Benefit effects of aerobic exercise and resistance training on the management of type 2 diabetes

Taoli Wang1*, Yang Liu2*, Rongzhou Zhong1, Donghong Xu3, Huifang Wang1, Bruma Sai-Chuen Fu2

1Department of Musculoskeletal Rehabilitation, Shanghai Yang Zhi Rehabilitation Hospital (Shanghai Sunshine Rehabilitation Center), Shanghai 201620, China; 2Department of Orthopaedics and Traumatology, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, China; 3Department of Cardiopulmonary Rehabilitation, Shanghai Yang Zhi Rehabilitation Hospital (Shanghai Sunshine Rehabilitation Center), Shanghai 201620, China. *Co-first authors.

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Abstract: To examine the effects of combined exercise (aerobic exercise and resistance training) on the management of type 2 diabetes. Articles published in English and Chinese based on a search of MEDLINE, Excerpta Medica Database (EMBASE) and China National Knowledge Infrastructure (CNKI) databases were the source for this meta-analysis. A significant difference in maximal oxygen consumption \( \text{VO}_{2\text{max}} \) was demonstrated between the combined exercise and non-exercise groups (Weighted mean difference: WMD = 2.66 ml/[kg/min], 95% CI = 1.80~3.51, P < 0.05). Combined exercise reduced the HbA1c concentration (WMD = -0.40%, 95% CI = -0.54~-0.26, P < 0.05), BMI (WMD = -1.09 kg/m\(^2\), 95% CI = -1.70~-0.49, P < 0.05), decreased the waist circumstance (WMD = -3.48 cm, 95% CI = -5.28~-1.6, P < 0.05), reduced the amount of abdominal subcutaneous fat (WMD = -104.14 cm\(^2\), 95% CI = -136.02~-72.27, P < 0.05), and reduced the amount of abdominal visceral fat (WMD = -32.26 cm\(^2\), 95% CI = -56.87~-7.66, P < 0.05). In addition, combined exercise reduced the SBP (WMD = -5.47 mmHg, 95% CI = -7.74~-3.20, P < 0.05), and DBP (WMD = 2.75 mg/dl, 95% CI = -4.10~-1.41, P < 0.05) and TG (WMD = -12.61 mg/dl, 95% CI = -24.00~-1.21, P < 0.05), and increased the HDL-C (2.91 mg/dl, 95% CI: 1.22-4.61, P < 0.05). Combined exercise is recommended in the management of type 2 diabetes patients.

Keywords: Combined exercise, aerobic exercise, resistance exercise, type 2 diabetes

Introduction

Type 2 diabetes is a metabolic disorder which is characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency [1-3]. In 2010, it was estimated that there were 285 million diabetics worldwide and 80% live in less developed areas. Physical activity, combined with diet and medication, are recommended treatments for type 2 diabetes by the World Health Organization. Aerobic and resistance exercises have been confirmed to be effective physical activities on improving glycemic control for type 2 diabetes patients [4-7]. Aerobic exercise is physical exercise that involves large muscle groups to improve cardiovascular endurance. Resistance exercise is physical exercise that causes the muscles to contract against an external resistance, the purpose of which is to increase muscle strength and muscle mass [8].

A recent study indicated that combined aerobic and resistance exercise could maximize the impact on the management of type 2 diabetes patients with characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency [5, 7]; however, the effects or effective dose (i.e., intensity, duration, and frequency) of combined aerobic and resistance exercise have been inconsistent. Thus, we performed a meta-analysis to determine the effects and effective dose of combined aerobic and resistance exercise on the management of type 2 diabetes patients based on current exercise regimen evidence.

Materials and methods

Search strategy

Articles published in English and Chinese based on a search MEDLINE, EMBASE and China
National Knowledge Infrastructure (CNKI) databases were the source for this meta-analysis. The search strategy for English databases used the following keywords: “combined exercise”; “aerobic exercise”; “resistance exercise”; “aerobic and resistance exercise”; “physical activity”; or “physical exercise”; and “type 2 diabetes”. The search strategy for Chinese databases used the following keywords: “aerobic and resistance exercise” and “type 2 diabetes”.

