024). However, Prior investigations have largely concentrated on the singular influence of a single intervention on blood glucose or sleep and lacked a comprehensive assessment of the "blood glucose-sleep" improvement. This study sought to examine the therapeutic potential of combining resistance training with metformin therapy in older adults presenting with both T2DM and comorbid sleep disturbances. Resistance exercise can improve sleep quality through multi-targets (neurological, metabolic and psychological) and it can also enhance insulin sensitivity, promote myoglycogen storage and improve postprandial glucose, which is especially suitable for elderly patients with T2DM. Combining resistance training with metformin treatment may form a synergistic treatment strategy of "lowering glucose and helping sleep", proposing a non-drug-dependent adjuvant therapy to compensate for the limitations of metformin in improving sleep. We propose a non-drug-dependent adjunctive therapy to compensate for the limitations of metformin in improving sleep. We hope to provide a low-cost and highly feasible intervention program for the comprehensive management of elderly patients with T2DM and to reduce the burden on public health.

MATERIALS AND METHODS

Study participant

Geriatric patients with T2DM attending our endocrinology and metabolism department between January 2022 and June 2024 were selected for this study. From the EMR system, we screened 216 age and diagnosis-qualified patients and 180 were finally enrolled to complete the full follow-up. This clinical study adheres to relevant ethical guidelines, including the Declaration of Helsinki (Wen *et al.*, 2025) and received approval from the Huanggang Central Hospital Ethics Committee prior to commencement. Researchers are required to provide a detailed explanation of the study's objectives, procedures and potential risks to the participants or their legal representatives and obtain written informed consent.

Inclusion criteria

(1) age ≥60 years and gender-neutral; (2) meeting the American Diabetes Association (ADA) 2022 diagnostic criteria for T2DM (fasting blood glucose ≥7.0 mmol/L or glycated hemoglobin HbA1c ≥6.5%); (3) presence of sleep disorders, with a Pittsburgh Sleep Quality Index (PSQI) score of ≥7 and lasting ≥3 months; (4) stable treatment with metformin (1000-2000 mg/d); (5) basic motor ability (able to independently complete a 6-minute step test); (6) in accordance with ethical guidelines, all participants submitted signed consent.

The exclusion criteria

(1) severe cardiovascular and cerebrovascular diseases (*e.g*., unstable angina, heart failure, stroke, *etc*.); (2) contraindications to exercise (e.g., severe arthritis, bone fracture, *etc*.); and (3) other disorders that affect sleep (e.g., major depression, sleep apnea syndrome, *etc*.). (4) Are using other medications that may affect blood glucose or sleep (e.g., glucocorticoids, sedative-hypnotics, *etc*.); (5) Are unable to cooperate in completing the study protocol.

Dropout criteria: those who did not meet the inclusion criteria or had incomplete information; those who had poor compliance; those who dropped out; those who had a sudden onset of other illnesses during the study period; those who developed serious psychological or emotional problems that prevented them from continuing to participate in the study; and those who changed or added a new surgical procedure.

Study design

This study is a retrospective clinical controlled study, with data collection and analysis conducted by researchers who were not involved in the patients' treatment. A total of 216 patients were enrolled in this study, of which 36 patients were ultimately not included in the trial (15 patients did not meet the inclusion requirements, 18 refused to participate and 3 for other reasons) and 180 completed the follow-up, which was allocated to either the study (n=90) or control (n=90) group, all of whom completed the trial, as shown in fig. 1.

Intervention measures

The control group was given metformin (National Drug Code H20040971; specification: 0.5 g), 0.5 g/d, 2 times/d, with meals for 12 weeks. Routine health education was given, including risk factors for diabetes mellitus, medication precautions, diabetes mellitus dietary recipes and blood glucose self-testing methods. The patients continued to maintain their original daily life exercise status without change.

