Muscle mass and strength after weight loss in Japanese obese men

by

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LIST OF ABBREVIATIONS

% MMI: Percentage of muscle mass index

% whole body fat: Percentage of whole body fat

BMI: Body mass index

DEXA: Dual energy x-ray absorptiometry

HGS: Handgrip strength

IKT180 AP = Isokinetic180 average power

IKT180 PTQ = Isokinetic180 peak torque

IKT180 PTQ/BW = Isokinetic180 peak torque/body weight

IKT180 TW = Isokinetic180 Total work

IKT180 WF = Isokinetic180 work fatigue

IKT60 AP: Isokinetic60 average power

IKT60 PTQ: Isokinetic60 peak torque

IKT60 TW: Isokinetic60 total work

IMT60 PTQ: Isometric60 peak torque

SMI: Skeletal muscle mass index

CHAPTER 1. INTRODUCTION

1.1. Background

The dramatic increase in obesity has been reported in both developed and underdeveloped countries over the last decade (Kolata, 1985; Mokdad et al., 2003; WHO, 1998). In Japan, obese population has become a 1.5-fold in the past 30 years and the incidence of obesity is over 30% in adult men between the age of 30-69 years (MHLW, 2011). Such an increase of obesity in middle-aged men is a major public health concern in Japan (McCurry, 2007). It is because, obesity is responsible for a wide range of chronic diseases, including heart disease, hypertension and certain cancers (WHO, 2002). Furthermore, obesity is deeply associated with musculoskeletal conditions such as pain, stiffness, loss of joint mobility and osteoarthritis that, though not fatal, decrease the quality of life and life expectancy by disturbing social exchange and aggravating obesity (Vincent et al., 2012; WHO, 2003).

The individual and social costs related to musculoskeletal conditions are considerable: their direct and indirect costs reach $214.9 billion in the USA, equivalent to three percent of the country's annual gross domestic product (WHO, 2003). In Europe, musculoskeletal conditions have been recognized as having the highest cost burden of all disease categories (Lindgren, 1998). In Australia, the costs of musculoskeletal conditions are second only to cardiac and vascular diseases, the most cost-intensive disease categories (AIHW, 2004). At present, there is not a report on individual and social costs associated with musculoskeletal conditions in Japan. However, from the above reports, it is considered that substantial costs related to musculoskeletal conditions may have been incurred in Japan. On these individual and socio-economic grounds, musculoskeletal conditions require effective management.

The effects of weight reduction on musculoskeletal conditions have been reported as follows: achieving 5% decrease in body weight would relieve some joint pain, but a loss of 10% of body weight is associated with moderate to large clinical improvements in joint pain (Christensen et al., 2007). It would reduce osteoarthritis cases by more than 50% by means of lowering BMI to 20-24.9 kg/m^2 (Coggon et al., 2001). Given these reports, it is recognized that weight loss has a positive effect on musculoskeletal conditions.

However, the concomitant loss of muscle mass and strength after weight loss may have undesirable effects on physical function and metabolism (Chomentowski et al., 2009; Weiss et al., 2007; Wolfe, 2006); low muscle mass and strength after weight loss are also related to occurrence of musculoskeletal conditions (Toda et al., 2000; Vincent et al., 2012; Wolfe, 2006). Accordingly, it is necessary to decrease fat mass while maintaining muscle mass and strength in order to prevent or improve obesity related musculoskeletal conditions.

It has long been recognized that a decline in muscle strength is a result of decreases in muscle mass, and muscle strength is directly proportional to muscle mass (Doherty, 2001, 2003). However, reports in which muscle strength decline is not correlated with decreases in muscle mass have increased in recent years (Auyeung et al., 2014; Goodpaster et al., 2006; Hughes et al., 2001; Kim et al., 2015; Schaap et al., 2013; Wang et al., 2007).

To date, only a limited number of studies on changes in muscle mass and strength after weight loss have been reported. This is due, in large part, to the fact the importance of muscle mass and strength in the obese men has been underappreciated. Therefore, the purpose of this study was to investigate changes in muscle mass and strength resulting from a weight loss program.

1.2. Literature review

1.2.1. Musculoskeletal conditions related to obesity

As obesity develops, both muscle and fat mass increases (Forbes, 1987; Harris, 1997). Heavier individuals have greater muscle mass, and because muscle strength is related to muscle mass, heavier individuals can generate more muscle strength (Forbes, 1987; Maffiuletti et al., 2007). However, compared to fat mass, the increased quantity in muscle mass is relatively low, and it causes low body weight normalized muscle mass and strength in obese individuals. Excessive body fat mass is a physical burden which compresses load bearing joints such as knees and low back (Andersen et al., 2003; Lementowski and Zelicof, 2008; Vincent et al., 2012). With inadequate body weight normalized muscle mass and strength, less absorption of physical burden on weight-bearing joints occurs, and it is insufficient to endure increased physical burden. Because of this, obese individuals may attempt to compensate for muscle weakness and instability by altering patterns and adopting different body transfer patterns to move body weight.

Hinman et al. (2010) have reported that joint misalignment in the load bearing joints may occur with increased body weight, altered posture, skeletal muscle strength imbalance and weakness in muscles which control joint motion. In addition, skeletal muscle becomes laden with intramuscular fat, and this fat is linked to elevated systemic levels of proinflammatory biomarkers in obese individuals. As the degree of obesity increases, these biomarkers cause a self-propagating process of muscle catabolism and loss of muscle strength (Schrager et al., 2007). Over time, the cumulative effects of excessive body fat, in addition to physical burden on load bearing joints and abnormal joint motion, contribute to the onset in musculoskeletal conditions (Sowers and Karvonen-Gutierrez, 2010).

Obese individuals with musculoskeletal conditions express fear related to conducting weight bearing exercise (Vincent et al., 2010). This fear may contribute to the evasion of weight bearing exercise and subsequent worsening of muscle weakness and obesity (Nebel et al., 2009; Sullivan et al., 2009).

1.2.2. Effects of weight loss in musculoskeletal conditions

Weight loss has been known as the most significant way for prevention and improvement of musculoskeletal conditions and is recommended by American College of Rheumatology (ACR, 2000). As a matter of fact, Messier et al. (2005) have reported that each pound of weight loss lead to a 4-fold reduction in the load exerted on the knee per step. Coggon et al. (2001) and Christensen et al. (2007) have reported the significance of weight loss on musculoskeletal conditions as follow: decrease in body weight by no more than 5 kg may reduce 25 % of cases and lowering BMI to 20-24.9

kg/m^2 may prevent more than 50% of all cases. Achieving 5% of reduction in body weight decreases joint pain and accomplishing 10% reduction in body weight is related to moderate to considerable clinical improvements in joint pain. Considering these reports, there is no doubt that weight loss has positive effects on prevents and improves musculoskeletal conditions.

1.2.3. The concomitant loss in muscle mass and strength after weight loss

Weight loss results not only in decrease in fat mass but also in muscle mass (Chomentowski et al., 2009; Henriksen et al., 2012). Muscle plays a key role in whole body glucose metabolism, therefore decrease in muscle mass can lead to augment of insulin resistance and reduction in capacity for insulin mediated glucose disposal in some case (McGregor et al., 2014).

Since muscle strength is positively associated with muscle mass, steep decline in muscle mass caused by substantial weight loss may decrease muscle strength and then is likely to decrease physical performance (Toda et al., 2000; Weiss et al., 2007). Existing researches have reported that low muscle mass and strength are also related to occurrence of musculoskeletal conditions. Conventional wisdom and experimental data suggest that muscles serve as shock absorbers in human body (Hill, 1960). As recognized from this report, ground-reaction forces and related rates of loading during physical activity are increased in combination with decline in muscle mass and strength (Mikesky et al., 2000). Furthermore, it has been reported that muscle mass is an independent predictor of medial-tibial cartilage volume and is linked to a reduction in the rate of tibial cartilage (Cicuttini et al., 2005).

On the one hand, recent researches have reported that decline in muscle strength seem to be a better indicator for poor cardio-respiratory function, functional limitations and mortality that that in muscle mass (Barbat-Artigas et al., 2012; Rantanen, 2003; Visser et al., 2000). In the light of these reports, it is essential to maintain muscle mass and strength during weight loss.

1.2.4. Effects of aerobic or resistance exercise on muscle mass and strength

For maintenance or improvement in muscle mass and strength, resistance exercise has been widely recommended, whereas aerobic exercise has not been suggested for a long period of time (Braith and Stewart, 2006; Bryner et al., 1999; Castaneda et al., 2002; Davidson et al., 2009; Donnelly et al., 2009; Schmitz et al., 2003; Sigal et al., 2007; Willis et al., 2012). Recent researches have reported, however, that moderate aerobic exercise attenuates the loss of muscle mass during caloric restriction as well as accelerates body weight and fat mass loss (Chomentowski et al., 2009; Yoshimura et al., 2014). If so, moderate aerobic exercise may have positive effects on maintaining muscle strength. For the present, it has not become obvious.

There are conflicting reports on whether resistance exercise induces decrease in fat mass. Schmitz et al. (2003) found that resistance training causes significant reduction in fat mass and potential mechanisms how resistance training lead to fat mass loss have been reported by American College of Sports Medicine (Donnelly et al., 2009). However, other previous researches did not find a significant trend or changes in fat mass (Castaneda et al., 2002; Davidson et al., 2009; Olson et al., 2007; Sigal et al., 2007). Given these reports, it is necessary to explore the effects of aerobic and resistance exercise on body composition and strength in obese individuals. In addition, the objects in these existing researches are European or American. It is widely accepted that they have more muscle mass and strength than Japanese. Therefore, the study of changes in muscle mass and strength is needed in Japanese obese men after resistance or aerobic exercise.

1.2.5. The relation between muscle mass and strength

In general, muscle strength is defined as the force-producing capacity of muscle. The association between muscle strength and functional impairments triggers interest in understanding the causes and mechanisms. Absolute muscle strength is the easiest way to show muscle strength, whereas relative muscle strength (muscle strength per body weight or muscle mass) may be more relevant to indicate the functional impairments (Barbat-Artigas et al., 2012; Ploutz-Snyder et al., 2002). Muscle strength per body weight or muscle mass has been widely employed to determine muscle quality (Barbat-Artigas et al., 2012; Goodpaster et al., 2006; Wang et al., 2007).

As cited above, it has been commonly considered that a decline in muscle strength is a result of decreases in muscle mass, and muscle strength completely depends on muscle mass. However, recently, reports in which muscle strength decline does not completely depend on decreases in muscle mass have increased (Auyeung et al., 2014; Doherty, 2001, 2003; Goodpaster et al., 2006; Hughes et al., 2001; Schaap et al., 2013; Wang et al., 2007).

1.3. Purpose

The purpose of this study was to investigate changes in muscle mass and strength, an appropriateness of the changes and the relation between muscle mass and strength after completing weight loss program. In order to fulfill this purpose (1) a cross-sectional study to investigate the relation between obesity and characteristics of muscle mass and strength in obese male adults. (2) Intervention studies to investigate changes in muscle mass and strength, and the relation between muscle mass and strength after completing weight loss program. For that, three different kinds of intervention were executed as follows: (2-1) weight loss program with dietary modification, (2-2) weight loss program with aerobic or resistance exercise, (2-3) weight loss program consisting of dietary modification and exercise. (3) Finally, one-year follow-up study for participants in weight loss program consisting of dietary modification and exercise to investigate whether weight loss leads to detrimental decreases in muscle mass, muscle strength that could lead to health problems was conducted.

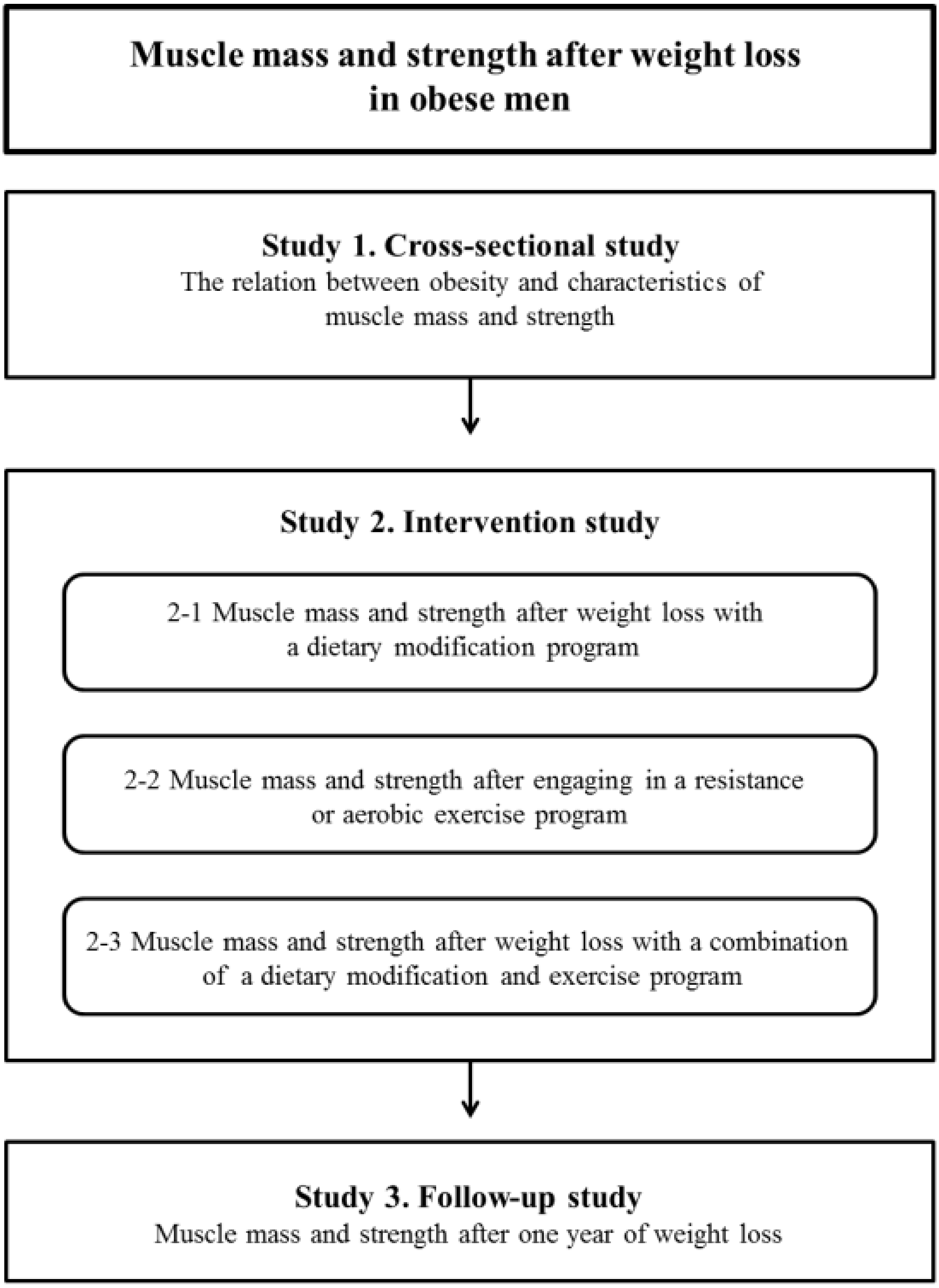


Figure 1. Flow of the studies in the doctoral thesis

1.4. Significance

First of all, it should be stated that this is the first study in which Japanese obesity guidelines have been used to study the relation between obesity and characteristics of muscle mass and strength in adult males. The results in this thesis can be used as a reference to characteristics of muscle mass and strength in obese male adults. It would promote understanding the characteristics of body composition and muscle strength in obese individuals.

Second, it would be possible to suggest a desirable weight loss program which minimizes decrease in muscle mass and strength while maximizing fat mass loss. The effects of resistance exercise on fat mass and change in muscle strength after performing aerobic exercise are unclear. There were a lot of existing researches which evaluated body composition after weight loss. However, at present, muscle strength is not fully evaluated though recent researches have reported that decline in muscle strength seem to be a better indicator for poor cardio-respiratory function, functional limitations and mortality (Barbat-Artigas et al., 2012; Rantanen, 2003; Visser et al., 2000).

Third, it has long been believed that the concomitant loss of muscle mass and strength after weight loss may cause adverse effects. However, before the onset of this thesis, there have been no reports on whether weight loss leads to detrimental decreases in muscle mass and muscle strength that could lead to health problems. This study would clear it.

1.5. Definition of terms

1.5.1. Obesity

Obesity is defined as BMI $\geq$ 25 kg/m^2 in this study according to the definition of obesity in Japan Society for the study of Obesity. It should be noted, however, that Body mass index ≧ 30 kg/m^2 is defined as obese by the World Health Organization.

1.5.2. Muscle mass

Muscle tissue is a soft tissue, and is one of the four fundamental types of tissue present in animals. There are three types of muscle tissue such as skeletal muscle, smooth muscle, and cardiac muscle. In the present study, a quantity of skeletal muscle is defined as muscle mass. (Mackenzie, 1918)

1.5.3. Muscle strength

Muscle strength is a capacity of muscle to produce force. It can be assessed through either a static (isometric) or dynamic (isokinetic) contraction. Isometric assessment reveals the amount of tension a muscle can generate against a resistance permitting no observable joint movement. Isokinetic assessment, muscle contraction at constant rate of speed, has been used to quantity a muscle group's ability to generate torque or force. (perrin, 1993)

CHAPTER 2. GENERNAL METHOD

2.1. Cross-sectional study

In the study 1, cross-sectional study was performed to investigate the relation between obesity and characteristics of muscle mass and strength.

2.1.1. Ethical consideration

We performed this study in accordance with the guidelines proposed in the Declaration of Helsinki, and the study protocol was approved by the Ethics Committee of the University of Tsukuba, Japan. Every participant was explained verbally and by document, regarding the purpose of the study, muscle mass and strength assessments, and handling of the data including anonymity. It was also clarified that their consent was based on free will and could be withdrawn any time without disadvantage. Confirming these points, the participants provided written informed consent.

2.1.2. Setting and participants

A total of 259 Japanese male adults, aged 30-64 years, were recruited by advertising in local newspapers in Ibaraki in 2012-2015. The required study inclusion criteria were as follows: 1) males aged 30-64 years; 2) no terminal disease, recent muscle injury, or surgery; 3) no history of drug or alcohol abuse.

2.1.3. Assessments

2.1.3.1. Anthropometric variables

Height was assessed to the nearest 0.1 cm using a wall-mounted stadiometer (YG-200; Yagami, Nagoya, Japan), and body weights, in light clothing and without shoes, were assessed to the nearest 0.1 kg using a digital scale (TBF-551; Tanita, Tokyo, Japan). BMI value was calculated as weight (in kg) divided by height (in m) squared

2.1.3.2. Body composition

Body composition was assessed using whole-body dual energy x-ray absorptiometry (DEXA; QDR 4500, Hologic Inc., Bedford, MA). Participants lay supine with the arms held against the sides of the body. Hologic software was employed to estimate the fat, lean, and bone tissue masses (in kg). Extended analyses were performed to obtain separate fat, lean and bone tissue masses for the arms, legs, and trunk. As for skeletal muscle mass evaluation, existing studies have reported as follows: computerized axial tomography and magnetic resonance imaging are the most accurate methods of assessing skeletal muscle mass (Wang et al., 1996). DEXA closely agreed with skeletal muscle mass assessed by CT, although DEXA tend to systematically overestimate skeletal muscle mass by ~5% (Wang et al., 1996). Especially, lean mass, excluding bone mineral content, is a valid representation of skeletal muscle mass in the extremities (Heymsfield et al., 1990; Visser et al., 1999). We calculated the appendicular skeletal muscle mass of each participant as the sum of the lean mass, excluding bone mineral content, of both upper and lower extremities. A height-adjusted index was then calculated by dividing a participant's appendicular skeletal muscle mass in kg by the square of his or her height in m (m^2) (Heymsfield et al., 2007; Kelly et al., 2009; Sanada et al., 2010). We defined the height-adjusted appendicular skeletal muscle index as the skeletal muscle mass index (SMI). The percentage of muscle mass index (% MMI) was calculated by dividing a participant's appendicular skeletal muscle mass in kg by 100 × his weight.

2.1.3.3. Muscle strength

To evaluate muscle strength, we measured handgrip strength for the upper extremity and knee extensor strength for the lower extremity. Handgrip strength (HGS) has been widely adopted to evaluate muscle strength because it is easy to measure. Measuring knee extensor strength is especially important (Andersen et al., 2003; Lementowski and Zelicof, 2008; Maffiuletti et al., 2007) because it evaluates the femoral muscle at the most common site of musculoskeletal conditions. HGS and knee extensor strength were measured and evaluated as follows.

2.1.3.3.1. Handgrip strength

Participants gripped a dynamometer (Grip-D, T.K.K. 5401; Takei Scientific Instruments, Tokyo, Japan) in each hand, alternately, with maximum effort, while lowering the arm naturally to the side of the body (Shinkai S, 2003). The assessment was executed twice in each hand, and the best result was recorded as the HGS for each hand. Handgrip strength was expressed as an absolute, body weight-normalized, and arm muscle mass-normalized value.

