

Elina Sillanpää

Adaptations in Body Composition,  
Metabolic Health and Physical Fitness  
during Strength or Endurance Training  
or Their Combination in Healthy Middle-  
Aged and Older Adults



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## ABSTRACT

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Adaptations in body composition, metabolic health and physical fitness during strength or endurance training or their combination in healthy middle-aged and older adults

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The purpose of this thesis was to investigate the effects of a 21-week endurance, strength and combined training period on body composition, metabolic health, physical fitness and health-related quality life (HRQoL) in healthy 39-77-year-old men and women. The experimental measures (body composition, metabolic variables, maximal oxygen uptake, muscle strength etc.) were assessed before and after training. During the intervention period both endurance and strength training groups trained two times a week. Endurance was performed by cycling, and strength training included high-intensity progressive training for all main muscle groups. The combined group trained four times a week, performing strength and endurance training protocols on different days. The 21-week training period led to large gains in muscle strength and maximal oxygen uptake in the combined strength and endurance group. The magnitude of these increases did not differ from the corresponding changes observed in the group that performed either strength or endurance training alone. Combined training was also of greater value than either endurance or strength training alone in optimizing body composition, i.e. decreasing body fat and increasing lean mass in older adults. Both endurance and strength training may modestly improve metabolic health characterized by abdominal obesity, blood lipids and lipoproteins, glucose and insulin metabolism and blood pressure even in healthy normal or slightly overweight men and women. Combined training did not produce additional benefits in any of the metabolic health factors over endurance or strength training alone. Endurance training alone and combined with strength training positively affected some dimensions of HRQoL and combined training especially improved the vitality dimension of the HRQoL over endurance or strength training only. To conclude, the present combined training program did not produce synergistic benefits for metabolic health over endurance or strength training only, but was especially effective in improving body composition and both aerobic performance and muscle strength, which may be of high value in preventing worsening metabolic syndrome risk factors even in low-risk individuals without the metabolic syndrome.

**Keywords:** body composition, metabolic health, combined strength and endurance training, health-related quality of life, randomized controlled trial

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*Dedicated to my best friend and husband, Janne*



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Jyväskylä, January 2011,  
Elina Sillanpää

## LIST OF ORIGINAL PUBLICATIONS

The present thesis is based on the following original articles, which are referred to in the text by their Roman numerals.

- I Sillanpää E., Häkkinen A., Nyman K., Mattila M., Cheng S., Karavirta L., Laaksonen DE., Huuhka N., Kraemer WJ, Häkkinen K. Body composition and fitness during strength and/or endurance training in older men. *Medicine and Science in Sport and Exercise* 2008 40(5):950-958.
- II Sillanpää E., Häkkinen A., Punnonen K., Häkkinen K., Laaksonen DE. Effects of strength and endurance training on metabolic risk factors in healthy 40-65-year-old men. *Scandinavian Journal of Medicine and Science in Sports* 2009 19(6):885-895.
- III Sillanpää E., Laaksonen DE., Häkkinen A., Karavirta L., Jensen B., Kraemer WJ., Nyman K., Häkkinen K. Body composition, fitness and health during strength and endurance training in middle-aged and older women. *European Journal of Applied Physiology* 2009 106(2):285-96.
- IV Sillanpää E., Häkkinen A., Laaksonen DE, Kraemer WJ, Karavirta L., Häkkinen K. Serum basal hormone concentrations, nutrition and physical fitness during strength and/or endurance training in 39-64-year-old women. *International Journal of Sports Medicine* 2010 31(2):110-7.
- V Sillanpää E., Häkkinen K., Häkkinen A. Combined strength and endurance training improves health-related quality of life in healthy older adults. *Submitted for publication.*

## ABBREVIATIONS

1RM	one repetition maximum load
ACSM	American College of Sports Medicine
AUC	area under the curve
BMI	body mass index
C	control
CSA	cross-sectional area
CT	computed tomography
DAG	diacylglycerol
DBP	diastolic blood pressure
DHEAS	dehydroepiandrosterone sulfate
DXA	dual-energy X-ray absorptiometry
E	endurance
HDL-C	high-density lipoprotein
HRQoL	health-related quality of life
ICC	intraclass correlation coefficient
IDF	International Diabetes Federation
IGF-1	insulin-like growth factor 1
LDL-C	low-density lipoprotein
MRI	magnetic resonance imaging
NCEP	National Cholesterol Education Program
OGTT	oral glucose tolerance test
QF	quadriceps femoris
RCT	randomized controlled trial
RMR	resting metabolic rate
S	strength
SBP	systolic blood pressure
SD	standard deviation
SE	standard error
SE	strength and endurance
SHBG	sex-hormone binding globulin
T	testosterone
TB	triceps brachii
TC	total cholesterol
TG	triglycerides
US	ultrasound
VL+VI	vastus lateralis + vastus intermedius
VO <sub>2</sub> max	maximal oxygen uptake
WHO	World Health Organization
W <sub>max</sub>	maximal cycling power
%fat	percentage of body fat

## CONTENTS

ABSTRACT

ACKNOWLEDGEMENTS

LIST OF ORIGINAL PUBLICATIONS

ABBREVIATIONS

1	INTRODUCTION .....	13
2	REVIEW OF THE LITERATURE .....	16
2.1	Aging .....	16
2.1.1	Age-related changes in body composition .....	16
2.1.2	Metabolic consequences of aging.....	17
2.1.3	Changes in physiological performance with aging.....	18
2.2	Physical training and body composition.....	20
2.2.1	Body composition assessment in intervention studies .....	20
2.2.2	Effects of endurance training on body composition .....	23
2.2.3	Effects of strength training on body composition .....	24
2.3	Improving metabolic health through physical training.....	25
2.3.1	Prevalence of metabolic risk factors .....	25
2.3.2	Physical training and total and abdominal obesity.....	26
2.3.3	Physical training and glucose and insulin metabolism .....	27
2.3.4	Physical training and blood lipids and lipoproteins.....	29
2.3.5	Physical training and resting blood pressure.....	30
2.4	Physical training and performance .....	31
2.4.1	Effects of endurance training on physical fitness .....	31
2.4.2	Effects of strength training on physical fitness .....	33
2.4.3	Training response at different ages .....	34
2.4.4	Special effects of combined endurance and strength training..	36
3	PURPOSE OF THE STUDY .....	40
4	RESEARCH METHODS.....	41
4.1	Subjects.....	41
4.2	Study design.....	42
4.3	Training protocols.....	43
4.3.1	Endurance training protocol.....	43
4.3.2	Strength training protocol.....	44
4.4	Measurements .....	44
4.4.1	Body composition.....	44
4.4.2	Metabolic health indicators.....	45
4.4.3	Muscle strength .....	46
4.4.4	Aerobic performance .....	47
4.4.5	Serum basal hormone concentrations .....	48

