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Physical Activity and Obesity in Adults

Hidetaka Hamasaki

Abstract

Both obesity and physical inactivity are global health problems responsible for the risk increment of non-communicable diseases. Obese individuals usually cannot perform the recommended level of physical activity because of their low physical fitness and comorbidities. The purpose of this chapter is summarizing and evaluating the effects of physical activity on obesity. The author also focuses on the association between non-exercise activity thermogenesis (NEAT) and obesity. The author has reviewed 13 systematic reviews and meta-analyses of randomized controlled trials investigating the effects of physical activity on obesity. Exercise is essential for the management of obesity. However, exercise alone is not sufficient for long-term weight loss and improving cardiovascular disease (CVD) risk factors. Diet seems to be more effective for treating obesity than exercise. On the other hand, exercise improves cardiorespiratory fitness and skeletal muscle fitness, which leads to prevent sarcopenic obesity in the elderly. Exercise therapy should be performed in conjunction with diet therapy to improve obesity. NEAT is the main determinant of variability in daily energy expenditure, which considerably contributes to weight change in humans. The current evidence regarding NEAT is limited; however, NEAT appears to be effective for the management of metabolic diseases as well as weight loss. To reveal the optimal mode of physical activity and to elucidate the effects of NEAT on health beyond weight lowering, further well-designed studies are warranted.

Keywords: obesity, physical activity, exercise, systematic review and meta-analysis, non-exercise activity thermogenesis

1. Introduction

Obesity prevalence rapidly increases in the world. A recent epidemiological study reported that an estimated 1.46 billion adults were overweight (body mass index (BMI) > 25 kg/m^2), and 502

million adults were obese (BMI > 30 kg/m^2) [1]. Such global obesity pandemic has serious health problems. Obesity is an established risk factor for type 2 diabetes, cancers, and cardiovascular diseases (CVD), which cause large disease burden in many low-income countries as well as high-income countries [2]. Meanwhile, physical inactivity is also a global health problem responsible for the risk increment of non-communicable diseases such as type 2 diabetes, coronary heart disease, and breast and colon cancers [3]. If physical inactivity disappears, the life expectancy of humans would rise by 0.68 years [3]. The American College of Sports Medicine and the American Heart Association have recommended that obese individuals engage in moderate-intensity aerobic physical activity for at least 30 minutes for 5 days per week, or vigorous-intensity aerobic physical activity for at least 20 minutes for 3 days per week [4]. However, obese individuals have usually physical, social, and psychological barriers to perform the recommended level of physical activity [5], it is quite difficult to resolve these two major health problems worldwide; obesity and physical inactivity pandemic. Nevertheless, a large number of clinical studies investigating the effects of physical activity on obesity have been conducted, and the evidence has been accumulated. This review is aimed at summarizing the current literature related to physical activity and obesity, and evaluating the effects of physical activity on obesity. This review will help clinicians, researchers, and obese individuals in the management of obesity. In addition to the literature review, the author focuses on the association between non-exercise activity thermogenesis (NEAT) and obesity to explore the possibility of applying NEAT to the treatment of obesity.

2. Methods

The author searched the English literature on physical activity and obesity using PubMed/MEDLINE and Cochrane Database of Systematic Reviews in the last 5 years (from June 2011 to May 2016). The author reviewed systematic reviews and meta-analyses of randomized controlled trials (RCTs) in principle. The search terms were "physical activity or exercise", "obesity", "systematic review", and "meta-analysis". The search returned 175 published articles. If the study participants were younger than 18 years, pregnant and women in the perinatal, and study outcomes were not related to weight loss, metabolic diseases, and CVD risk factors, the studies were excluded from this review. The titles and abstracts of the identified articles were reviewed to determine their relevance. Thirteen articles met the criteria for this review.

3. Results

3.1. The effect of lifestyle intervention on obesity

Obviously, the first-line treatment for obesity is lifestyle habit improvement. Peirson et al. [6] updated the previous review of the effectiveness of behavioral and pharmacologic interventions for treating obesity in adults. Of 68 identified studies, eight studies were diet interventions, four studies were exercise interventions, 10 studies were diet plus exercise interventions,

and 19 studies were lifestyle modifications. The exercise intervention had −1.49 kg reduction in weight, and the diet plus exercise intervention had −3.83 kg reduction in weight, respectively. Interventions by exercise alone did not achieve the greater reduction in weight, while interventions by diet alone showed the largest reduction in weight compared with the control group. However, the quality of evidence rating of these interventions was low. Additionally, this meta-analysis showed improvements in metabolic parameters in behavioral intervention subjects; TC (−0.10 mmol/L), low-density lipoprotein cholesterol (LDL-C) (−0.14 mmol/L), fasting blood glucose (−0.14 mmol/L), systolic blood pressure (−1.76 mmHg), and diastolic blood pressure (−1.60 mmHg). The incidence of type 2 diabetes was also less in the behavioral intervention group than in control group (risk ratio = 0.55, absolute risk reduction = 8.88%). No significant difference between behavioral and pharmacologic interventions for obesity-related outcomes was observed, although the potential adverse effects occurred more frequently in pharmacologic interventions than behavioral interventions. This result is of importance. Lifestyle intervention including an increase in physical activity is a safer and highly effective strategy for the management of obesity. However, this review also showed that the effectiveness of physical activity alone on obesity was small.