2.1.3.3.2. Knee extensor strength

Isometric and isokinetic knee extensor strengths were assessed using a Biodex System 3 dynamometer (Biodex Medical Systems, Shirley, NY). Participants performed warm-up and cool-down exercises with experienced staff before and after the tests to prevent injury and muscular pain. A 3-min rest was allowed between the isometric and isokinetic assessments. The participants were seated in the Biodex System 3 dynamometer tightly secured by the chest, pelvis and thigh straps, with the back supported and the hips flexed at 120°. The axis of rotation of the knee and the Biodex System 3 dynamometer were precisely aligned before each test by visual inspection. The knee was extended to 60° for the isometric assessment because this angle provides the quadriceps with close-to-optimum muscle lengths to produce maximal force

(Henriksen et al., 2012). The protocol in the isometric assessment consisted of 3 maximal extension efforts, each lasting 3 seconds, with intervening 15-second pauses. The isokinetic assessment comprised 3 maximal extensions at an angular velocity of 60°/s, as is widely employed for isokinetic muscle strength evaluation. The highest muscular force output at any moment during the assessment was defined as the peak torque and is reported in absolute terms (Nm) and normalized to body weight, represented as the body-weight-normalized (Nm/kg) peak torque. The amount of work accomplished for an entire assessment is defined as the total work and is reported as an absolute (W), whereas the average of total work divided by time defines the average power and is reported as an absolute value (J). Every assessment was performed on each leg, and the average strength in both legs was calculated for the lower-extremity muscle strength. The results were expressed as an absolute, body weight-normalized, and leg muscle mass-normalized value.

2.2. Intervention studies

2.2.1. Study design

In the study 2, three different kinds of intervention studies were performed to investigate changes in muscle mass and strength after weight loss program. For study 2-1, obese men took part in a 12-week dietary modification program. Data were obtained with assessments executed before and after the program. The main outcomes in the present study were the effects of weight loss with dietary modification program on muscle mass and strength. Study 2-2 was a 2-armed intervention trial which focused on examining the short-term effects of aerobic exercise or resistance exercise over a 12-week intervention. Study 2-3 was that obese men took part in a 12-week weight loss program consisting of a dietary modification and a comprehensive exercise program. Every assessment was executed before beginning the weight loss program and repeated within 2 weeks after completing the weight loss program.

2.2.2. Ethical consideration

The study protocol was developed in accordance with the guidelines proposed in the Declaration of Helsinki and was approved by the Research Ethics Committee of the Faculty of Health and Sport Sciences of the University of Tsukuba, Japan.

2.2.3. Setting and participants

The trials were conducted at the University of Tsukuba, five times from 2012 to 2015. Study participants were recruited from communities which are advertised in local newspapers and distributing study flyers. The eligibility criteria for study 2 were as follows: 1) body mass index (BMI) ≥ 25 kg/m^2 according to the Japanese obesity guidelines; 2) males aged between 30 and 64 years; 3) not to decrease body weight greater than 5 % in the past 12 months, intentionally; 4) no terminal disease, recent muscle injury, or surgery and not to restricted from exercising by a doctor; 5) not to engage in exercise frequently. Applicants were excluded if they were applicable to any of those criteria and had taken part in another clinical trial during previous years. The numbers of participants were decided according to the capacity and safety of the program. If a participant was unable to take part in the allocated program after he was informed of what program he took part in, he was excluded from the study and considered to be dropped out. We then held an explanatory meeting for the included study participants and obtained written informed consent.

2.2.4. Intervention program

2.2.4.1. Dietary modification program

We performed a 12-week dietary modification program focused at positively influencing the participant's dietary modification. This program was on the basis of the Four-Food-Group Point Method and each group based instructional session was run for 90 min, and held 8 times during 12 weeks (Kagawa, 1983). As shown in Fig. 2, in the Modified Four-Food-Group Point Method, diet was divided into four food groups based

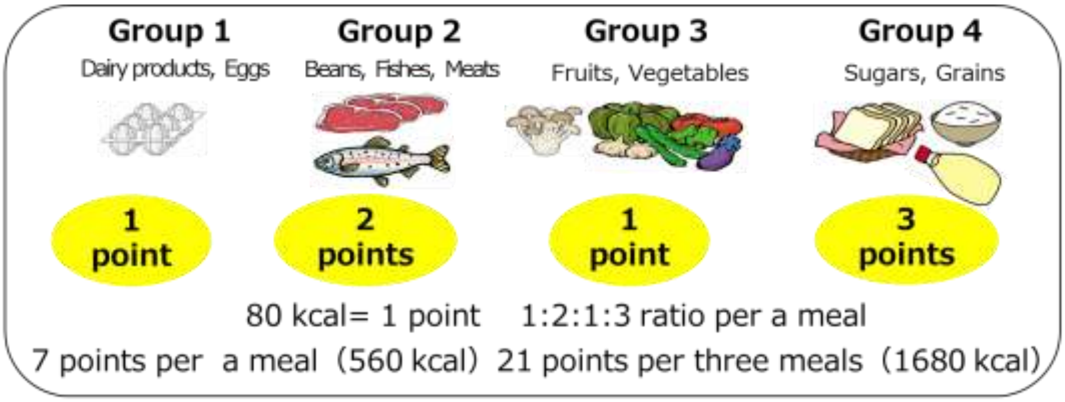


Figure 2. Modified Four-Food-Group Point Method

on nutrient content as follow: group 1 (dairy products and eggs), group 2 (beans, fish and meat), group 3 (fruits and vegetables) and group 4 (sugar and grains). For concise nutrient balance calculations and energy intake, all foods were portioned into 80 kcal amounts and each portion was regarded as 1 point. Participants selected 1, 2, 1 and 3 points value of diverse food in the Four-Food-Group, respectively, to ingest a well-balanced daily diet. Accordingly, participants ingested approximately a total of 21 points which corresponded to approximately 1,680 kcal/day. Participants maintained a daily food diary in which they recorded all the food they ate. At each class, the dieticians reviewed the participants' diaries and provided participants with individualized feedback regarding energy intake and nutritional balance.

2.2.4.2. Aerobic exercise program

Every participant took part in a 90-min aerobic exercise program 3 days/week for 12 weeks. Each session began with 10-20 min of warm-up activities such as stretching. This was followed by the main exercise, 40-60 min of brisk walking and jogging in the outdoors. On rainy days, indoor exercise using stationary cycling and lad-der climbing was the main exercise. Each session concluded with 10-20 min of resistance exercise with body weight and cool-down exercises. Every exercise was executed under the supervision of several trained physical trainers at the University of Tsukuba. Participants were encouraged to exercise at their maximum heart rates' level or near their maximum heart rates' level. Heart rates were monitored by short-range telemetry (Polar RS400, Kempele, Finland). This method has been previously described in detail elsewhere (Nakata, 2003; Okura et al., 2003; Sasai et al., 2009).

2.2.4.3. Resistance exercise program

It was run 3 days/week for 12 weeks. Before the beginning of resistance exercise program, 1 RM muscle strength assessment was executed to adjust the load in resistance training machine and around 50% of 1 RM muscle strength was adopted for the load. Exercise was began and done with 15 min of warm up and cool down, and conducted on six resistance exercise machine (Techno Gym) for 60 min. The resistance program consisted of three sets of the following seven exercise: crunch, high lat pull down, seated low, chest press, leg press, leg extension and leg curl. Participants conducted 10-12 repetitions to failure for each set except crunch. Crunch was performed with their body weight around 15 repetitions. Participants could get 1-2 min rest between each set. When participants could easily performed the recommended repetitions, the load was inclined. Our trainers gave them verbal encourage to ensure that participants performed to volitional fatigue.

2.2.5. Assessments

At baseline, information regarding clinical history, medication use and lower back or knee pain over the past year were collected. Items and method of assessments used to assess the effects of interventions were described here after.

2.2.5.1. Anthropometric variables

The detail methods of each measurement has been described previously (see 2.1.3.1, in page 18).

2.2.5.2. Body composition

The detail methods of each measurement has been described previously (see 2.1.3.2, in page 18-19).

2.2.5.3. Muscle strength

2.2.5.3.1. Handgrip strength

The detail methods of each measurement has been described previously (see 2.1.3.3.1, in page 20).

2.2.5.3.2. Knee extensor strength

Biodex System 3 (Biodex Medical Systems, Shirley, NY) was used to assess isometric and isokinetic knee extensor strength. The knee was extended to 60° for the isometric assessment because this angle provides the quadriceps with close-to-optimum muscle lengths to produce maximal force.(Henriksen et al., 2012) The protocol in the isometric assessment consisted of 3 maximal extension efforts, each lasting 3 seconds, with intervening 15-second pauses. We surmised that there might be a possibility of different results in isokinetic assessments when angular velocities were different. Therefore, we assessed isokinetic muscle strength at different angular velocities. Angular velocities of 60°/s and 180°/s have been widely used in isokinetic assessments to evaluate isokinetic muscle strength. In the isometric assessment, the protocol consisted of 3 maximal efforts (each extension lasted 3 seconds), with a 15-second pause between extensions. In the isokinetic assessment of angular velocity at 60°/s and 180°/s, participants executed 3 and 12 maximal extensions, respectively. The highest muscular force output at any moment during a repetition was defined as the peak torque, reported in absolute terms (Nm), and normalized to body weight, represented as body weight-normalized (Nm/kg) peak torque. The amount of work accomplished for an entire assessment was defined as the total work and was reported as an absolute (W), whereas the average of total work divided by time defines the average power and was reported as an absolute value (J). Every assessment was performed on each leg, and the average strength in both legs was calculated for the lower-extremity muscle strength. The results were expressed as an absolute, body weight-normalized, and leg muscle mass (LMM)-normalized value.

2.3. Follow-up study

2.3.1. Study design

This study was a one-year follow-up of a prospective study designed to investigate long-term effects of changes in muscle mass and strength resulting from a weight loss program consisting of dietary modification and comprehensive exercise program.

2.3.2. Ethical consideration

This study was performed in accordance with the Declaration of Helsinki guidelines, and the study protocol was reviewed and approved by the Ethics Committee of the University of Tsukuba, Japan.

2.3.3. Setting and participants

To investigate the appropriateness of the changes in muscle mass and strength after the weight loss, we compared the physical parameters in the weight loss program participants with those of a reference group at the completion of the weight loss program and at a year after completion of the weight loss program. The Japanese obesity guidelines define obesity as a BMI $\geq$ 25 kg/m^2. On the basis of this guideline, the participants who decreased their BMI to less than 25 kg/m^2 during the weight loss program and maintained their BMI at less than 25 kg/m^2 one year after the weight loss program were defined as the analysis subjects. Individuals who have not experienced intentional weight loss and whose BMI have not exceeded 25 kg/m^2 were defined as the reference group.

2.3.4. Assessments

Variables and methods of assessments used to evaluate the long term effects resulting from a weight loss program consisting of dietary modification and exercise were previously described in 2.1.3, in page 18-21.

CHAPTER 3. STUDY 1. Cross-sectional study

The relation between obesity and characteristics of muscle mass and strength

3.1. Purpose

The purpose of this study was to assess the association between obesity and characteristics of muscle mass and strength.

3.2. Methods

3.2.1. Study design

A total of 259 Japanese males aged 30-64 years were recruited via advertising in local newspapers in Ibaraki from 2012-2015. The participants were classified into groups A (Non-obese, n = 60), B (Obesity class I, n = 142), C (Obesity class II, n = 47) and D (Obesity class III, n = 10) based on Japanese obesity guidelines (Examination Committee of Criteria for 'Obesity Disease' in Japan, 2002).

3.2.2. Assessment variables

Body composition was evaluated as follows: whole body lean mass, whole body fat mass, percentage of whole body fat, arm muscle mass, leg muscle mass, skeletal muscle mass index and percentage of muscle mass index. Handgrip strength and knee extensor strength which evaluated muscle strength in upper and lower extremity was expressed as an absolute, body weight-normalized, and arm and leg muscle mass-normalized value.

3.3. Statistical analyses

Values are expressed as the means ± standard deviations (SDs) or standard errors (SEs). We used one-way analysis of variance (ANOVA) to analyze the differences between groups. One-way analysis of covariance (ANCOVA), with age as a covariate, was utilized to test for differences in mean body composition and muscle strength among the four groups. We applied the Bonferroni post hoc test when the ANCOVA results exhibited significant differences ($P < 0.05$). The Jonckheere-Terpstra test was used to assess the trends among the values in the four groups. The Jonckheere-Terpstra test was also employed to assess the trends of muscle mass and strength with aging. The trend test was 2-tailed, with a significance level of $P < 0.05$. SPSS software, version 18.0 (IBM, Inc., Armonk, NY, USA), was used for the statistical analyses.

3.4. Results

The anthropometric characteristics and trends among the 4 groups are presented in Table 1. The ANOVA results demonstrated that body weight and BMI differed significantly among the 4 groups. A progressive trend toward decreasing age from group A to group D was observed (standardized statistic = -2.43, $P < 0.05$).

To evaluate the trends of muscle mass and strength with aging, the trends of whole body lean mass and knee extensor strength in isokinetic 60°/s were employed, respectively. As described in Fig 3 and 4, significant decreasing trends of muscle mass and strength with aging were detected (standardized statistic = -3.46 and -7.19, respectively; $P < 0.01$ for both).

Table 2 presents the body composition results for the 4 groups. To avoid the influence of age on the results, ANCOVA was performed with age as a covariate. The post hoc tests demonstrated significant differences among the 4 groups for all variables. Groups A, B, C and D ranked in descending order for all variables except % MMI. The trend test also demonstrated increases from group A to group D for all variables except % MMI (standardized statistic = 10.40, 13.35, 9.78, 8.34, 7.16, 9.05, respectively; $P < 0.01$ for all). The % MMI trended in the opposite direction for all other variables (standardized statistic = -7.03; $P < 0.01$). These results indicate that both body fat and muscle mass increase in parallel with obesity.

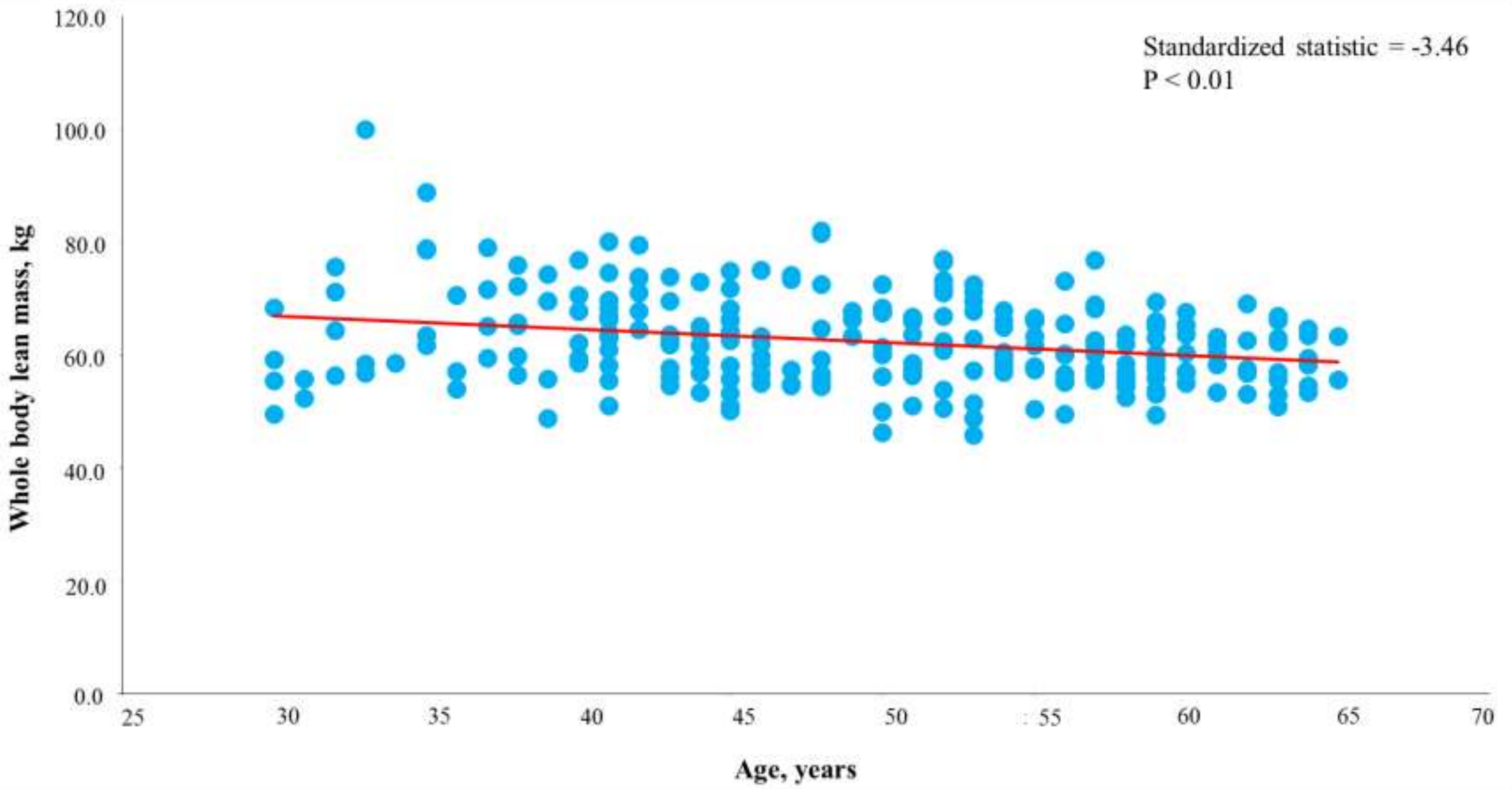
Table 3 presents the muscle strength for the 4 groups. Multiple comparisons demonstrated significant differences among the 4 groups for all variables except LMM normalized strength. Although there was no trend in the absolute values of handgrip strength among groups A to D, the handgrip strength values normalized for body weight and AMM exhibited a statistically significant trend (standardized statistic = -8.82 and -6.66, respectively; $P < 0.01$ for both). The leg muscle strength absolute values did not differ significantly between groups A and B or between groups C and D but were significantly higher in groups C and D than in groups A and B. The trend test indicated that the absolute muscle strength value for each leg increased progressively from group A to group D (standardized statistic = 6.41, 6.30, 6.18, 5.32, respectively; $P < 0.01$ for all). When leg muscle strength was normalized for body weight, there were no significant differences among groups B, C and D aside from IKT60 AP/Body weight, although their values were significantly lower than those for group A. Although the IKT60 AP/Body weight values for groups A, B, C and D were ranked in ascending order, no significant differences were observed between groups B and C or between groups C and D. IKT60 AP/Body weight was significantly higher in group A than in groups B, C and D. When analyzed for trend, the decrease in the body-weight-normalized leg muscle strength from group A to group D was statistically significant (standardized statistic = -3.08, -3.15, -3.23, -3.09, respectively; $P < 0.01$ for all). The mean values for groups A, B and C did not differ significantly, although each was significantly higher than the value for group D. These results indicate that leg muscle strength correlates positively with increasing obesity, but the increases in leg muscle strength that accompany increases in obesity do not improve body weight-normalized leg muscle strength.