4.4.6	Dietary intake.....	48
4.4.7	Health-related quality of life (HRQoL).....	49
4.5	Statistical methods.....	49
4.6	Study approval.....	50
5	RESULTS .....	51
5.1	Subject characteristics.....	51
5.2	Drop-outs and compliance to experimental training .....	51
5.3	Body composition.....	52
5.3.1	Body weight and BMI.....	53
5.3.2	Total body fat.....	54
5.3.3	Abdominal fat.....	54
5.3.4	Body lean mass and muscle thickness .....	55
5.3.5	Reproducibility of different body composition methods.....	57
5.3.6	Relationships between different body composition methods ..	57
5.4	Metabolic health indicators.....	57
5.4.1	Glucose and insulin metabolism.....	57
5.4.2	Lipid and lipoprotein metabolism.....	59
5.4.3	Blood pressure .....	61
5.4.4	Relationships between body composition and metabolic health indicators .....	63
5.5	Physical performance .....	63
5.5.1	Aerobic performance .....	65
5.5.2	Relationships between metabolic health indicators and physical fitness.....	65
5.6	Nutrition intake.....	67
5.7	Basal hormone concentrations.....	67
5.8	Health-related quality of life.....	68
6	DISCUSSION .....	71
6.1	Changes in body fat and fat distribution during training .....	71
6.2	Training effects on metabolic health indicators .....	75
6.3	Changes in aerobic performance and muscle strength and mass during training.....	79
6.4	Training effects on health-related quality of life.....	82
6.5	Methodological strengths and limitations .....	83
6.6	Practical applications and suggestion for future research.....	85
7	PRIMARY FINDINGS AND CONCLUSIONS.....	86
	YHTEENVETO (FINNISH SUMMARY).....	88
	REFERENCES.....	91

## 1 INTRODUCTION

Aging and obesity are major and mounting public health concerns. Worldwide the aging population is growing. During 2000-2030, the worldwide population aged  $\geq 65$  years is projected to increase by approximately 550 million to 973 million (U.S. Census Bureau 2010), increasing from 6.9% to 12.0% worldwide and from 15.5% to 24.3% in Europe. Aging, and especially age-related diseases and loss of independence, is a major socioeconomic and public health challenge. The loss of independence occurs due to loss of mobility, in part, due to loss of muscle mass, strength and endurance.

Obesity has reached pandemic proportions globally. More than 1 billion adults are overweight and at least 300 million are clinically obese (World Health Organization (WHO) 2010). Obesity and overweight are a major risk for several serious diseases, including cardiovascular diseases, hypertension and stroke, type 2 diabetes, and certain forms of cancer. Even before these diseases exist, obesity reduces the overall quality of life by diminishing physiological, psychological and, in some cases, social well-being.

Obesity results from a long-term positive energy balance. A decrease in total physical activity may be the dominant reason for increased prevalence of obesity. Increased leisure time physical activity has not compensated decreased physical activity at work and in transportation (Petersen et al. 2010).

The growing number of older adults increases demands on the public health system and on medical and social services. At the same time as Western countries are struggling with rapidly increasing health care costs due to the aging population, the costs of obesity-related disorders are exploding. It is estimated that obesity accounts 2-7% of the total health care costs in several developed countries (WHO 2000a). Not all obesity-related costs are included in the calculations, so the true costs are undoubtedly much greater.

Obesity and physical inactivity, and very often also aging, lead to adverse metabolic effects on blood triglycerides, high-density cholesterol, blood pressure and glucose and insulin metabolism. A cluster of these risk factors has been referred to as the metabolic syndrome (Alberti et al. 2009). The prevalence of metabolic syndrome in different populations have varied widely, mostly due



to the differences in the definitions of the syndrome, and in part because of differences in the characteristics of the populations studied. In the year 2002, the prevalence of the metabolic syndrome according to the International Diabetes Federation (IDF) criteria was 55.6% in men and 45.3% in women in the Finnish adult population (Hu et al. 2008).

Health promotion focuses on prevention of disability and development and progression of the disease through modification of risk factors. Effective prevention and treatment of obesity involves promotion of healthy behavior through exercise and nutrition. Both these factors are also of great importance in preventing the age-associated decline in muscle strength and mass, aerobic fitness and functional capacity.

The current American College of Sports Medicine (ACSM) recommendations on the types and amounts of physical activity needed by healthy adults to improve and maintain health includes moderate-intensity aerobic activity for a minimum of 30 min on five days each week or vigorous intensity activity for a minimum of 20 min on three days each week. In addition, every adult should perform activities that maintain or increase muscular strength and endurance a minimum of two days each week (Haskell et al. 2007). Although there is extensive evidence on the health benefits of both strength and endurance training, few studies have compared the effects of strength training, endurance training, and combined training on healthy middle-aged and older subjects.

Knowledge of the impact of strength or endurance training on metabolic health in men and women with relatively few risk factors is important from the perspective of public health (Lakka and Laaksonen 2007). Cardiovascular disease risk starts to rise approximately 15 years before the diagnosis of type 2 diabetes (Hu et al. 2002), and prediabetes develops up to 10 years before the onset of diabetes. Thus, the key to the successful treatment of type 2 diabetes is primary prevention. One major weapon against the metabolic syndrome and type 2 diabetes is physical activity. Sedentary behavior is an independent risk factor of type 2 diabetes itself. In addition, increased physical training may also affect several other major risk factors related to body composition and lipid and glucose metabolism.

Both endurance and strength training may ameliorate total and abdominal obesity, glucose and insulin metabolism, and other manifestations of metabolic health. Strength and endurance training-induced improvements in body composition, metabolic health, and physical fitness have been observed both in obese, type 2 diabetic and healthy subjects even without corresponding weight loss (DiPietro et al. 2006; Evans et al. 2005; Lee et al. 2005; Miller et al. 1994). Many questions regarding the type, intensity, duration, and frequency of training are still unanswered. Endurance training improves insulin sensitivity and muscle oxidative capacity, decreases intramuscular lipid content and increases whole body rates of fat oxidation and turnover (Boule et al. 2001; Bruce and Hawley 2004). In contrast to endurance training, strength training increases muscle mass and muscle glucose disposal (Fenicchia et al. 2004). The possible synergistic benefits are of high interest. In some studies, however, combining

strength training to endurance training has led to diminished adaptation in strength or muscle mass development, especially during high-intensity or high-volume physical training (Dolezal and Potteiger 1998; Glowacki et al. 2004; Hickson 1980). This mechanism has been referred to as the interference effect (Hickson 1980). Current data related to possible interference effects with regard to combined high intensity strength and endurance training are sparse.

Maintaining quality of life in aging populations is also a major issue in public health. In addition to indicators of aerobic and neuromuscular performance and health risk factors, there is growing use of health-related quality of life (HRQoL) measures to assess the subject's perception of his own health. Most of the interventions and cross-sectional studies that have studied the relationships between physical activity or training and HRQoL have been performed in chronically diseased populations. As yet, there are few studies on the effect of exercise interventions on HRQoL in generally healthy individuals.

