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ORIGINAL ARTICLE

Effects of a 12-week Exercise Training on Insulin Sensitivity, Quality of Life, and Depression Status in Patients with Type 2 Diabetes

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Background: Exercise is one of the optimal and alternative treatments for type 2 diabetes (T2DM). Although the effect of a single bout of exercise on insulin sensitivity is reported to persist only for 2–3 days, effects remain unclear of a 12-week aerobic exercise training on insulin sensitivity, quality of life (QOL), and depression status over time as exercise training duration increases in patients with T2DM. **Objectives:** To investigate the effects over time in patients with T2DM of a 12-week aerobic exercise training on insulin sensitivity, QOL, and depression status. **Materials and Methods:** Purposive sampling was used to recruit 17 T2DM patients. Participants underwent a 12-week, supervised, moderate-intensity aerobic exercise training three times per week, 30 min per session. Outcome indicators including insulin sensitivity (measured by a 2-h oral glucose tolerance test [OGTT] and homeostatic model assessment-insulin resistance [HOMA-IR]), QOL (Medical Outcomes Study Short Form 36), and depression status (beck depression inventory scale) were evaluated at baseline and at 4-week intervals. **Results:** A final 13 eligible participants completed the study. For every 4-week increase in duration of exercise training, there was an increase over time in insulin sensitivity, including a decrease over time in OGTT glucose area under the curve of 66.92 min/mmol/L. Glucose concentrations decreased over time at 60, 90, and 120 min after an oral glucose challenge. Further, the HOMA-IR decreased over time as the duration of exercise training increased. QOL and depression status improved significantly during the training. **Conclusions:** Moderate-intensity exercise training improves insulin sensitivity, QOL, and depression status in T2DM patients, particularly over time within a 12-week exercise training course.

Key words: Exercise, insulin sensitivity, type 2 diabetes, quality of life, depression status

INTRODUCTION

Type 2 diabetes (T2DM) is a global illness. The World Health Organization reports that the number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014, and diabetes will be the seventh leading cause of death in 2030.[1] It has been predicted that by 2025, the worldwide burden of diabetes will be 5.4% of the adult population.[2]

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T2DM, a major risk factor for coronary artery diseases and serious complications, has a severe adverse effect on quality of life (QOL).[2] T2DM patients have impaired QOL[3,4] and a high incidence of depression.[5,6] Their impaired QOL is associated with glycemic control, severity of symptoms, and multiple medical complications.[4,7] In addition, impaired QOL and depression status predict earlier and higher mortality.[8] Therefore,

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developing optimal strategies to improve insulin sensitivity combined with QOL and depression status is imperative.

Diabetes treatment aims primarily to prevent progression of the disease and its complications. Among treatment strategies, exercise can be one of the most natural, effective remedies. Regular exercise improves blood glucose control, increases insulin sensitivity, reduces cardiovascular risk factors, enhances psychological well-being, delays the onset of T2DM,[9,10] and decreases diabetes-related mortality.[11,12] Given that insulin sensitivity in T2DM patients is benefitted by exercise,[11,12] the effect seems to require regularity and continuity. Previous reports have advocated that the effect of exercise on insulin sensitivity persists for 2–3 days.[13] Yet, it is uncertain whether the effect on insulin function is only immediate or if residual benefit occurs after the exercise is stopped. Therefore, its effect over time remains unclear. Exercise has also been found to improve QOL and depression status in patients with an insufficient immune system, cardiovascular disease, major depressive disorder, or those undergoing dialysis.[14-16] However, a meta-analysis showed no significant improvement in QOL among T2DM patients,[17] and a review even concluded that the effects of exercise training remain conflicting on psychological outcomes in people with T2DM.[11]

Previous studies have focused separately on exercise training's effect on glycemic control, insulin sensitivity, cardiorespiratory fitness, and QOL, as well as depression status. However, few studies examined the effects of exercise training on insulin sensitivity, combined with health status and psychological well-being. The impact remains unclear of exercise training on insulin sensitivity, QOL, and depression status over time in T2DM patients.[18] Thus, the aim of this study was to investigate the effect of a 12-week aerobic exercise training program on insulin sensitivity, QOL, and depression status over time in patients with T2DM.