In addition, the references of the included studies and review articles which were not captured by our database searches were also reviewed for further relevant studies.

**Eligibility criteria**

The inclusion criteria were as follows: (1) all randomized controlled trials (RCTs) comparing combined aerobic and resistance exercise with aerobic/resistance/non-exercise control groups in type 2 diabetes patients with characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency; (2) trials ≥ 12 weeks were included because an exercise period < 12 weeks would be too short to show an alteration in the glycated hemoglobin (HbA1c) concentration or body mass index (BMI); and (3) the diagnostic criteria for type 2 diabetes was described in the study. The acceptable diagnostic criteria included the criteria described by the World Health Organization (WHO 1999; WHO 2006) or the American Diabetes Association standards (ADA 1997; ADA 2003; ADA 2010). To be consistent with the changes over the years, the related standards were based on the publication year of the study or the author cited in the study.

The exclusion criteria were as follows: (1) studies with a single bout exercise interventions; (2) studies with a combined aerobic and resistance exercise intervention group only; (3) studies with mere recommendations as interventions, without further details; (4) studies in which the combined aerobic and resistance exercise was not either directly supervised or well-documented; and (5) studies in which there was a co-intervention in the experimental group, such as a dietary alteration that was not applied to the control group.

**Variables coded from each study**

The value of HbA1c, which represents the average plasma glucose concentration over prolonged periods of time, before and after long-term exercise was collected to reflect the effect of combined aerobic and resistance exercise on glycemic control [9]. Moreover, because some studies showed that physical activity can help to decrease fat mass or increase muscle mass in type 2 diabetes patients, body mass indices were also collected. Furthermore, because many type 2 diabetes patients always have abnormal blood lipid profiles or blood pressure, the related values before and after exercise were collected. Adverse events were collected from any related study reports. The detailed items are shown below: (1) primary findings included the HbA1c concentration, body mass indices (BMI, body mass, fat mass, abdominal subcutaneous fat, abdominal visceral fat, waist circumstance, and mid-thigh muscle cross-sectional area), and adverse events (injuries and hypoglycaemic reactions; and (2) secondary findings included blood lipids (triglycerides [TG], total cholesterol [TC], high-density lipoprotein-cholesterol [HDL-C], low-density lipoprotein-cholesterol [LDL-C], blood pressure (systolic blood pressure SBP) and diastolic blood pressure [DBP]); and fitness (maximal oxygen consumption [VO_{2max}]).

**Data collection**

The following information was independently extracted by two investigators from all studies: first author; year of publication; trial characteristics (trial design and randomization); participants (total number in intervention/control groups, gender, age, diagnostic criteria, and dropouts); exercise interventions (type, intensity, frequency, and duration), and outcomes.

**Statistical analysis**

Pooled measures were calculated on the weighted mean difference (WMD) with 95% confidence intervals (CIs) of each outcome of interest (i.e., HbA1c, muscle mass, and fat mass) to assess the effect of combined exercise on the management of type 2 diabetes. Forest plots were used to show the outcomes of this meta-analysis.