The health benefits of various combinations of moderate and high-intensity physical training have not been sufficiently examined using randomized controlled trials (Haskell et al. 2007), especially in primary prevention. The present thesis investigated adaptations in total and regional body composition, metabolic health indicators, and HRQoL during endurance, strength, and combined training in healthy middle-aged and older men and women. Moreover, the focus of this study was to analyze the training-specific changes in physical fitness during a prolonged period of training to assess possible interference in muscle mass or physical fitness development during combined training in previously untrained subjects.

## 2 REVIEW OF THE LITERATURE

### 2.1 Aging

The worldwide population is growing older. The individual aging process depends on both environmental and genetic factors. However, physiological aging is universal and affects body function at both the cellular and organ level. Of all the physiological changes that occur during the aging process, among the most important with regard to quality of life and functional independence are declines in muscle strength and aerobic capacity. Physical performance decreases with aging, even in healthy subjects. It is mostly a consequence of age-related changes in body composition, i.e., decreases in the amount of muscle fibers and fiber size with concomitant increases in body fat.

#### 2.1.1 Age-related changes in body composition

The aging process affects nearly every facet of human body composition. Although the pattern and magnitude of the changes are influenced by gender, ethnicity, and physical activity patterns, aging is generally associated with increased general adiposity and changes in fat deposition (Kuk et al. 2009). Longitudinal studies have shown that fat mass increases with age and peaks at about age 60-75 years (Droyvold et al. 2006; Rissanen et al. 1988). Moreover, with aging, body fat is redistributed so that subcutaneous fat tends to decline at the same time as visceral and intramuscular fat tend to increase (Beaufrere and Morio 2000; Zamboni et al. 1997). Increases in total adiposity can occur independently of changes in body weight (Zamboni et al. 1997).

In contrast, muscle mass starts to decrease progressively at the age of 30 years and a more accelerated loss starts around at age of 60 (Bassey 1998; Frontera et al. 2000; Häkkinen and Häkkinen 1991). According to cross-sectional studies, muscle cross-sectional area (CSA) diminishes between the ages of 20 to 60 years by ~1% per year and the decline is even steeper (1-3% per year) according to longitudinal studies (Porter et al. 1995; Vandervoort 2002). This age-

associated reduction in muscle mass and strength is often referred as sarcopenia (Rosenberg 1997).

The loss of muscle mass is caused by reductions in the amount and size of muscle fibers. The number of muscle fibers starts to decrease after 30 years and accelerates rapidly after the age of 50. Between the ages of 20 and 80 years, the total number of muscle fibers is reduced by 50% (Lexell et al. 1988). The proportions of type I and II muscle fibers are affected by age to a similar extent. However, the fast twitch type II fibers lose more of their CSA compared to slow-twitch type I fibers.

A key contributing factor behind the loss of lean tissue is reduced physical activity, which results in muscle atrophy. Various other factors contribute to the development of sarcopenia, including loss of skeletal muscle fibers, reduced testosterone and growth hormone levels, and inadequate energy and protein intake (Doherty 2003).

### **2.1.2 Metabolic consequences of aging**

Age-related changes in body composition (i.e. reduced lean mass and accumulation of fat) and function (i.e. decreased muscle strength and endurance) influence health in several ways. A decrease in lean mass during aging results in a decrease in metabolically active cell mass and, furthermore, to a decline in resting metabolic rate (RMR). A progressive decline in whole-body RMR is at a rate of 1-2% per decade after 20 years of age (Elia et al. 2000). Less lean mass also means less insulin sensitive tissue available for glucose metabolism, which may result in decreased glucose tolerance.

With aging, adipose tissue is often redistributed from peripheral areas into the central visceral adipose depot, skeletal and cardiac muscle, liver and bone marrow (Kuk et al. 2009). The accumulation of non-subcutaneous fat is strongly associated with several risk factors and adverse outcomes, such as dyslipidemia (Hunter et al. 2010), insulin resistance, type 2 diabetes, cardiovascular disease, and mortality (Kuk et al. 2006; Tiikkainen et al. 2002).

Visceral adipose tissue is an important source of inflammatory substances, which also contribute to the development of insulin resistance, the metabolic syndrome, type 2 diabetes, and cardiovascular disease (Lau et al. 2005; Trayhurn 2007). These inflammatory proteins are associated not only with chronic diseases and insulin resistance, but also with catabolism of muscle tissue, reducing muscle strength and contributing to the development and progression of sarcopenia (Cesari et al. 2005; Schrager et al. 2007). The combination of age-related loss of muscle strength and mass and obesity may be more strongly associated with health risk and disability than either condition alone (Stephen and Janssen 2009).

Intramuscular fat increases with aging in two depots. Both inter-muscular fat that lies between the muscle fibers and intra-muscular fat that is located within the myocytes increases. The metabolic consequences of intermuscular fat are unclear, but it is generally thought to be metabolically inert (Hwang et al. 2001). In contrast, intramuscular fat is commonly associated with metabolic de-

rangements, which are known to be central in the development of peripheral insulin resistance and the metabolic syndrome (Kelley et al. 1999; Ryan and Nicklas 1999). This lipid accumulation in skeletal muscle is most likely due to enhanced fatty acid intake into the muscle coupled with diminished mitochondrial lipid oxidation (Corcoran et al. 2007). The excess fatty acids are esterified and either stored or metabolized to various molecules that may participate or interfere with normal cellular signaling, particularly insulin-mediated signal transduction, thus altering cellular and, subsequently, whole-body glucose metabolism (Corcoran et al. 2007). Intracellular fatty acid metabolites that have been suggested to play a role as primary mediators in lipid-induced insulin resistance are diacylglycerol (DAG) or ceramides. DAG is a fatty acid metabolite, which is expected to increase with increased lipid deposition within the muscle. This increase in intracellular DAG concentration has been associated with the blunting of insulin signaling (Yu et al. 2002).

As skeletal muscle is responsible for 90% of insulin stimulated glucose uptake (DeFronzo et al. 1985), increased intramuscular fat may be partly responsible for the decline in glucose tolerance often associated with aging. It is, however, uncertain, how strong the independent association between intramuscular fat and insulin resistance is after controlling for visceral and liver fat. (Kelley et al. 2003). Furthermore, elite endurance athletes have extremely high concentrations of muscle lipid, yet they are quite insulin sensitive (Goodpaster et al. 2001). The nature of this metabolic paradox seems to indicate that it is not the size of the intramyocellular triacylglycerol pool, but rather the balance between fatty acid availability, cellular uptake, and oxidation (i.e. lipid turnover) (Corcoran et al. 2007).

In those with a genetic predisposition to pancreatic beta-cell dysfunction and impaired insulin secretion, insulin resistance and the associated abnormalities may progress to impaired glucose tolerance and further to type 2 diabetes (Kilpeläinen et al. 2008).