MATERIALS AND METHODS

Setting and participants

Purposive sampling was conducted at a medical center in northern Taiwan to select patients aged 20–60, diagnosed as having T2DM according to criteria of the American Diabetes Association.[19] Inclusion criteria were (1) being treated with oral hypoglycemic drugs; (2) without visual or hearing impairments; (3) able to brisk walk without assistance; (4) able to communicate in Mandarin. Excluded were those with complicating conditions (i.e., stroke, Parkinson's disease, renal failure, cardiac arrhythmia, cardiac failure, pulmonary emphysema, or thyrotoxicosis) and those unable to participate due to comorbid neurological and musculoskeletal conditions that produce physical disability. All eligible patients underwent graded exercise testing (GXT) by a physician and a research assistant before receiving 12 weeks of treadmill exercise training. Insulin sensitivity, cardiorespiratory fitness, QOL, and depression status were assessed before, at 4-week intervals during, and after training.

Ethics

After the study purpose was explained to participants, qualifying patients were selected upon their written consent, which was reviewed by the hospital's institutional review board (TSGHIRB: 097-05-157). Our research procedure followed the Helsinki Declaration. All participants were assured that their participation was entirely voluntary and that they could withdraw at any time.

Graded exercise testing

A motorized treadmill (Trackmaster 400, JAS fitness system, USA) was used. The GXT allowed identification of cardiorespiratory fitness (maximum oxygen uptake: VO_{2max}) and maximum heart rate (HR_{max}), as well as risk for potentially life-threatening myocardial infarction.[20] A modified Balke protocol was used in the GXT procedures, wherein the speed of the treadmill was kept below 3 mph and the inclination was increased by 2.5% every 2 min up to a maximum of 20%.[21] Two observers were involved with each patient throughout the GXT. Prior to the test, blood pressure, heart rate (HR), and electrocardiogram (ECG) were measured at rest. During the test, blood pressure, HR, rating of perceived exertion (RPE), and ECG were recorded every 1–2 min. GXT was stopped if patients complained of exhaustion based on RPE; reached maximum HR or VO_{2max}; had a respiratory exchange ratio >1.15; developed symptoms such as chest pain, dyspnea, pallor, diaphoresis or dizziness; had systolic pressure >250 mmHg or diastolic pressure >120 mmHg; had a decrease in systolic pressure of more than 10 mmHg compared to the systolic pressure at rest; requested stopping the test; or if monitoring equipment became detached from the patient.[20]

Intervention

The 12-week aerobic exercise training was applied to those participants who passed the GXT. Treadmills (928ME2C, Takasuma, Japan) were used for aerobic exercise training three times per week on alternating days for 12 weeks. The duration of each session was 30 min and took 1–2 h after a meal. Blood glucose was monitored before and after each session using a One Touch glucometer (FreeStyle Blood Glucose Monitoring System, TheraSense, USA). If blood glucose before exercise was <20 mmol/L, a snack containing 25 g carbohydrate and 7 g protein was provided. The intensity of exercise training was set at 60% VO_{2max} (72% HR_{max}) obtained from the participant's GXT. The appropriate speed and grade were used to achieve target HR monitored by Heart Rate Monitor (Polar S510, Electro Oy, Finland) and to accurately control the required exercise intensity.[20]

Measurements

Biochemical measurement and subjective data were collected before the training and every 4 weeks during the training until the end of the 12-week program.

Subjective information

Participants' subjective information was collected including demographic characteristics (e.g., gender, age, marital status, and education level), lifestyles (smoking status, regular exercise [exercise at least 3 times/week and 30-min per session] or sedentary [exercise under 3 times per week]), duration of T2DM diagnosis, presence of complication (e.g., proteinuria and visual impairment), and antidiabetic medication use.