Behavioral weight management interventions can achieve weight reduction by 8–10%; however, most obese individuals regain weight after interventions end. A systematic review reported that the effect of extended care on weight-loss maintenance resulted in an additional 3.2 kg weight loss than normal care [7]. Dombrowski et al. [8] systematically reviewed the long-term effects of non-surgical treatments for weight-loss maintenance. Among 45 eligible studies, the weighted average age and BMI before interventions were 47.3 years and 35.2 kg/m², respectively. The weighted average weight loss across studies was −10.8 kg during the initial weight loss treatment (ranged from 2 to 12 months). The physical activity recommendations for weight loss were various. The most common recommendation was walking. Physical activity frequency varied from three to five times per week with a 20–30 minutes session; however, physical activity intensity was not described in detail. Most studies did not provide details of physical activity interventions. For weight-loss maintenance, recommendations for physical activity promoted a general increase in physical activity in most studies. Some studies provided specific recommendations such as walking, resistance training, and exercise classes. Extended behavioral/lifestyle management showed a mean weight change of −1.56 kg at 12 months, −1.96 kg at 18 months, and −1.48 kg at 24 months. However, there were no evidence of effectiveness for physical activity interventions and adding aerobic exercise or physical activity such as walking to a dietary intervention. Similarly, Johansson et al. [9] evaluated the effects of diet, exercise, or anti-obesity drugs on weight-loss maintenance after low-calorie diet interventions. A total of 20 RCTs met the criteria, which included three exercise (one of the three studies investigated the effect of both diet and exercise) intervention studies. The mean age and BMI of participants ranged from 28 to 48 years and from 27.9 to 41.6 kg/m², respectively. After the weight-loss intervention using very-low-calorie diet (<800 kcal/day) or low-calorie diet (800–1000 kcal/day), the studies randomly assigned participants to a weight-loss maintenance intervention group or a control group. Exercise interventions were resistance training, walking, and arthritis-adapted knee exercises. Exercise did not improve weight-loss maintenance, and a significant heterogeneity among studies was observed. When included

two studies that focused on the only exercise, weight-loss maintenance was improved; weighted mean difference was 1.6 kg with 8 months of maintenance phase duration. However, if the unsupervised follow-up (median follow-up duration: 24 months) was included in the analysis, weight-loss maintenance was not improved; the weighted mean difference was −0.7 kg. Going on a diet without physical activity instructions seems to be quite difficult.

Several systematic reviews have examined the effectiveness of workplace physical activity interventions [10,11] and eHealth using the internet and smartphones [12], or interactive computer-based interventions [13] on obesity. They are effective for weight loss and weight maintenance than no behavioral intervention. However, there is insufficient evidence for improving obesity by such interventions. Daily physical activity in workplace and home besides structured exercise plays a crucial role in the management of obesity [14]. Hence, to elucidate the role of daily physical activity, NEAT is important in controlling body weight. The details are described later.

Table 1 shows a summary of published systematic reviews of the effectiveness of lifestyle interventions on obesity.

Authors, year	Number of studies	Summary of inclusion and exclusion criteria	Physical activity	Results
Peirson et al., 2014 [6]	68 RCTs	Subjects: BMI ≥25 kg/m², <40 kg/m² Study duration: no restrictions Outcomes: changes in weight, WC and BMI Language: English or French Surgical treatments were excluded	No detailed description	The exercise intervention: −1.49 kg The diet plus exercise intervention: −3.83 kg Behavioral intervention: TC −0.10 mmol/L, LDL-C −0.14 mmol/L, FBG −0.14 mmol/L, SBP −1.76 mmHg, DBP −1.60 mmHg The incidence of type 2 diabetes↓ No significant differences between behavioral and pharmacologic interventions for obesity were found
Dombrowski et al., 2014 [8]	45 RCTs	Subjects: BMI ≥30 kg/m², weight loss >5% of body weight at baseline within 24 months Study duration: ≥12 months Outcomes: weight change during the weight loss phase and maintenance treatment period Language: any language Surgical treatments and alternative interventions were excluded	Walking Exercise classes	The initial weight loss treatment: −10.8 kg Extended behavioral/lifestyle management: −1.56 kg at 12 months, −1.96 kg at 18 months, and −1.48 kg at 24 months No evidence of effectiveness for physical activity interventions and adding aerobic exercise or physical activity such to a dietary intervention