### **2.1.3 Changes in physiological performance with aging**

Maximal aerobic power, muscle strength, and explosive power decline even with healthy aging. Under normal conditions human muscle strength reaches its peak between the ages of 20-30 years after which it declines very slowly for the next 20 years. After the 5<sup>th</sup> decade a steeper decline in maximal strength begins (Frontera et al. 1991; Häkkinen et al. 1998a; Porter et al. 1995). The age-related decrease in muscle strength varies between different muscle groups. The loss of muscle strength seems to be greater in lower than in upper extremities (Frontera et al. 1991).

The decline in muscle strength with advancing age is due to the anatomical and functional changes in skeletal muscles associated with alterations in hormone balance, especially with decreased androgen levels, and often also with reduced amount and intensity of physical activity. The majority of the loss in strength results from an age-related decrease in muscle mass (Frontera et al. 1991). Although the losses in muscle CSA during aging can be as high as 1-3%

per year, the losses in dynamic muscle strength can be even greater, at least in lower extremities (Hughes et al. 2001), suggesting that the quality of skeletal muscle or efficiency of muscle strength per muscle mass is also reduced with age (Greenlund and Nair 2003). In addition to a decline in muscle mass and quality, decreased maximal strength might also be in part due to a decrease in maximal voluntary neural input.

Aging leads to decreased muscle strength, but also to even greater worsening in explosive force production (Häkkinen and Häkkinen 1991; Häkkinen et al. 1998a). The decrease in explosive force production is associated with age-related changes in muscle fibers, such as selective loss of fast-twitch fibers compared to slow-twitch fibers.

Cross-sectional studies have demonstrated a decline in aerobic capacity, measured by peak  $\text{VO}_2$ , of 5 to 10% per decade in untrained individuals (Fitzgerald et al. 1997; Fleg and Lakatta 1988; Jackson et al. 1995; Wilson and Tanaka 2000; Åstrand 1960). In longitudinal studies, declines in peak  $\text{VO}_2$  have varied from 5% to > 20% per decade, but most of the studies done, are limited to small samples and narrow age ranges, or have focused on elite athletes (Fleg et al. 2005). Fleg et al. (2005) reported, in a large longitudinal study, that the decline in peak  $\text{VO}_2$  is not constant across the age span in healthy adults. They found that the decrease in peak  $\text{VO}_2$  accelerated with age from 3 to 6% per decade between the 20-30s and 30-40s and up to >20% per decade in the 70s and beyond.

The decline in aerobic capacity with advancing age is explained by the aging process itself and also by age-associated decreases in vigorous physical activity and muscle mass (Ogawa et al. 1992; Talbot et al. 2000). The role of habitual physical activity on the age-associated decline in peak  $\text{VO}_2$  is controversial. Although greater levels of physical activity increases the peak  $\text{VO}_2$  at any age, it does not prevent the accelerated decline with advancing age, which is relatively similar in endurance trained and sedentary subjects (Fitzgerald et al. 1997; Fleg et al. 2005).

Although maximal heart rate declines with advancing age, this does not fully explain the accelerated reduction in peak  $\text{VO}_2$  (Fleg et al. 2005). A part of peak  $\text{VO}_2$  decline can be explained by the decrease in  $\text{O}_2$  pulse, which is the product of stroke volume and the difference between the arterial and venous blood (a-v peak  $\text{VO}_2$ ). Potential factors affecting stroke volume and a-v peak  $\text{VO}_2$  include cardiac and peripheral changes, for example, reduced ability to deliver blood to exercising muscle and intrinsic changes in muscle tissue that impair oxygen utilization (Fleg et al. 2005; Grimby and Saltin 1983; Ho et al. 1997).

Muscle strength has been shown to be closely associated with functional capacity, such as walking and stair climbing speed, and stand ups (Bassey et al. 1992; Brown et al. 1995). Problems in performing these basic movements can increase disability and finally lead to loss of independence.

Decreases in aerobic capacity may also reduce the probability to live independently. Aerobic capacity between 18 to 20 ml/kg/min has been defined as



an aerobic threshold for independent living, and below this threshold the decline in physical function per milliliter of oxygen uptake was 8-fold greater than the corresponding decline above the threshold (Cress and Meyer 2003; Morey et al. 1998). A higher aerobic capacity provides aerobic reserve, which enables, for example, active leisure activities and reduces the risk of falling below the minimum physiological thresholds required to perform daily tasks (Arnett et al. 2008).

## 2.2 Physical training and body composition

### 2.2.1 Body composition assessment in intervention studies

Body composition assessment is indispensable to evaluate nutritional status and health, both at the population level and individual level, and to assess the efficacy of nutritional and exercise interventions. For example, the primary goal of weight-loss interventions is to maximize the loss of fat mass while preserving or increasing fat free mass. Several methods have been used for estimating total and regional body composition and fat distribution, but less is known of their suitability for assessing the differential changes in body composition following endurance and strength training.

Each body composition method has some advantages and limitations, and method selection depends on the information needed. In selecting the method, one must take into account cost (equipment and personnel), possible radiation exposure, time required to obtain the information, and accuracy of the information (Andreoli et al. 2009).

Simple anthropometric measurements such as body mass index (BMI), waist circumference and waist-hip-ratio are used as indirect and crude estimates of adiposity and abdominal obesity. These measures are simple, standardized and ideal for use in epidemiological studies. Body mass index, the ratio of body weight to height in meters squared ( $\text{kg}/\text{m}^2$ ), has gained international acceptance because of its associations with adiposity, disease risk (Must et al. 1999), and mortality (Calle et al. 1999). BMI is, however, a crude measure of overall adiposity. Moreover, BMI is unreliable in body composition analyses among people with abnormally low or high muscle mass (Racette et al. 2006). In intervention studies, BMI seems to be a rather good method for analyzing changes in body fat, if the intervention includes energy restriction (Evans et al. 1999; Fogelholm and van Marken Lichtenbelt 1997). However, BMI cannot be used to estimate changes in body composition in interventions that include increases in fat free mass.

More recently, girth measurements, such as waist circumference and waist-hip ratio have been suggested to be more closely associated with subsequent morbidity and mortality (Bigaard et al. 2005; Huxley et al. 2010; Wei et al. 1997; Welborn and Dhaliwal 2007). These measurements reflect central adiposity and seem to be superior to BMI in predicting cardiovascular disease risk (Lee

et al. 2008, Huxley R 2009). The WHO current recommendations for waist circumference between 94.0-101.9 cm in men and 80.0-87.9 cm in women, correspond with the BMI overweight range of 25-29.9 kg/m<sup>2</sup> (WHO 2000b). Similarly, waist-hip ratio >0.9 and 0.8 in men and women has corresponded to a BMI of 25.0 or greater.

Especially during intervention studies, more detailed information about fat mass and fat free mass are needed to estimate the intervention effects. Simple measurements for body composition analyses in field and in clinical settings are also skin fold thickness measurements and bioelectrical impedance analyses. These methods provide only an indirect measure of body composition and, therefore, can include quite a large measurement error.