All data were initially analyzed with a fixed effect model. Heterogeneity among studies was assessed using the I^2 of Higgins and Thompson. The I^2 parameter was used to quantify any inconsistencies [10]. If substantial heterogeneity was present (I^2 > 40%), the Der-Simonian and Laird random effect model (REM)
## Table 1. Characteristics of included randomized controlled combined aerobic and resistance exercise intervention trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Study Design</th>
<th>Study Length</th>
<th>Exercise Prescription (frequency and duration of period)</th>
<th>Primary Findings</th>
<th>Secondary Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stefano et al, 2010</td>
<td>563 T2D Men</td>
<td>Com vs. Control</td>
<td>2 times/week</td>
<td>150 min/wk, moderate intensity AE: From 4 to 10 MET-h/week RT: 3 MET-h/week</td>
<td>↓HbA1c</td>
<td>SBP, SBP, H-DLC, L-DLC</td>
</tr>
<tr>
<td></td>
<td>275 Com, 288 Con</td>
<td></td>
<td>12 months</td>
<td>↓BMI</td>
<td>↓TC, ↑UBS, ↑LBS, ↑Fasting Blood Glucose, ↓VO₂max, ↑Waist Circumference</td>
<td></td>
</tr>
<tr>
<td>Timothy et al, 2010</td>
<td>262 T2D Men</td>
<td>Com vs. Control</td>
<td>150 min/week</td>
<td>Com: AE: 50-80% of VO₂peak, 10 kcal/kg/week RT: 9 exercise, 4 S/MG/W, 10-12 RM</td>
<td>↓HbA1c</td>
<td>VO₂peak, ↓BMI, ↓Total Abdominal Fat, ↓BMI, ↓Fat Mass</td>
</tr>
<tr>
<td></td>
<td>76 Com, 72 AE</td>
<td></td>
<td>9 months</td>
<td>↓BMI</td>
<td>↓TC, ↑UBS, ↓LBS, ↓Fasting Blood Glucose, ↓VO₂max, ↓Waist Circumference</td>
<td></td>
</tr>
<tr>
<td></td>
<td>73 RT, 41 Con</td>
<td></td>
<td></td>
<td>↑Mid-Thigh Skeletal Muscle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Darcye et al, 2003</td>
<td>28 Post-Menopausal Women with T2D</td>
<td>Com vs. Control</td>
<td>3 times/week</td>
<td>Com: AE: 60-75% of HRmax RT: 5 exercises, 6 S/MG/W, 12 RM</td>
<td>↓BMI</td>
<td>↓Total Abdominal Fat</td>
</tr>
<tr>
<td></td>
<td>16 weeks</td>
<td></td>
<td>12 months</td>
<td>↓BMI</td>
<td>↓L-DLC, ↓BMI, ↓Body Mass, ↓Fat Mass</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 Com, 9 AE</td>
<td></td>
<td>12 months</td>
<td>↓BMI</td>
<td>↓Fat Mass, ↓Waist Circumference</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 Com, 9 AE</td>
<td></td>
<td>12 months</td>
<td>↓BMI</td>
<td>↓Abdominal Subcutaneous Fat</td>
<td></td>
</tr>
<tr>
<td>Antti et al, 2003</td>
<td>49 T2D Men</td>
<td>Com vs. Control</td>
<td>2 times/week</td>
<td>AE: 65-75% of the VO₂peak RT: 8 exercise, 6 S/MG/W, 10-12 of 70-80% RM</td>
<td>↓BMI</td>
<td>↓L-DLC, ↓H-DLC, ↓TC, ↓BMI, ↓DBP</td>
</tr>
<tr>
<td></td>
<td>24 Com, 25 Con</td>
<td></td>
<td>12 months</td>
<td>↓BMI</td>
<td>↓L-DLC, ↓BMI, ↓Body Mass, ↓Fat Mass</td>
<td></td>
</tr>
<tr>
<td>Ronald et al, (Publised through 6 studies) 2007</td>
<td>251 T2D Men</td>
<td>Com vs. Control</td>
<td>3 times/week</td>
<td>DARE trial AE: From 25 min/time at 70% of HRmax to 45 Min/time at 75% of HRmax RT: 7 exercises, 6-9 S/MG/W, 7-9 RM</td>
<td>↓BMI</td>
<td>VO₂peak, ↑UBS, ↑LBS, ↑Body Mass</td>
</tr>
<tr>
<td></td>
<td>64 Com, 60 AE</td>
<td></td>
<td>22 weeks</td>
<td>↓BMI</td>
<td>↓Fat Mass, ↓BMI, ↓Waist Circumference</td>
<td></td>
</tr>
<tr>
<td></td>
<td>64 RT, 63 Con</td>
<td></td>
<td></td>
<td>↓BMI</td>
<td>↓Abdominal Subcutaneous Fat</td>
<td></td>
</tr>
<tr>
<td></td>
<td>22 weeks</td>
<td></td>
<td></td>
<td>↓BMI</td>
<td>↓Mid-thigh Muscle Cross Sectional Area Health Status</td>
<td></td>
</tr>
<tr>
<td>Li SN, 2013</td>
<td>36 T2D</td>
<td>High intensity Com vs. Control</td>
<td>3 times/week</td>
<td>Com: before 2 wks, 20-30 min/times, 50-60% of HRmax</td>
<td>↓BMI</td>
<td>Fastingblood-glucose, ↑H-DLC</td>
</tr>
<tr>
<td></td>
<td>12 High Com</td>
<td></td>
<td>12 weeks</td>
<td>↓BMI</td>
<td>↓L-DLC, ↓BMI, ↓Body Mass, ↓Fat Mass</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 Low Com</td>
<td></td>
<td>12 weeks</td>
<td>↓BMI</td>
<td>↓Fat Mass</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 con</td>
<td></td>
<td></td>
<td>↓BMI</td>
<td>↓TC</td>
<td></td>
</tr>
</tbody>
</table>