Table 1 Anthropometric characteristics and trends among four groups

	A. Non obesity (95% CI) (n = 60)		B. Obesity class Ⅰ (95% CI) (n = 142)		C. Obesity class Ⅱ (95% CI) (n = 47)		D. Obesity class Ⅲ (95% CI) (n = 10)		post hoc	Standardized statistic[b]
Age, year	50.9 ± 9.3	(48.5, 53.3)	50.3 ± 9.0	(48.8, 51.8)	47.7 ± 8.6	(45.2, 50.2)	44.0 ± 8.5	(37.9, 50.1)	Ns	-2.43[†]
Height, cm	171.4 ± 5.7	(169.9, 172.9)	171.5 ± 6.1	(170.5, 172.5)	171.6 ± 5.3	(170.1, 173.2)	172.8 ± 6.4	(168.2, 177.3)	Ns	0.36
Body weight, kg[*]	69.0 ± 6.1	(67.4, 70.6)	80.7 ± 6.9	(79.6, 81.8)	94.1 ± 7.7	(91.8, 96.4)	119.8 ± 19.3	(106.0, 133.6)	A < B < C < D	13.95[††]
BMI, kg/m^2[*]	23.5 ± 1.3	(23.1, 23.8)	27.4 ± 1.4	(27.2, 27.7)	31.9 ± 1.4	(31.5, 32.3)	40.0 ± 4.9	(36.5, 43.5)	A < B < C < D	16.29[††]

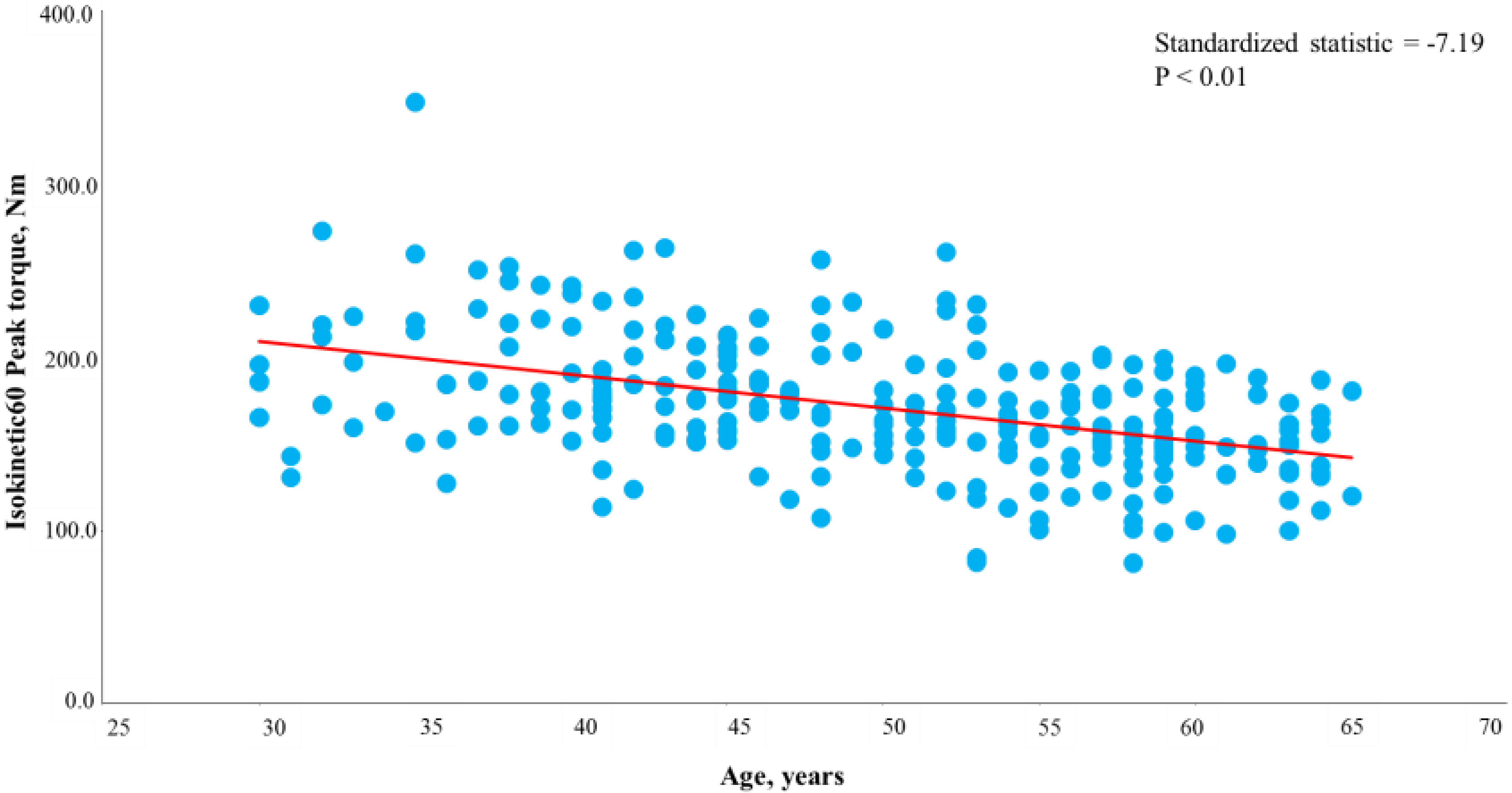
NOTES: Values are means ± SD. Significant group differences were found among four groups ([*] $P < 0.05$). Significant trend was found among four groups ([†] $P < 0.05$, [††] $P < 0.01$). [b]Jonckheere-Terpstra test was used to assess the trend among four groups. NS = not significant; BMI = body mass index

Figure 3. The trend of muscle mass with aging



Note: To evaluate the trend of muscle mass with aging, the trend of whole body lean mass was employed.

Figure 4. The trend of muscle strength with aging



Note: To evaluate the trend of muscle strength with aging, the trend of knee extensor strength in isokinetic 60 °/s was employed.

Table 2 Characteristics and trends of body composition among four groups

	A. Non obesity (95% CI) (n = 60)		B. Obesity class Ⅰ (95% CI) (n = 142)		C. Obesity class Ⅱ (95% CI) (n = 47)		D. Obesity class Ⅲ (95% CI) (n = 10)		post hoc	Standardized statistic[b]
Whole body lean mass, kg*	56.6 ± 0.8	(55.1, 58.0)	61.7 ± 0.5	(60.7, 62.6)	68.9 ± 0.9	(67.2, 70.6)	76.8 ± 1.9	(73.1, 80.4)	A < B < C < D[a]	10.40††
Whole body fat mass, kg*	13.3 ± 0.5	(12.3, 14.3)	19.6 ± 0.3	(18.9, 20.2)	24.5 ± 0.6	(23.4, 25.7)	34.9 ± 1.3	(32.4, 37.4)	A < B < C < D[a]	13.05††
% whole body fat, %*	18.9 ± 0.5	(18.0, 19.9)	23.9 ± 0.3	(23.3, 24.5)	26.0 ± 0.5	(25.0, 27.1)	30.3 ± 1.2	(28.0, 32.6)	A < B < C, D	9.78††
AMM, kg*	5.9 ± 0.1	(5.7, 6.1)	6.4 ± 0.1	(6.3, 6.6)	7.3 ± 0.1	(7.0, 7.5)	7.7 ± 0.3	(7.2, 8.2)	A < B < C, D[a]	8.34††
LMM, kg*	17.5 ± 0.3	(16.8, 18.1)	18.7 ± 0.2	(18.3, 19.2)	20.8 ± 0.4	(20.0, 21.6)	23.1 ± 0.9	(21.4, 24.8)	A < B < C, D[a]	7.16††
SMI, kg/m^{2*}	7.9 ± 0.1	(7.7, 8.2)	8.5 ± 0.1	(8.4, 8.7)	9.6 ± 0.1	(9.3, 9.8)	10.5 ± 0.3	(9.9, 11.1)	A < B < C < D[a]	9.05††
% MMI, %*	33.7 ± 0.4	(32.9, 34.5)	31.1 ± 0.3	(30.6, 31.7)	30.0 ± 0.5	(29.1, 30.9)	26.4 ± 1.0	(24.4, 28.4)	A > B, C > D	-7.03††

NOTES: Values are means ± SE. Significant group differences were found among four groups (* $P < 0.05$). Significant trend was found among four groups († $P < 0.05$, †† $P < 0.01$). [a]Kruskal Wallis permutation test was consistent with the ANCOVA analysis. [b]Jonckheere-Terpstra test was used to assess the trend among four groups. % whole body fat = percentage of whole body fat; AMM = Arm muscle mass; LMM = Leg muscle mass; SMI = Skeletal muscle index; % MMI = percentage of muscle mass Index

Table 3 Characteristics and trends of muscle strength and physical performance among four groups

	A. Non obesity (95% CI)		B. Obesity class Ⅰ (95% CI)		C. Obesity class Ⅱ (95% CI)		D. Obesity class Ⅲ (95% CI)		post hoc	SS[b]
	(n = 60)		(n = 142)		(n = 47)		(n = 10)			
HGS, kg*	43.49 ± 0.88	(41.77, 45.22)	42.14 ± 0.57	(41.02, 43.26)	45.69 ± 0.99	(43.73, 47.65)	44.18 ± 2.16	(39.93, 48.43)	B < C	1.45
HGS/BW, kg*	0.63 ± 0.01	(0.61, 0.65)	0.52 ± 0.01	(0.51, 0.54)	0.49 ± 0.01	(0.47, 0.51)	0.38 ± 0.03	(0.33, 0.43)	A > B, C > D	-8.82††
HGS/AMM, kg*	7.42 ± 0.12	(7.20, 7.65)	6.59 ± 0.08	(6.44, 6.74)	6.31 ± 1.13	(6.05, 6.57)	5.89 ± 0.29	(5.33, 6.46)	A > B, C, D	-6.66††
IMT60 PTQ, Nm*	182.35 ± 4.91	(172.68, 191.01)	194.78 ± 3.19	(188.50, 201.06)	226.51 ± 5.56	(215.56, 237.46)	235.67 ± 12.09	(211.86, 259.49)	A, B < C, D	6.41††
IMT60 PTQ/BW, Nm/kg*	2.63 ± 0.06	(2.52, 2.75)	2.41 ± 0.04	(2.34, 2.49)	2.42 ± 0.07	(2.29, 2.54)	1.97 ± 0.14	(1.70, 2.25)	A > B, C, D[a]	-3.08††
IMT60 PTQ/LMM, Nm/kg	10.59 ± 0.28	(10.03, 11.15)	10.51 ± 0.19	(10.15, 10.87)	10.97 ± 0.32	(10.34, 11.60)	10.43 ± 0.70	(9.06, 11.81)	Ns	1.13
IKT60 PTQ, Nm*	156.23 ± 4.08	(148.20, 164.26)	169.12 ± 2.65	(163.91, 174.34)	192.30 ± 4.62	(182.21, 201.40)	203.31 ± 10.05	(183.52, 223.09)	A, B < C, D	6.30††
IKT60 PTQ/BW, Nm/kg*	2.26 ± 0.05	(2.16, 2.35)	2.10 ± 0.03	(2.03, 2.16)	2.04 ± 0.05	(1.94, 2.15)	1.72 ± 0.12	(1.48, 1.95)	A > C, A > B > D	-3.15††
IKT60 PTQ/LMM, Nm/kg	9.04 ± 0.25	(8.56, 9.53)	9.13 ± 0.16	(8.82, 9.45)	9.34 ± 0.28	(8.80, 9.89)	9.00 ± 0.60	(7.81, 10.19)	Ns	1.08
IKT60 TW, J*	440.22 ± 11.77	(417.04, 463.39)	472.44 ± 7.64	(457.39, 487.49)	535.28 ± 13.33	(509.03, 561.53)	592.18 ± 28.99	(535.08, 649.27)	A, B < C, D	6.18††
IKT60 TW/BW, J/kg	6.36 ± 0.14	(6.08, 6.64)	5.86 ± 0.09	(5.68, 6.04)	5.70 ± 0.16	(5.39, 6.01)	5.02 ± 0.35	(4.34, 5.71)	A > B, C, D	-3.23††
IKT60 TW/LMM, J/kg	25.47 ± 0.66	(24.16, 26.77)	25.45 ± 0.43	(24.60, 26.30)	26.06 ± 0.75	(24.57, 27.54)	26.16 ± 1.64	(22.94, 29.38)	Ns	1.02
IKT60 AP, W*	97.47 ± 2.81	(91.94, 103.01)	103.53 ± 1.82	(99.93, 107.78)	117.26 ± 3.18	(110.99, 123.53)	130.57 ± 6.92	(116.94, 144.20)	A, B < C, D	5.32††
IKT60 AP/BW, W/kg*	1.41 ± 0.03	(1.34, 1.48)	1.28 ± 0.02	(1.24, 1.33)	1.25 ± 0.04	(1.17, 1.32)	1.10 ± 0.08	(0.94, 1.27)	A > B, C, D	-3.09††
IKT60 AP/LMM, W/kg	5.65 ± 0.16	(5.33, 5.97)	5.59 ± 0.11	(5.38, 5.80)	5.69 ± 0.19	(5.33, 6.05)	5.78 ± 0.40	(4.99, 6.67)	Ns	0.75

NOTES: Values are means ± SE. Significant group differences were found among four groups (*P < 0.05). Significant trend was found among four groups (†P < 0.05, ††P < 0.01). [a]Kruskal Wallis permutation test was consistent with the ANCOVA analysis. [b]Jonckheere-Terpstra test was used to assess the trend among four groups. NS = not significant; HGS = Handgrip strength; BW = Body weight; AMM = Arm muscle mass; LMM = Leg muscle mass; IMT60 PTQ = Isometric60 peak torque; IKT60 PTQ = Isokinetic60 peak torque; IKT60 TW = Isokinetic60 total work; IKT60 AP = Isokinetic60 average power; SS = Standardized statistic

3.5. Discussion

Our primary finding was that body fat and muscle mass increased as obesity progressed. Leg muscle strength correlated positively with obesity; however, increases in leg muscle strength without weight loss might not improve body weight-normalized leg muscle strength. Cross-sectional and interventional research showed positive correlations between the loss of muscle mass and strength and musculoskeletal conditions and between the amelioration of musculoskeletal conditions and muscle strengthening with resistance training (Gur et al., 2002; Lange et al., 2008; Penninx et al., 2001; Slemenda et al., 1998; Vincent and Vincent, 2012). However, the findings of the present study indicate that an increase in muscle strength requires an increase in muscle mass, which in turn increases body fat.

Body weight is a major determinant of muscle mass, and lean mass correlates positively with body fat (Forbes, 1987; Harris, 1997). We observed that SMI tended to increase as obesity increased and that % whole-body fat increased as whole-body lean mass increased. These findings are consistent with the observation that heavier adult males have more muscle mass, and because muscle strength correlates positively with muscle mass, heavier adult males generate more muscle strength.

Maffiuletti et al (2007) reported that adult males with a BMI > 40 kg/m^2 had

18% more lean mass and created significantly more leg muscle power and maximum muscle strength (16-20%) compared with adult males with a BMI < 25 kg/m^2. This finding is consistent with the results of our study. A possible explanation for this finding is that the heavier body weights of obese adults serve as a training stimulus to gain muscle mass and, consequently, to increase muscle strength (Duche et al., 2002; Harris, 1997; Hulens et al., 2002; Hulens et al., 2001). Because the lower extremities' muscles must maintain and support all of the body's weight, these muscles are stimulated more strongly than those of the upper extremities. This condition likely accounts for the absence of significant obesity-related increases in handgrip strength despite increases in every absolute value of leg muscle strength.

Body weight-normalized leg muscle strength is significantly lower in obese men than in non-obese men (Andersen et al., 2003; Hulens et al., 2001). As the trend test indicated, the increase in whole-body fat mass (standardized statistic = 13.05) with increasing obesity was greater than the increase in whole-body lean mass (standardized statistic = 10.40). Excessive increases in body fat are a physical burden on the musculoskeletal system; as obesity develops, the amount of whole-body fat increases faster than whole-body lean mass does.

This was the first study in which Japanese obesity guidelines were used to study the relationship between obesity and muscle mass and strength in adult males. Although this cross-sectional study characterized the basis of the relationship between obesity and muscle mass and strength, scientific evidence of the relationship is limited. Consequently, long term and prospective studies will be needed to explore the mechanisms involved.

3.6. Conclusion

Both body fat and muscle mass increase as obesity develops. Muscle mass and strength correlate positively with obesity. In the presence of obesity, increases in LMM and strength may not improve body weight-normalized muscle strength. From these results, it is recognized that it is easier to prevent and ameliorate musculoskeletal conditions with weight loss than with increased muscle mass and strength.

CHAPTER 4. STUDY 2. Intervention studies

2-1. Changes in muscle mass and strength after weight loss with dietary modification

2-2. Changes in muscle mass and strength after executing resistance or aerobic exercise

2-3. Changes in muscle mass and strength after weight loss with a combination of dietary modification and exercise

4.1. Study 2-1. Changes in muscle mass and strength after weight loss with dietary modification program

4.1.1. Purpose

The purpose of this study was to investigate how weight loss due to dietary modification program affects muscle mass and strength in obese men.

4.1.2. Methods

4.1.2.1. Participants

Study participants were recruited from communities through advertisements in local newspapers and distributed study flyers. The following inclusion criteria were applied: 1) body mass index (BMI) ≥ 25 kg/m^2, according to the Japanese obesity guidelines; 2) males between 30 and 64 years of age; 3) no intentional decrease in body weight greater than 5% in the past 12 months; and 4) no terminal disease, recent muscle injury, or surgery (Examination Committee of Criteria for 'Obesity Disease' in Japan and Japan Society for the Study of Obesity, 2002). As shown in Fig. 5, 33 obese men who fulfilled the inclusion criteria served as the study group, and they were enrolled in a 12-week weight loss program. We excluded 9 participants who dropped out of the weight loss program, had incomplete data, or did not participate in the assessments used for the analyses. Consequently, 24 participants were included in the analysis. Each participant provided signed informed written consent, which was approved by the institutional review board. This study was conducted in accordance with the guidelines

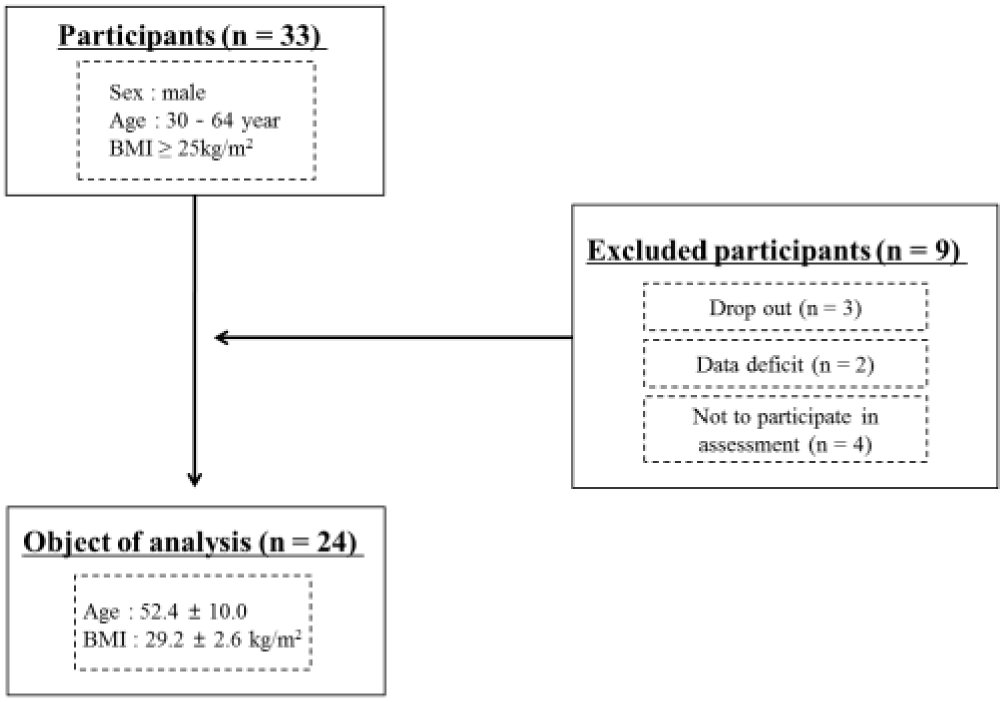


Figure 5. Flow chart of the study participants

proposed in the Declaration of Helsinki, and the study protocol was reviewed and approved by the Ethics Committee of the University of Tsukuba, Japan. Participants were eligible for the present study if complete dietary modification program data on body composition and muscle strength from the baseline and 12-week follow-up assessments were available.

4.1.2.2. Assessment variables

Body composition was evaluated as follows: whole body lean mass, whole body fat mass, arm muscle mass, leg muscle mass, skeletal muscle mass index and percentage of muscle mass index. Handgrip strength and knee extensor strength which evaluated muscle strength in upper and lower extremity was expressed as an absolute and body weight-normalized value. Total energy intake and the amounts of each nutrient was measured before and after weight loss program.

4.1.3. Statistical analyses

Statistical analysis was conducted with SPSS software, version 20.0 (IBM Inc., Armonk, NY, USA). Data are presented as the means ± standard deviations. A paired t-test was employed to assess the differences between the variables before and after the weight loss program. Partial correlation analysis was performed to remove the age effect between variables before the weight loss program and between changes in variables from before the weight loss program to the follow-up after the weight loss program. To evaluate whether muscle mass change is correlated with body weight change and whether muscle strength change is correlated with muscle mass change, partial correlation analysis was performed to remove the age effect. Statistical significance was set at $P < 0.05$.

4.1.4. Results

Table 4 shows the patients' demographic information, body composition, muscle strength and daily energy intake before and after the dietary modification program. After the program, the following significant changes were observed in body weight, body composition, muscle strength, and daily energy intake. Body weight decreased by an average of 8.8 ± 3.6 kg (-10.5 ± 4.1%, $P < 0.01$). Whole body fat mass and leg muscle mass, as well as the SMI, were significantly decreased (by -5.0 ± 2.3 kg, -1.2 ± 0.7 kg, and -0.5 ± 0.3 kg, respectively; $P < 0.01$). Static maximal muscle strength (-21.5 ± 30.4 Nm at 60°, $P < 0.01$), dynamic maximal muscle strength (-16.7 ± 14.9 Nm at 60°/s, $P < 0.01$), dynamic muscle endurance (-34.3 ± 35.8 Nm at 60°/s, $P < 0.01$), and dynamic muscle power (-8.4 ± 8.7 Nm at 60°/s, $P < 0.01$) declined significantly, and the % MMI (2.0 ± 1.6%; $P < 0.01$) and handgrip strength per body weight (0.05 ± 0.05 kg; $P < 0.01$) were significantly improved. However, arm muscle mass, handgrip strength, body weight-normalized static and dynamic maximal muscle strength (-0.2 ± 0.5 kg, -1.0 ± 3.2 kg, 0.03 ± 0.36 Nm/kg at 60° and 0.03 ± 0.19 Nm/kg at 60°/s, respectively) were not significantly changed. Total energy intake (-634.9 ± 559.8

kcal/day, $P < 0.01$), carbohydrate (-75.1 ± 88.9 g/day, $P < 0.01$), protein (-10.9 ± 19.7 g/day, $P < 0.05$), and fat (-21.5 ± 27.7 g/day, $P < 0.01$) were significantly reduced.