The study group implemented an resistance exercise program (Crossman, 2023) based on the control group. An exercise therapy team was set up, consisting of the head nurse of the department (team leader), a rehabilitation physician (to develop the resistance exercise program) and six diabetes specialist nurses (to assess and distribute the patients), with the rehabilitation physician instructing the team members on the training points and steps of resistance exercise. Prior to the commencement of resistance exercise, the specialist nurses conducted a comprehensive health assessment of each patient to ensure that the patient was physically fit for resistance exercise. Exercise intensity was set at 50% to 65% of each patient's maximum heart rate (HRmax), with adjustments based on individual fitness and tolerance. HRmax was primarily determined using the age-predicted formula (220 - age), per guidelines like those from the American College of Sports Medicine. For patients in good condition without major cardiovascular complications, submaximal exercise testing was used to fine-tune HRmax as needed. The nurse in charge of the specialty focused on the patients and their families to provide on-site guidance on the essentials and methods of movement and monitored whether the patients adhered to the training through follow-up visits; the nurse in charge of the specialty reminded the patients of the training every day through WeChat or text messages and followed up with them by phone every 7 days to learn about the patients' exercise condition and any adverse reactions and provided timely and more professional exercise guidance feedback to the patients. The resistance training protocol was administered thrice weekly, on alternate days, for 12 weeks. The content included: dynamic stretching and low-intensity aerobic warm-up (10 min), elastic band push-ups for upper limbs (3 sets × 12 repetitions, 60 s rest between sets), instrumented leg lifts for lower limbs (3 sets × 10 repetitions, 60% 1-RM), modified plate support for core muscle training (3 sets × 30s) and relaxation exercises with static stretching and breathing exercises at the end of the exercise (10 min). For the determination of 1-RM in instrumented leg lifts among elderly participants, including those who were frail, we used a gradual loading protocol: starting with a light weight (5-10 kg) that could be easily lifted 10-15 times, then increasing the load by 2.5-5 kg per attempt, with 2-3 minutes of rest between trials, until the participant could complete only 1 repetition with proper form. Safety precautions included continuous monitoring of blood pressure and heart rate before and after testing, having a physical therapist present to guide movement form and stopping immediately if signs of dizziness, chest discomfort, or excessive fatigue occurred.

Evaluation indicators and data collection

Main indicators

Indicators of glucose metabolism

Fasting blood glucose (FBG): measured using venous blood in the early morning in the fasting state after abstaining from caloric intake for ≥8 hours overnight. 2-hour postprandial glucose (2hPG): measured using venous blood two hours after a standard mixed meal (containing 75 g of carbohydrate). Glycated hemoglobin (HbA1c): an important indicator for for evaluating chronic glucose regulation in diabetes management, reflecting the average blood glucose level over the past 2-3 months, detected by high performance liquid chromatography.

Sleep indicators

Sleep quality: the Pittsburgh Sleep Quality Index (PSQI) scale, which consists of seven components: sleep latency, daytime dysfunction, sleep disruption, sleep efficiency, subjective sleep quality, sleep duration and use of sleep medications, with scores ranging from 0 to 3 for each component and a total score ranging from 0 to 21. A higher total score indicates poorer sleep quality (Buysse *et al.*, 1989). Degree of improvement of sleep disorders: eight-channel electroencephalograph (ND-82B, China) was used to assess patients' sleep disorders before and after treatment. Sleep process and sleep structure were recorded. Sleep processes included sleep latency, REM sleep latency, total sleep time and sleep efficiency. Sleep structure included sleep cycle, non-rapid eye movement (NREM) duration and rapid eye movement sleep duration.

Secondary indicators

Fasting serum insulin: Elevated fasting serum insulin levels are usually a marker of insulin resistance, using a venous blood test in the early morning in the fasted state after abstaining from caloric intake for ≥8 hours overnight.

Insulin Resistance Index (HOMA-IR): calculated as fasting glucose x fasting insulin/22.5, expresses the reduced sensitivity of body tissues to insulin, the higher the HOMA-IR index, the more severe the insulin resistance(Mona *et al.*, 2024).

Melatonin (MT) levels: salivary melatonin levels were measured using saliva; clinically, salivary melatonin is used as a biomarker for the diagnosis of circadian rhythm sleep disorders; normally, melatonin is elevated at night and helps to promote sleep. Salivary melatonin levels were measured using Abcam Human Melatonin Salivary ELISA Kit, which has been validated for clinical use with a sensitivity of 0.6 pg/mL. Samples were collected at 22:00-

23:00 (consistent with the nocturnal peak of melatonin secretion) to align with its circadian rhythm and results were reported in pg/mL.

Record adverse reactions, including gastrointestinal reactions (nausea, diarrhea, bloating), hypoglycemic events, muscle soreness/injury, dizziness/weakness and abnormal liver function.

Data collection

Baseline data on patients were collected prior to treatment, including demographic characteristics (demographic characteristics, glycemic metabolic indexes, cardiovascular indexes, lipid indexes, medication use, concomitant diseases and medical history, sleep disorders and assessment of motor function.). Main and secondary indicators related to glucose metabolism and sleep were tested before treatment, 6 weeks and 12 weeks of treatment, respectively.