was adopted as the pooling method; otherwise, the inverse-variance fixed effect model (FEM) was adopted. Once the heterogeneity was found, the potential sources of heterogeneity with various subgroup and sensitivity analyses were determined.

**Sub-group analysis:** Sub-group analysis included age, gender (male or female), body mass (BMI < 25 kg/m² or > 25 kg/m²), medication (receiving medication or not receiving medication), and exercise dose (intensity, frequency, and duration).

**Sensitivity analysis:** ‘Leave one out’ sensitivity analysis [5] was used to evaluate the key studies with substantial impact on between-study heterogeneity.

Furthermore, an evaluation form was used to assess the study quality according to the Cochrane Collaboration tool. All of the data was analyzed with Review Manager 5 software, which can be downloaded from the Cochrane Collaboration.

### Results

#### Characteristics of studies

The initial search yielded 11470 studies from the 3 databases (Embase [n = 22], Pubmed [175] and CNKI [11273]). Based on the content of the abstract, 16 studies were selected for further examination. Among these studies, 6 met the inclusion criteria [8, 11-18] and 1 study reported the results through 6 studies [8, 14-16, 18, 19]. Ten studies were excluded; 2 studies had a duration of intervention < 16 weeks [20, 21], 5 studies had no control group [20-24], the participants in the control group of 1 study did not have type 2 diabetes [25]; 3 studies was not RCTs [26-28]; and 1 study did...
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Table 4. Comparison Outline for Combined exercise vs. Resistance exercise

<table>
<thead>
<tr>
<th>Outcome of measurement title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size (Combined exercise groups vs. Resistance exercise groups)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Glycated haemoglobin (%)</td>
<td>2</td>
<td>236</td>
<td>Mean Difference (95% CI)</td>
<td>-0.25 [-0.45, -0.44]</td>
</tr>
<tr>
<td>2. Body mass (kg)</td>
<td>2</td>
<td>277</td>
<td>Mean Difference (95% CI)</td>
<td>-1.28 [-0.70, 4.52]</td>
</tr>
<tr>
<td>3. Upper body strength (kg)</td>
<td>1 (2 measurements)</td>
<td>256</td>
<td>Mean Difference (95% CI)</td>
<td>3.10 [-5.13, 11.32]</td>
</tr>
</tbody>
</table>

Figure 1. Combined exercise vs. Non-exercise, Glycated Haemoglobin (%).

not reveal the details of the exercise intervention [24] (Table 1).

**Study types:** All 6 of the included studies were RCTs. The studies were conducted in 5 different countries (Canada, Italy, the Netherlands, Finland and China) [11-13, 17, 18]. The types of exercise intervention were combined aerobic and resistance exercise in all of the studies, with a non-exercise group as the control group. Three studies also had aerobic exercise or resistance exercise alone as the control group [12, 13, 18].