Table 5 presents partial correlations. We only investigated the correlations between body weight, leg muscle mass, and leg muscle strength because there were no significant changes in arm muscle mass and handgrip strength after the dietary modification program. The results indicate that every measurement of absolute change in leg muscle strength was moderately-to-highly related to leg muscle mass, as well as that absolute change in leg muscle mass was related to body weight before and after the dietary modification program. Body weight-normalized muscle strength was not significantly associated with body weight or leg muscle mass before or after the dietary modification program. Considering these results, it seems clear that changes in leg muscle strength derived from changes in leg muscle mass and leg muscle strength are directly proportional to leg muscle mass. However, we found that rates of change in leg muscle mass do not absolutely correlate with rates of change in body weight, as well as that rates of change in leg muscle strength do not absolutely correlate with rates of change in leg muscle mass, based on the results summarized in Table 6. This finding implies that changes in muscle mass do influence muscle strength; however, changes in other factors also influence muscle strength.

Table 4 Descriptive characteristics and their changes before and after a 12-week dietary modification program

	Pre (range)		Post (range)		Change (95% CI)		*P*
Age, year	52.4 ± 10.0	(32.0, 64.0)					
Height, cm	168.8 ± 6.4	(156.1, 184.6)					
Weight, kg	83.4 ± 11.0	(70.4, 102.7)	73.2 ± 14.3	(61.7, 97.2)	-8.8 ± 3.6	(-10.3, -7.2)	< 0.01
Body mass index, kg/m^2	29.2 ± 2.6	(25.7, 34.7)	26.1 ± 2.6	(22.5, 32.7)	-3.1 ± 1.3	(-3.6, -2.5)	< 0.01
Whole body lean mass, kg	62.8 ± 7.6	(53.0, 79.1)	58.6 ± 7.7	(48.3, 73.0)	-4.1 ± 2.0	(-5.0, -3.3)	< 0.01
Whole body fat mass, kg	21.4 ± 5.0	(13.6, 34.3)	16.4 ± 5.1	(9.6, 28.2)	-5.0 ± 2.3	(-6.0, -4.1)	< 0.01
Arm muscle mass, kg	6.6 ± 1.0	(5.1, 9.2)	6.4 ± 1.1	(4.7, 9.1)	-0.2 ± 0.5	(-0.4, 0.1)	0.12
Leg muscle mass, kg	19.6 ± 3.1	(15.9, 26.4)	18.4 ± 3.1	(14.3, 25.3)	-1.2 ± 0.7	(-1.5, -0.9)	< 0.01
SMI, kg	9.2 ± 0.9	(7.8, 11.2)	8.7 ± 0.9	(7.0, 10.8)	-0.5 ± 0.3	(-0.6, -0.4)	< 0.01
% MMI, %	31.5 ± 3.0	(25.3, 37.2)	33.5 ± 3.9	(26.9, 40.2)	2.0 ± 1.6	(1.3, 2.6)	< 0.01
HGS	45.3 ± 6.1	(34.5, 56.6)	44.2 ± 5.8	(35.9, 57.6)	-1.0 ± 3.2	(-2.4, 0.3)	0.13
HGS/BW, kg	0.55 ± 0.08	(0.44, 0.73)	0.64 ± 0.22	(0.43, 0.77)	0.05 ± 0.05	(0.03, 0.07)	< 0.01
IMT60 PTQ, Nm	214.1 ± 53.8	(136.2, 347.9)	192.6 ± 43.3	(116.0, 322.0)	-21.5 ± 30.4	(-34.3, -8.7)	< 0.01
IMT60 PTQ/BW, Nm/kg	2.56 ± 0.51	(1.79, 3.52)	2.77 ± 1.07	(1.61, 3.58)	0.03 ± 0.36	(-0.12, 0.19)	0.38
IKT60 PTQ, Nm	177.8 ± 53.2	(101.3, 347.9)	161.1 ± 46.6	(73.8, 281.8)	-16.7 ± 14.9	(-23.0, -10.3)	< 0.01
IKT 60 PTQ/BW, Nm/kg	2.13 ± 0.50	(1.27. 3.43)	2.29 ± 0.88	(1.02, 3.14)	0.03 ± 0.19	(-0.04, 0.11)	0.38
IKT60 TW, J	496.5 ± 136.8	(272.1, 838.4)	462.1 ± 127.3	(213.6, 793.4)	-34.3 ± 35.8	(-49.5, -19.2)	< 0.01
IKT60 AP, W	110.8 ± 34.8	(62.0, 209.1)	102.4 ± 30.8	(47.0, 188.3)	-8.4 ± 8.7	(-12.0, -4.7)	< 0.01
Total energy intake, kcal/day	2228.8 ± 570.6	(1385.0, 3546.0)	1593.9 ± 198.3	(1187.0, 2013.0)	-634.9 ± 559.8	(-871.3, -398.5)	< 0.01
Carbohydrate, g/day	279.5 ± 92.5	(133.6, 566.8)	204.4 ± 27.0	(144.9, 261.1)	-75.1 ± 88.9	(-112.6, -37.6)	< 0.01
Protein, g/day	83.2 ± 17.9	(49.2, 119.0)	72.3 ± 14.6	(42.6, 103.1)	-10.9 ± 19.7	(-19.3, -2.6)	< 0.05
Fat, g/day	68.6 ± 24.4	(24.8, 132.0)	47.2 ± 10.6	(28.8, 74.8)	-21.5 ± 27.7	(-33.2, -9.8)	< 0.01

NOTES: SMI = Skeletal muscle mass index; % MMI = Percentage of muscle mass index; HGS = Hand grip strength; HGS/BW = Hand grip strength/body weight; IMT60 PTQ = Isometric60 peak torque; IMT60 PTQ/BW = Isometric60 peak torque/body weight; IKT60 PTQ = Isokinetic60 peak torque; IKT60 PTQ/BW = Isokinetic60 peak torque/body weight; IKT60 TW = Isokinetic60 total work; IKT60 AP = Isokinetic60 average power. Mean ± standard deviation (range).

Table 5 Partial correlation coefficients adjusted for age#

	Weight	Leg muscle mass	IMT60 PTQ in Nm	IMT60 PTQ/BW in Nm/kg	IKT60 PTQ in Nm	IKT60 PTQ/BW in Nm/kg	IKT60 TW in J	IKT60 AP in W
Weight, kg	×	**0.47 ***	**0.07**	**-0.75 ****	**0.11**	**-0.72 ****	**0.09**	**0.12**
Leg muscle mass, kg	0.63 **	×	**0.63 ****	**0.07**	**0.64 ****	**0.08**	**0.67 ****	**0.61 ****
IMT60 PTQ in Nm	0.33	0.70 *	×	**0.47 ***	**0.86 ****	**0.43 ***	**0.86 ****	**0.87 ****
IMT60 PTQ/BW in Nm/kg	-0.29	0.29	0.80 **	×	**0.42 ***	**0.97 ****	**0.42 ***	**0.40**
IKT60 PTQ in Nm	0.23	0.58 **	0.80 **	0.64 **	×	**0.60 ***	**0.97 ****	**0.98 ****
IKT60 PTQ/BW in Nm/kg	-0.33	0.20	0.61 **	0.82 **	0.83 **	×	**0.49 ***	**0.47 ***
IKT60 TW in J	0.22	0.68 **	0.82 **	0.68 **	0.92 **	0.77 **	×	**0.97 ****
IKT60 AP in W	0.23	0.62 **	0.80 **	0.67 **	0.96 **	0.81 **	0.95 **	×

#Values in the lower left half represent correlations between variables before weight loss program; values in the right half (bold face) represent correlations between changes in variables after weight loss program. NOTES: IMT60 PTQ = Isometric60 peak torque; IMT60 PTQ/BW = Isometric60 peak torque/body weight; IKT60 PTQ = Isokinetic60 peak torque; IKT60 PTQ/BW = Isokinetic60 peak torque/body weight; IKT60 TW = Isokinetic60 total work; IKT60 AP = Isokinetic60 average power. * $P < 0.05$; ** $P < 0.01$

Table 6 Correlation between change rates in lower extremity muscle mass and body weight, and lower extremity muscle strength adjusted for age

	Change rates in lower extremity muscle mass				
	Change rates in body weight	Change rates in IMT60 PTQ	Change rates in IKT60 PTQ	Change rates in IKT60 TW	Change rates in IKT60 AP
	-10.5 ± 4.1 %	-8.7 ± 12.5 %	-6.0 ± 3.6 % -9.3 ± 7.6 %	-6.8 ± 7.7 %	-7.2 ± 8.2 %
R^2	0.03	0.03	0.06	0.11	0.01
p	0.41	0.46	0.25	0.12	0.84

NOTES: IMT60 PTQ = Isometric60 peak torque; IKT60 PTQ = Isokinetic60 peak torque; IKT60 TW = Isokinetic60 total work; IKT60 AP = Isokinetic60 average power. Values are mean ± standard deviation.

4.1.5. Discussion

The primary findings of this study were that a 12-week dietary modification program induced weight loss that resulted in an independent decrease in lower extremity muscle mass and strength, whereas upper extremity muscle mass and strength were maintained. Decreased lower extremity muscle mass contributed to decreases in the SMI, and lower extremity muscle strength per body weight was maintained. In addition, decreases in the percentage of whole body fat mass and an increase in % MMI were observed. It is beneficial for obese men to decrease their percentage of whole body fat mass and increase their % MMI because excessive body fat is a physical burden on the musculoskeletal system, and this system is sustained by muscle mass. However, the preservation of muscle mass and strength in the femoral muscle is particularly important after weight loss because the incidence of musculoskeletal conditions is greatest in the knee joints, and femoral muscle mass and strength support and control the knee joints (Andersen et al., 2003; Kim et al., 2015).

After an average weight loss of 10.5%, the percentage of whole body fat mass and SMI were significantly decreased. Because body weight is a major determinant of muscle mass and lean mass is positively related to body fat, these results are reasonable (Forbes, 1987; Harris, 1997). However, the trends in lower and upper extremity muscle mass changes differed. Many previous studies have reported that a heavy body weight in obese adults serves as a training stimulus to gain muscle mass and, accordingly, to increase muscle strength (Duche et al., 2002; Hulens et al., 2002; Hulens et al., 2001). In particular, when people perform physical activities, the lower extremities get a greater influence than the upper extremities. Consequently, as body weight decreased, the training stimulus in the lower extremities declined, but the upper extremities were not greatly affected by the weight loss. These results explain why the muscle mass and strength in the upper extremities were maintained despite the decrease in lower extremity muscle mass and strength.

As demonstrated in study 2-3, a weight loss program consisting of dietary modification and exercise led to a 14.1% weight loss, which was accompanied by a significant decrease in lower extremity muscle mass and strength, as well as a significant increase in lower extremity muscle strength per body weight (Kim et al., 2015). In the present study, a 10.5% weight loss through dietary modification triggered a decrease in lower extremity muscle mass and strength. It is natural to lose lower extremity muscle mass and strength in situations involving considerable weight loss. However, compared with our previous study, the rates of decline in leg muscle mass and strength were relatively greater in the present study, and the lower extremity muscle strength per body weight was not significantly increased. Assessing absolute muscle strength is the simplest method of evaluating muscle strength, while lower extremity muscle strength per body weight may be more relevant for indicating functional impairments (Barbat-Artigas et al., 2012; Ploutz-Snyder et al., 2002). Recently, the importance of relative muscle strength has attracted attention. Chomentowski et al. (Yoshimura et al., 2014) and Yoshimura et al. (Yoshimura et al., 2014) reported that engaging in exercise during dietary modification helps to preserve muscle mass during weight loss. Based on these reports and the findings in our previous and present studies, it is recognized that engaging in exercise along with dietary modifications yielded significant improvement in lower extremity muscle strength per body weight. Conversely, without exercise, there were no improvements in lower extremity muscle strength per body weight. Thus, engaging in exercise is recommended during weight loss.

It has been long thought that a change in muscle strength stems from changes in muscle mass and that muscle strength is directly proportional to muscle mass (Doherty, 2001, 2003). In recent years, more studies have reported that a change in muscle strength is not directly proportional to a change in muscle mass; changes in muscle mass can only explain 5% of the changes in muscle strength (Hughes et al., 2001). Individuals who gained lean mass did not get stronger, which may have been expected

(Goodpaster et al., 2006). The resulting relationship between the rates of decreased muscle mass and muscle strength after weight loss was in accordance with recent reports. Barbat-Artigas et al. (Barbat-Artigas et al., 2012) suggested a few possible factors contributing to this discrepancy, including obesity, physical activity, sex hormones, and fibrosis. To date, however, no clear evidence exists to explain this discrepancy between muscle mass and strength.

The present study has some limitations. First, the sample size may not be sufficiently large. However, the 10.5% weight loss at the expense of the 6% decrease in leg muscle mass is highly consistent with the results of an existing report in which a 13% weight loss resulted in a 4.6% decrease in lower extremity muscle mass (Henriksen et al., 2012). Thus, it is recognized that the sample size did not affect the results in the present study. Second, the age range of participants was comparatively large. It was reported that the decline in the cross-sectional area of the femoral muscle was smaller with the combination of dietary modification and exercise compared with dietary modification alone, even after adjusting for age (Yoshimura et al., 2014). Consequently, the age range of participants is unlikely to influence the results in the present study. Third, we cannot precisely explain why the change in muscle strength was out of sync with the change in muscle mass after weight loss. This finding must be further investigated.

4.1.6. Conclusion

Weight loss accomplished through dietary modification induced independent losses in lower extremity muscle mass and strength, and decreases in lower extremity muscle mass led to decreases in SMI. Additionally, the weight loss observed in the present study was accompanied by maintained body weight normalized lower extremity muscle strength. Based on these results, we recommend that engaging in exercise during weight loss with dietary modification to minify losses in muscle mass and strength.

4.2. Study 2-2. Changes in muscle mass and strength after engaging in resistance or aerobic exercise

4.2.1. Purpose

Recent guidelines on exercise for weight loss and health promotion include aerobic or resistance exercise as a part of the exercise prescription. However, few studies have investigated the effects of these two different mode of exercise on body composition and muscle strength in obese men. Thus, we investigated these effects.

4.2.2. Methods

4.2.2.1. Participants

Thirty-seven individuals were allocated to the resistance (n = 20) or aerobic (n = 17) exercise group. During the exercise program, 10 participants were excluded due to missing an assessment, dropping out, missing data, and so on (Figure 6). Consequently, a total of 27 participants who remained in the present study after the post-intervention assessment (n = 14 in the resistance exercise group, n = 13 in the aerobic exercise group) were included in the final analysis. The study purpose and design were explained to every participant before they gave written informed consent. The research protocol was approved by the institutional review board of the University of Tsukuba.

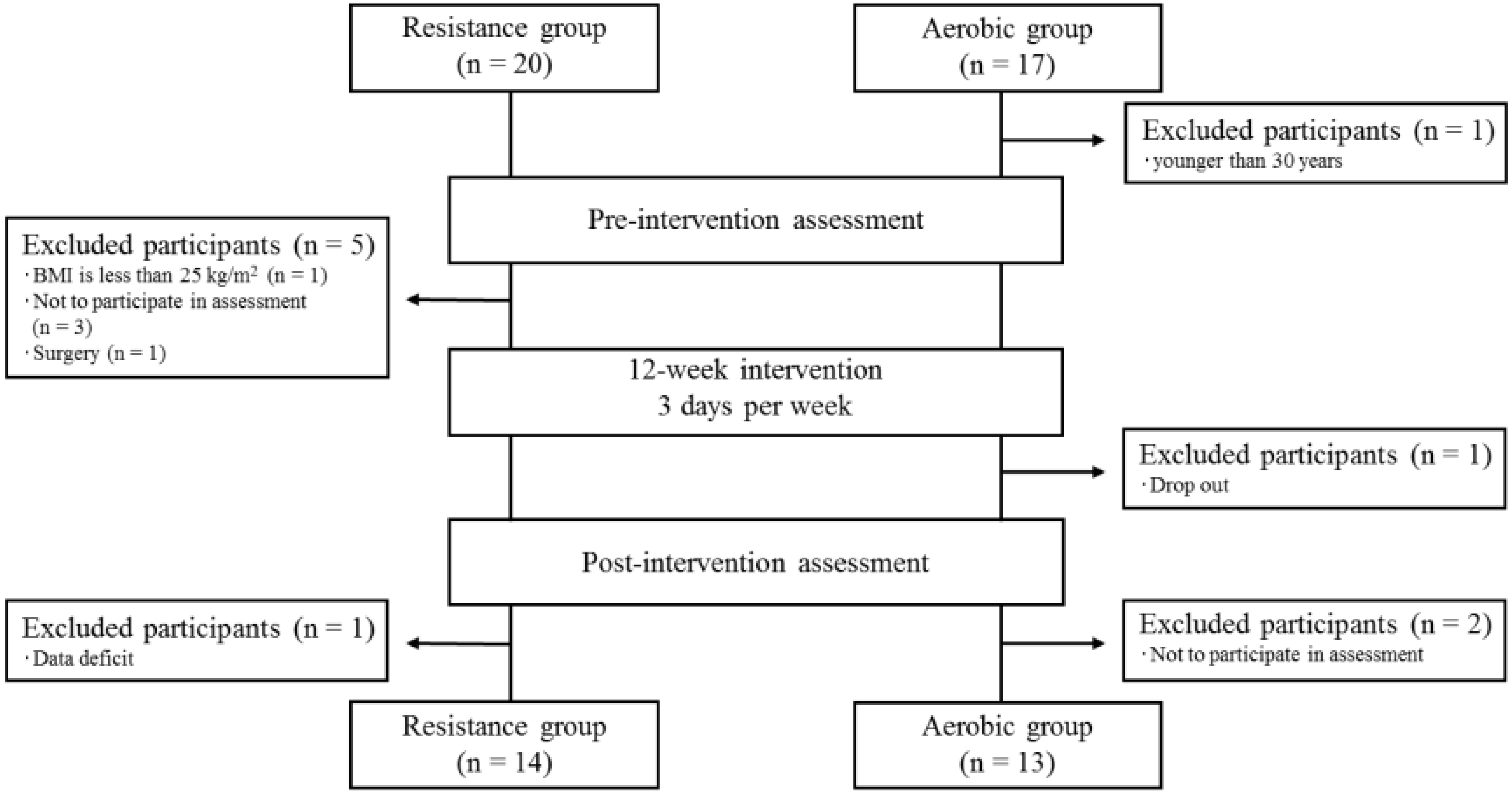


Figure 6. Flow chart of the study participants

4.2.2.2. Assessment variables

Body composition was evaluated as follows: whole body lean mass, whole body fat mass, arm muscle mass, leg muscle mass, skeletal muscle mass index and percentage of muscle mass index. Handgrip strength and knee extensor strength which evaluated muscle strength in upper and lower extremity was expressed as an absolute and body weight-normalized value.

4.2.2.3. Exercise protocol

Both of aerobic exercise and resistance exercise were designed to gradually increase the amount and intensity of exercise, and executed under the supervision of several well experienced physical trainers at the University of Tsukuba. The details of each exercise has been described previously (see 2.2.4.2 and 2.2.4.3, in page 25-26).

4.2.3. Statistical analyses

Values are expressed as the means ± standard deviations or standard errors. Unpaired *t*-tests were employed to evaluate the statistical significance of between-group differences at baseline. The comparison of variables before and after the weight loss program was conducted using paired *t*-tests. To compare changes between groups, we applied a two-way repeated measures analysis of variance. Partial correlations were used to remove the effect of age on the relationships among variables before the weight loss program and on the relationships among variables' changes from before to after the weight loss program. To evaluate whether changes in muscle mass were correlated with changes in body weight and whether changes in muscle strength were correlated with changes in muscle mass, partial correlations were again used to remove the effect of age. $P < 0.05$ was set as the threshold for statistical significance. Statistical analyses were performed with SPSS software, version 20.0 (IBM Inc., Armonk, NY, USA).