Authors, year	Number of studies	Summary of inclusion and exclusion criteria	Physical activity	Results
		Subjects with mental disorders were excluded		
Johansson et al., 2014 [9]	20 RCTs	Subjects: treatment with a very-low-calorie diet (<800 kcal/day) or low-calorie diet (<1000 kcal/day) Study duration: no restrictions Outcomes: weight change during the calorie restriction phase and the weight-loss maintenance phase Language: English	Resistance training Walking Arthritis-adapted knee exercises	The weighted mean difference was 1.6 kg with 8 months of maintenance phase duration The weighted mean difference was −0.7 kg if the unsupervised follow-up was included in the analysis

RCT, randomized controlled trial; BMI, body mass index; WC, waist circumference; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; FBG, fasting blood glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 1. Systematic reviews and meta-analyses investigating the effects of lifestyle interventions on obesity.

3.2. Diet or exercise: comparing the effectiveness of management option for obesity

Which then is more effective for long-term weight loss, diet or exercise? There are four systematic reviews of RCTs to assess the effect of weight loss method on long-term change in weight and CVD risk factors. Schwingshackl et al. [15] compared the long-term effectiveness of (1) diet plus exercise vs. diet, (2) diet plus exercise vs. exercise, and (3) diet vs. exercise in overweight or obese individuals. Twenty one RCTs met the criteria and were analyzed. The mean age and BMI of subjects varied from 35 to 70 years and from 25.6 to 38.2 kg/m^2, respectively. Among eligible trials, 17 trials compared diet plus exercise vs. diet, 11 trials compared diet plus exercise vs. exercise, and 14 trials directly compared diet vs. exercise. Exercise interventions include aerobic exercise (walking, jogging, circuit training) and resistance training with the intensity of 50–85% of maximal heart rate. The weighted mean differences in change of body weight (−1.38 kg), waist circumference (−1.68 cm), waist-to-hip ratio (−0.01 U), and fat mass (−1.65 kg) were more significant in diet plus exercise group than in diet only group. The diet plus exercise group also had a more significant increase in cardiorespiratory fitness represented by maximal oxygen uptake (VO$_2$max) (3.61 mL/kg/min) and HDL-C (1.62 mg/dL), and a decrease in TG (−10.08 mg/dL) and diastolic blood pressure (−1.2 mmHg). When comparing diet plus exercise group with exercise only group, body weight (−4.13 kg), waist circumference (−3 cm), waist-to-hip ratio (−0.01 U), and fat mass (−3.6 kg) had more distinctive reductions in diet plus exercise group than in exercise only group. The weighted mean difference in change of VO$_2$max (2.13 mL/kg/min) was larger in diet plus exercise group. TC (−11.36 mg/dL), LDL-C (−10.03 mg/dL), systolic blood pressure (−2.84 mmHg), and diastolic blood pressure (−2.06 mmHg) changed more substantially by diet plus exercise interventions compared with exercise only interventions. Direct comparison between the effectiveness of

diet and exercise revealed that diet interventions were more effective for reductions in body weight (−2.93 kg), fat mass (−2.2 kg), HDL-C (−0.96 mg/dL), and systolic blood pressure (−2.19 mmHg). However, the significant difference in change of cardiorespiratory fitness was not observed. This systematic review found that a combination of diet and exercise intervention was more effective in improving obesity-related anthropometric parameters, lipid profile, and blood pressure. Exercise is less effective for improving obesity than diet. However, the authors could not conclude which treatment is more effective for HDL-C. Washburn et al. [16] compared the effect of energy restriction, aerobic and resistance exercise, and various combinations of them on long-term (≥12 months) weight loss and metabolic parameters. A total of 20 studies were included in quantitative synthesis. Seven studies were selected for the review of the effectiveness of diet vs. exercise. Aerobic exercise included various modes such as walking/jogging, treadmill or cycle ergometer, and Nordic Track exercise machine. When subjects were engaged in exercise, two trials were supervised, two trials were partially supervised, and three trials were not supervised. Exercise intensity, frequency, and duration were also various. The median age and BMI for exercise groups were 58.1 years and 28.9 kg/m^2, respectively. The median weight loss for five out of seven trials with long-term comparisons was 7.2% in diet groups and 2.4% in exercise groups. Waist circumference reduced by 1.9 cm in exercise groups and 3.7 cm in diet groups. The median long-term change in fat mass was −6.1 kg by diet interventions and −0.6 kg by aerobic exercise interventions. A long-term trial evaluated the change in metabolic parameters such as lipid profile and blood pressure; however, no significant differences between groups were reported. Three trials provided data on weight change in follow-up periods of 6 months, 12 months, and 18 months. Briefly, weight regains in the diet and exercise groups were 77 and 148% of their weight loss, respectively. Diet tends to be more effective for long-term weight loss than exercise. Adding aerobic exercise to diet results in greater weight loss than diet alone. However, in most trials of exercise for obesity, the exercise intensity, frequency, and duration is not well-controlled and physical activity level is not accurately measured, prescribed exercise level is also insufficient for significant weight loss [17]. Therefore, exercise protocol should probably be standardized to perform "head-to-head" comparison of diet vs. exercise in obesity. For example, energy expenditure by exercise should be objectively measured (e.g., using accelerometry or doubly labeled water method) to match the energy deficit by diet interventions.