Insulin sensitivity

Insulin sensitivity was reflected in the oral glucose tolerance test (OGTT). After an 8–14-h fast, 75 g of glucose was given orally, and blood was drawn for plasma glucose and insulin determinations at 30, 60, 90, and 120 min.[22] This study used the trapezoidal method for pharmacokinetics modeling to calculate the area under the curve (AUC) for the 2-h integrated plasma glucose and insulin response to oral glucose challenge, which represents insulin sensitivity at different time points during the OGTT.[23] A lower AUC of glucose and insulin level reflects a higher insulin sensitivity. Besides, a homeostatic model assessment-insulin resistance (HOMA-IR) index was evaluated. A lower HOMA-IR reflects a lower insulin resistance and also a higher insulin sensitivity.[24]

Plasma glucose level was determined by a YSI model 2300 glucose analyzer (Yellow Springs Instrument Company, USA). Another glucose analyzer (YSI model 1500 glucose analyzer, Yellow Springs Instrument Company, USA) was used simultaneously to confirm validity. The correlation coefficient between the two analyzers was 0.90 (criterion-related validity) based on the Pearson product-moment correlation analysis. Plasma insulin concentration was measured by radioimmunoassay with a coefficient of variation of 0.2%.

Cardiorespiratory fitness, heart rate, and blood pressure

Fitness level VO_{2max} was assessed by GXT. Baseline HR and blood pressure were measured by an electronic blood pressure monitor device (Terumo, ESP2000, Tokyo, Japan) after the patient had been sitting 5–10 min. Blood pressure was measured to the nearest 2 mmHg.

Quality of life

QOL involves one's satisfaction with the activities of daily life such as participating in or interacting with community events, and it usually has five generic health concepts: physical health, mental health, social functioning (SF), role functioning, and general health (GH) perceptions.[25] The reliable and valid Medical Outcomes Study Short Form 36 was used, consisting of 36 items that measure eight dimensions of health: physical function (PF), role function limitation due to physical conditions (RP), bodily pain (BP), GH, vitality (VT), SF, role function limitation due to emotional problems (RE), and mental health (MH). In addition, two summary scales, the physical components summary (PCS) and the mental components summary (MCS), can be derived.[25] These two summary QOL scales that include PCS and MCS are calculated by all of the physically relevant questions (e.g., PF, role function limitations caused by physical problems, bodily pain, and GH) and all of the emotionally relevant items (e.g., role function limitations caused by emotional problems, VT, SF, and mental health).[25] Higher scores (score range, 0–100) indicate better QOL.

Depression status

Depression comprised of negative mood (e.g., sadness, guilt), negative views of the self (e.g., worthlessness, self-criticism), decreased positive affect and engagement (e.g., loss of interest, loss of meaning, and purpose), and negative social cognition (e.g., loneliness, interpersonal alienation).[26] Beck's Depression Inventory, with well-documented reliability and validity, was used to evaluate the depression status in the last week.[26] It consists of 21 self-reported items and has been employed in numerous groups such as dialysis patients, cancer patients, and psychiatric patients, as well as patients with diabetes.[27,28] Each item is rated on a 3-point Likert-type scale ranging from 0 to 3. The higher the score (range 0-63), the higher the depression status: 0–9 indicates minimal depression, 10–18 mild depression, 19–29 moderate depression, and 30–63 severe depression.

Statistics

Data were collected at baseline, and after 4, 8, and 12 weeks of the exercise training. SAS V8.2/Win98 statistics software (SAS Inc., NC, USA) was used to evaluate the effects on insulin sensitivity, QOL, and depression status over time as the training duration increased every 4 weeks. To compensate for our small sample size, we applied repeat measurements to increase the statistical power. The study power was estimated using G-Power version 3.1 analysis and calculated based on repeat measures (within–between interactions). We selected a total sample size of 13, with an effect size of 0.3, four numbers of measurements, and an alpha of 0.05, resulting in an estimated study power >0.70. Data analysis was performed mainly on longitudinal data of general linear model, using generalized estimating equation (GEE).[29] Effects of the training were analyzed after adjusting for covariates including gender, age, educational level, regular exercise habits, smoking, duration of diabetes, and presence of diabetes complications. Results were considered statistically significant if $P < 0.05$.

RESULTS

Subject characteristics

Of the 17 beginning participants, 13 completed the study. Two patients were excluded during the GXT (one because of symptoms of cardiac ischemia, the other because of unexpected hypertension), and two patients dropped out. The remaining 13 subjects included seven males and six females, with an average age of 48.2 years. Most were married (n = 12). Five (38.5%) were high school graduates. The average time since diabetes diagnosis was 62.8 months, ranging from 1 month to 16 years. Four patients (30.8%) had complications such as proteinuria and visual impairment, and two were smokers. Three patients had previously exercised occasionally, while the other 10 led a sedentary lifestyle [Table 1].