4.2.4. Results

Baseline levels and changes in anthropometric measures and body composition for each group are presented in Table 7. There were no significant differences between the two groups in any baseline measure. Significant decreases were observed in body weight and BMI in the aerobic exercise group and in whole body lean mass, leg muscle mass and percentage of muscle mass in the resistance exercise group. Both exercises decreased whole body fat mass. ANOVA revealed no significant interactions (P = 0.076-0.675) between two groups in any variable except whole body lean mass. This results highlights that resistance exercise increases whole body lean mass more (P = 0.003) than does aerobic exercise. Overall, these findings indicate that resistance exercise induces decreases in whole body fat mass and increases muscle mass. AE is not only beneficial for decreasing body weight and fat mass but also for maintaining muscle mass.

Table 8 contains baseline levels of and changes in muscle strength for each group. At baseline, no significant differences were found between the two groups in any variable. After completing the exercise program, significant increases in all muscle strength variables were detected in the resistance exercise group, while no significant changes were found in the aerobic exercise group. There were significant interactions between exercise group and all variables except isokinetic180 average power. These results highlight several insights. Resistance exercise leads to significant increases in muscle strength, while aerobic exercise aids in the maintenance of muscle strength. However, engaging in aerobic exercise is less likely to increase muscle strength than is resistance exercise.

Table 9 and 10 present partial correlations between body weight, leg muscle mass and leg muscle strength in the resistance and aerobic exercise group, which showed significant changes in leg muscle mass after completing the exercise program. The results indicate that almost every measure of absolute change in leg muscle strength is unrelated to leg muscle mass. Additionally, we found that rates of change in leg muscle mass are not necessarily related to rates of change in body weight and that rates of change in strength are unrelated to rates of change in leg muscle mass (Table 11 and 12). Given these findings, it seems that changes in factors other than muscle mass influence muscle strength.

Table 7 Changes in anthropometric characteristics and body composition, differences between resistance (n = 14) and aerobic (n = 13) group

Variables	Group	Before	After	Change	*p* for difference	*p* for interaction
Age, yr	R	51.79 ± 8.22				
	A	50.15 ± 5.84				
Height, cm	R	171.56 ± 4.93				
	A	171.90 ± 4.90				
Weight, kg	R	80.79 ± 8.43	80.66 ± 7.66	-0.14 ± 1.64	0.76	0.083
	A	82.26 ± 7.87	80.39 ± 7.63	-1.87 ± 3.07	< 0.05	
BMI, kg/m^2	R	27.39 ± 1.87	27.35 ± 1.56	-0.04 ± 0.56	0.79	0.076
	A	27.85 ± 2.62	27.20 ± 2.33	-0.65 ± 1.05	< 0.05	
Whole body lean mass, kg	R	60.91 ± 6.80	62.20 ± 6.09	1.29 ± 1.40	< 0.01	0.003
	A	62.63 ± 5.49	61.56 ± 5.20	-1.08 ± 2.13	0.09	
Whole body fat mass, kg	R	20.40 ± 3.27	19.51 ± 2.93	-0.90 ± 1.18	< 0.05	0.626
	A	20.02 ± 4.85	18.83 ± 4.37	-1.18 ± 1.59	< 0.05	
Arm muscle mass, kg	R	6.35 ± 0.97	6.35 ± 1.02	0.02 ± 0.39	0.86	0.675
	A	6.53 ± 0.78	6.47 ± 0.97	-0.05 ± 0.46	0.69	
Leg muscle mass,kg	R	19.37 ± 2.65	19.74 ± 2.56	0.37 ± 0.39	< 0.01	0.310
	A	19.35 ± 1.95	19.45 ± 1.66	0.11 ± 0.93	0.69	
SMI, kg/m^2	R	8.70 ± 0.79	8.84 ± 0.80	0.13 ± 0.23	0.05	0.334
	A	8.75 ± 0.63	8.76 ± 0.55	0.02 ± 0.40	0.89	
% MMI, %	R	31.77 ± 1.84	32.25 ± 1.68	0.48 ± 0.80	< 0.05	0.374
	A	31.54 ± 2.49	31.64 ± 2.87	0.11 ± 1.40	0.79	

Notes: Values are means ± SD. BMI = body mass index; SMI = Skeletal muscle index; % MMI = percentage of muscle mass Index

Table 8 Changes in muscle strength and differences between resistance (n = 14) and aerobic (n = 13) group

Variables	Group	Before	After	Change	*p* for difference	*p* for interaction
IKT60 PTQ, Nm	R	168.16 ± 29.79	182.30 ± 26.28	14.14 ± 13.11	< 0.01	< 0.001
	A	181.02 ± 28.69	175.17 ± 25.55	-5.86 ± 12.87	0.13	
IKT60 PTQ/Weight, Nm/kg	R	2.08 ± 0.28	2.27 ± 0.27	0.18 ± 0.14	< 0.01	0.006
	A	2.20 ± 0.26	2.19 ± 0.33	-0.01 ± 0.19	0.85	
IKT60 TW, J	R	468.81 ± 97.53	520.36 ± 80.20	51.55 ± 55.25	< 0.01	0.015
	A	502.16 ± 84.97	503.63 ± 75.55	1.47 ± 40.41	0.90	
IKT60 AP, W	R	106.86 ± 20.39	117.89 ± 21.52	11.03 ± 10.46	< 0.01	0.012
	A	112.79 ± 19.03	113.29 ± 18.48	0.51 ± 10.78	0.87	
IKT180 PTQ, Nm	R	113.01 ± 20.83	119.72 ± 18.21	6.71 ± 7.71	< 0.01	0.016
	A	118.35 ± 17.15	115.84 ± 17.78	-2.51 ± 9.78	0.37	
IKT180 PTQ/Weight, Nm/kg	R	1.40 ± 0.21	1.49 ± 0.19	0.09 ± 0.09	< 0.01	0.124
	A	1.44 ± 0.16	1.45 ± 0.24	0.01 ± 0.14	0.77	
IKT180 TW, J	R	1276.42 ± 284.57	1388.58 ± 241.26	112.15 ± 95.65	< 0.01	0.006
	A	1323.47 ± 211.65	1304.02 ± 216.77	-19.45 ± 122.57	0.58	
IKT180 AP, W	R	174.38 ± 42.32	186.24 ± 37.84	11.85 ± 16.91	< 0.05	0.098
	A	180.81 ± 30.15	180.24 ± 35.54	-0.58 ± 17.86	0.91	

Notes: Values are means ± SD. IKT60 PTQ = Isokinetic60 peak torque; IKT60 TW = Isokinetic60 total work; IKT60 AP = Isokinetic60 average power; IKT180 PTQ = Isokinetic180 peak torque; IKT180 TW = Isokinetic180 total work; IKT180 AP = Isokinetic180 average power.

Table 9 Partial correlation coefficients in resistance exercise group adjusted for age[#]

	Weight	LMM	IKT60 PTQ in Nm	IKT60 PTQ/BW in Nm	IKT60 TW in J	IKT60 AP in W	IKT180 PTQ in Nm	IKT180 PTQ/BW in Nm	IKT180 TW in J	IKT180 AP in W
Weight, kg	×	**0.93** **	**0.46**	**-0.23**	**0.39**	**0.47**	**0.53**	**-0.17**	**0.31**	**0.47**
LMM, kg	0.89 **	×	**0.52**	**-0.11**	**0.42**	**0.50**	**0.52**	**-0.14**	**0.32**	**0.42**
IKT60 PTQ in Nm	0.58 *	0.54	×	**0.76** **	**0.91** **	**0.92** **	**0.79** **	**0.50**	**0.66** *	**0.65** *
IKT60 PTQ/BW in Nm/kg	-0.01	0.03	0.81 **	×	**0.70** **	**0.65** *	**0.48**	**0.69** **	**0.49**	**0.37**
IKT60 TW in J	0.59 *	0.51	0.86 **	0.62 *	×	**0.94** **	**0.85** **	**0.64** **	**0.85** **	**0.80** **
IKT60 AP in W	0.60 *	0.56 *	0.95 **	0.74 **	0.92 **	×	**0.84** **	**0.56** *	**0.76** **	**0.79** **
IKT180 PTQ in Nm	0.59 *	0.50	0.84 **	0.62 *	0.80 **	0.88 **	×	**0.74** **	**0.91** **	**0.94** **
IKT180 PTQ/BW in Nm/kg	-0.03	-0.06	0.56 *	0.73 **	0.51	0.61 *	0.79 **	×	**0.81** **	**0.72** **
IKT180 TW in J	0.45	0.36	0.76 **	0.62 *	0.75 **	0.81 **	0.98 **	0.86 **	×	**0.94** **
IKT180 AP in W	0.60 *	0.45	0.76 **	0.51	0.80 **	0.83 **	0.97 **	0.75 **	0.96 **	×

[#]Values in the lower left half represent correlations between variables before weight loss program; values in the right half (bold face) represent correlations between changes in variables after weight loss program. NOTES: LMM = Leg muscle mass; IKT60 PTQ = Isokinetic60 peak torque; IKT60 PTQ/BW = Isokinetic60 peak torque/body weight; IKT60 TW = Isokinetic60 total work; IKT60 AP = Isokinetic60 average power; IKT180 PTQ = Isokinetic60 peak torque; IKT180 PTQ/BW = Isokinetic180 peak torque/body weight; IKT180 TW = Isokinetic60 total work; IKT180 AP = Isokinetic60 average power * $p < 0.05$; ** $p < 0.01$

Table 10 Partial correlation coefficients in aerobic exercise group adjusted for age[#]

	Weight	LMM	IKT60 PTQ in Nm	IKT60 PTQ/BW in Nm	IKT60 TW in J	IKT60 AP in W	IKT180 PTQ in Nm	IKT180 PTQ/BW in Nm	IKT180 TW in J	IKT180 AP in W
Weight, kg	×	**0.75** *	**0.24**	**-0.44**	**0.31**	**0.39**	**0.09**	**-0.50**	**0.06**	**0.12**
LMM, kg	0.69 *	×	**0.20**	**-0.31**	**0.42**	**0.32**	**0.05**	**-0.39**	**0.09**	**0.02**
IKT60 PTQ in Nm	0.61 *	0.47	×	**0.76** **	**0.91** **	**0.96** **	**0.75** **	**0.50**	**0.55**	**0.66** *
IKT60 PTQ/BW in Nm/kg	-0.06	0.03	0.76 **	×	**0.62** *	**0.63** *	**0.62** *	**0.78** **	**0.44**	**0.50**
IKT60 TW in J	0.68 *	0.68 *	0.88 **	0.55	×	**0.91** **	**0.72** **	**0.43**	**0.62** *	**0.63** *
IKT60 AP in W	0.67 *	0.50	0.93 **	0.62 *	0.94 **	×	**0.81** **	**0.47**	**0.65** *	**0.75** **
IKT180 PTQ in Nm	0.61 *	0.50	0.74 **	0.40	0.72 **	0.72 **	×	**0.82** **	**0.92** **	**0.95** **
IKT180 PTQ/BW in Nm/kg	-0.13	0.02	0.36	0.53	0.29	0.29	0.71 *	×	**0.77** **	**0.76** **
IKT180 TW in J	0.49	0.52	0.58 *	0.30	0.61 *	0.56	0.91 **	0.71 *	×	**0.94** **
IKT180 AP in W	0.45	0.34	0.66 *	0.42	0.63 *	0.68 *	0.95 **	0.78 **	0.92 **	×

[#]Values in the lower left half represent correlations between variables before weight loss program; values in the right half (bold face) represent correlations between changes in variables after weight loss program. NOTES: LMM = Leg muscle mass; IKT60 PTQ = Isokinetic60 peak torque; IKT60 PTQ/BW = Isokinetic60 peak torque/body weight; IKT60 TW = Isokinetic60 total work; IKT60 AP = Isokinetic60 average power; IKT180 PTQ = Isokinetic60 peak torque; IKT180 PTQ/BW = Isokinetic180 peak torque/body weight; IKT180 TW = Isokinetic60 total work; IKT180 AP = Isokinetic60 average power * $p < 0.05$; ** $p < 0.01$

Table 11 Correlation between change rates in lower extremity muscle mass and body weight, and lower extremity muscle strength in resistance exercise group (n = 14) adjusted for age

	Change rates in lower extremity muscle mass						
	Change rates in body weight	Change rates in IKT60 PTQ	Change rates in IKT60 TW	Change rates in IKT60 AP	Change rates in IKT180 PTQ	Change rates in IKT180 TW	Change rates in IKT180 AP
				1.94 ± 2.07 %			
	-0.11 ± 2.03 %	7.93 ± 7.68 %	10.09 ± 10.79 %	9.17 ± 8.94 %	6.86 ± 7.88 %	10.86 ± 13.03 %	8.92 ± 14.00 %
R^2	0.14	0.10	0.01	0.01	0.11	0.05	0.05
p	0.21	0.30	0.79	0.69	0.27	0.47	0.46

NOTES: Values are mean ± standard deviation. IKT60 PTQ = Isokinetic60 peak torque; IKT60 TW = Isokinetic60 total work; IKT60 AP = Isokinetic60 average power; IKT180 PTQ = Isokinetic180 peak torque; IKT180 TW = Isokinetic180 total work; IKT180 AP = Isokinetic180 average power.

Table 12 Correlation between change rates in lower extremity muscle mass and body weight, and lower extremity muscle strength in aerobic exercise group (n = 13) adjusted for age

	Change rates in lower extremity muscle mass						
	Change rates in body weight	Change rates in IKT60 PTQ	Change rates in IKT60 TW	Change rates in IKT60 AP	Change rates in IKT180 PTQ	Change rates in IKT180 TW	Change rates in IKT180 AP
	0.76 ± 4.83 %						
	-2.21 ± 3.55 %	-2.87 ± 7.00 %	0.85 ± 8.43 %	0.93 ± 9.12 %	-1.97 ± 8.58 %	-1.17 ± 8.97 %	-0.39 ± 9.81 %
R^2	0.68	0.003	0.06	0.20	0.002	0.001	0.11
p	0.001	0.88	0.44	0.14	0.89	0.91	0.30

NOTES: Values are mean ± standard deviation. IKT60 PTQ = Isokinetic60 peak torque; IKT60 TW = Isokinetic60 total work; IKT60 AP = Isokinetic60 average power; IKT180 PTQ = Isokinetic180 peak torque; IKT180 TW = Isokinetic180 total work; IKT180 AP = Isokinetic180 average power.

4.2.5. Discussion

We have been interested in what types of exercise are most beneficial for health promotion. Existing research has reported that resistance exercise improves glucose tolerance and levels of glycosylated hemoglobin, as well as muscle mass and strength. Aerobic exercise has the advantage of improving several metabolic variables and decreasing weight and fat mass. To date, however, there are still unexplored effects of aerobic and resistance exercise, including the effect of resistance exercise on fat mass and the effect of aerobic exercise on muscle mass and strength. Consequently, we investigated the effects of resistance exercise or aerobic exercise in previously inactive obese men. The main findings of the present study were as follows: 1) Resistance exercise induces decreases in whole body fat mass and increases in muscle mass and muscle strength. 2) Aerobic exercise is beneficial not only for decreasing body weight and fat mass but also for maintaining muscle mass and strength. However, engaging in aerobic exercise is unlikely to increase muscle strength as effectively as resistance exercise. 3) Changes in leg muscle strength do not depend on changes in leg muscle mass. Overall, these findings suggest that resistance exercise induces independent increases in muscle mass and muscle strength, as well as in fat mass loss. Aerobic exercise has a positive effect on the maintenance of muscle mass and strength as well as on loss of fat and body weight.

It is broadly accepted that RE induces increases in muscle mass and strength. In the present study, variables that reflect muscle mass increased or showed a tendency to increase after RE, and the percentage of muscle mass also increased. Considering these results, there is no doubt that resistance exercise has positive effects on muscle mass and strength. However, whether resistance exercise induces fat mass loss has remained a point of controversy. Some existing studies have reported no change in fat mass, whereas others have found that resistance exercise decreases fat mass. The findings in the present study were consistent with the latter reports. After completing a resistance exercise program, participants observed decreases in whole body fat mass without changes in body weight. The lack of a change in body weight was due to increased whole body lean mass. The American College of Sports Medicine (2009) has suggested the following potential mechanism by which resistance exercise might cause fat mass loss: though the energy expenditure related to resistance exercise is not great, resistance exercise increases muscle mass, and increased muscle mass causes increases in resting energy expenditure. On these grounds, it can be expected that executing resistance exercise for a long period leads to fat mass loss as well as muscle mass and strength gains.

Aerobic exercise has long been recommended for fat mass and body weight loss, and the effectiveness of this strategy was demonstrated in the present study. Despite insufficient evidence, it had long been assumed that aerobic exercise has no positive influence on muscle mass and strength. However, in recent years, reports of aerobic exercise having positive effects on maintenance of muscle mass during intentional weight loss have increased. The results of the present study showed no change in variables measuring muscle mass despite significant weight loss. This pattern suggests that engaging in aerobic exercise supports the maintenance of muscle mass. In addition, every muscle strength measurement in the present study was statistically unchanged after an aerobic exercise program. Carolina et al (2010) reported that both aerobic exercise and resistance exercise increase motor unit conduction velocity, with both exercise types having similar effects on electrophysiological adaption of the muscle fiber membrane properties. Given this previous report and the results of the present study, it seems evident that muscle mass and strength are positively affected by aerobic exercise. However, given the interaction between exercise type and most muscle strength variables, engaging in aerobic exercise cannot be expected to increase muscle strength as effectively as resistance exercise.

For decades, it has been believed that there is a direct link between changes in muscle mass and strength. (Doherty, 2001, 2003) However, recently, reports in which change in muscle strength is not directly proportional to change in muscle mass have increased: for example, changes in muscle mass can explain only 5% of the change in muscle strength. (Hughes et al., 2001) Individuals who gained lean mass did not increase in strength as much as might have been expected. (Goodpaster et al., 2006) In the present study, the relationship between rates of change in muscle mass and in muscle strength after completing resistance exercise was in line with recent reports. Barbat-Artigas et al (2012) identified a few factors which impact this discrepancy such as obesity, physical activity, sex hormone and fibrosis. Neuromuscular factors may be more likely than mechanical and architectural factors to explain the discrepancy with resistance exercise (Ivey et al., 2000; Young et al., 1983). To date, however, objective evidence for this discrepancy between muscle mass and muscle strength has not been adequate.

One limitation of the present study was that all participants were middle-aged Japanese men. Factors such as race, age and sex can have effects on changes in body composition and muscle strength in response to exercise. Therefore, a prospective cohort study is required in the future.

4.2.6. Conclusion

Resistance exercise resulted in a tendency for muscle mass and muscle strength to independently increase, as well as decreases in whole body fat mass. Aerobic exercise produced decreases in fat mass and body weight and was associated with maintenance of muscle mass and strength. Resistance exercise was more effective than aerobic exercise in producing gains in muscle strength. If increasing muscle mass is the goal, engaging in resistance exercise is recommended. However, considering the effects of aerobic exercise on muscle strength and body weight and composition, which are two important variables for health promotion, aerobic exercise alone may be sufficient, particularly because aerobic exercise is easier to approach than resistance exercise.

4.3. Study 2-3. Changes in muscle mass and strength after weight loss with a combination of dietary modification and exercise program

4.3.1. Purpose

The purpose of this study was to investigate the changes in muscle mass and strength resulting from a weight loss program consisting of dietary modification and exercise program.

4.3.2. Methods

4.3.2.1. Participants

Participants were eligible for the present study if complete weight loss program data on body composition and muscle strength from baseline and12-week follow up were available. As described in Fig. 7, 97 participants were included in the study, but only 60 participants were included in the data analysis. The remaining 37 participants were not participants included in the analysis for the following reasons: 2 dropped out of weight loss program for private reasons, 4 of them had incomplete data and 31 did not take part in the muscle strength assessment. We permitted participants not to take parts in the muscle strength assessment among participants who do not desire for muscle strength assessment, because one of the purposes on study was the health support in the region. The study purpose and design were adequately explained to every participant before they gave written informed consent. The research protocol was approved by the institutional review board at the University of Tsukuba.