Johns et al. [18] examined the effectiveness of combined behavioral weight management programs in comparison with diet only or physical activity only programs on weight loss. Eight studies were included in the analysis, four of which included both diet only and physical activity only arms. Seven studies compared a combined program with diet only intervention, and five studies compared a combined program with physical activity intervention. The mean age and BMI of subjects ranged from 32 to 70 years and from 29.2 to 37.3 kg/m^2, respectively. As is common in clinical studies investigating weight change, there were more female subjects than male subjects. Physical activity interventions were various; however, most studies advised moderate to vigorous intensity physical activity (e.g., brisk walking, using upstairs, step aerobics) three to five times per week. Seven studies had supervised exercise sessions, and two studies performed resistance training as well as aerobic exercise. Weight loss at 3–6 months was significantly higher in combined programs than in physical activity alone interventions

(mean difference = −5.33 kg) Weight loss at 12 months was also higher in combined programs than in physical activity alone interventions (mean difference = −6.29 kg). Measurement of physical activity was reported in four trials; step count, VO_2max, and a 400 m walking time. No significant differences in the improvement of physical activity were reported in two studies; however, one trial reported an increase of step count, and the other reported a greater improvement in VO_2max by combined behavioral weight management programs compared with physical activity alone interventions. Weight management by physical activity alone is less effective than combined weight management programs in both short- and long-term. Miller et al. [19] investigated the specific effects of exercise on physical function, fitness, and body composition in obesity during diet interventions alone than the combination of diet and exercise interventions. Fourteen studies were included in this systematic review. The mean age and BMI of subjects across all trials ranged from 37 to 75 years and 31 to 37 kg/m^2, respectively. Ten studies included older individuals and postmenopausal women. The duration of trials ranged from 3 to 12 months. Exercise interventions included aerobic exercise, resistance training, or both of them. Aerobic exercise was mostly performed at moderate to vigorous intensities (65–85% maximum heart rate) and for 90–225 minutes per week. Resistance training was typically performed 2–3 sets of 8–12 repetitions at approximately 65–85% of one repetition maximum. All aerobic exercise groups showed a significant improvement in VO_2max than in energy restriction alone. All exercise interventions demonstrated improvement in upper and/or lower extremity muscle strength. On the other hand, all energy restriction groups showed no significant change or decrease in muscle strength following weight loss. Fat mass loss between diet alone groups and diet plus exercise groups was not different in the studies that showed similar weight loss. The lean mass loss in diet alone groups and diet plus exercise groups ranged from 0.4 ± 1.0 kg to 4.1 ± 1.9 kg and from 0.5 ± 1.1 kg to 3.4 ± 2.0 kg, respectively. Six trials reported that skeletal muscle mass loss was smaller in diet plus exercise groups than that in diet alone groups. Adding exercise to energy restriction for obese individuals has beneficial effects for physical fitness and body composition. Exercise is crucial for lifestyle modifications in the improvement of cardiorespiratory fitness and body composition in obese individuals. **Table 2** summarizes published systematic reviews that compared the effectiveness of diet with exercise.

Authors, year	Number of studies	Summary of inclusion and exclusion criteria	Exercise	Results
Schwingshackl et al., 2014 [15]	21 RCTs	Subjects: BMI ≥25 kg/m^2 Study duration: ≥12 months Outcomes: BW, WC, WHR, FM, TC, LDL-C, HDL-C, TG, SBP, DBP, VO_2max Language: no restrictions Participants with coronary heart disease were excluded	Partly supervised Aerobic exercise (jogging, walking, flexibility, circuit training) Resistance training 50–85% of maximal heart rate	Diet + exercise vs. diet: BW −1.38 kg, WC −1.68 cm, WHR −0.01 U, FM −1.65 kg, HDL-C 1.62 mg/dL, TG −10.08 mg/dL, DBP −1.2 mmHg, VO_2max 3.61 mL/kg/min Diet + exercise vs. exercise: BW −4.13 kg, WC −3 cm, WHR −0.01 U, FM −3.6 kg, TC