Statistical analysis

Statistical analyses were performed using SPSS version 25.0. Continuous variables are presented as mean ± standard deviation (SD) and repeated-measures data across time points were analyzed using repeated-measures ANOVA to account for within-subject correlations and control Type I error. For baseline comparisons between groups, Student's *t*-tests were used. Categorical data are expressed as proportions (%) and analyzed with χ^2 tests. A two-tailed *p*-value <0.05 defined statistical significance. And the sample size was estimated using G-power software.During the estimation process, we chose an effect size of 0.5, set the significance level (α) to 0.05 (two-tailed test) and set the statistical efficacy ($1-\beta$) to 0.8. Based on these parameters, the calculated sample size for each group was 64 participants and the total sample size was 128. The number of actually recruited participants for the experiment was 180, which exceeded the planned sample size and therefore met the statistical requirements of the study design.

RESULTS

Main indicators

Comparison of baseline information

No statistically significant differences were observed in baseline characteristics between the two groups in demographic characteristics, glycemic metabolic indexes, cardiovascular indexes, lipid indexes, medication use, concomitant diseases and medical history, sleep disorders and assessment of motor function (P>0.05), suggesting that the two groups were comparable in terms of their basic pre-treatment characteristics. See table 1.

Indicators of blood glucose metabolism

Before treatment, there was no statistically significant difference between the FBG, 2hPG and HbA1c levels of the two groups compared to each other (P>0.05). At 6 weeks of treatment, patients in the study group had lower FBG, 2hPG and HbA1c than those in the control group (P<0.05), suggesting that the treatment regimen in the study group had a faster onset of action, especially postprandial glycemic 2hPG improved more significantly, which could reduce the risk of cardiovascular events. At 12 weeks of treatment, Across all outcome measures, the treatment group exhibited significantly enhanced results versus the control condition (P<0.001 between groups) and the FBG of the study group was close to the normal range (3.9-6.1 mmol/L), whereas the control group was still in the pre-diabetic stage (≥ 6.1 mmol/L), suggesting that the study group was more effective in improving basal insulin secretion. HbA1c decreased to 5.83% in the study group, indicating that long-term glycemic control was close to normal human levels, which significantly reduced the risk of retinopathy and nephropathy. Therefore, resistance exercise combined with metformin is more prominent in glycemic control and has significant clinical value in preventing chronic complications of diabetes. See table 2.

Sleep quality

Prior to treatment,the two cohorts demonstrated comparable baseline values on all Pittsburgh Sleep Quality Index (PSQI) components,there was no statistically significant difference (P>0.05) and the scores of all the indexes of the study group were significantly lower than those of the control group at 6 weeks of treatment (P<0.05), which indicated that the therapeutic measures of the study group had a rapid onset of action in a short period of time and were more effective in improving the patients' sleep quality. At 12 weeks of treatment, the difference between the scores of the study group and the control group was highly significant (P<0.001 between groups) and the sleep time and sleep quality scores of the study group were stabilized at a low level, indicating that the intervention effect was ideal and long-lasting and may reduce the risk of insomnia recurrence. Therefore, resistance exercise combined with metformin is more effective in improving sleep quality in elderly T2DM patients in all dimensions. See table 3.

Degree of improvement in sleep disorders

There was no statistically significant difference in sleep progression and sleep structure between the two groups before treatment (P>0.05) and at 6 weeks of treatment, the study group was significantly better than the control group in all indexes (P<0.05), especially REM time and sleep efficiency were closer to the normal level and ideal range. At 12 weeks of treatment, the study group was further optimized in all indicators (P<0.05), sleep efficiency reached healthy standards and the proportion of sleep structure was normalized. Resistance exercise combined with metformin treatment was significantly better than the control group in both sleep process and sleep structure (P<0.001 between groups) and the effect was enhanced with longer treatment duration. This overall improvement may have synergistic benefits on glycemic control, mood regulation and long-term prognosis in diabetic patients. See table 4.

Secondary indicators

The difference between the two groups was not statistically significant compared to the fasting insulin, HOMA-IR and melatonin (MT) levels before treatment (P>0.05). At 6 weeks of treatment, the fasting insulin, HOMA-IR and the study group demonstrated significantly higher melatonin concentrations compared to controls (P<0.05), indicating that the treatment in the study group was more rapidly effective. At 12 weeks of treatment, fasting insulin in the study group was close to normal (<10 μU/mL) and HOMA-IR reached mild resistance (2.5-3.0 is considered as mild resistance), suggesting that the combination of resistance exercise and metformin may alleviate insulin resistance by decreasing visceral fat and improving hepatic glucose output and that the level of melatonin (MT) was close to the peak of nighttime physiology, which is more conducive to the regulation of the sleep-wake cycle. See table 5.