**Participants:** The included studies involved 1,189 participants, who were all diagnosed with type 2 diabetes. The number of participants in a single study ranged from 28 to 563. Four hundred seventy-three participants received the combined aerobic and resistance exercise intervention. The mean age of all the participants was approximately 50 years.

**Interventions:** The types of aerobic exercise interventions included aerobic, yoga, aerobic dancing, treadmill, recumbent steppers, elliptical cycle ergometer, stationary bicycles, rowing machines, step up, jogging, or walking. Resistance exercise included weight training targeting all body muscle groups. For the upper body, bench press, seated row, shoulder press, pull down, chest press, abdominal crunches, or back extensions were included. For the lower body, leg press, leg extension, leg extension, leg curls, or hip extension were included.

The duration of the exercise intervention was 12 weeks, 16 weeks, 22 weeks, 9 months, and 1 year [12, 13, 18]. For single exercise intervention, the duration of aerobic exercise varied from 30-75 min, and 4-9 exercises per session, and 2-3 sessions per time for resistance exercise.

Most exercise interventions involved 2-3 times per week, lasting 60-150 min.

The intensity of aerobic and resistance exercise was from moderate-to-high. For aerobic exercise, the intensity was 50%-80% of the VO2max or 60%-75% of the maximum heart rate (HRmax). The resistance exercise involved 2-9 exercises per set targeting all muscle groups and 4-9 sets per week; each exercise was conducted with 7-22 maximal repetitions.

**Quantitative synthesis**

The comparison outlines for the meta-analysis between the combined exercise and control groups are shown in tables (Tables 2-4).
Blood glucose: All of the 6 studies (one of the studies with two kinds of strength training) reported the HbA1c concentration, which was the primary measurement of blood glucose. Specifically, HbA1c was significantly reduced in the combined exercise group compared with the non-exercise group (WMD = -0.40%, 95% CI = -0.54~0.26, I² = 3%, P < 0.05) (Figure 1).

Stefano et al also showed that the fasting blood glucose level were reported after 12 months and 12 weeks of exercise intervention. One study showed significant reduction in the fasting blood glucose level before and after the training in the combined exercise group compared with the non-exercise group (WMD = -0.40%, 95% CI = -0.54~0.26, I² = 3%, P < 0.05) (Figure 1).

Two studies were eligible for testing the effect of combined exercise and aerobic exercise or resistance exercise alone on blood glucose [12, 18]. No significant reduction in the HbA1c occurred in the combined exercise group compared to the aerobic exercise group (WMD = -0.13%, 95% CI = -0.36~0.11, I² = 4%), but a significant difference existed in the combined exercise versus the resistance exercise group (WMD = -0.25%, 95% CI = -0.45~0.04, I² = 48%, P < 0.05).
Body mass index: Three studies were included to assess the effect of exercise on the BMI [12, 17, 18]. There was a significant reduction in the BMI in the combined exercise group compared to the non-exercise group (WMD = -1.09 kg/m$^2$, 95% CI = -1.70~0.49, $I^2$ = 0%, $P < 0.05$) (Figure 2).

Waist circumference: Two studies were included to assess the effect of exercise on waist circumference. There was a significant decrease in the waist circumference in the combined exercise group compared to the non-exercise group (WMD = -3.48 cm, 95% CI = -5.28~1.6, $I^2$ = 0%, $P < 0.05$) (Figure 3). Another study showed the changes in waist circumference before and after exercise [12]. There was a 2.8 cm reduction in the combined exercise group, which was the greatest reduction among all groups in the study. The reduction was also significantly different from the non-exercise group.

Abdominal subcutaneous fat and abdominal visceral fat: Two studies [13, 18] were included to assess the effect of exercise on abdominal subcutaneous fat and abdominal visceral fat. There was a significant reduction of abdominal subcutaneous fat (WMD = -104.14 cm$^2$, 95% CI = -136.02~72.27, $I^2$ = 78%, $P < 0.05$) and abdominal visceral fat (WMD = -32.26 cm$^2$, 95% CI = -56.87~7.66, $I^2$ = 0%, $P < 0.05$) in the combined exercise group compared with the non-exercise group.