Authors, year	Number of studies	Summary of inclusion and exclusion criteria	Exercise	Results
				−11.36 mg/dL, LDL-C −10.03 mg/dL, SBP −2.84 mmHg, DBP −2.06 mmHg, VO$_2$max 2.13 mL/kg/min Diet vs. exercise: BW −2.93 kg, FM −2.2 kg, HDL-C −0.96 mg/dL, SBP −2.19 mmHg
Washburn et al., 2014 [16]	20 RCTs	Subjects: BMI ≥25 kg/m^2, age ranged from 18 to 65 years Study duration: ≥6 months Outcomes: BW, body composition, TC, HDL-C, LDL-C, TG, insulin, glucose, HbA1c, blood pressure Language: English	Aerobic exercise: walking/jogging, treadmill or cycle ergometer, and Nordic Track exercise machine	Diet vs. exercise: weight loss 7.2% vs. 2.4%, WC −1.9 cm vs. −3.7, FM −6.1 kg vs. −0.6, weight regain 77% vs. 148%
Johns et al., 2014 [18]	8 RCTs	Subjects: BMI ≥25 kg/m^2, BMI ≥2 kg/m^2 in Asian populations Study duration: ≥12 months Outcomes: weight change Language: any language Studies in pregnant women, participants with eating disorders, and specific diseases were excluded	Moderate to vigorous intensity physical activity (e.g., brisk walking, using upstairs, step aerobics) three to five times per week. Supervised sessions Two studies performed resistance training as well as aerobic exercise	BWMPs vs. physical activity alone: mean difference −5.33 kg at 3–6 months, −6.29 kg at 12 months
Miller et al., 2013 [19]	14 RCTs	Subjects: BMI ≥30 kg/m^2 Study duration: no description Outcomes: body composition (by DXA and MRI), cardio-respiratory fitness Language: English	Aerobic exercise: at moderate to vigorous intensities and for 90–225 minutes per week Resistance training: 2–3 sets of 8–12 repetitions at approximately 65–85% of one repetition maximum	Exercise: VO$_2$max↑, extremity muscle strength↑ Energy restriction: VO$_2$max→ Skeletal muscle mass loss was smaller in diet plus exercise groups than that in diet alone groups

RCT, randomized controlled trial; BMI, body mass index; BW, body weight; WC, waist circumference; WHR, waist-to-hip ratio; FM, fat mass; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; FBG, fasting blood glucose; HbA1c, hemoglobin A1c; SBP, systolic blood pressure; DBP, diastolic blood pressure; BWMP, behavioral weight management program; DXA, dual-energy X-ray absorptiometry; MRI, magnetic resonance imaging.

Table 2. Systematic reviews and meta-analyses comparing the effects of exercise interventions with diet interventions on obesity.

3.3. The effect of isolated exercise on obesity

There are two systematic reviews evaluating the effects of isolated exercise on weight loss and lipid profile. Kuhle et al. [20] conducted a systematic review and meta-analysis to appraise the evidence regarding the effect of aerobic exercise and/or resistance training on body composition and serum lipids in older individuals. Nine RCTs were included in the analysis. Studies enrolling patients with diabetes, cognitive impairment, and cardiovascular disease were excluded. The mean age ranged between 60 ± 1.6 years and 80.8 ± 4.7 years. Aerobic exercise with moderate to vigorous intensity based on 50–80% of maximal heart rate and resistance training with an increase in weight load depending on individuals' muscle strength were performed. Exercise significantly reduced BMI (-1.01 kg/m^2) and waist circumference (-3.09 cm). However, exercise did not statistically change LDL-C levels in older subjects. In addition, data on TG and HDL-C were insufficient for analysis. This review is notable for focusing on the effect of exercise on obesity in individuals over the age of 60 years. Sarcopenic obesity, which is defined as the age-related decrease in muscle mass and increase in fat mass [21], increase the risk of mortality as well as disability [21, 22]. Sarcopenic obesity is an important issue for countries in which society is aging. Losing weight without loss of lean body mass will not be achieved by only exercise. Exercise programs in combination with dietary interventions such as protein supplements will be required to combat sarcopenic obesity in older individuals.

Thorogood et al. [23] evaluated the isolated efficacy of aerobic exercise (without energy restriction) programs on weight loss in overweight and obese individuals. Six trials met the inclusion/exclusion criteria of their review. The mean age of subjects ranged from 19 to 72 years. The mean BMI of subjects was unclear because three trials did not report baseline BMI. Exercise included various modes such as walking, jogging, cycle ergometer, aerobics, mini-trampoline, and rowing ergometer. Exercise was performed with the intensity of 40–85% maximum heart rate and 40–70% VO$_2$max. Exercise durations were 120–240 minutes per week. The mean difference of weight between the exercise groups and the control groups ranged from 0.8 to -2.5 kg. Two studies reported weight gain in the exercise groups (0.5 kg and 0.6 kg, respectively). However, the exercise groups had significant weight loss in all 6- and 12-month exercise programs. Additionally, exercise was beneficial for waist circumference reduction in all 6- and 12-month exercise interventions. Five studies reported a significant decrease in systolic and diastolic blood pressure, and the mean differences ranged from -1.7 to -5.6 mmHg and -0.8 to -3.0 mmHg, respectively. Four out of six trials reported a decrease in TC levels (-1.6 to -18.2 mg/dL), and five trials also reported a decrease in TG levels (-8.9 to -36.5 mg/dL) by aerobic exercise. Pooled analysis revealed that 6- and 12-month aerobic exercise programs were associated with a decrease in weight (-1.6 kg and -1.7 kg, respectively), a reduction in waist circumference (-2.12 cm and -1.95 cm, respectively). At 6 months, aerobic exercise programs had beneficial effects on blood pressure and TC; however, the number of studies was insufficient for performing pooled analysis at 12 months. This systematic review shows that 6–12 month moderate-intensity aerobic exercise programs have modest benefits to obesity, but isolated aerobic exercise is not sufficiently effective for weight loss. The authors recommend that exercise therapy be performed in conjunction with diet therapy to improve obesity.