Table 1: Demographic characteristics of participants (n=13)

Variables	Mean (SD)	*n* (%)
Gender (male)		7 (53.8)
Age (years)	48.2 (4.1)	
Marriage (married)		12 (92.3)
Education (high school and above)		5 (38.5)
Duration of diagnosed disease (months)	62.8 (55.5)	
Presence of complication (e.g., proteinuria and visual impairment)		4 (30.8)
Lifestyle		
Smoker		2 (15.4)
Regular exercise		3 (23.1)
Sedentary		10 (76.9)
Antidiabetic medication		
Metformin		8 (61.5)
Sulfonylureas		7 (53.8)
Repaglinide		3 (23.1)

SD=Standard deviation

Changes in glucose, insulin sensitivity, fitness level, and blood pressure

Table 2 shows the physiological indices and survey scores before and after the exercise training. As the exercise training duration increased every 4 weeks, the patients' fasting blood glucose levels decreased by 0.5 mmol/L (P = 0.003), and the OGTT glucose level at the 120-min point decreased by 1.0 mmol/L (P = 0.009) [Table 3]. All time-point glucose levels of OGTT, except for the 30-min point, decreased over time as the duration of exercise increased [Table 3].

Table 2 shows a trend toward improvement of glucose AUC as the exercise duration increased (P = 0.016) and an average decrease in glucose AUC of 66.9 min/mmol/L. No change in insulin level was observed at any time point. In addition, the HOMA-IR decreased by 0.85 (P < 0.001) over time as the duration of exercise training increased every 4 weeks [Table 3].

The cardiorespiratory fitness (VO_{2max}) showed a gradual increase (P < 0.001), as presented in Table 3. Furthermore, the improvement rate in VO_{2max} was greater for males than for females, and the improvement rates in VO_{2max} were greater in patients who had exercised formerly than in sedentary participants. There was a decline trend over time in HR_{rest} (P < 0.001). Both systolic and diastolic BP showed gradually decreasing trends over time (P < 0.001). SBP and DBP decreased by 7.4 and 3.7 mmHg, respectively [Table 3].

IMPROVEMENTS IN QUALITY OF LIFE AND DEPRESSION STATUS

In the general linear model of GEE analysis after adjusting for covariates (gender, age, educational level, exercise habits, smoking, duration of diabetes, and diabetes complications), the "PCS" increased gradually as the training duration increased, which was not statistically significant. The "MCS," however, showed significant improvements over time (P < 0.001) [Table 3].

All eight subscales of QOL, except "bodily pain," increased over time (P < 0.01) after controlling for covariates. The increase in "PF" was higher in sedentary patients. Improvements in "role function limitation due to emotional problems" were lower in females than in males. A similar effect was found on depression status, where there was also a gradual improvement over time (P < 0.001) [Table 3].

DISCUSSION

This study suggests that exercise training can stimulate metabolism and utilization of blood glucose in T2DM patients, in accordance with previous findings that exercise

Table 2: Comparison of physiological indicators, quality of life, and depression status between pre- and post-training