The skin fold is an indirect measure of thickness of subcutaneous adipose tissue at a specific site. Because 50 to 70% of fat is located subcutaneously, selected skin folds have been found to relate to overall body fatness. The two most commonly used equations are Jackson Pollock (1980) and Durnin and Womersley (1974) skin fold equations. Both these equations have been validated in a large sample of white adults. The accuracy of measurements is highly dependent on the technical skill, type of calipers, and client factors (Heyward 2001).

Bioelectrical impedance method (BIA) is a rapid non-invasive, and relatively inexpensive method for evaluating total and regional body composition (Malavolti et al. 2003). Although BIA is considered to be more accurate than most of the other field measurements, it is not as accurate as underwater weighing, computed tomography (CT), magnetic resonance imaging (MRI), or dual-energy X-ray absorptiometry (DXA) (Fogelholm and van Marken Lichtenbelt. 1997; Fuller et al. 1999; Levine et al. 2000; Malavolti et al. 2003). BIA methods also provide systematically lower values for fat mass than, for example, DXA (Bolanowski and Nilsson 2001; Volgyi et al. 2008). This error can be diminished by using empirically derived and validated formulas instead of manufacturer's equations. BIA also has a poor accuracy in detecting small changes in body fat and composition and it is quite sensitive to hydration status, temperature, body symmetry and position (Andreoli et al. 2009).

For years, a water displacement method, known as hydrostatic weighting, has been considered as the golden standard method for body fat analyses in light of the relatively small technical error associated with the accuracy of the measurement (0.7%) (Heyward 2001). There are, however, several limitations related to hydrostatic weighting. It is inconvenient, wet, and requires considerable subject co-operation for multiple trials. The availability of specialized equipment may also be a problem.

DXA is considered to be a valid technique for total and regional fat and muscle tissue assessment and also the most sensitive method for assessing small changes in body composition (Houtkooper et al. 2000; Pritchard et al. 1993). It permits the direct measurement of lean tissue, fat tissue and bone mineral with high precision and accuracy (precisions for soft tissue measurements 2-3%) (Jebb et al. 1993) and, therefore, in recent studies DXA has been referred



to as the golden standard method for body composition analyses (van der Ploeg et al. 2003). Other advantages are relatively fast scanning time 10-15min, and low radiation dose. However, DXA is not free of hydration assumptions and in some regions of the body it cannot distinguish between soft tissue and bone. The equipment is also rather expensive and machines and software from different manufacturers cannot be used interchangeably (Tylavsky et al. 2003).

A couple of studies have compared the utility of different methods to assess changes in body composition in intervention studies (Evans et al. 1999; Houtkooper et al. 2000; Mahon et al. 2007; Nelson et al. 1996). These studies have used different designs, as well as different analyzing and statistical methods and subjects. The results have been inconsistent. For example, Nelson et al. (Nelson et al. 1996) concluded that hydrostatic weighting is superior to anthropometry, BIA and DXA to estimate changes in body fat mass in strength trained, older, weight-stable women. In contrast, Houtkooper et al. (Houtkooper et al. 2000) reported that DXA was more sensitive than hydrostatic weighing and a multicomponent model for assessing small changes in body composition in postmenopausal, weight-stable women after physical training.

### **Assessing muscle mass**

In addition to total body measurements, especially in research settings, more pronounced information about changes muscle mass are needed. These measurements are important, for example, in longitudinal aging studies, when the effect of aging on muscular development and function is studied, and also to monitor the efficacy of exercise and nutritional interventions on muscular development and function. The reference methods for regional body composition assessment are MRI and CT, which can measure skeletal muscle mass and adipose tissue volumes (Lee et al. 2001). Unfortunately, the use of these methods is often limited by access and cost, as well as ionizing radiation (CT), which reduces its appropriateness for repeated measurements (Lukaski 1987).

In addition to MRI and CT, regional muscle mass can be analyzed by DXA (lean mass) and ultrasound (muscle CSA and thickness). Also, anthropometric measurements such as arm and leg circumferences corrected for subcutaneous adipose tissue have been used, but the problem in these circumference measurements is high intraindividual error and low sensitivity to monitor small changes in muscle mass (Lukaski 1996).

CT-measured thigh skeletal muscle correlates well with DXA-measured thigh fat free mass (Levine et al. 2000). Nevertheless, there are systematic differences between the two techniques that seem to relate to nonskeletal muscle tissues that are measured as fat free mass by DXA. More specifically, DXA fat free mass includes skin as well as the fat free components of adipose tissue (Levine et al. 2000). Therefore DXA systematically overestimates CT-measured thigh skeletal muscle. A single-slice CT may be an appropriate method for muscular measurements for the purposes related to muscle strength (Schantz et al. 1983). If tissue mass is needed as a denominator for the metabolic measurements, DXA is preferred over single-slice CT, because fat mass measured by DXA in

both abdomen and thigh compares well with multi-slice CT-measures (Jensen et al. 1995; Svendsen et al. 1993).

MRI measurements are widely used in training studies to estimate muscle growth (Häkkinen and Häkkinen 1991; Häkkinen et al. 1998a; Häkkinen et al. 2001; Kraemer et al. 2004). It is almost radiation free and can be used to measure regional body composition, and by calculations also total body composition. Like CT, MRI is capable of quantifying intramuscular adipose tissue (Forsberg et al. 1991). The primary disadvantage related to MRI is the expense of the apparatus.

Ultrasound measurements can be used to estimate regional skeletal muscle growth (Sipilä and Suominen 1991). There are some important limitations related to these measurements. Considerable practice is needed to obtain a good image with the ultrasound method. In addition, the ultrasound probe needs to be kept directly perpendicular to the skin surface. Measurement error in repeated ultrasound measurements can be diminished by always using the same anatomical places marked with tattoo points and by using an experienced operator. This method, however, includes more error than, for instance, MRI (Miyatani et al. 2002).

### **2.2.2 Effects of endurance training on body composition**

Endurance training is commonly undertaken to promote reductions in body weight. The size of the reduction is related to the total weekly energy expenditure via exercise and total energy intake during intervention period (Ballor and Keesey 1991). Also other factors, such as baseline body composition and fitness level, may affect weight changes during the exercise period (Ballor and Keesey 1991). Moreover, older persons and men may be more likely to lose weight in response to exercise training than younger people and women (Andersson et al. 1991; Kohrt et al. 1992).

During moderate exercise induced weight loss, fat free mass is usually preserved. In contrast, weight loss including diet restriction is usually a combination of both reduced fat and fat free mass (Weiss et al. 2007). Body fat is reduced by training until total energy expenditure and total energy intake are equal.

Although more fat is oxidized during high-intensity training, several studies have shown that high and low intensity exercise has similar effects on the percentage of weight loss as fat (Ballor et al. 1990; Grediagin et al. 1995).

Aerobic training is also associated with small or moderate increases in skeletal muscle mass, with a similar response in both men and women (Marti and Howald 1990; Kohrt et al. 1992). Both high-intensity cycling (Harber et al. 2009) and walking/jogging training (Coggan et al. 1992) have been shown to be effective in increasing muscle mass in previously untrained individuals.