3.4. Comparison of the effectiveness for obesity between aerobic exercise and resistance training

One systematic review directly compared the effectiveness of aerobic exercise and resistance training for visceral adipose tissue [24]. A total of 35 studies met the eligibility criteria. The mean age of subjects ranged from 28 to 83 years. Eighteen studies had obese subjects, 15 had overweight subjects, and study participants of two studies were within normal weight. The most common mode of aerobic exercise was cycle ergometer, and resistance training on a weight machine was most commonly prescribed. The intensity of aerobic exercise ranged from 40 to 55% (expressed as a percentage of maximum heart rate or VO_2peak) in initial weeks, which progressed to 60–90% in the final week. The most common intensity of aerobic exercise was moderate intensity: 60–75% of maximal heart rate. The intensity of resistance training expressed as one repetition maximum ranged from 30 to 100%. The frequency of aerobic exercise was commonly 3–5 days per week. The frequency of resistance training was commonly 2–3 days per week. Six studies combined aerobic exercise and resistance training. We should have a particular concern about dietary intake during the study period. Indeed, diet was not controlled in ten studies, and eight studies did not report on diet. When compared aerobic exercise therapy with control, a significant pooled effect size (ES) was found (ES = −0.33; 95% CI, −0.52 to −0.14, $p < 0.01$). However, the pooled ES for progressive resistance training therapy when compared with control was not significant (ES = 0.09: 95% CI, −0.17 to 0.36, $p = 0.49$). Heterogeneity among studies was observed in both analyses. The pooled ES for the comparison between aerobic exercise and resistance training therapy did not reach statistical significance, which tended to favor aerobic exercise (ES = 0.23; 95% CI, −0.02 to 0.50, $p = 0.07$). Moreover, the combined aerobic exercise and resistance training therapy was not significantly effective for reducing visceral fat tissue compared with control. This review suggests that not resistance training but aerobic exercise is relatively effective for improving visceral fat obesity; however, exercise intervention alone is insufficient for ameliorating obesity.

3.5. The effect of weight loss on glycemic control and the prevention of obesity

Franz et al. [25] investigated the effect of lifestyle weight-loss interventions on glycemic control in overweight and obese patients with type 2 diabetes. A total of 11 trials were eligible for meta-analysis. The mean weight at baseline with weight loss <5% and ≥5% were 98.4 kg and 99.9 kg, respectively. Unfortunately, only three weight-loss intervention trials [26–28] measured and reported physical activity (goal setting: 175 minutes per week of physical activity), although physical activity was recommended as a lifestyle intervention. The effect of physical activity on glycemic control in obese patients with type 2 diabetes was not described in this review. Moreover, no significant beneficial effects on hemoglobin A1c (HbA1c), lipid profile, and blood pressure were reported by this meta-analysis. However, two trials that included regular physical activity intervention and frequent contact with health professionals reported beneficial effects on HbA1c, lipid profile, and blood pressure. The Mediterranean-style diet study group in newly diagnosed patients with type 2 diabetes reported a decrease in HbA1c of 1.2%, TC of 15.1 mg/dL, TG of 39.0 mg/dL, systolic blood pressure of 2.3 mmHg, and diastolic blood pressure of 4.0 mmHg, and an increase in HDL-C of 3.9 mg/dL [28]. The intensive

lifestyle intervention in the LooK AHEAD trial reported a decrease in HbA1c of 0.6%, LDL-C of 4.4 mg/dL, TG of 29.3 mg/dL, systolic blood pressure of 9.9 mmHg, and diastolic blood pressure of 3.1 mmHg, and an increase in HDL-C of 3.4 mg/dL [26, 29]. This review concluded that over 5% of weight loss is necessary for beneficial effects on glycemic control, lipid profile, and blood pressure. Not only energy restriction but energy expenditure, namely regular physical activity, is essential for improving metabolic diseases in obese patients with type 2 diabetes.