Variable	Baseline	4-week	8-week	12-week
OGTT glucose level (min)				
0	9.1±2.9	7.5±2.5	7.7±2.9	7.2±1.8
30	13.7±4.0	12.8±3.6	13.1±3.2	12.6±2.5
60	17.6±3.6	15.2±2.9	16.2±2.5	15.3±2.9
90	18.9±4.3	16.0±4.0	17.2±4.0	15.7±3.6
120	18.9±6.1	14.8±4.3	15.9±4.3	14.7±4.3
OGTT insulin level (min)				
0	42±43	48±57	18±36	10±18
30	83±79	99±101	83±104	81±108
60	169±133	138±129	127±151	123±133
90	168±151	141±144	152±155	156±191
120	152±144	150±183	153±155	107±191
OGTT glucose AUC	1925±479	1655±377	1753±369	1624±341
OGTT insulin AUC	14456±10860	13317±13340	12515±13942	11671±13355
HOMA-IR	2.4±0.8	2.3±0.9	0.9±0.7	0.5±0.2
Cardiorespiratory fitness				
VO_{2max}	30.6±5.4	-	-	34.5±7.6
HR_{rest}	83.8±9.0	77.1±9.7	73.2±8.3	71.5±8.7
SBP	133.5±14.1	119.1±14.1	110.6±9.4	112.0±8.7
DBP	83.4±10.5	74.2±10.1	71.8±7.6	71.5±7.9
Quality of life				
PCS	50.6±9.4	54.7±6.9	54.5±5.8	56.0±3.6
MCS	47.2±7.6	50.1±8.3	55.6±5.0	54.0±4.3
PF	85.0±14.1	93.5±11.9	96.2±7.2	96.5±7.6
RP	69.2±39.7	78.8±37.9	86.5±33.2	90.4±28.1
BP	86.3±17.3	90.6±10.8	90.6±10.1	93.2±8.7
GH	50.8±18.0	68.8±18.7	73.1±13.7	73.8±12.3
VT	61.9±14.1	73.5±15.9	76.2±18.0	78.8±9.0
SF	78.8±14.1	81.7±15.9	95.2±6.5	91.3±10.8
RE	76.9±28.5	84.6±32.1	100.0±0	94.9±18.4
MH	69.8±11.5	75.7±13.0	83.4±9.7	81.5±9.0
Depression status	10.5±4.7	6.4±4.0	4.3±4.0	2.9±2.5

Data are means±SD. OGTT=Oral glucose tolerance test; OGTT glucose level=Blood glucose level after OGTT (mmol/L); OGTT insulin level=Insulin level after OGTT (pmol/L); OGTT glucose AUC: OGTT glucose area under curve (min/mmol/L); OGTT insulin AUC: OGTT insulin area under curve (min/pmol/l); VO_{2max}=Maximal oxygen uptake (ml/kg/min); HR_{rest}=Resting heart rate (beats/min); SBP=Systolic pressure (mmHg); DBP=Diastolic pressure (mmHg); PCS=Physical components summary; MCS=Mental components summary; PF=Physical function; RP=Role function limitation due to physical conditions; BP=Bodily pain; GH=General health; VT=Vitality; SF=Social function; RE=Role function limitation due to emotional problems; MH=Mental health; -=Indicates no measure taken; SD=Standard deviation; HOMA-IR=Homeostatic model assessment-insulin resistance

increases glucose uptake and insulin action.[30,31] However, inconsistencies exist among studies regarding the effect of exercise on glucose tolerance and utilization and on insulin sensitivity. Differences are possibly explained by variation in subject selection criteria, diabetes severity, and exercise prescription.[30,31] Given that extensive evidence supports the effects of exercise training on insulin sensitivity,[13,30,31] our study presents a new finding that regular engagement in a 12-week exercise training improves insulin sensitivity over time in patients with T2DM. A previous meta-analysis indicated the improvement in insulin sensitivity in favor of exercise versus control between 48 and 72 h after exercise, and this persisted even when insulin sensitivity was measured more than 72 h after the last exercise

Table 3: Effects of exercise training on physiological indicators, quality of life, and depression scores

Variable	Parameter	Estimates	*P*
OGTT glucose (min)			
0	Time	−0.5	0.003
30	Time	−0.3	0.271
60	Time	−0.4	0.039
90	Time	−0.7	0.027
120	Time	−1.0	0.009
OGTT insulin (min)			
0	Time	−10.7	0.079
30	Time	−2.6	0.670
60	Time	−3.8	0.197
90	Time	−2.0	0.802
120	Time	−8.2	0.062
OGTT glucose AUC	Time	−66.9	0.016
OGTT insulin AUC	Time	−915.1	0.203
HOMA-IR	Time	−0.85	<0.001
Cardiorespiratory fitness			
VO_{2max}	Time	1.6	<0.001
	Gender × time[b]	−0.7	0.006
	Exercise habit × time[a]	−0.4	0.017
HR_{rest}	Time	−3.8	<0.001
SBP	Time	−7.4	<0.001
DBP	Time	−3.7	<0.001
Quality of life			
PF	Time	2.2	<0.001
	Exercise habit × time[a]	2.4	0.008
RP	Time	9.3	0.022
BP	Time	−1.5	0.053
	Exercise habit × time[a]	4.6	0.023
GH	Time	7.3	0.0003
VT	Time	5.2	0.0002
SF	Time	6.4	0.010
RE	Time	15.8	<0.001
	Gender × time[b]	−17.3	<0.001
MH	Time	4.7	<0.001
MCS	Time	2.9	<0.001
PCS	Time	1.0	0.113
Depression status	Time	−2.6	<0.001