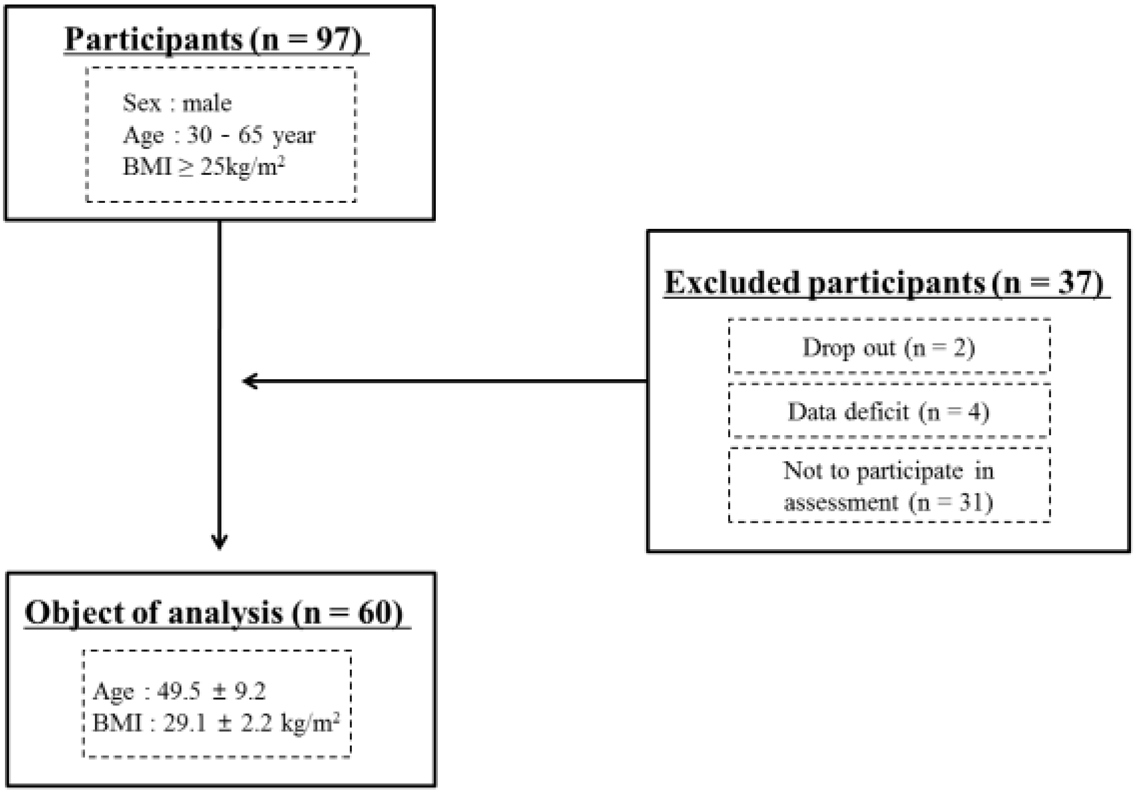


Figure 7. Flow diagram of the participants

4.3.2.2. Assessment variables

Body composition was evaluated as follows: whole body lean mass, whole body fat mass, arm muscle mass, leg muscle mass, skeletal muscle mass index and percentage of muscle mass index. Handgrip strength and knee extensor strength which evaluated muscle strength in upper and lower extremity was expressed as an absolute and body weight-normalized value.

4.3.3. Statistical analyses

Data are expressed as the mean ± standard deviation (SD) values. A comparison of variables before and after the weight loss program was made using the paired *t*-test. Partial correlation analysis was performed to remove the effect of age between variables before the weight loss program and between changes in variables before the weight loss program to follow up after the weight loss program. To evaluate whether change in muscle mass is correlated with change in body weight and whether change in muscle strength is correlated with change in muscle mass, partial correlation analysis was applied to remove the effect of age. $P < 0.05$ was considered to indicate statistical significance. Every statistical analysis was performed with SPSS software, version 20.0 (IBM Inc., Armonk, NY, USA).

4.3.4. Results

Demographic information, body composition and muscle strength characteristics before and after taking part in the weight loss program are presented in Table 13. During the weight loss program, the participants lost an average −12.1 ± 4.0 kg (−14.1 ± 4.4%, $P < 0.01$) of body weight. After weight loss, significant changes were found in both body composition and muscle strength. Except % MMI, other variables including whole body lean mass, whole body fat mass, arm muscle mass, leg muscle mass and SMI were significantly decreased (by −5.1 ± 2.3 kg, −6.6 ± 2.1 kg, −0.7 ± 0.4 kg, −1.6 ± 2.3 kg and −0.8 ± 0.9 kg, respectively; $P < 0.01$). % MMI was significantly increased (2.1 ± 3.1 %; $P < 0.01$). Handgrip strength (-0.3 ± 2.9 kg; $P = 0.49$) did not decline significantly and handgrip strength per body weight (0.08 ± 0.05 kg; $P < 0.01$) was significantly increased. Static maximal muscle strength (−9.1 ± 28.2 Nm at 60◦; $P < 0.05$), dynamic maximal muscle strength(−11.9 ± 23.9 Nm at 60◦/s and −6.9 ± 14.8 Nm at 180◦/s, respectively; $P < 0.01$) and dynamic muscle endurance (−24.5 ± 68.4 Nm at 60◦/s and−71.2 ± 189.5 Nm at 180◦/s, respectively; $P < 0.01$) declined significantly, whereas dynamic muscle power (−1.9 ± 15.4 Nm at 60◦/s; $P = 0.34$ and −3.4 ± 28.5 Nm at 180◦/s; $P = 0.36$) did not decline significantly and body weight-normalised muscle strength (0.3 ± 0.3 Nm/kg at 60◦, 0.2 ± 0.3 Nm/kg at 60◦/s and 0.7 ± 0.3 Nm at 180◦/s, respectively; $P < 0.01$) was significantly increased. Every result in the dynamic strength assessment was correlated at angular velocities of 60◦/s and 180◦/s, contrary to our assumption before the weight loss program.

Partial correlations are presented in Table 14.The results show that every measure of absolute change in leg muscle strength is moderately-to-highly related to leg muscle mass, and absolute change in leg muscle mass is related to body weight before and after the weight loss program. Everybody weight-normalised muscle strength measure has no relation to body weight and leg muscle mass before and after the weight loss program. Given these results that it appears to be clear that a change in muscle strength is a result of changes in muscle mass and muscle strength is directly proportional to muscle mass. However, we found that change rates in leg muscle mass do not completely depend on change rates in body weight and change rates in leg muscle strength do not completely depend on change rates in leg muscle mass on the basis of the results presented in Table 15. This suggests that not only muscle strength is influenced by changes in muscle mass but also influenced by changes in other factors.

Table 13 Characteristics of the participants before and after weight loss program

	Pre (range)		Post (range)		Change (95% CI)		*P*
Age, year	49.5 ± 9.2	(31.0, 64.0)					
Height, cm	171.8 ± 5.6	(161.2, 193.0)					
Weight, kg	86.1 ± 8.9	(70.3, 120.0)	74.0 ± 9.1	(60.4, 114.0)	-12.1 ± 4.0	(-11.1, -13.1)	< 0.01
Body mass index, kg/m^2	29.1 ± 2.2	(25.0, 36.3)	25.0 ± 2.4	(21.3, 31.1)	-4.1 ± 1.3	(-3.8, -4.4)	< 0.01
Whole body lean mass, kg	61.5 ± 6.5	(51.2, 76.3)	56.4 ± 6.1	(46.7, 74.2)	-5.1 ± 2.3	(-4.5, -5.7)	< 0.01
Whole body fat mass, kg	21.5 ± 4.6	(14.6, 36.7)	14.9 ± 4.8	(8.2, 34.9)	-6.6 ± 2.1	(-6.1, -7.2)	< 0.01
Arm muscle mass, kg	6.7 ± 0.9	(5.1, 9.5)	6.0 ± 0.8	(4.7, 8.2)	-0.7 ± 0.4	(-0.8, -0.6)	< 0.01
Leg muscle mass, kg	20.3 ± 2.9	(16.8, 26.8)	18.8 ± 2.0	(15.7, 25.8)	-1.6 ± 2.3	(-1.0, -2.2)	< 0.01
SMI, kg/m^2	9.2 ± 1.1	(7.3, 15.4)	8.4 ± 0.7	(7.1, 10.1)	-0.8 ± 0.9	(-1.0, -0.6)	< 0.01
% MMI, %	31.5 ± 3.2	(26.7, 35.6)	33.5 ± 2.3	(29.4, 38.3)	2.1 ± 3.1	(1.3, 2.9)	< 0.01
HGS, kg	43.3 ± 6.8	(30.0, 67.9)	43.0 ± 6.1	(30.5, 60.7)	-0.3 ± 2.9	(-0.5, -1.0)	0.49
HGS/BW, kg	0.51 ± 0.08	(0.37, 0.69)	0.59 ± 0.09	(0.41, 0.77)	0.08 ± 0.05	(-0.09, -0.07)	< 0.01
IMT60 PTQ, Nm	204.0 ± 41.2	(106.2, 300.0)	194.9 ± 37.8	(108.7, 313.5)	-9.1 ± 28.2	(-1.8, -16.4)	< 0.05
IMT60 PTQ/BW, Nm/kg	2.4 ± 0.4	(1.2, 3.1)	2.6 ± 0.4	(1.5, 3.7)	0.3 ± 0.3	(0.2, 0.4)	< 0.01
IKT60 PTQ, Nm	180.4 ± 38.1	(99.3, 263.8)	168.5 ± 31.1	(106.1, 288.7)	-11.9 ± 23.9	(-5.7, -18.1)	< 0.01
IKT 60 PTQ/BW, Nm/kg	2.1 ± 0.4	(1.1, 2.7)	2.3 ± 0.3	(1.3, 3.2)	0.2 ± 0.3	(0.1, 0.3)	< 0.01
IKT60 TW, J	501 ± 97.1	(221.4, 719.5)	476.5 ± 79.5	(283.2, 646.3)	-24.5 ± 68.4	(-6.8, -42.2)	< 0.01
IKT60 AP, W	108.3 ± 25.2	(44.0, 163.8)	106.4 ± 22.8	(71.1, 190.0)	-1.9 ± 15.4	(-2.1, -5.9)	0.34
IKT180 PTQ, Nm	117 ± 28.0	(55.8, 202.8)	110.1 ± 22.7	(58.0, 216.2)	-6.9 ± 14.8	(-3.0, -10.7)	< 0.01
IKT180 PTQ/BW, Nm/kg	1.4 ± 0.3	(0.6, 1.9)	2.0 ± 0.4	(0.7, 1.9)	0.7 ± 0.3	(0.6, 0.8)	< 0.01
IKT180 TW, J	1323.8 ± 307	(561.1, 1976.3)	1252.7 ± 238.9	(648.1, 2197.7)	-71.2 ± 189.5	(-22.2, -120.1)	< 0.01
IKT180 AP, W	165.6 ± 46.7	(62.9, 268.2)	162.2 ± 41.0	(96.1, 342.6)	-3.4 ± 28.5	(-4.0, 10.7)	0.36

NOTES: SMI = Skeletal muscle mass index; % MMI = Percentage of muscle mass index; HGS = Hand grip stremgth; HGS/BW = Hand grip strength/body weight; IMT60 PTQ = Isometric60 peak torque; IMT60 PTQ/BW = Isometric60 peak torque/body weight; IKT60 PTQ = Isokinetic60 peak torque; IKT60 PTQ/BW = Isokinetic60 peak torque/body weight; IKT60 TW = Isokinetic60 total work; IKT60 WF = Isokinetic60 work fatigue; IKT60 AP = Isokinetic60 average power; IKT180 PTQ = Isokinetic180 peak torque; IKT180 PTQ/BW = Isokinetic180 peak torque/body weight; IKT180 TW = Isokinetic180 Total work; IKT180 AP = Isokinetic180 average power. Mean ± standard deviation (range).

Table 14 Partial correlation coefficients adjusted for age#

	Weight	Leg muscle mass	IMT60 PTQ in Nm	IMT60 PTQ/BW in Nm/kg	IKT60 PTQ in Nm	IKT60 PTQ/BW in Nm/kg	IKT60 TW in J	IKT60 AP in W	IKT180 PTQ in Nm	IKT180 PTQ/BW in Nm/kg	IKT180 TW in J	IKT180 AP in W
Weight, kg	×	**0.80** **	**0.52** **	**0.08**	**0.65** **	**-0.09**	**0.49** **	**0.59** **	**0.64** **	**-0.08**	**0.58** **	**0.58** **
Leg muscle mass, kg	0.55 **	×	**0.59** **	**0.17**	**0.70** **	**0.16**	**0.59** **	**0.66** **	**0.60** **	**0.44**	**0.58** **	**0.58** **
IMT60 PTQ in Nm	0.45 **	0.27 *	×	**0.70** **	**0.87** **	**0.65** **	**0.89** **	**0.87** **	**0.77** **	**0.53** **	**0.70** **	**0.70** **
IMT60 PTQ/BW in Nm/kg	0.16	0.09	0.86 **	×	**0.50** **	**0.55** **	**0.58** **	**0.50** **	**0.47** **	**0.52** **	**0.50** **	**0.47** **
IKT60 PTQ in Nm	0.50 **	0.36 **	0.79 **	0.60 **	×	**0.69** **	**0.91** **	**0.94** **	**0.89** **	**0.57** **	**0.80** **	**0.80** **
IKT60 PTQ/BW in Nm/kg	-0.06	0.06	0.63 **	0.73 **	0.84 **	×	**0.73** **	**0.67** **	**0.53** **	**0.81** **	**0.50** **	**0.47** **
IKT60 TW in J	0.40 **	0.34 **	0.77 **	0.64 **	0.93 **	0.82 **	×	**0.88** **	**0.78** **	**0.58** **	**0.70** **	**0.70** **
IKT60 AP in W	0.45 **	0.34 *	0.76 **	0.60 **	0.95 **	0.81 **	0.92 **	×	**0.88** **	**0.62** **	**0.85** **	**0.85** **
IKT180 PTQ in Nm	0.53 **	0.37 **	0.77 **	0.60 **	0.86 **	0.65 **	0.82 **	0.84 **	×	**0.71** **	**0.92** **	**0.93** **
IKT180 PTQ/BW in Nm/kg	0.02	0.10	0.63 **	0.70 **	0.72 **	0.81 **	0.73 **	0.73 **	0.85 **	×	**0.68** **	**0.67** **
IKT180 TW in J	0.40 **	0.29 *	0.67 **	0.52 **	0.76 **	0.62 **	0.81 **	0.76 **	0.93 **	0.86 **	×	**0.93** **
IKT180 AP in W	0.37 **	0.27 *	0.67 **	0.54 **	0.76 **	0.65 **	0.77 **	0.81 **	0.91 **	0.86 **	0.94 **	×

#Values in the lower left half represent correlations between variables before weight loss program; values in the right half (bold face) represent correlations between changes in variables after weight loss program. NOTES: IMT60 PTQ = Isometric60 peak torque; IMT60 PTQ/BW = Isometric60 peak torque/body weight; IKT60 PTQ = Isokinetic60 peak torque; IKT60 PTQ/BW = Isokinetic60 peak torque/body weight; IKT60 TW = Isokinetic60 total work; IKT60 AP = Isokinetic60 average power; IKT180 PTQ = Isokinetic180 peak torque; IKT180 PTQ/BW = Isokinetic180 peak torque/body weight; IKT180 TW = Isokinetic180 Total work; IKT180 AP Isokinetic180 average power. * $p < 0.05$; ** $p < 0.01$

Table 15 Correlation between change rates in lower extremity muscle mass and body weight, and lower extremity muscle strength adjusted for age

	Change rates in lower extremity muscle mass							
	Change rates in body weight	Change rates in IMT60 PTQ	Change rates in IKT60 PTQ	Change rates in IKT60 TW	Change rates in IKT60 AP	Change rates in IKT180 PTQ	Change rates in IKT180 TW	Change rates in IKT180 AP
	-7.2 ± 6.9 %							
	-14.1 ± 4.4 %	-3.0 ± 16.9 %	-4.8 ± 15.5 %	-2.9 ± 18.4 %	-0.3 ± 17.8 %	-3.9 ± 15.1 %	-2.9 ± 18.4 %	-1.6 ± 24.3 %
R^2	0.20	0.05	0.11	0.09	0.09	0.09	0.05	0.03
p	0.13	0.72	0.41	0.50	0.49	0.49	0.71	0.82

NOTES: IMT60 PTQ = Isometric60 peak torque; IKT60 PTQ = Isokinetic60 peak torque; IKT60 TW = Isokinetic 60 total work; IKT60 AP = Isokinetic60 average power; IKT180 PTQ = Isokinetic180 peak torque; KT180 TW = Isokinetic180 Total work; IKT180 AP = Isokinetic180 average power. Values are mean ± standard deviation.

4.3.5. Discussion

Weight loss induced by a combination of caloric reduction and an exercise program led to a14.1% weight loss accompanied by independent losses of leg muscle mass and static maximal muscle strength, dynamic maximal muscle strength and dynamic muscle endurance. However, dynamic muscle power was not significantly decreased and body weight-normalised muscle strength was increased. Though the augmentation of bodyweight-normalised muscle strength is beneficial for obese men, low muscle mass and muscle strength are also related to the occurrence of musculoskeletal system disorders after weight loss (Barbat-Artigas et al., 2012; Toda et al., 2000).

Weiss et al. (2007) have reported that a weight loss program with exercise did not induce a significant decrease in leg muscle volume as assessed by MRI and in leg muscle strength as assessed by an isokinetic dynamometer. Conversely, a weight loss program with caloric reduction was associated with the significant decreases which moderate intensity in both leg muscle volume and leg muscle strength (Weiss et al., 2007; Yoshimura et al., 2014). In addition, it has been shown that aerobic exercise induces quantitative and qualitative amelioration in the musculoskeletal system (Chomentowski et al., 2009). Aerobic exercise also increases resistance to fatigue, while resistance exercise increases maximum muscle output (Vila-Cha et al., 2010). These reports indicate that a weight loss program with exercise is beneficial for maintaining leg muscle mass and muscle strength. Despite this, prescribing weight loss programs with exercise for all obese men may not be appropriate. Because of the mechanical factors in joints, exercises that involve excessive weight bearing or joint loading may be deleterious to joints (Hunter and Felson, 2006). Existing reports have reported that losses in whole body fat-free mass and the cross-sectional area of the femoral muscle through a weight loss program consisting of caloric restriction and exercise were less than those through a weight loss program with caloric restriction (Chomentowski et al., 2009; Yoshimura et al., 2014). Given these findings, exercise during caloric reduction is not only expected to suppress losses of leg muscle mass and muscle strength but also may decrease the risk of injury during weight loss. Therefore, we conclude that a weight loss program consisting of both caloric reduction and exercise was appropriate for obese men in the present study (Fig.2)

Kraemer et al. (1999) reported that though whole body mass was decreased by −9.4%, 1-RM strength in a squat exercise increased +27.8% after a 12-week weight loss program consisting of caloric reduction and exercise in obese men. This result contradicts those of the present study. The reason for this discrepancy may be due to the rate of weight loss. The weight loss rate in existing research is almost 5% lower than the weight loss rate in the present study. From the existing studies described above, it is clear that exercise during caloric reduction had desirable effects on maintaining muscle strength (Chomentowski et al., 2009; Vila-Cha et al., 2010). However, on the basis of the results of the present study, we conclude that maintaining muscle strength is difficult in situations involving abundant losses in body weight.

It has long been recognised that a decline in muscle strength is a result of decreases in muscle mass and muscle strength is directly proportional to muscle mass (Doherty, 2001, 2003). However, reports in which muscle strength decline is not correlated with decreases in muscle mass have increased in recent years. Hughes et al. (2001) reported that changes in muscle mass muscle mass explain only 5% of the changes in strength, and according to Goodpaster et al. (2006), individuals who gained weight and lean mass did not become stronger as might have been expected. In the present study, the resulting association between the rate of muscle mass loss and that of muscle strength after weight loss was consistent with recent reports. At this point, the reason for the discrepancy between muscle mass and muscle strength has not been clearly identified. However, existing research has proposed a few factors influencing this discrepancy, including physical activity, sex hormones, obesity and fibrosis (Barbat-Artigas et al., 2012).

There are several limitations associated with the present study. First, there was no control group (weight loss program with caloric reduction) according to the capitalised study on a sample of convenience. Future studies will benefit from a study protocol that includes a control group. Second, the age range of participants in this study was relatively wide. Yoshimura et al. (2014), however, found that the decrease in cross-sectional area of the femoral muscle was smaller in the weight loss program consisting of caloric reduction and exercise compared with the weight loss program with caloric reduction alone, even after adjusting for age. Therefore, the age range of participants did not likely affect the results of the present study. Third, there was no objective data to explain why the loss of muscle strength was not coincident with the loss of leg muscle mass. Future avenues for research should include data on changes in the neuromuscular system and the quality of musculoskeletal system as a result of exercise during weight loss.

4.3.6. Conclusion

Weight loss achieved by a combination of a caloric reduction program and a comprehensive exercise program led to independent losses of leg muscle mass and leg muscle strength (except dynamic muscle power). The weight loss observed in this study was accompanied by increased body-weight-normalised muscle strength. Based on these results, we recommend utilizing resistance exercise to restore muscle mass and muscle strength in the legs after substantial weight loss.

CHAPTER 5. STUDY 3. Follow up study

Changes in muscle mass and strength after a year of weight loss

5.1. Purpose

The aim of this study was to investigate whether weight loss leads to detrimental decrease in muscle mass and strength that could lead to health problems.

5.2. Methods

5.2.1. Participants

As described in Figure 8, 31 participants whose BMI decreased to 25 kg/m^2 from BMI over 25 kg/m^2 were included as analysis subjects at the completion of the weight loss program. For the one-year follow-up data collection, we sent study flyers to the 31 participants to notify them of the follow up assessment and to survey their participation in the follow-up assessment 11 months after completing the weight loss program. We executed the follow-up assessment at the beginning of August in 2013 and 2014. Of these Participants, 17 were excluded because of nonattendance at the follow-up assessment. In total, 14 participants who maintained their BMI under 25 kg/m^2 were included as analysis subjects for the one-year follow-up.