Security analysis

In this study, 22 cases of adverse reactions occurred in the control group, 12 cases of gastrointestinal discomfort, 3 cases of hypoglycemia, 1 case of muscle soreness, 4 cases of dizziness and fatigue and 2 cases of liver function abnormality; 36 cases of adverse reactions occurred in the study group, 14 cases of gastrointestinal discomfort, 5 cases of hypoglycemia, 8 cases of muscle soreness, 5 cases of dizziness and fatigue and 3 cases of liver function abnormality. The difference in the incidence of adverse reactions between the two groups was statistically significant and the incidence of adverse reactions in the study group was higher than that in the control group (χ^2=4.986, P=0.026), which was mainly attributed to exercise-related side effects (muscle soreness), which is an expected response to resistance exercise and can be alleviated by adjusting the intensity of exercise. All adverse were mild to moderate and there were no serious adverse events; the increase in adverse effects in the study group was mainly from the exercise intervention, but the improvements in glucose metabolism and sleep were significantly better than the risks. This suggests an overall favorable safety profile for resistance exercise combined with metformin. See table 6.

DISCUSSION

Glucose metabolism is the core metabolic process of the body to maintain normal life activities and it is crucial for the regulation of blood glucose levels. By raising glucose metabolism, insulin sensitivity can be improved and insulin resistance can be reduced, which is crucial for the long-term management of T2DM (Hahn *et al.*, 2024). Metformin is a commonly used drug in the clinical treatment of T2DM, although it can improve glucose metabolism level, the overall efficacy of single drug is not ideal and there are certain adverse reactions, such as gastrointestinal discomfort (Yuxin *et al.*, 2020). In this study, resistance exercise combined with metformin co-intervention achieved a large reduction in FBG, 2hPG and HbA1c in elderly patients with T2DM and the magnitude of glycemic improvement is of significant clinical value. This may be related to the unique metabolic characteristics of elderly patients with T2DM. On the one hand, sarcopenia is prevalent in the elderly, leading to a decrease in basal metabolic rate and an increase in insulin resistance (Sanz-Cánovas *et al.*, 2022); on the other hand, age-associated decline in β-cell function makes glycemic control more difficult (Vidmar *et al.*, 2023). Resistance exercise may partially reverse age-related muscle loss by increasing muscle mass and strength, thus providing a better metabolic basis for metformin to work (Graham *et al.*, 2021). It is worth noting that although the HbA1c in our intervention group reached 5.83% (near normal), tight control below 6.0% may raise hypoglycemia risk in elderly T2DM patients-who often have comorbidities and impaired hypoglycemia awareness, with potential harms like falls or cardiovascular events. No severe hypoglycemia occurred in our study, but we lack detailed analysis of episodes and long-term follow-up, limiting safety assessment. Future studies should monitor this risk closely, individualizing glycemic targets by age, comorbidities and hypoglycemia history to balance benefits and harms.

Sleep disorders occur in up to 50-60% of elderly T2DM patients and form a vicious circle with poor glycemic control (Mikołajczyk-Solińska *et al.*, 2020). In this study, a significant reduction in PSQI score was found after resistance exercise combined with metformin treatment. And sleep process and sleep structure were significantly improved. Several studies have shown that resistance training is effective in improving glycemic control in T2DM and improved glycemic control may directly or indirectly enhance sleep quality. Hyperglycemia may lead to increased nocturia, affecting sleep continuity (Jansson *et al.*, 2022; Picard *et al.*, 2021; Su *et al.*, 2022). Resistance training may affect sleep by modulating the endocrine system and inflammatory responses, in a controlled trial, resistance-based exercise protocols were shown to elevate walking performance while simultaneously decreasing fasting glucose measures in those with type 2 diabetes and that improvements in physical functioning reduced nocturnal discomfort, which in turn promoted sleep (Manju *et al.*, 2024). While prior studies demonstrate independent benefits of resistance exercise on T2DM, our results reveal its synergistic potential with metformin. For example, the intervention group's 39.8% melatonin increase aligns with metformin's AMPK-mediated AANAT upregulation, a mechanism absent in exercise-only studies.