[a]Reference group=Has regular exercise habits; [b]Reference group=Male. Estimates were data after adjusting for gender, age, educational level, regular exercise habits, smoking, duration of diabetes, and the presence of complications of diabetes. OGTT=Oral glucose tolerance test; OGTT glucose level=Blood glucose level after OGTT (mmol/L); OGTT insulin level=Insulin level after OGTT (pmol/L); OGTT glucose AUC=OGTT glucose area under curve (min/mmol/l); OGTT insulin AUC=OGTT insulin area under curve (min/pmol/L); VO_{2max}=Maximal oxygen uptake (ml/kg/min); SBP=Systolic pressure (mmHg); DBP=Diastolic pressure (mmHg); HR_{rest}=Resting heart rate (beats/min); PCS=Physical components summary; MCS=Mental components summary; PF=Physical function; RP=Role function limitation due to physical conditions; BP=Bodily pain; GH=General health; VT=Vitality; SF=Social function; RE=Role function limitation due to emotional problems; MH=Mental health; Time=Exercise training duration (4 weeks per unit); Exercise habit × time=Interaction between variable time with exercise habit; Gender × time=Interaction between variable time with gender

session.[13] However, little is known about the chronic effects of exercise training; therefore, we have an innovative perspective to investigate the effect of a 12-week aerobic exercise training program on insulin sensitivity over time and prove whether or not an exercise bout has only an acute effect on insulin sensitivity.

Our findings confirm that the intensity of exercise would be the most important factor in its effect on insulin sensitivity, with exercise at 70% VO_{2max} leading to significant improvement, as compared to a previous study that concluded no effect was observed at 50% VO_{2max} of training.[32,33] This can highlight the fact that a moderate-intensity exercise training contributes to a better metabolic control for patients with T2DM.

For patients with a long-term diagnosis or those who have low insulin concentrations, exercise training alone has limited effect on insulin sensitivity.[32,33] Evidence has shown that exercise training is more beneficial to patients in early stages of T2DM characterized by hyperinsulinemia.[32,33] In our study, the average duration of diabetes was about 5 years, with six patients having had diabetes for more than 6 years (46.2%). Average fasting glucose before exercise was 9.1 mmol/L, and insulin concentration was 42 pmol/L. During the OGTT, average blood glucose levels at 30, 60, 90, and 120 min were 13.7, 17.6, 18.9, and 18.9 mmol/L, and insulin response was 83, 169, 168, and 152 pmol/L, respectively, presenting impaired glucose tolerance and impaired insulin-secreting function among T2DM patients. However, our results showed a significant improvement in insulin sensitivity, which was found in a decrease of OGTT glucose AUC and HOMA-IR index. More studies are required to confirm that a 12-week moderate exercise training still has benefits in promoting insulin sensitivity among patients with a diagnosis of T2DM for more than 5 years.

Whether improvement in insulin sensitivity after exercise is a chronic effect of long-term exercise or an immediate residual effect is still uncertain.[34] Besides, evidence so far indicates that the effects of exercise on improvement of insulin sensitivity last only several days.[13,35] And, delaying the OGTT may underestimate the effect of regular exercise on insulin function.[31,36] Therefore, in this study, the OGTT was performed within 24 h after each 4 weeks of training. Besides, due to inconsistent results in the chronic effect of exercise, our study used a longitudinal design with four measurements to examine whether moderate exercise has an accumulated effect over time on insulin sensitivity within a 12-week training duration. Our results were consistent with previous studies but without similar effects on fasting insulin and OGTT insulin AUC.[33,36] This might be because our limited sample of only 13 patients had potential variations of individual characteristics. However, in the HOMA-IR index, we found a significant decrease over time, indicating an improvement of insulin sensitivity. Such a result suggests that exercise may induce a chronic effect.