Considering that the number of obese individuals is rapidly increasing, the prevention of weight gain in non-obese individuals is also important. Hebden et al. [30] reviewed RCTs of lifestyle interventions for preventing weight gain among healthy young (18–35 years) individuals. This systematic review excluded interventions for obese subjects (BMI ≥ 30 kg/m^2) because such subjects did not represent the general population. Eight studies were included in the analysis. The average BMI of subjects at baseline was <30 kg/m^2. Lifestyle interventions consisted of face to face or group sessions for weight control, dietary counseling, physical activity recommendations, and feedback by using the internet. Three out of eight studies performed supervised exercise sessions such as treadmill walking, resistance training, and walking/running measured by pedometer. Although the independent effect of physical activity on preventing weight gain was not described, the combined weighted mean weight change in lifestyle intervention subjects and controls were −0.87 kg and +0.86 kg, respectively. Interventions for longer than 4 months were associated with greater weight loss. However, the authors stated that the effectiveness of lifestyle intervention for preventing weight gain in young individuals was unclear because of the small number of subjects, short duration, and large heterogeneity of the studies. Further large-scale RCTs with standard lifestyle intervention methods are warranted to reveal the effect of lifestyle modification for preventing obesity.

4. Non-exercise activity thermogenesis (NEAT) and obesity

Many previous studies have shown that sedentary lifestyle and daily physical inactivity contribute to obesity [31–35]. A recent systematic review and meta-analysis showed that obesity was associated with higher all-cause mortality than normal weight [36], and physical inactivity is a crucial problem for the prevention and treatment of obesity. Increasing energy expenditure in daily life is essential. NEAT is the main determinant of variability in total daily energy expenditure [37]. It is defined as the energy expenditure due to physical activities besides volitional exercise and includes various activities in daily life such as walking for pleasure, going to work, gardening, doing housework, singing, and dancing [38]. NEAT covers a wide range of intensity that at times reaches to the recommended level for obese individuals [39]. The energy expenditure by sitting and watching television is no more than 9 kcal per hour, but gardening and cleaning reach higher levels of energy expenditure; 100–150 kcal per hour and 500 kcal/day, respectively [40]. Steeves et al. [41] conducted a randomized controlled pilot study to examine the 6-month effects of two interventions; stepping in house during TV commercials vs. walking 30 minutes per day in sedentary and