Table 1: Comparison of baseline characteristics between the two groups of patients

norm	Control group (n=90)	Study group (n=90)	Statistic χ^2/t	*P*-value
Demographic characteristics				
Age (years)	67.30±5.10	68.00±4.80	t=-0.94	0.347
Sex (m/f)	46/44	48/42	χ^2=0.08	0.765
Weight (kg)	72.51±8.30	73.20±7.95	t=-0.57	0.572
Waist circumference (cm)	94.24±7.53	93.87±6.91	t=0.34	0.733
BMI (kg/m²)	26.33±2.72	26.58±2.54	t=-0.63	0.527
Indicators of glucose metabolism				
Duration of diabetes (years)	8.40±2.30	8.10±2.00	t=0.93	0.353
HbA1c (%)	7.82±0.88	7.88±0.92	t=-0.53	0.600
2hPG (mmol/L)	12.42±2.01	12.49±2.10	t=-0.22	0.821
FBG (mmol/L)	8.51±1.20	8.58±1.25	t=-0.38	0.700
HOMA-IR	5.66±1.34	5.75±1.43	t=-0.43	0.662
Cardiovascular indicators				
SBP (mm Hg)	138±11	136±12	t=1.15	0.248
DBP (mm Hg)	82±8	83±7	t=-0.88	0.376
Heart rate (beats/min)	76.30±8.50	75.10±7.90	t=0.97	0.330
Lipid Indicators				
Total cholesterol (mg/dL)	198±32	201±29	t=-0.65	0.513
HDL-C (mg/dL)	42±7	43±6	t=-1.02	0.308
LDL-C (mg/dL)	118±28	120±25	t=-0.50	0.616
Medications				
Biguanides (n)	90	90	-	1.000
Sulfonylurea (n)	35	38	χ^2=0.20	0.649
DPP-4 inhibitors (n)	42	40	χ^2=0.09	0.765
Alpha-glucosidase inhibitors (n)	42	40	χ^2=0.09	0.765
GLP-1 (n)	15	12	χ^2=0.39	0.531
Insulin (n)	20	18	χ^2=0.13	0.715
Concomitant diseases and medical history				
Hypertension (n)	58	62	χ^2=0.40	0.527
Dyslipidemia (n)	65	63	χ^2=0.10	0.742
Hepatic steatosis (n)	32	29	χ^2=0.22	0.637
Diabetic retinopathy (n)	18	15	χ^2=0.33	0.563
Osteoarthritis (n)	25	28	χ^2=0.24	0.624
sleep disorder				
HADS-Anxiety	6.21±2.16	6.06±1.90	t=0.49	0.621
HADS-Depression	5.82±1.80	6.11±2.09	t=-0.99	0.322
PSQI score	13.28±2.40	13.47±2.61	t=-0.50	0.613
Sleep efficiency (%)	68.58±6.33	67.94±6.12	t=0.68	0.494
Total sleep time (min)	320.61±35.26	318.40±34.71	t=0.42	0.674
Melatonin levels (pg/mL)	25.31±5.80	25.10±5.92	t=0.23	0.812
Motor function assessment				
6-minute walk test (m)	382±52	378±49	t=0.52	0.598
Sitting tests (times)	12.50±2.30	12.80±2.10	t=-0.91	0.364
One-legged balance test(s)	18.22±5.10	17.86±4.82	t=0.48	0.629
number of steps	4582±1023	4459±978	t=0.82	0.413
HGS Grip Strength (kg)	24.30±5.20	23.90±4.90	t=0.52	0.598

Note: 1. All enrolled participants satisfied the inclusion requirements concerning baseline metformin treatment (a consistent metformin dosage [≥1500 mg daily or a maximally tolerated dose of at least 1000 mg] maintained within the 60-day period before screening).
2. Prior to randomization, all subjects had stopped taking other antidiabetic medications except biguanides.

Table 2: Comparison of major indices of blood glucose ($\bar{x}$±s)

groups	FBG (mmol/L)	2hPG (mmol/L)	HbA1c (%)
Control group (n=90)			
pre-treatment	8.51±0.92	12.44±1.23	7.81±0.77
6 weeks of treatment	7.58±0.85$^{\&}$	11.58±1.16$^{\&}$	7.02±0.69$^{\&}$
12 weeks of treatment	6.63±0.73$^{\&*}$	10.22±1.13$^{\&*}$	6.41±0.68$^{\&*}$
Study group (n=90)			
pre-treatment	8.58±1.05	12.49±2.11	7.89±0.69
6 weeks of treatment	6.96±0.76$^{\&\#}$	10.21±1.49$^{\&\#}$	6.91±0.67$^{\&\#}$
12 weeks of treatment	5.82±0.67$^{\&*\#}$	9.03±1.24$^{\&*\#}$	5.83±0.49$^{\&*\#}$
P-value between groups (12 weeks)	<0.001	<0.001	<0.001