Body mass: Two studies were included to assess the effect of exercise on body mass [12, 13]. No significant difference existed between the three groups on the reduction of body mass (WMD = -3.25 kg, 95% CI = -7.52~1.03, $I^2$ = 0%, $P = 0.14$).

Two studies were used to determine the difference in body mass between the combined exercise and aerobic exercise or resistance exercise group, but no significant difference was found between the two groups (WMD = -1.60 kg, 95% CI = -7.39~4.19, $I^2$ = 0%, $P = 0.59$ [combined exercise vs. aerobic exercise] and WMD = -1.28 kg, 95% CI = -7.08~4.52, $I^2$ = 0%, $P = 0.67$ [combined exercise vs. resistance exercise]).

Adverse events: Two studies reported the prevalence of adverse events during training.
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[11, 18]; most adverse events were sports injuries and hypoglycemia. The prevalence of the three most common sports injuries (shoulder pain, low back pain, and spin splints) were analyzed in this meta-analysis, and all the results showed no significant difference on the prevalence of sports injuries between the combined exercise and non-exercise groups (P > 0.1). Moreover, no severe hypoglycemia, which indicates the need for medication, was reported during the training.

Maximal oxygen consumption (VO\textsubscript{2max}): Three studies [11, 12, 17] were included to assess the effect of exercise on the VO\textsubscript{2max} after excluding one study [13], which showed the VO\textsubscript{2max} data after training. A significant difference in VO\textsubscript{2max} was found between the combined exercise and non-exercise groups (WMD = 2.66 ml/[kg/min], 95% CI = 1.80–3.51, I\textsuperscript{2} = 0%, P < 0.05) (Figure 4).

TG: Two studies reported the effect of combined exercise on TG [11, 14]. This meta-analysis showed a significant change in TG levels between the combined exercise and non-exercise groups (WMD = -12.61 mg/dl, 95% CI = -24.00–1.21, I\textsuperscript{2} = 0%, P < 0.05) (Figure 5).

LDL-C and HDL-C: Two studies were included in this meta-analysis to assess the effect of combined exercise on LDL-C and HDL-C [11, 14]. As a result, there was a significant increase in HDL-C (WMD = 2.91 mg/dl, 95% CI: 1.22 to 4.61, I\textsuperscript{2} = 0%, P < 0.05) in the combined exercise group when compared with the non-exercise group (Figure 6), but there was no significant difference in LDL-C (WMD = 16.27 mg/dl, 95% CI = -9.58–42.11, I\textsuperscript{2} = 91%, P = 0.22) between the combined exercise group and non-exercise group.

Blood pressure: Three studies [11, 17, 18] were included to assess the effect of combined exercise on SBP and two studies [11, 17] measured the DBP. As a result, there was a 5.47 mmHg significant reduction of SBP (WMD = -5.47 mmHg, 95% CI = -7.74–3.20, I\textsuperscript{2} = 0%, P < 0.05) (Figure 7) and a 2.75 mmHg reduction of DBP (WMD = 2.75 mg/dl, 95% CI = -4.10–1.41, I\textsuperscript{2} = 0%, P < 0.05) in the combined exercise group compared with the non-exercise group.

Muscle strength: Two studies [11, 18] with three measurements were included to assess the effect of combined exercise on upper body muscle strength (UBS). There was a significant increase in UBS in the combined exercise group.
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Compared with the non-exercise group (WMD = 11.98 kg, 95% CI = 9.27~14.70, I² = 0%, P < 0.05) (Figure 8). Moreover, one study [11] with two measurements was included to compare the difference in UBS between the combined exercise group and the aerobic exercise or resistance exercise group alone. No significant increase existed in the combined exercise group compared with the aerobic exercise (WMD = 8.10 kg, 95% CI = -0.44~16.63, I² = 0%, P = 0.06) and resistance exercise groups (WMD = 3.10 kg, 95% CI = -5.13~11.32, I² = 0%, P = 0.46).