If the exercise induced energy cost is compensated by increased energy intake, body weight does not change. However, endurance training even without weight loss results in changes in body composition. In several studies, aerobic training without weight loss has resulted in reductions in total body fat mass, as

well as in visceral and adipose tissue both in obese and lean men and women (Lee et al. 2005; Ross et al. 2004; Ross et al. 2000).

### **2.2.3 Effects of strength training on body composition**

Resistance training results in increased energy expenditure, which is caused by increased lean body mass, increased requirements of metabolically active lean tissue (Campbell et al. 1994; Pratley et al. 1994) and increased energy needed for physical activity during training.

Body composition changes following strength training interventions have been variable because of differences in training programs. Overall, those programs that have trained only small muscle groups have reported only local adaptations, while those programs that have included large muscle groups have resulted in larger changes in body composition. The main effect of strength training on body composition is a shift from fat to muscle mass with individuals remaining in caloric balance (Hunter et al. 2004). A number of studies have reported strength training-associated decreases in fat mass and a concomitant increase in fat free mass, with no change in body weight (Bamman et al. 2003; Campbell et al. 1994; Pratley et al. 1994; Treuth et al. 1994).

High-intensity strength training increases fat free mass, muscle CSA and muscle fiber area. Typical increases in muscle CSA have been 5-10%, which indicates that a large part of strength increases are also caused by neural factors (Charette et al. 1991; Frontera et al. 1988; Grimby et al. 1992; Häkkinen et al. 1998a; Häkkinen et al. 2001a). Both fast and slow twitch fibers adapt to strength training by increasing size.

In addition to increases in fat free mass and decreases in total body fat mass, strength training may also modify body composition by decreasing abdominal fat (Ibañez et al. 2005; Treuth et al. 1995; Tsuzuku et al. 2007). Especially total body strength training with progressive training load seems to be effective in modifying body composition. Ibañez et al. (2005) showed that 2 times per week of progressive strength training (50-80% 1RM) decreased visceral and subcutaneous abdominal fat by more than 10% without concomitant changes in body mass in older type 2 diabetic men. Significant improvements in body composition after strength training have also been found in non-diabetic elderly men and women. Tsuzuku et al. (2007) observed that even relatively short-term (3 times per week for 12 weeks), non-instrumental strength training using body weight as a load may be effective in improving fat distribution and metabolic profiles in healthy elderly people without weight loss. Moreover, Treuth et al. (1995) found significant improvements in intra-abdominal adipose tissue after 16 weeks of strength training for 3 times per week in older healthy women. In the studies by Treuth et al. (1995) and Ibañez et al. (2005) successful strength training also resulted in large increases in mean muscle strength (from 17 to 65%).

## 2.3 Improving metabolic health through physical training

Epidemiological studies have shown that moderate and high levels of cardiorespiratory fitness provide substantial protection against developing metabolic syndrome in both men and women (Laaksonen et al. 2002; LaMonte et al. 2005). The mechanisms through which exercise modifies chronic disease risk may be mediated by decreases in total and abdominal fat, plasma concentrations of lipids and lipoproteins, blood pressure and improvements in insulin sensitivity and glycemic control. Less information is available, whether the health benefits of resistance training are independent of, or additive to, those already established for dynamic aerobic training that activates large muscle groups. The following paragraphs summarize the independent effects of physical training on these risk factors.

### 2.3.1 Prevalence of metabolic risk factors

Several factors have been found to increase the risk for the metabolic syndrome, type 2 diabetes and cardiovascular disease. These factors include obesity, especially central obesity, abnormal glucose tolerance, increased blood pressure and triglycerides and decreased HDL-cholesterol (HDL-C), as well as low physical activity. The incidence of metabolic risk factors and an associated increase in several cardiometabolic diseases has reached pandemic proportions throughout the world, also in the Finnish population.

The most important risk factor for type 2 diabetes is obesity, especially in the abdominal area. According to the latest statistics, in the 45 to 74-year-old population, 70% of Finnish men and 63% of women are overweight or obese (Salopuro et al. 2010). During the last couple of years the prevalence of obesity seems to have leveled off among Finnish middle-aged population, but obesity-related disorders, especially type 2 diabetes, continue to rise rapidly (Saaristo et al. 2008; Salopuro et al. 2010). Type 2 diabetes and abnormal glucose tolerance are closely related to abdominal obesity, which has shown increasing trends in both genders (Lahti-Koski 2001; Saaristo et al. 2008). Among middle-aged and older subjects, 65% of men and 75% of women have increased waist circumference (>94cm in men or >80cm in women) in Finland (Salopuro et al. 2010).

Among Finnish middle-aged adults (45-65-year-old) the prevalence of other metabolic risk factors was also significantly higher in men than in women: obesity 80 vs. 33%, hypertension 66 vs. 55% and dyslipidemia 52 vs. 29% of men and women, respectively. Abnormal glucose metabolism was found in 35% of the men and 21% of the women, and diabetes in 10 and 7% of the men and women, respectively. Only 37% of the subjects with type 2 diabetes were aware of their condition. (Ilanne-Parikka et al. 2004).

These findings indicate that the proportion of subjects with major obesity-related health risks is increasing rapidly and, therefore, the prevention of abdominal obesity and other metabolic risk factors is highly important.

A cluster of several metabolic risk factors has been referred to as the metabolic syndrome. Several diagnostic criteria for metabolic syndrome have been published. The most commonly used definitions have been proposed by the National Cholesterol Education Program (NCEP) Expert Panel (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults 2001), and later modified slightly by the American Heart Association/National Heart Lung and Blood Association and the International Diabetes Federation (IDF). More recently, a new definition attempting to unify the criteria for the metabolic syndrome has been proposed (Alberti et al. 2009). In all of these definitions, criteria related to increased fasting glucose, abdominal obesity, serum triglycerides, and increased blood pressure, and decreased HDL-C are included. Even though insulin resistance plays a major pathological role in the development of the metabolic syndrome, these definitions do not include a measure of insulin resistance. At the present time, clinically practical and standardized measurements of insulin resistance are not yet available (Laaksonen et al. 2004).

In the Finnish population, at the beginning of the 21<sup>st</sup> century, the prevalence of metabolic syndrome has varied between 39 and 56% in men and 22 and 45% in women, depending on the criteria used for the metabolic syndrome (Hu et al. 2008; Ilanne-Parikka et al. 2004). Between 1992 and 2002 the prevalence of the metabolic syndrome increased by 7.3% in 45 to 64-year-old women, but not among men (4.2%) (Hu et al. 2008). The increase in prevalence of metabolic syndrome was caused by increased glucose abnormalities and abdominal obesity. In contrast, mean blood pressure and serum triglyceride levels, and the prevalence of high blood pressure significantly decreased, and the mean HDL-C level significantly increased in both genders (Hu et al. 2008; Ilanne-Parikka et al. 2004).