Note: pre-treatment baseline comparison, $^{\&}P < 0.05$; 6-week within-group comparison, $^{\#}P < 0.05$; concurrent control comparison, $^{*}P < 0.05$

Table 3: Comparison of sleep quality (scores, $\bar{x}$ ± s)

groups	sleep latency	Daytime dysfunction	sleep disorder	sleep efficiency	Subjective sleep quality	Sleep duration	sleep medicine
Control group (n=90)							
pre-treatment	1.92±0.31	1.88±0.30	1.93±0.40	1.91±0.33	1.85±0.30	1.90±0.31	1.89±0.33
6 weeks of treatment	1.87±0.41	1.80±0.31	1.88±0.32	1.85±0.22	1.78±0.21	1.82±0.41	1.81±0.22
12 weeks of treatment	1.83±0.31	1.76±0.20	1.83±0.21	1.82±0.61	1.73±0.20	1.80±0.31	1.74±0.61
Study group (n=90)							
pre-treatment	1.95±0.32	1.90±0.37	1.94±0.32	1.94±0.39	1.89±0.39	1.93±0.32	1.92±0.32
6 weeks of treatment	1.19±0.33$^{\&*}$	1.22±0.29$^{\&*}$	1.20±0.28$^{\&*}$	1.28±0.14$^{\&*}$	1.19±0.26$^{\&*}$	1.18±0.32$^{\&*}$	1.28±0.13$^{\&*}$
12 weeks of treatment	0.67±0.32$^{\&\#*}$	0.71±0.33$^{\&\#*}$	0.69±0.34$^{\&\#*}$	0.67±0.31$^{\&\#*}$	0.69±0.31$^{\&\#*}$	0.66±0.31$^{\&\#*}$	0.68±0.36$^{\&\#*}$
P-value between groups (12 weeks)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Note: pre-treatment baseline comparison, $^{\&}P < 0.05$; 6-week within-group comparison, $^{\#}P < 0.05$; concurrent control comparison, $^{*}P < 0.05$

This dual action explains the significant PSQI reduction and underscores the novelty of our combined approach. However, it is important to acknowledge the limitations in interpreting these melatonin findings. The observed increase should be considered with caution due to large inter-individual variability in salivary melatonin levels among participants. Additionally, we did not strictly control for light exposure, a key factor influencing melatonin secretion, which may have introduced confounding effects. These limitations weaken the robustness of our conclusions regarding the magnitude and specificity of the melatonin response to the intervention.

In this study, the combined intervention regimen demonstrated a favorable safety and tolerability profile, which is consistent with clinical studies and guideline recommendations in recent years.

Table 4: Comparison of the degree of improvement in sleep disorders ($\bar{x}$±*s*)

groups	sleep process				sleep architecture		
	Sleep latency (minutes)	REM latency (minutes)	Total sleep time (minutes)	Sleep efficiency (%)	Sleep cycle (minutes)	NREM time (minutes)	REM sleep time (minutes)
Control group (n=90)							
pre-treatment	45.21±8.74	120.50±15.40	320.61±35.46	68.58±6.36	90.52±10.28	260.41±28.86	60.29±10.60
6 weeks of treatment	42.12±7.55	116.80±14.27	325.24±33.01	72.83±5.93	89.72±8.65	265.36±26.54	64.91±9.88
12 weeks of treatment	39.61±6.96	114.40±13.67	327.72±30.68	72.85±5.93	88.17±7.84	269.63±24.26	68.16±8.74
Study group (n=90)							
pre-treatment	44.81±7.89	121.81±15.28	318.40±34.90	67.94±6.15	91.91±5.78	258.70±24.47	59.72±8.40
6 weeks of treatment	32.62±5.06$^{\&*}$	95.74±10.09$^{\&*}$	375.63±27.11$^{\&*}$	82.41±5.78$^{\&*}$	85.32±5.17$^{\&*}$	300.26±20.38$^{\&*}$	75.44±6.56$^{\&*}$
12 weeks of treatment	25.42±4.46$^{\&\#*}$	82.32±10.98$^{\&\#*}$	412.50±22.45$^{\&\#*}$	88.62±4.83$^{\&\#*}$	82.43±5.22$^{\&\#*}$	325.48±17.79$^{\&\#*}$	87.15±6.43$^{\&\#*}$
P-value between groups (12 weeks)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Note: pre-treatment baseline comparison, $^{\&}P < 0.05$; 6-week within-group comparison, $^{\#}P < 0.05$; concurrent control comparison, $*P < 0.05$