We conducted a health survey event to collect data for the reference group in April 2014 at the University of Tsukuba, Japan. The participants in the health survey event were recruited from communities by advertising in local newspapers and distributing study flyers. The eligibility criteria for participation in the health survey event were as follows: 1) males aged 30-64 years; 2) no terminal disease, recent muscle injury, or surgery; and 3) no history of drug or alcohol abuse. As shown in Figure 6, a total of 46 men took part in the health survey event, and 29 participants with a BMI < 25 kg/m^2 were included as the reference group.

5.2.2. Assessment variables

Body composition was evaluated as follows: percentage of whole body fat, arm muscle mass, leg muscle mass, skeletal muscle mass index and percentage of muscle mass index. Handgrip strength and knee extensor strength which evaluated muscle strength in upper and lower extremity was expressed as an absolute, body weight-normalized, and arm and leg muscle mass-normalized value.

5.3. Statistical analyses

Statistical analyses were performed with SPSS software, version 18.0 (IBM, Inc., Armonk, NY, USA). The independent sample *t*-test was employed for normally distributed data. Otherwise, the Mann Whitney *U* test was employed. The data are expressed as the mean ± standard deviation (SD) values, and $P < 0.05$ was considered statistically significance.

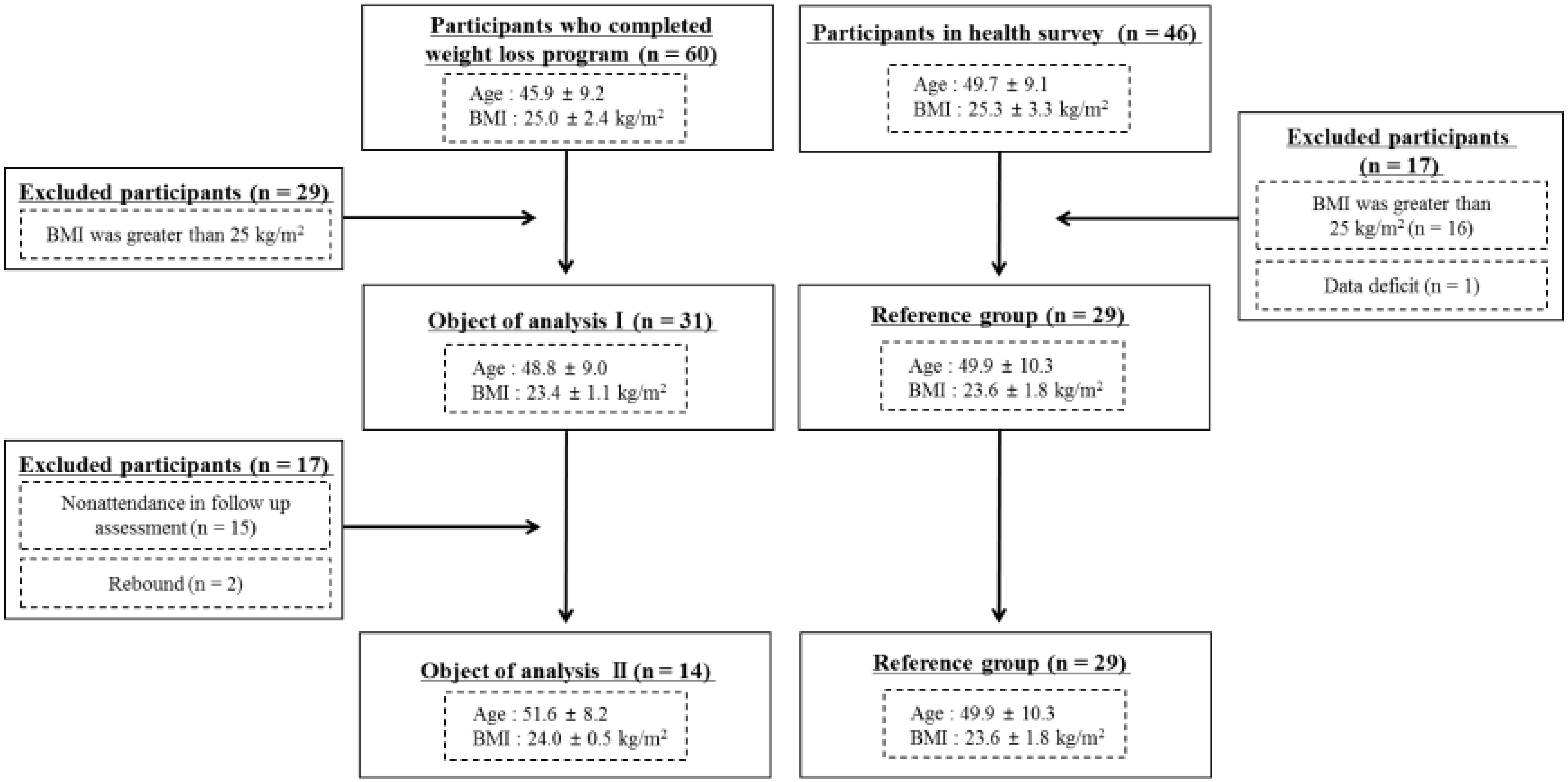


Figure 8. Flow chart of the study participants

5.4. Results

Table 16 contains characteristics of object of analysis I before and after weight loss program. During the weight loss program, the participants lost an average −13.7 ± 3.7 kg (−16.5 ± 3.8%, $P < 0.01$) of body weight. After weight loss, significant changes were found in both body composition and muscle strength. Except % MMI, other variables including whole body lean mass, whole body fat mass, arm muscle mass, leg muscle mass and SMI were significantly decreased (by −5.5 ± 2.0 kg, −7.2 ± 1.9 kg, −0.8 ± 0.3 kg, −1.3 ± 0.7 kg and −0.7 ± 0.3 kg, respectively; $P < 0.01$). % MMI was significantly increased (3.2 ± 1.2 %; $P < 0.01$). Handgrip strength (-0.4 ± 2.5 kg; $P = 0.37$) did not decline significantly and handgrip strength per body weight (0.10 ± 0.05 kg; $P < 0.01$) was significantly increased. Static maximal muscle strength (−14.4 ± 29.1 Nm at 60◦; $P < 0.05$), dynamic maximal muscle strength(−12.1 ± 25.4 Nm at 60◦/s; $P < 0.01$) declined significantly, whereas dynamic muscle endurance (−25.6 ± 79.8 Nm at 60◦/s; $P = 0.08$) and dynamic muscle power (−1.7 ± 15.6 Nm at 60◦/s; $P = 0.54$; $P = 0.54$) did not decline significantly and body weight-normalised muscle strength (0.3 ± 0.4 Nm/kg at 60◦, 0.2 ± 0.3 Nm/kg at 60◦/s, respectively; $P < 0.01$) was significantly increased.

The anthropometry and body composition characteristics as well as the differences between the two groups after completing the weight loss program are presented in Figure 9. The age, height, body weight and BMI did not significantly differ between the two groups. There were no significant differences in the total body fat percentages and leg muscle mass between the two groups. With respect to the arm muscle mass, SMI and %MMI, the values in the weight loss group were significantly lower than those of the reference group ($P < 0.01$, 0.05 and 0.05, respectively). The arm muscle mass in the weight loss group contributed to the difference between the groups with respect to the SMI and % MMI.

Figure 10 presents the muscle strength results for the two groups after completing the weight loss program. With the exception of the handgrip strength per arm muscle mass, there were no significant differences in any of the variables between the two groups. Although the arm muscle mass of the weight loss group was significantly lower than that of the reference group, a significant difference was not observed with respect to the handgrip strength between the two groups. The handgrip strength per arm muscle mass in the weight loss group was significantly higher than that in the reference group ($P < 0.01$). The upper extremity muscle mass decreased significantly after completion of the weight loss program, but it did not induce an undesirable decrease in the upper extremity muscle strength.

Table 17 and 18 present the results of the one-year follow-up assessment and the differences between the weight loss group and reference group. No significant differences were observed between the two groups with respect to any of the variables. These results revealed that weight loss resulting from a combination of caloric restriction and an exercise program did not induce an undesirable decline in muscle mass and strength.

Table 16 Characteristics of object of analysis I before and after weight loss program

	Pre (range)		Post (range)		Change (95% CI)		*P*
Age, year	48.8 ± 9	(31.0, 63.0)					
Height, cm	171.8 ± 5.1	(161.2, 180.0)					
Weight, kg	82.8 ± 6.5	(70.3, 96.1)	69.0 ± 5.0	(60.4, 79.0)	-13.7 ± 3.7	(-15.1, -12.4)	< 0.01
Body mass index, kg/m^2	28.0 ± 1.4	(25.6, 31.3)	23.4 ± 1.1	(21.3, 24.9)	-4.6 ± 1.2	(-5.1, -4.2)	< 0.01
Whole body lean mass, kg	61.9 ± 5.8	(53.4, 75.2)	56.4 ± 4.8	(49.4, 67.4)	-5.5 ± 2.0	(-6.2, -4.7)	< 0.01
Whole body fat mass, kg	19.7 ± 3.8	(14.6, 28.6)	12.5 ± 3.4	(8.2, 21.9)	-7.2 ± 1.9	(-7.9, -6.5)	< 0.01
Arm muscle mass, kg	6.5 ± 0.7	(5.1, 8.0)	5.7 ± 0.6	(4.7, 7.1)	-0.8 ± 0.3	(-0.9, -0.7)	< 0.01
Leg muscle mass, kg	19.4 ± 1.8	(16.8, 23.2)	18.8 ± 1.6	(15.8, 22.3)	-1.3 ± 0.7	(-1.6, -1.1)	< 0.01
SMI, kg/m^2	8.8 ± 0.6	(7.3, 10.0)	8.1 ± 0.5	(7.5, 9.3)	-0.7 ± 0.3	(-0.8, -0.6)	< 0.01
% MMI, %	31.3 ± 1.8	(27.8, 34.9)	34.5 ± 2.1	(30.1, 38.3)	3.2 ± 1.2	(2.8, 3.7)	< 0.01
HGS, kg	42.1 ± 5.7	(31.7, 52.7)	41.7 ± 5.6	(30.5, 50.5)	-0.4 ± 2.5	(-1.3, -0.5)	0.37
HGS/BW, kg	0.51 ± 0.08	(0.38, 0.69)	0.61 ± 0.10	(0.42, 0.77)	0.10 ± 0.05	(0.08, 0.11)	< 0.01
IMT60 PTQ, Nm	199.6 ± 40.6	(106.2, 300.0)	185.2 ± 33.3	(108.7, 257.2)	-14.4 ± 29.1	(-25.1, -3.7)	< 0.05
IMT60 PTQ/BW, Nm/kg	2.4 ± 0.4	(1.2, 3.1)	2.7 ± 0.5	(1.5, 3.7)	0.3 ± 0.4	(0.1, 0.4)	< 0.01
IKT60 PTQ, Nm	172.6 ± 37.3	(99.3, 263.8)	160.5 ± 23.2	(128.0, 224.7)	-12.1 ± 25.4	(-21.4, -2.8)	< 0.05
IKT 60 PTQ/BW, Nm/kg	2.1 ± 0.4	(1.2, 2.7)	2.3 ± 0.3	(1.8, 3.2)	0.2 ± 0.3	(0.1, 0.4)	< 0.01
IKT60 TW, J	485.7 ± 103.5	(221.4, 719.5)	460.1 ± 65.8	(351.5, 630.6)	-25.6 ± 79.8	(-54.8, 3.7)	0.08
IKT60 AP, W	102.4 ± 25.1	(44.0, 156.5)	100.6 ± 17.0	(74.1, 148.0)	-1.7 ± 15.6	(-7.5, 4.0)	0.54

NOTES: SMI = Skeletal muscle mass index; % MMI = Percentage of muscle mass index; HGS = Hand grip stremgth; HGS/BW = Hand grip strength/body weight; IMT60 PTQ = Isometric60 peak torque; IMT60 PTQ/BW = Isometric60 peak torque/body weight; IKT60 PTQ = Isokinetic60 peak torque; IKT60 PTQ/BW = Isokinetic60 peak torque/body weight; IKT60 TW = Isokinetic60 total work; IKT60 WF = Isokinetic60 work fatigue; IKT60 AP = Isokinetic60 average power. Mean ± standard deviation (range).

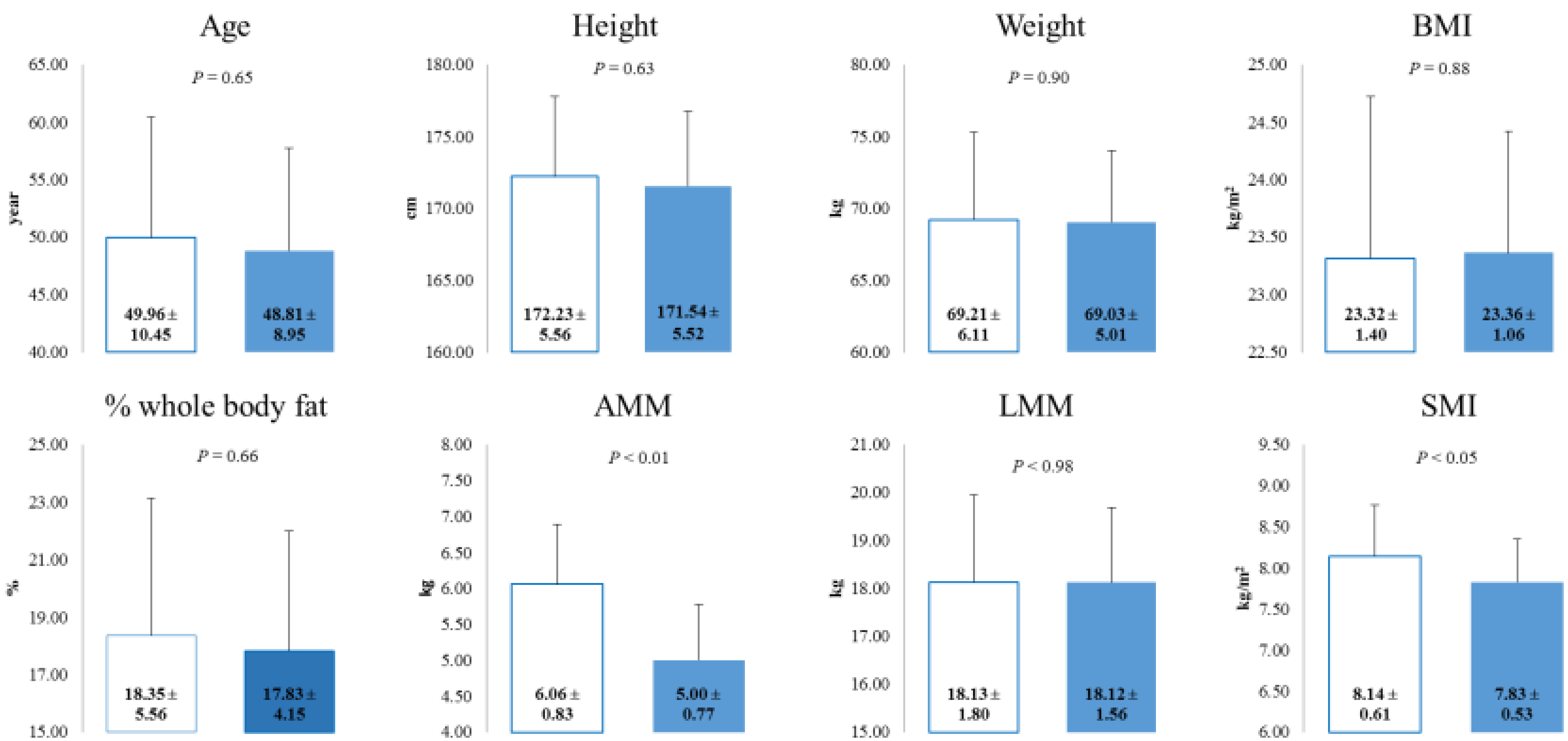
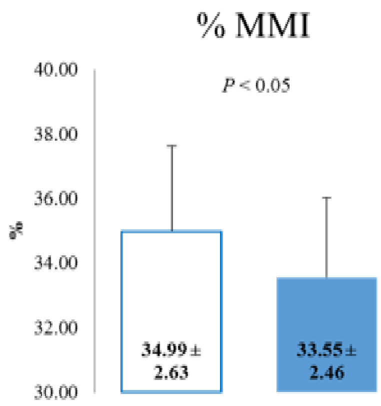


Fig 9. Characteristics of anthropometry and body composition, and differences between two groups after completing the weight loss program



NOTES:BMI = body mass index ; % whole body fat = percentage of whole body fat ; SMI = Skeletal muscle index ; % MMI = Percentage of muscle mass Index

Reference group Weight loss group

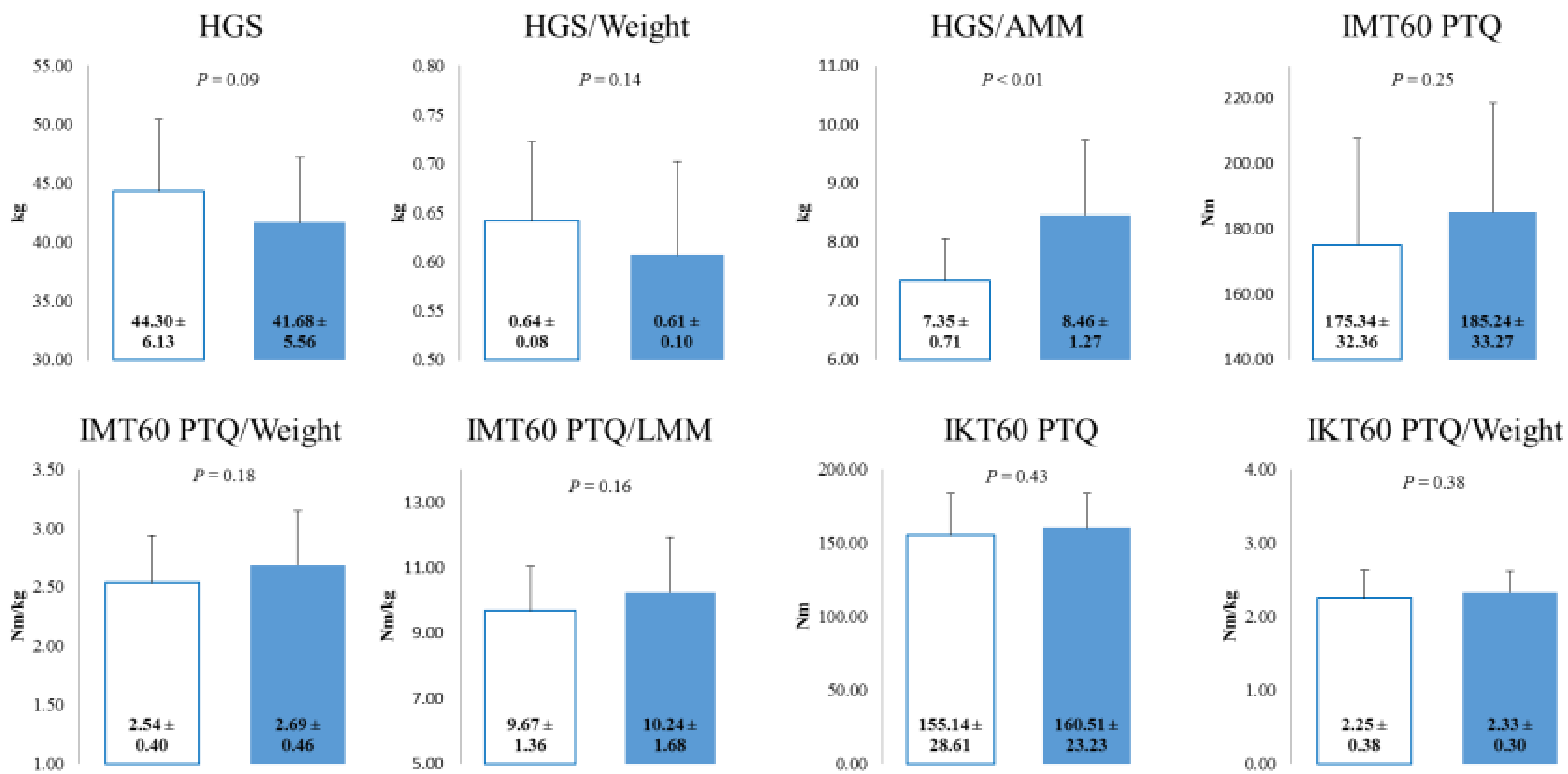
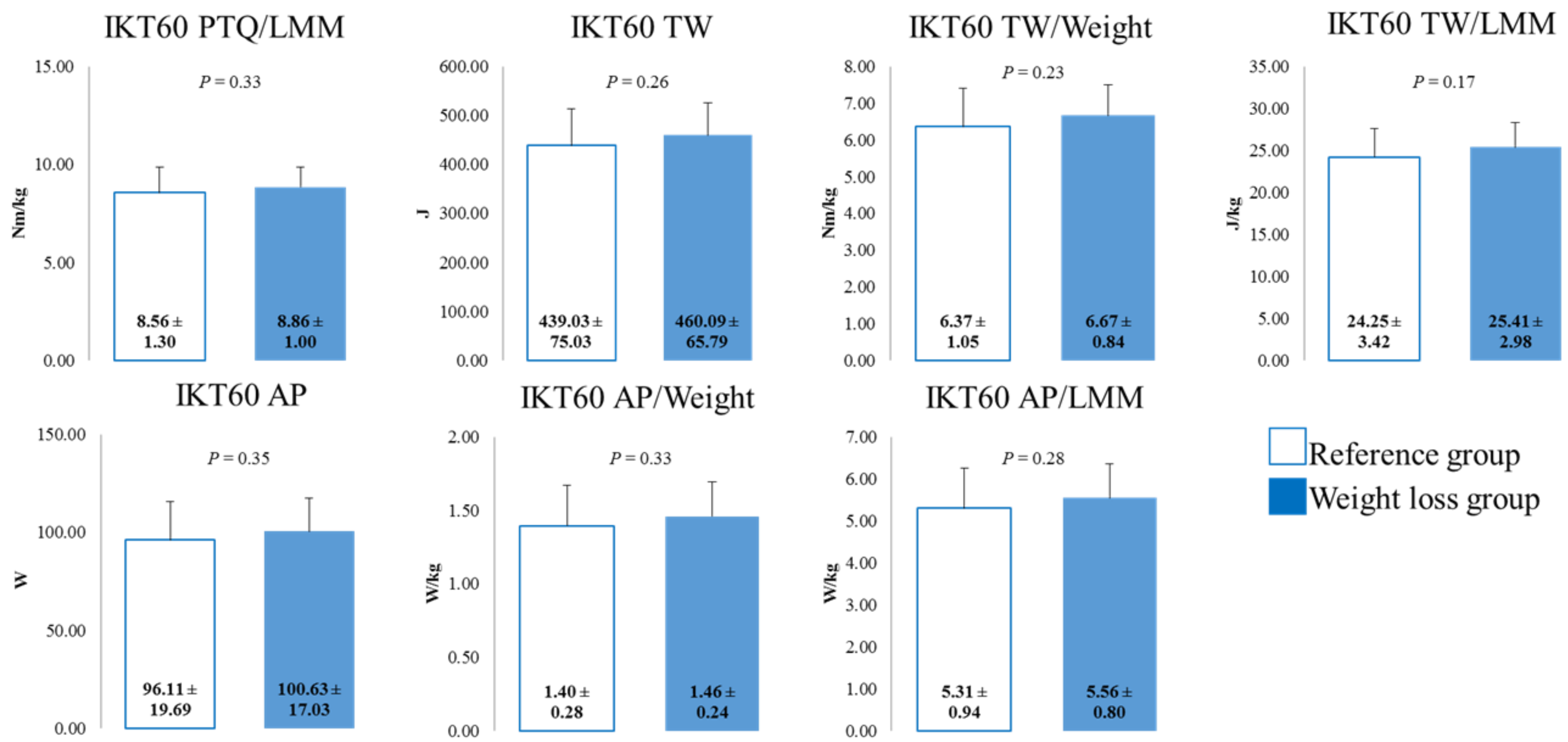