### **2.3.2 Physical training and total and abdominal obesity**

Continued inactivity, even for short periods such as 6 months, can significantly increase total fat and visceral abdominal fat in middle-aged subjects (Slentz et al. 2005). In contrast, cross-sectional studies have showed that physical activity is associated with more favorable body composition. In active individuals the amount of total body fat and abdominal fat is smaller and the amount of muscle mass is larger than in inactive individuals. Also, various physical activity interventions have been shown to decrease total and abdominal fat.

It is clear that aerobic training interventions are associated with increased energy expenditure during the exercise session and, therefore, it often leads to negative energy balance and reduced body weight. Strength training, however, is less frequently associated with decreased body weight. In some studies, strength training has, however, been shown to promote weight loss in obese subjects (Rice et al. 1999; Sarsan et al. 2006). A significant number of studies have also showed that strength training is associated with a decrease in fat mass and a concomitant increase in lean body mass and, thus, has little or no effect on body weight (Cauza et al. 2005; Dunstan et al. 2002; Hunter et al. 2000; Treuth et al. 1994; Treuth et al. 1995). Increased lean body mass produced by



strength training can translate into clinically important increases in daily energy expenditure and associated losses in body fat (Strasser and Schobersberger 2011). For example, strength training interventions for a couple of months in duration have been shown to produce at least 1-2kg increases in lean body mass. A rather small difference of 2.5kg in lean body mass translates into a difference in energy expenditure of 50 kcal per day, which is equivalent to a loss of 2.4 kg fat mass per year (Wolfe 2006).

Not only the amount of body weight or the total amount of fat, but the location of the excess weight is of particular importance. Visceral fat is often considered the major culprit, and the relationship between abdominal obesity and metabolic disease risk is well documented (Shen et al. 2006; Fox et al. 2007; Racette et al. 2006).

Waist circumference measurements are included in the definition of metabolic syndrome and are commonly used to estimate abdominal obesity. Although waist circumference does not distinguish visceral and subcutaneous fat in the abdominal area, it predicts cardiovascular disease and type 2 diabetes in both obese and lean subjects (Goodpaster et al. 2005; Klein et al. 2004; Rexrode et al. 1998; Shen et al. 2006).

Both aerobic training and progressive strength training have been shown to be effective in reducing abdominal fat in type 2 diabetic people and in healthy obese subjects even without weight loss (Ibañez et al. 2005; Lee et al. 2005; Ross et al. 2000; Strasser and Schobersberger 2011). In weight loss interventions, aerobic training has decreased abdominal fat by 5.6-6.9 cm<sup>2</sup> in per kilogram of weight loss (Irwin et al. 2003; Slentz et al. 2005; Ross et al. 2000). There seems to be also a clear dose-response relationship between the change in abdominal fat and the change in both exercise intensity and amount of exercise (Slentz et al. 2005; Slentz et al. 2009).

Several strength training studies have also demonstrated decreases in visceral adipose tissue following strength training programs (Cuff et al. 2003; Hunter et al. 2002; Ross et al. 1996; Treuth et al. 1994; Treuth et al. 1995). For example, Treuth et al. (1994, 1995) observed significant decreases in visceral fat in older men and women after 16 weeks of training. Additional improvements in decreases in visceral fat have also been observed when strength or aerobic training has been combined to a diet-induced weight loss intervention (Hunter et al. 2002).

### **2.3.3 Physical training and glucose and insulin metabolism**

Both endurance, strength and combined training have both acute and chronic beneficial effects on glucose control (fasting glucose, post prandial glucose, insulin sensitivity and fasting insulin) in type 2 diabetic subjects. Acutely, physical exercise and contraction of skeletal muscle increases insulin sensitivity and glucose uptake in skeletal muscles (Hawley and Lessard 2008). Acute exercise-induced improvement in glucose uptake into skeletal muscles is mediated by activation of AMP-activated protein kinase, upregulation of glucose transporter

4 and glycogen synthase, changes in muscle fibre type and increased muscle capillarisation (Hawley and Lessard 2008; Rockl et al. 2008).

As exercise intensity is increased, muscle glycogen becomes a more important substrate source (Kjaer et al. 1990). The depletion and resynthesis of muscle glycogen stores are coupled to the post-exercise improvement in glucose tolerance and insulin sensitivity (Snowling and Hopkins 2006). Therefore, it seems logical that exercise intensity is a key factor to enhanced insulin sensitivity caused by physical training. The data is, however, quite inconsistent. Some data suggest that only vigorous, intense (i.e.  $\geq 70\%$   $\text{VO}_2\text{max}$ ) exercise can enhance insulin sensitivity (DiPietro et al. 2006; Kang et al. 1996; Seals et al. 1984), while others have shown improvements in relatively lower intensities (Mayer-Davis et al. 1998; Oshida et al. 1989). Houmard et al. (2004) found similar, significant improvements after moderate (40-55% peak  $\text{VO}_2$  consumption,  $\text{VO}_2\text{peak}$ ) and high 65-80%  $\text{VO}_2\text{peak}$  intensity endurance training when total exercise volume was the same in both groups.

Over longer training periods, endurance training improves insulin sensitivity and glucose uptake in healthy and insulin-resistant subjects (Kirwan et al. 1993; Lakka and Laaksonen 2007; Rockl et al. 2008). The mechanisms are likely related to the reductions in body fat, improvements in muscle oxidative capacity, decreases in muscle lipid content and increases in whole-body rates of fat oxidation and turnover (Bruce and Hawley 2004).

Strength training has improved glycemic control in type 2 diabetic subjects (Castaneda et al. 2002; Dunstan et al. 2002; Fenicchia et al. 2004; Ibañez et al. 2005), but findings in non-diabetic individuals has been inconsistent (Rice et al. 1999; Ross et al. 2000). Conflicting results in healthy older subjects may be related to concurrent changes in body composition. Progressive resistance training has been shown to decrease adipose tissue, which is closely related to insulin resistance, for example during aging (Ibañez et al. 2005). This relationship is, however, somewhat unclear. DeNino et al. (2001) did not find a clear relationship between accumulation of visceral fat during aging and insulin sensitivity.

Strength training also increases muscle mass, which affects insulin sensitivity and glucose tolerance. Increased muscle mass enhances the available glucose storage area, and thereby facilitates the clearance of glucose from the circulation and reduces the amount of insulin required to maintain normal glucose tolerance (Miller et al. 1984).

According to some studies, the training-induced enhancement in insulin sensitivity and glucose homeostasis seems to present independently of changes in body weight or composition (Boule et al. 2001). The mechanisms may be related, for example, to enhanced insulin signaling (Braith and Stewart 2006; Holten et al. 2004) or increased insulin sensitivity.

There is some evidence of additional benefits resulting from combined endurance and strength training (Balducci et al. 2004; Snowling and Hopkins 2006). Sigal et al. (2007) found that, in type 2 diabetic patients, combined training led to greater improvements in glycemic control than aerobic and resistance training alone, especially among patients with poor glycemic control at baseline.