Two studies [11, 17] were included to assess the effect of combined exercise on lower body strength (LBS). There was a 38.26 kg significant increase in LBS in the combined exercise group compared with the non-exercise group (WMD = 38.26 kg, 95% CI = 27.15~49.37, I² = 0%, P < 0.05).

Study quality

All of the included studies were RCTs. Allocation concealment was also reported in two studies [11, 18]. There were no significant differences with respect to the main characteristics among participants in all of the studies at baseline. The dropout rates of the included studies were 0% [13], to 2% [17], 6% [12], 7% [11], and 12% [18] (Figure 8).

Sub-group analysis

We noted that there was a significant heterogeneity in the meta-analysis of LDL-C (I² = 91%, X² = 32.97, P < 0.00001) between the combined exercise and non-exercise groups. Therefore, in order to investigate the source of the heterogeneity of the results, we conducted subgroup analyses of the included trails based on exercise duration and BMI. The results showed that there was a significant difference in the LDL-C concentration between the combined exercise and non-exercise groups (WMD = 38.80%, 95% CI = 23.64~53.96, I² = 0%, P < 0.05) and WMD = -7.42%, 95% CI = -12.38~2.46, I² = 0%, P < 0.05) for the BMI (< 25 kg/m²) group and BMI (> 25 kg/m²) group, respectively. There was, however, no significant difference for the > 6 months or < 6 months exercise duration group. This finding reflected that the BMI of patients may be the causes of the heterogeneity of the results of LDL-C.

Discussion

From the results shown in the meta-analysis and relevant studies, we found that combined, aerobic, and resistance exercise can make a contribution to blood glucose control for type 2 diabetes patients. In this meta-analysis there was a 40% reduction in the HbA1c concentration in the combined exercise group compared with the non-exercise group. Some studies have confirmed that the glucose level of patients and the benefits derived from exercise have a positive correlation [9, 11, 30]; however, the HbA1c concentration was 0.40% less than other meta-analyses analyzing the effects of aerobic or resistance exercise alone on the management of HbA1c [9, 30]. This result may be because the HbA1c baseline in all of the included studies was approximately 7%, which is less than the baseline value in other reviews [9, 30]. Moreover, two of the included studies also showed a significant reduction on fasting blood glucose and insulin resistance in the combined exercise group.

However, no significant difference in the HbA1c concentration was found between the com-
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Combined exercise tends to increase cardiopulmonary fitness for type 2 diabetes. According to this meta-analysis, the VO_{max}, blood pressure (SBP and DBP), and blood lipids (HDL-C, other than LDL-C) showed a significant difference between the combined exercise group and non-exercise group after training. Type 2 diabetes patients always have abnormalities in cardiorespiratory fitness, which are the main risk factors for metabolic disorders [9, 14, 30]. Studies have shown that the prevalence of type 2 diabetes has a tendency to increase with age, and aging is also associated with a decline in cardiorespiratory fitness [30-34]. Thus, combined exercise was advisable for aging type 2 diabetes patients. Moreover, most studies have reported that aerobic or resistance exercise alone have limited effects on cardiorespiratory fitness, especially on control of blood pressure or blood lipids [9, 30, 35]. In this review, combined exercise was shown to have an effect on the control of both blood pressure and blood lipids. Furthermore, studies have also confirmed that combined exercise can increase endothelial function, such as the main coronary artery, and cardiovascular autonomic regulation, which may have clinical importance on preventing sudden death in type 2 diabetes patients [17, 36]. In the Sadanori RCT study [30], the prevalence of cardiovascular events was also shown to be lower in the combined exercise group than the non-exercise group.

Combined exercise and aerobic exercise or resistance exercise group, but the Joanie study arrived at the opposite conclusion [8]. One non-randomized control trial also showed that combined exercise reduced the HbA1c concentration more than aerobic exercise alone [26].