Fig 10. Characteristics of muscle strength and differences between two groups after completing the weight loss program



NOTES: HGS = Handgrip strength ; AMM = Arm muscle mass ; LMM = Leg muscle mass ; IMT60 PTQ = Isometric60 peak torque; IKT60 PTQ = Isokinetic60 peak torque; IKT60 TW = Isokinetic60 total work; IKT60 AP = Isokinetic60 average power

Table 17 Characteristics of anthropometry and body composition, and differences between two groups after a year of weight loss program

	Reference (n = 28)	Weight loss[b] (n = 14)	Mean Difference (95% CI)	*P*
Age, year	49.96 ± 10.45	48.71 ± 8.19	1.25 ± 2.95 (-4.75, 7.25)	0.70
Height, cm	172.23 ± 5.56	170.87 ± 6.20	1.35 ± 1.96 (-2.70,5.41)	0.48
Weight, kg	69.21 ± 6.11	70.20 ± 5.07	-0.99 ± 1.78 (-4.62, 2.64)	0.61
BMI, kg/m^{2}[a]	23.32 ± 1.40	24.02 ± 0.47	-0.70 ± 0.29 (-1.30, -0.11)	0.11
% whole body fat, %	18.35 ± 4.77	17.63 ± 3.30	0.73 ± 1.26 (-1.84, 3.29)	0.61
Arm muscle mass, kg	6.06 ± 0.83	6.01 ± 0.60	0.05 ± 0.22 (-0.41, 0.51)	0.84
Leg muscle mass, kg	18.13 ± 1.80	18.67 ± 1.51	-0.54 ± 0.53 (-1.61, 0.54)	0.34
SMI, kg/m^{2}[a]	8.14 ± 0.61	8.45 ± 0.42	-0.30 ± 0.16 (-0.63, 0.02)	0.13
% MMI, %	34.99 ± 2.63	35.18 ± 1.85	-0.19 ± 0.70 (-1.61, 1.24)	0.81

NOTES: BMI = body mass index ; % whole body fat = percentage of whole body fat ; AMM = Arm muscle mass ; LMM = Leg muscle mass ; SMI = Skeletal muscle index ; % MMI = percentage of muscle mass Index ; [a]Mann Whitney U test was employed ; [b]Values are means ± standard deviation or means ± standard error; CI = confidence interval

Table 18 Characteristics of muscle strength, and differences between two groups after a year of weight loss program

	Reference (n = 28)	Weight loss[b] (n = 14)	Mean Difference (95% CI)	*P*
HGS, kg	44.30 ± 6.13	43.25 ± 6.13	1.05 ± 2.06 (-3.19, 5.29)	0.61
HGS/Weight, kg	0.64 ± 0.08	0.62 ± 0.10	0.02 ± 0.03 (-0.04,0.09)	0.45
HGS/AMM, kg	7.35 ± 0.71	7.23 ± 0.99	0.12 ± 0.29 (-0.50,0.74)	0.66
IMT60 PTQ, Nm	175.34 ± 32.36	194.36 ± 33.51	-19.03 ± 10.84 (-41.35, 3.29)	0.08
IMT60 PTQ/Weight, Nm/kg	2.54 ± 0.40	2.78 ± 0.52	-0.25 ± 0.16 (-0.57, 0.08)	0.10
IMT60 PTQ/LMM, Nm/kg	9.67 ± 1.36	10.49 ± 2.08	-0.82 ± 0.61 (-2.10,0.46)	0.13
IKT60 PTQ, Nm	155.14 ± 28.61	160.73 ± 31.45	-5.59 ± 9.99 (-26.22, 15.03)	0.57
IKT60 PTQ/Weight, Nm/kg	2.25 ± 0.38	2.30 ± 0.45	-0.05 ± 0.14 (-0.34, 0.24)	0.72
IKT60 PTQ/LMM, Nm/kg	8.56 ± 1.30	8.65 ± 1.72	-0.09 ± 0.52 (-1.17, 1.00)	0.86
IKT60 TW, J	439.03 ± 75.03	461.90 ± 89.67	-22.88 ± 27.86 (-80.60, 34.85)	0.39
IKT60 TW/Weight, Nm/kg	6.37 ± 1.05	6.60 ± 1.25	-0.23 ± 0.39 (-1.03, 0.58)	0.54
IKT60 TW/LMM, J/kg	24.25 ± 3.42	24.83 ± 4.75	-0.58 ± 1.42 (-3.55, 2.39)	0.65
IKT60 AP, W	96.11 ± 19.69	102.38 ± 21.83	-6.27 ± 6.92 (-20.56, 8.01)	0.35
IKT60 AP/Weight, Nm/kg	1.40 ± 0.28	1.46 ± 0.31	-0.07 ± 0.10 (-0.27, 0.13)	0.48
IKT60 AP/LMM, W/kg[a]	5.31 ± 0.94	5.51 ± 1.19	-0.20 ± 0.37 (-0.96, 0.56)	0.65

NOTES: HGS = Handgrip strength ; AMM = Arm muscle mass ; LMM = Leg muscle mass ; IMT60 PTQ = Isometric60 peak torque ; IKT60 PTQ = Isokinetic60 peak torque ; IKT60 TW = Isokinetic60 total work ; IKT60 AP = Isokinetic60 average power ; [a]Mann Whitney U test was employed ; [b]Values are means ± standard deviation or means ± standard error; CI = confidence interval

5.5. Discussion

The purpose of this study was to investigate whether weight loss significantly decreases muscle mass and strength to cause health problems; the primary findings of this study were as follows. First, the arm muscle mass in the weight loss group was significantly less than that in the reference group after completion of the weight loss program. Low arm muscle mass contributed significantly to low SMI and % MMI in the weight loss group compared with the reference group. Second, there were no significant differences between the two groups with respect to the absolute and relative (strength per body weight and muscle mass) values for muscle strength except in the handgrip strength per arm muscle mass, which was significantly higher in the weight loss group than in the reference group. Third, no significant differences between the two groups were observed for any the variables after a one-year weight loss program. These findings are inconsistent with existing reports that weight loss can cause an undesirable decrease in muscle mass and strength, which is thus likely to decrease physical performance.

The results after the completion of the weight loss program indicate that there were no significant differences between the reference and weight loss groups with respect to total body fat percentages and leg muscle mass, whereas the arm muscle mass, SMI and % MMI in the weight loss group were significantly lower than those in the reference group. The low SMI and % MMI in the weight loss group were derived from the low arm muscle mass. Low arm muscle mass after the completion of a weight loss program might be problematic. However, there was no significant difference between the reference and weight loss groups with respect to handgrip strength, and the handgrip strength per arm muscle mass in the weight loss group was significantly greater than that in the reference group. Absolute muscle strength is the easiest way to measure muscle strength, whereas relative muscle strength (the muscle strength per body weight or muscle mass) might be more relevant for indicating functional impairments (Barbat-Artigas et al., 2012; Ploutz-Snyder et al., 2002). Muscle strength per muscle mass has been widely employed to determine muscle quality (Barbat-Artigas et al., 2012; Goodpaster et al., 2006; Wang et al., 2007). Thus, our results indicate that the muscle quality in the arm muscle mass was improved after the completion of the weight loss program. The absolute and relative (strength per body weight and muscle mass) values of leg muscle strength in the weight loss group were not significantly lower than those of the reference group. Therefore, it is difficult to conclude that muscle mass and strength decreased inappropriately.

Previous studies have recommended utilizing resistance exercise to restore or increase muscle mass and strength after weight loss on the basis that ground-reaction forces and related rates of loading during physical activity are increased in combination with a decline in muscle mass and strength (Cicuttini et al., 2005; Henriksen et al., 2012; Kim et al., 2015; Mikesky et al., 2000). Resistance exercise to restore or increase muscle mass and strength might not be needed because a year after completion of the weight loss program, the muscle mass and strength returned to the pre-weight loss state. In addition, Santanasto et al (2010) reported that a weight loss program consisting of caloric restriction and exercise caused additional improvements in function compared with exercise alone because the thigh fat area decreased 6-fold relative to the lean area after weight loss. Beavers et al (2013) reported that a change in fat mass is a more significant predictor of change in physical function than a change in lean mass. Weight loss decreases the physical burden on the musculoskeletal system and does not cause an inappropriate decrease in muscle mass and strength. These changes after weight loss are very likely to contribute to an improvement in physical performance.

The conclusion in this study was confirmed with a weight loss program consisting of caloric reduction and exercise. It remains unclear whether similar conclusions could be drawn at the conclusion of a weight loss program based only on dietary modification. Further research is needed to determine whether a weight loss program with caloric reduction induces an undesirable decrease in muscle mass and strength.

5.6. Conclusion

The upper extremity muscle quality in the weight loss group was significantly greater than that in the reference group, and no significance was observed between the two groups with respect to the other variables at the completion of the weight loss program. A year after the completion of the program, no significant differences between the two groups were found in any of the variables. Weight loss does not induce a concerning decrease in muscle mass and strength.

CHAPTER 6. COMPREHENSIVE DISCUSSION

6.1. Major findings

This study was carried out to investigate changes in muscle mass and strength, as well as the association between muscle mass and strength after completing a weight loss program. The following major findings were obtained:

1) Both body fat and muscle mass increase as obesity develops. Muscle mass and strength correlate positively with obesity. In the presence of obesity, increases in leg muscle mass and strength may not improve body-weight-normalized muscle strength.

2) Weight loss achieved by either dietary modification alone or the combination of dietary modification and a comprehensive exercise program led to independent losses of leg muscle mass and leg muscle strength. The rates of decrease in leg muscle mass and strength induced by a dietary modification were greater than those caused by the combination program. Body-weight-normalized leg muscle strength increased after the combination program, whereas it remained constant after dietary modification.

3) RE produced a tendency for muscle mass to increase that was independent of increases in muscle strength. It also decreased whole body fat mass. AE decreased fat mass and body weight and was associated with maintenance of muscle mass and strength. RE was more effective than AE for muscle mass and strength gain.

4) One year after completion of the program, no significant differences between the

reference and weight loss group were found in any of the variables. Weight loss does not produce a worrisome decrease in muscle mass or muscle strength.

6.2. Limitations and future directions

For the cross sectional study, a total of 259 Japanese male adults were divided into groups A (Non-obese, n = 60), B (Obesity class I, n = 142), C (Obesity class II, n = 47) and D (Obesity class III, n = 10) based on Japanese obesity guidelines. The sample size differed across groups. In particular, there were only 10 participants in group D, which may constrain comparisons between groups. For example, there were several non-significant differences between groups C and D in Tables 2 and 3. These results may be due to the small sample size in group D. Considering this potential limitation, future studies need to investigate characteristics of muscle mass and strength in individuals whose BMI exceeds 35 kg/m^2.

In the intervention studies, the findings revealed that changes in muscle strength are not strongly correlated with changes in muscle mass. However, this study cannot explain what accounts for the discrepancy between muscle mass and strength. Previous researchers have suggested the following potential explanations for the discrepancy:

Obesity

Increases in intramuscular and intermuscular fat occur with both aging and obesity and compromise evaluation of muscle mass by methods such as DEXA and bio impedance analysis. In a cohort of 1454 elderly men, Rolland et al (2004) reported that muscle strength adjusted for muscle mass did not differ significantly between obese, normal-weight and lean subjects. However, DEXA does not exclude intermuscular fat from the muscle mass measured (Rolland et al., 2004). Consequently, overestimation of the muscle mass of obese individuals may have reduced the adjusted muscle strength.

Resistance exercise

Several mechanisms have been suggested to explain the increased muscle strength per muscle mass associated with strength training. Ivey et al (2000) have hypothesized that resistance training induces transformation of type II muscle fiber subtypes (from type IIb to IIa). However, to what extent, if any, this change explains muscle quality increases is unclear. Tracy et al (1999) also hypothesized that alterations in muscle architecture could affect changes in the muscle strength per muscle mass with resistance training. Kawakami et al (1995) reported greater pennation angles in subjects with hypertrophied muscles than in those with normal muscles. Increases in muscle fascicle angles have also been reported as a result of resistance training (Kawakami et al., 1995). On the other hand, it has been suggested that neuromuscular factors may be more likely than mechanical and architectural factors to account for the increase in muscle strength per muscle mass with resistance training (Ivey et al., 2000; Young et al., 1983). Hakkinen et al (1998) made similar conclusions with reference to the strength gains that are independent of hypertrophy during the first few weeks of resistance training.

Fibrosis

Evidence also tends to show an age-associated fibrotic tissue deposition in muscle (myofibrosis) that may alter muscle quality. Numerous findings from animal studies report an increase in fibrous connective tissue and an impairment of muscle regenerative potential, manifested by replacement of muscle with fibrous connective tissue (Serrano and Munoz-Canoves, 2010). Indeed, aging animal studies have reported increases in collagen concentration or advanced glycation end products, both of which have been associated with increased muscle stiffness and reduced muscle function. To date, few studies have investigated this phenomenon in human skeletal muscle. Researchers have found significantly increased advanced glycation end products cross-linking in older individuals compared with young individuals, which is paralleled by significantly decreased muscle mass, muscle strength, muscle power and muscle strength per cross-sectional area (Haus et al., 2007). Based on these results, it has been suggested that the formation of advanced glycation end products may contribute to increased muscle connective tissue protein stiffness and may thus contribute to impaired muscle function.

Further research is essential to narrow down the potential factors that might affect the discrepancy between changes in muscle mass and muscle strength.

Aging

An age-associated decline in the muscle strength per muscle mass would be estimated, because muscle strength declines at a higher rate than muscle mass. Two known main factors in muscle might explain the observed age-associated changes in the muscle strength per muscle mass: neuronal factors, and muscle fiber composition. Electrophysiological and histological studies show that motoneuron diseases become increasingly more prevalent in older individuals (Brown, 1972; Campbell et al., 1973; Grimby et al., 1982; Tomonaga, 1977). The remaining motor units are enlarged and tend to have fewer type II fibers. These enlarged motor units partially maintain muscle mass even while muscle strength deteriorates. To put it slightly differently, the denervated-reinnervated muscle become less efficient, which might explain some of the observed decline in muscle strength in excess of what is estimated based on the decline in muscle mass. The changes in muscle fiber composition with aging are controversial. It is unclear whether the proportion of type II muscle fibers declines with aging. However, it is agreed that type II fibers decrease in size in older individuals (Grimby et al., 1982; Tomonaga, 1977). Thus, some suggested that the decreased size and possibly decreased percentage of type II fiber may cause a loss of muscle strength out of proportion to the decline in muscle mass (Kallman et al., 1990; Overend et al., 1992).

To investigate the appropriateness of changes in muscle mass and strength resulting from weight loss, a follow up study was conducted. The findings indicated that weight loss does not lead to undesirable decreases in muscle mass and strength. However, this conclusion was based on evidence from a weight loss program consisting of a dietary modification program combined with a comprehensive exercise program. As a result, it is unclear whether weight loss through a dietary modification program alone could lead to detrimental changes in muscle mass and strength that could cause health problems. Thus, future studies need to perform a follow up study after weight loss with a dietary modification program.

6.3. Conclusion and suggestion

As obesity progresses, the absolute value of muscle mass and strength increases and strength per body weight decreases. Recently, the importance of relative muscle strength has attracted attention because muscle strength per body weight might be more relevant for functional impairments than absolute muscle strength (Barbat-Artigas et al., 2012; Ploutz-Snyder et al., 2002). On the basis of this evidence, weight loss has been recommended for obese individuals to improve strength per body weight.

On the one hand, weight loss with a dietary modification program does not improve strength per body weight in tandem with considerable decrease in absolute muscle mass and strength. Engaging in exercise mitigates muscle mass and strength loss during weight loss caused by a dietary modification program. Considering these factors, a combination of a dietary modification program and an exercise program is recommended. However, prescribing a weight loss program with exercise for all obese individuals may not be appropriate. Because of the mechanical limits of joints, exercises that involve excessive weight bearing or joint loading may be deleterious to obese individuals' joints (Hunter and Felson, 2006). Therefore, I suggest following a 12-week weight loss plan. As described in Figure 11, from the beginning to 6 weeks, a dietary modification program is implemented to induce weight loss and prevent musculoskeletal injuries resulting from executing exercise with heavy body weight. The decrease in muscle mass and strength may be slight when body weight loss is not considerable. After 6 weeks of a dietary modification program, an exercise program is added to the dietary

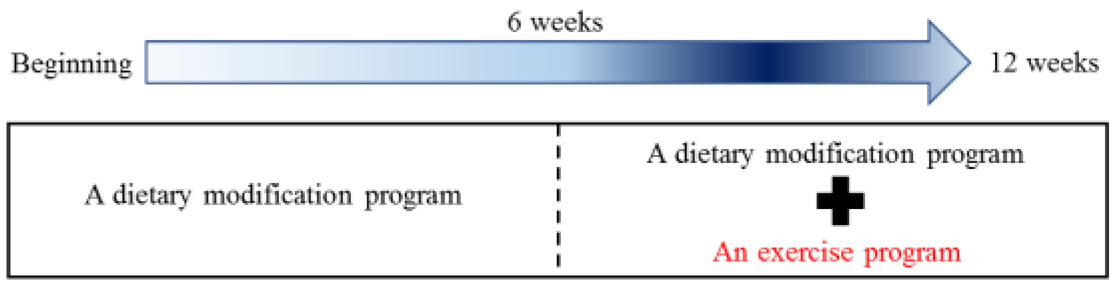


Figure 11. A 12-week weight loss plan

modification program. This addition will have positive effects on minimizing muscle mass and strength loss as well as on accelerating body weight loss. In terms of prescribing an exercise regimen, individual circumstances should be considered. Men whose most urgent need is maintenance of muscle mass and strength during weight loss are better off performing resistance exercise. However, to accelerate body weight loss, aerobic exercise may be the better prescription.

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