obese individuals. Although no significant difference between groups were observed, daily steps increased, and time of TV viewing, dietary intake, body fat percentage, waist and hip circumference significantly decreased after both interventions. Only stepping during watching TV could be a feasible approach for improving obesity. In the modern world, walking in a break during work is effective for weight loss. Levine and Miller [42] investigated whether the change of work environment affect individuals' energy expenditure at workplace. The vertical workstation that allows obese workers to use a personal computer while walking on a treadmill was established. The mean energy expenditure while walking at workplace was 191 kcal per hour, which was significantly higher than energy expenditure while seated at work (72 kcal per hour). This amount of energy expenditure could be equal to a weight loss of 20–30 kg per year. Furthermore, they assessed the effect of using an office-place stepping device housed under a desk on workers' energy expenditure [43]. The mean increase of energy expenditure in obese office workers was 335 kcal per hour, which could be equal to a weight loss of 20 kg per year. Changing living environments to change sedentary behavior will increase NEAT and decrease body weight. Each NEAT is small; however, "Many a little makes a mickle." To increase NEAT should be effective for improving obesity (**Figure 1**). NEAT is intricately regulated by endocrine, genetic, and sociological factors [39]. Sarcolipin [44] and ventromedial hypothalamic melanocortin receptor [45] have been of current interest as new mediators of NEAT. Sarcolipin, which consists of 31 amino acids and is highly expressed in skeletal muscle, plays a role in energy expenditure. Sopariwala et al. [44] showed that sarcolipin overexpression mice are more resistant to fatigue and more physically active compared with wild type. This newly identified regulator may increase non-shivering thermogenesis in humans [45] and could be effective to increase energy expenditure and control weight gain in obese individuals [46]. The ventromedial hypothalamus also has an important role in regulating energy balance, and the brain melanocortin system not only decreases appetite but increases physical activity [45, 47]. Gavini et al. [48] showed that intra-ventromedial hypothalamus melanocortin receptor activation increased physical activity and induced the elevation of mRNA expression of mediators of energy expenditure such as uncoupling proteins, peroxisome proliferator-activated receptors, peroxisome proliferator-activated receptor gamma coactivator 1-α, and AMP-activated protein kinase. Modulating melanocortin receptors in the ventromedial hypothalamus may contribute to increase of NEAT. Identifying such novel mechanisms to increase energy expenditure is expected to be applied in the treatment of obesity. Moreover, the significant associations of NEAT with metabolic diseases such as type 2 diabetes, hypertension, and dyslipidemia have been identified [49–53]. NEAT intervention in addition to structured exercise prescription certainly improves obesity and metabolic diseases. To elucidate the effectiveness of NEAT for metabolic diseases, and further CVD, as well as obesity, well-designed longitudinal studies in humans are warranted. On the other hand, how to measure NEAT accurately under free-living (accelerometry, doubly labeled water method, or a completely new method?) and how to intervene NEAT (recommendation or supervised program?) are still unknown. The development of measurement and intervention method of NEAT will be needed to conduct such clinical studies.
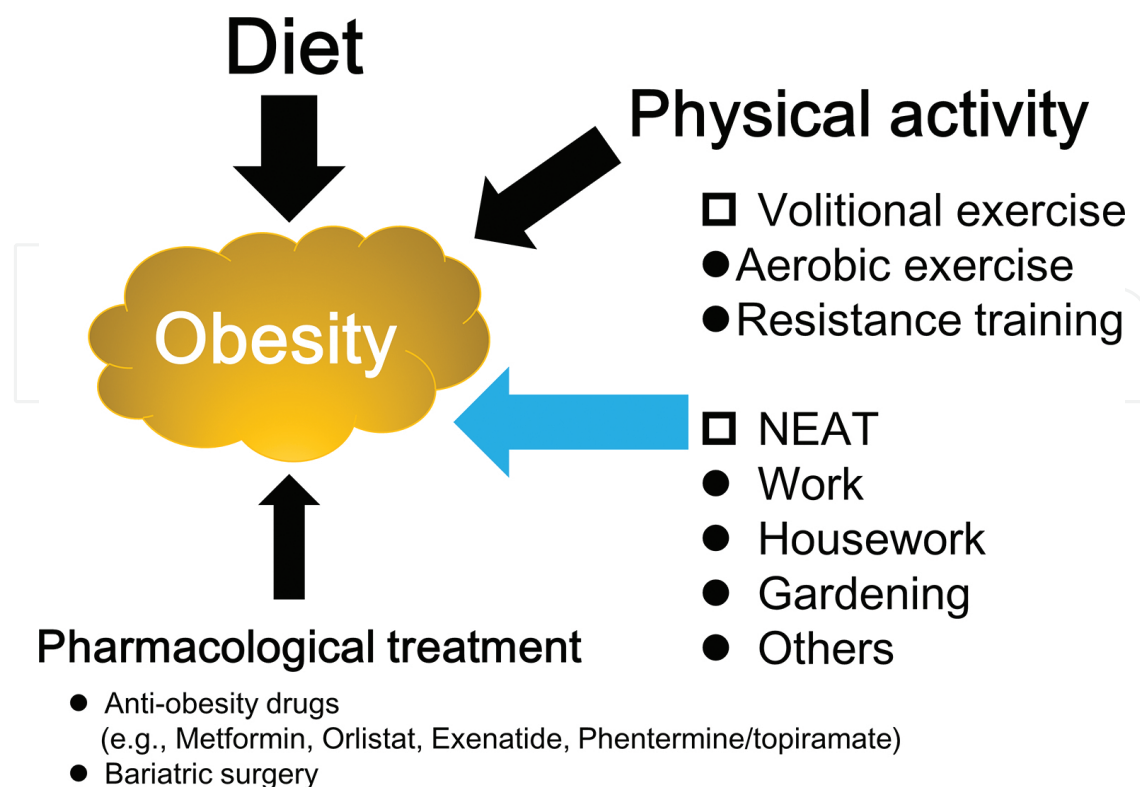
Diet

Physical activity

☐ Volitional exercise
● Aerobic exercise
● Resistance training

☐ NEAT
● Work
● Housework
● Gardening
● Others

Obesity

Pharmacological treatment

● Anti-obesity drugs
(e.g., Metformin, Orlistat, Exenatide, Phentermine/topiramate)
● Bariatric surgery

Figure 1. Obesity is treated with diet, physical activity, and pharmacologic therapy. Diet appears to be more effective for treating obesity than physical activity; therefore, physical activity intervention should be combined with dietary intervention in the management of obesity. Non-exercise activity thermogenesis (NEAT) beyond structured exercise may play a pivotal role in weight loss in obese individuals.

5. Conclusions

Exercise interventions are essential for the management of obesity. However, exercise alone is not sufficient for long-term weight loss and improving CVD risk factors. Diet seems to be more effective for treating obesity than exercise. On the other hand, exercise improves cardiorespiratory fitness and skeletal muscle fitness, which leads to prevent sarcopenic obesity in the elderly. Exercise therapy should be performed in conjunction with diet therapy to improve obesity. Although a number of systematic reviews have been conducted to assess the effectiveness of exercise for obesity, small number of subjects, short duration, and the heterogeneity of exercise modes between clinical studies makes it difficult to conclude. The optimal intensity, frequency, and duration of exercise to improve obesity and its comorbidities are not fully elucidated. In addition, NEAT is the main determinant of variability in daily energy expenditure, which considerably contributes to weight change in humans. The current evidence regarding NEAT is limited, but NEAT plays an important role for treating obesity. To my knowledge, there are no clinical studies which include "NEAT only" interventions besides volitional physical activity to investigate the effects of NEAT on obesity and metabolic diseases. This is a challenge for the future.

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