Furthermore, according to the suggestion by United Kingdom Prospective Diabetes Study Group [29], a 1% increase in the HbA1c concentration represents a 14% increased risk for myocardial infarction and a 37% increased risk for microvascular complications. As no severe adverse events were reported in the relevant studies herein, the 0.40% reduction in this meta-analysis may accompany a 6% decreased risk for myocardial infarction and a 15% decreased risk for microvascular complications for type 2 diabetes patients with a HbA1c concentration of 7%.

Combined exercise tends to increase muscle strength and indices of balance body for type 2 diabetes patients. This meta-analysis verified that combined exercise increases UBS and LBS. It has been shown that muscle strength is decreased in type 2 diabetes patients, especially on aging people. This phenomenon was due to a loss in both muscle mass and the metabolic quality of skeletal muscle, such as sarcopenia [30]. The loss of muscle mass also led to an increased risk for type 2 diabetes [37]. Moreover, skeletal muscle is the primary metabolic target organ for glucose and TG disposal and is an important determinant of the resting metabolic rate [30]. Thus, combined exercise can prevent the reduction in muscle strength and increasing the metabolic rate, especially for aging patients. In contrast, the meta-analysis also showed a significant effect of combined exercise on decreasing the BMI and waist circumstance. Three included studies also showed that fat mass was significant decreased between the combined exercise group and non-exercise group [13, 18]. Because weight control is one of the important recommendations for type 2 diabetes patients to prevent complications, the effects of combined exercise on balance body can be beneficial.

In this review, the effective volume of the exercise was 60-150 min per week at 50-80% VO_{max} or 60-75% HR_{max} for aerobic exercise and 4-9 exercises at 7-22 repetitions targeting major muscles per set and 2-9 sets per week for resistance exercise. The weekly volume in this review was consistent with the recommendation by the ADA [38]; however, there was a discrepancy regarding the frequency of exercise. In this review, the frequency of exercise was from 2-3 times per week, while the ADA recommended was ≤2 consecutive days without exercise. The discrepancy might be because it was not convenient for participants to go to special places taking part in the training >3 times a week. Because the entire exercise volume was similar to the ADA recommendation, the exercise volume in this review was recommended to type 2 diabetes patients and a higher frequency was suggested.

The exercise duration in the review ranged from 12 weeks to 1 year. In the sub-group analysis of LDL-C, we found that LDL-C was significant decreased both in the BMI (<25 kg/m²) group
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and BMI (> 25 kg/m²) group. This may indicate that the BMI of patients can make a contribution to the management of type 2 diabetes, such as the blood lipid level, but large-scale of studies need to be investigated in the future based on above classification features because of only three studies considered measuring LDL-C.

One study assessing the effect of combined exercise on quality of life showed that mental health status decreased in the combined exercise group [19]. The author explained that combined exercise might make people more fatigued than aerobic or resistance exercise alone. Due to insufficient data in this review, more related studies are suggested. Gradual combined exercise is suggested, which may help patients decrease the sense of fatigue during training [9].

For better interpretation of the results, several potential limitations of this meta-analysis should be acknowledged. The included study number in the meta-analysis was only six studies. Moreover, the statistics comparison about exercise effects between combined exercise and aerobic or resistance exercise alone was limited. Furthermore, less of the data were conducted from Asian countries.

In conclusion, combined exercise can be recommended in the management of type 2 diabetes patients, especially for elderly patients. Moreover, 2-3 times per week, moderate-to-high intensity of the combined aerobic and resistance exercise are suitable to be conducted for type 2 diabetes patients.

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None.

Address correspondence to: Bruma Sai-Chuen Fu, Department of Orthopaedics and Traumatology, Prince of Wales Hospital, The Chinese University of Hong Kong, 30-32 Ngan Shing Street, Shatin, New Territories, Hong Kong, China. Tel: 0086-52-2632-2211; Fax: 0086-52-26322415; E-mail: aebt39@sina.com

References

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[37] Sayer AA, Syddall HE, Dennison EM, Martin HJ, Phillips DI, Cooper C, Byrne CD and Hertfordshire C. Grip strength and the metabolic syndrome: findings from the Hertfordshire Cohort Study. QJM 2007; 100: 707-713.