Table 5: Comparison of blood glucose and sleep secondary indicators ($\bar{x}$±*s*)

groups	Fasting insulin (μU/mL)	HOMA-IR	Melatonin (pg/mL)
Control group (n=90)			
pre-treatment	15.59±2.52	5.79±0.94	25.31±5.83
6 weeks of treatment	14.59±2.49$^{\&}$	5.22±0.92$^{\&}$	26.19±6.13
12 weeks of treatment	13.02±2.38$^{\&\#}$	4.44±0.92$^{\&\#}$	26.60±6.33
Study group (n=90)			
pre-treatment	15.62±2.29	5.75±1.16	25.10±5.01
6 weeks of treatment	12.82±1.74$^{\&*}$	4.14±0.82$^{\&*}$	32.44±5.06$^{\&*}$
12 weeks of treatment	10.38±1.62$^{\&*\#}$	3.02±0.70$^{\&*\#}$	39.85±5.09$^{\&*\#}$
P-value between groups (12 weeks)	<0.001	<0.001	<0.001
P-value between groups (12 weeks)	<0.001	<0.001	<0.001

Note: pre-treatment baseline comparison, $^{\&}P < 0.05$; 6-week within-group comparison, $^{\#}P < 0.05$; concurrent control comparison, $*P < 0.05$

Table 6: Incidence of adverse reactions

groups	Gastrointestinal discomfort (nausea, diarrhea, bloating)	hypoglycemia	muscle pain	Dizziness/ weakness	liver dysfunction	Total Adverse Reaction Rate
Control group (n=90)	12 (13.3%)	3 (3.3%)	1 (1.1%)	4 (4.4%)	2 (2.2%)	22 (24.4%)
Study group (n=90)	14 (16.7 %)	5 (5.6%)	8 (8.9%)	5 (5.6%)	3 (3.3%)	36 (40.0%)
χ^2	0.180	0.523	5.731	0.117	0.206	4.986
P-value	0.672	0.469	0.017	0.732	0.650	0.026