Our study addressed whether chronic effects of exercise become more significant as the duration of exercise training increases. As duration increased, patients' blood glucose AUC and blood glucose level at various time points in the OGTT all showed gradually decreasing trends. However, insulin AUC and insulin concentration at various time points in the OGTT showed no significant change. This result is consistent with previous data[32,37] and may be due to the exercise intensity since previous research documented that the insulin AUC can be reduced by vigorous exercise.[38]

We found that 30 min of aerobic exercise training three times per week, at 60% VO_{2max}, lasting for 12 weeks, could significantly improve patients' cardiorespiratory fitness. On average, patients' VO_{2max} increased 12.4% (from 30.6 ml/kg/min to 34.5 ml/kg/min) and HR and BP decreased. These findings are similar to previous studies.[12,33] Decreased HR_{rest} and systolic and diastolic BP after exercise training suggest that exercise can improve functional heart capacity.[39] In particular, the effects of exercise on HR_{rest} and BP showed an improving trend over time during the 12 weeks. This finding requires further and larger trials with more samples to confirm, and studies with a longer training duration to realize whether the effects might reach a threshold.

Studies have shown that gender and exercise habits can influence VO_{2max}.[33] We found that as the training duration increased, improvement in VO_{2max} in males was greater than in females, even though males had a higher average VO_{2max} before training. This may be due to women's greater body fat stores, lower hemoglobin levels, smaller heart size, lower plasma volume, and greater susceptibility to exercise-induced arterial hypoxemia.[40] Some male patients preferred to exercise more than 30 min per session even though they had not exercised regularly before. Males also had better compliance throughout the program than the females. This may explain why, as the training duration increased, patients who exercised previously showed significantly more improvement in average VO_{2max} than patients who had not.

Our study revealed that, after 12 weeks of exercise training, all eight QOL subscales showed significant improvement from baseline, except for the score of "bodily pain." Thus, patients' perception of their own health appeared to be improved by exercise.[15] As the training continued, improvements in the score of "physical health" were more obvious in sedentary patients. It is possible that nonsedentary patients had higher scores in "physical health" at the beginning of the study; thus, further improvements were not as obvious for them. As the training duration increased, scores in "role function limitation due to emotion" improvement in females were less significant than in the males. However, females scored significantly higher at baseline, and thus, males had more room for improvement.

Depression status was significantly reduced over time in our study. Such results have not been found previously in diabetes patient groups but have been seen in other groups such as patients on dialysis[16,41] and patients with major depressive disorder.[14] In those studies, exercise reduced the extent of depression and increased psychological and emotional comfort. Cotman and Engesser-Cesar have suggested that this may be due to increased secretion of brain-derived neurotrophic factor after exercise.[42]

Patients with better metabolic control have a lower incidence of depression.[27] Whether this is causative is unknown. Potentially, exercise training may not only directly increase psychological comfort and satisfaction but also indirectly improve depression status by stabilizing blood glucose level. Exercise also provides patients with hope and something to look forward to, improves mentality and VT, increases self-confidence, and lowers anxiety.[41] After adjusting for confounding factors, the improvement of depression symptoms over time suggests a potential reciprocal relationship between exercise and depression. Feeling less depressed may make it more likely that patients comply with exercise, and exercise may make it less likely that patients will suffer from depressive mood.

Several limitations were the study's small sample size, not being randomized, lacking a control group, and generalizability due to its venue of a local medical center in northern Taiwan. Therefore, our results need confirmation by larger trials with control groups. Randomization is problematic, however, because of the difficulty of providing control exercise therapy. A crossover design could further clarify our findings. Regarding our small sample size, since recruiting participants to join a supervised exercise training with frequent blood testing is not easy; however, we could also provide a preliminary and feasibility study with a longitudinal design to uncover this interesting finding about the effects of a 12-week exercise training on insulin sensitivity, QOL, and depression status over time.

CONCLUSIONS

A moderate exercise training improves glucose utilization and tolerance, cardiorespiratory fitness, blood pressure, and QOL as well as depression status in patients with T2DM through a 12-week exercise training program after adjusting for covariates such as demographic features, disease characteristics, and lifestyle. Larger randomized trials of exercise in T2DM patients may further clarify its role in the physiology and psychology of diabetes.

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Conflicts of interest

There are no conflicts of interest.

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