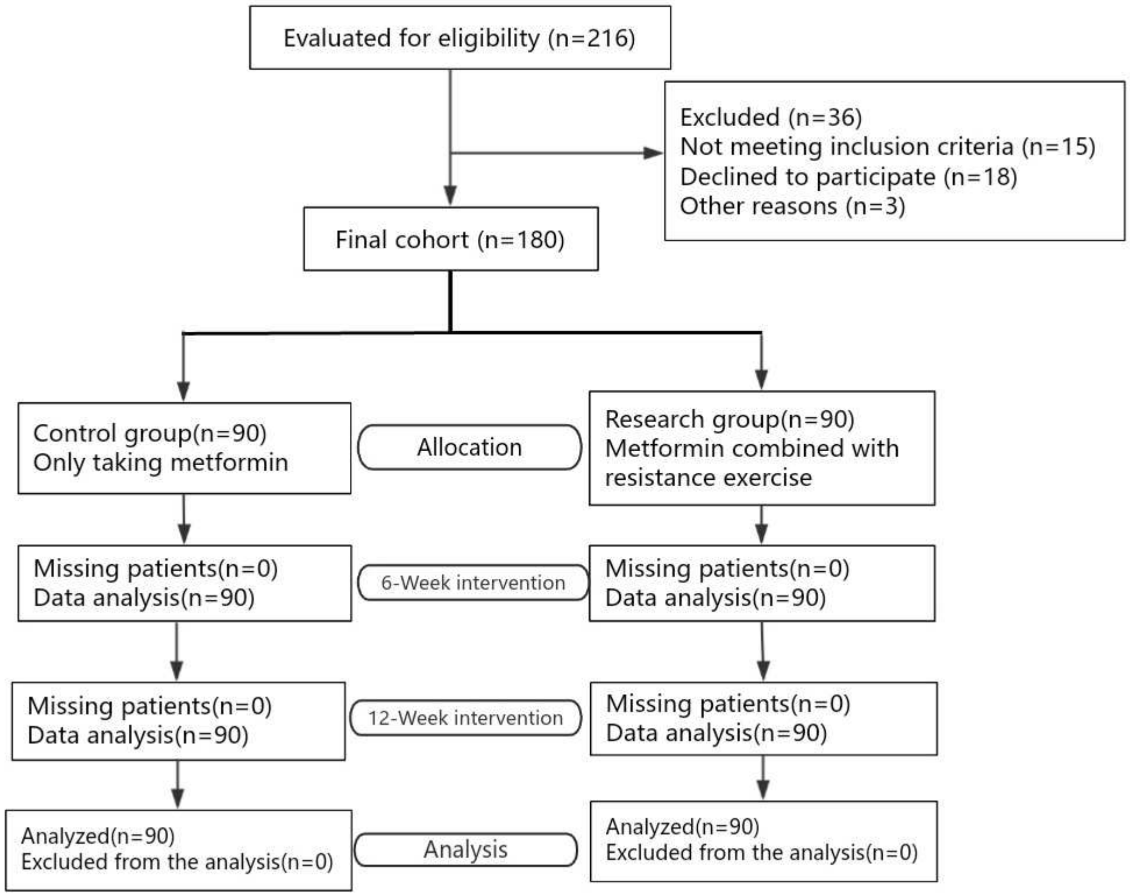

Fig. 1: Design flow chart

The 2022 American Diabetes Association (ADA) guidelines advise that Individuals with type 2 diabetes are advised to engage in a minimum of 150 minutes of moderate-to-vigorous aerobic physical activity weekly, with supplementary resistance training sessions (≥2 per week) further enhancing therapeutic efficacy (Davies *et al.*, 2022). In particular, the guidelines emphasize that resistance exercise is more suitable for older patients than aerobic exercise because it is less impactful on the joints and more effective in preventing and improving sarcopenia. In terms of safety, research indicates that during submaximal and maximal intensity resistance training, the frequency of myocardial ischemia, ventricular arrhythmias and abnormal hemodynamic responses is lower than that during aerobic training (Paluch *et al.*, 2024). This may be related to the lower heart rate and higher myocardial perfusion pressure during resistance training. Among the 23 trials (involving a total of 1,174 participants) that reported adverse events, 63 non-fatal cardiovascular-related complications occurred during aerobic training sessions and tests, whereas only 1 such complication occurred during resistance training sessions and none occurred during resistance training tests. This is consistent with our clinical observation that in this study, patient compliance with the intervention program was good and no serious adverse events occurred. Of particular note, no significant increase in hypoglycemia incidence was observed among participants in the combined intervention group, which is particularly important for seniors with diagnosed diabetes, as hypoglycemia can have serious consequences, including cognitive decline and increased risk of cardiovascular events (Ali *et al.*, 2023; Verhulst *et al.*, 2022). In terms of clinical practice, our findings support the use of resistance exercise as an important component of the comprehensive management of older patients with T2DM. Considering the heterogeneity of the elderly population, intervention protocols should be individualized and developed. For elderly patients with poor basal muscle strength, progressive resistance training can be used, starting with low-intensity elastic band training and gradually transitioning to equipment training to help elderly patients better adapt to resistance exercise training and improve blood glucose levels and sleep quality.

CONCLUSION

In conclusion, resistance exercise combined with metformin can significantly improve glycemic control and sleep quality in elderly T2DM patients and the treatment program has good safety and high patient tolerance. It can provide certain reference value for the clinic. There are several limitations of this study: first, the sample sizes of the control and study groups were comparatively small and sampled in a single center and the findings may lack representativeness. Second, the treatment period was 12 weeks and long-term follow-up assessment was lacking. Third, there was no immediate guidance on consistency and standardization of exercise. Further investigation through methodologically rigorous, long-duration randomized controlled trials is warranted to establish the enduring efficacy of combined metformin treatment and resistance-based physical activity in improving glycemic stability and sleep health indicators.

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Authors' contributions
[Xiang Li]: Developed and planned the study, performed experiments and interpreted results. Edited and refined the manuscript with a focus on critical intellectual contributions.
[Lihua Sun]: Participated in collecting, assessing and interpreting the date. Made significant contributions to date interpretation and manuscript preparation.
[Ruiying Li]: Provided substantial intellectual input during the drafting and revision of the manuscript.

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Data availability statement
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical approval
This experiment was approved by Huanggang Central Hospital Ethics Committee No: 2021-154. We secured a signed informed consent form from every participant.

Conflicts of interest
The authors declare that they have no financial conflicts of interest.

Consent to publish
The manuscript has neither been previously published nor is under consideration by any other journal. The authors have all approved the content of the paper.

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