Also, Cuff et al. (2003) reported that adding strength training to endurance training significantly enhanced glucose disposal capacity in type 2 diabetic postmenopausal women. Very few data are, however, available about the effects of combined training on glucose and insulin homeostasis in type 2 diabetic, glucose intolerant and especially normoglycemic subjects.

#### **2.3.4 Physical training and blood lipids and lipoproteins**

Regular physical activity has been associated with favorable serum lipids and lipoproteins in different populations (Hu et al. 2001; Panagiotakos et al. 2003). Intervention studies have, however, reported equivocal results. Effects of endurance or strength training have been either an increase in plasma HDL-C and/or a reduction in total cholesterol, low-density lipoprotein cholesterol (LDL-C) and triglycerides, or no change at all (Boardley et al. 2007; Leon and Sanchez 2001; Stefanick et al. 1998). Because of the varied exercise interventions, experimental designs, and participant characteristics, the influence of physical activity on lipid and lipoprotein levels remains elusive (Durstine et al. 2001; Halbert et al. 1999).

A meta-analysis from the year 2006 in men (49 trials) and 2004 in women (41 trials) evaluated randomized controlled trials investigating the effects of aerobic exercise on blood lipids and lipoproteins (Kelley et al. 2004; Kelley and Kelley 2006). Using random-effects modeling, statistically significant improvements were observed in all lipids and lipoproteins in women (Kelley et al. 2004) and in TC, HDL-C and TG in men, and also a trend for decreases was observed for LDL-C (Kelley and Kelley 2006). A decrease of 2% in TC and 3% of LDL-C was observed both in men and in women. Reductions of TG were approximately 5% and 9% and increases of HDL-C 3% and 2% in women and men, respectively.

The heterogeneity between training responses on blood lipids and lipoproteins can be explained by several factors. First, more favorable changes in response to training usually occur in those with more pronounced dyslipidemia at baseline (Kelley and Kelley 2006; Laaksonen et al. 2000). The improvements in the lipid profile due to physical training may also be dependent on loss of body fat (Leon and Sanchez 2001; Ross et al. 2000). Greater decreases in body fat may result in greater decreases in TC (Kelley et al. 2004) and greater increases in HDL-C have been observed in those with poorer body composition profile at baseline (Kelley and Kelley 2006).

Also, the effects of resistance training on blood lipids and lipoproteins are rather unclear. In less than half of the studies, resistance training has produced significant reductions in LDL-C, ranging from 5 to 23% (Tambalis et al. 2009). Improvements in TC, TG or HDL-C have been found only in less than one fourth of the resistance training studies. Also, studies that have compared both aerobic and resistance training have been inconsistent. Other studies have not found alterations in blood lipids in either aerobic or resistance training groups (Blumenthal et al. 1991; Hersey et al. 1994; Smutok et al. 1993), but other studies reported improvements in both groups (Fahlman et al. 2002; Fenkci et al. 2006).



Some studies suggest that combining aerobic and resistance training may confer a better effect on lipoprotein profile in healthy individuals than aerobic activities alone (Pitsavos et al. 2009). There are limited studies investigating effects of combined strength and endurance training on blood lipid levels. Combined training has been shown to improve LDL-C or HDL-C levels (Kodama et al. 2007; Park et al. 2003; Verney et al. 2006), but improvements in TC and TG have been less common. LeMura (2000) and Boardley (2007) did not find intervention effects in any of the training groups compared with the control groups.

Although the effects of exercise to improve the serum lipid profile have been known some time, the effects of different training volumes and intensities on serum lipids are little understood. Heterogeneity in the exercise responses can be explained, for example, by the differences in increases in physical performance. Greater increases in  $\text{VO}_2\text{max}$  have resulted in greater increases in HDL-C (Kelley et al. 2004). According to a recent review, training intensity seems also to be a strong influencing factor on training induced improvements in blood lipids and lipoproteins (Tambalis et al. 2009). Improvements, mainly an increase in HDL-C, were more often reported after high-intensity exercise programs. Twenty-one percent of moderate intensity studies reported improvements in serum lipids compared with 60% in high-intensity studies.

### 2.3.5 Physical training and resting blood pressure

Physical exercise causes both acute and chronic adaptations in blood pressure. A single endurance training session reduces blood pressure during the recovery period. This phenomenon referred as post-exercise hypotension is characterized both in normotensive and in hypertensive subjects and is significant in magnitude and lasts for several hours (Cardoso et al. 2010). Resistance training seems to have similar acute effects on blood pressure than aerobic training, but the magnitude, duration and mechanism of action needs to be more thoroughly investigated (Cardoso et al. 2010).

Both prolonged strength and endurance type of exercise decreases systolic (SBP) and diastolic (DBP) resting blood pressure (Cornelissen and Fagard 2005a; Cornelissen and Fagard 2005b; Kelley and Kelley 2000; Kelley et al. 2001). The average decrease caused by endurance training has been -1.9/-1.6 (SBP/DBP) mmHg (Kelley et al. 2001), and that caused by strength training is about 3 mmHg in both SBP and DBP (Cornelissen and Fagard 2005b; Kelley and Kelley 2000). Similar decreases have been observed after typical strength training and circuit training (Kelley and Kelley 2000).

Even though the training-induced decreases in blood pressure were quite small, it has been shown that even such small reductions will decrease risk for stroke and coronary heart disease (Chobanian et al. 2003). Moreover, the reductions in blood pressure caused by physical training have been more pronounced among hypertensive subjects (Cornelissen and Fagard 2005a). Hypothetically, the acute decreases in blood pressure following exercise may also decrease cardiovascular risk when exercise is practiced daily.

Increased body weight is a strong risk for hypertension. Weight loss is, therefore, important for the prevention and treatment of hypertension (Neter et al. 2003). However, regular physical activity can also reduce the risk of hypertension in both sexes regardless of the level of obesity or the changes in weight (Fagard 2006; Hu et al. 2004).

Knowledge of the underlying mechanisms responsible for the exercise-induced reduction in blood pressure is limited. Aerobic training decreases the activity of the sympathetic nervous system and enhances that of the parasympathetic nervous system, which decreases blood pressure and systemic vascular resistance. Similarly, exercise-induced decreases in plasma noradrenaline and renin activity may also reduce blood pressure.

Very few studies have addressed the underlying mechanisms behind the decrease in blood pressure in response to resistance training (Van Hoof et al. 1996; Cononie et al. 1991; Fagard 2006). Fagard et al. (2006) did not observe changes in resting heart rate in their meta-analysis and, therefore, concluded that the mechanism responsible for resistance training induced decreases in heart rate may be related to changes in sympathetic activity. However, Cononie et al. (1991) did not find concomitant changes in cardiac output, vascular resistance, plasma angiotensin or epi- and norepinephrine with decreases in blood pressure. It seems that the mechanisms behind the resistance-training induced decreases in blood pressure are still unclear.

## **2.4 Physical training and performance**

Physical adaptation caused by training is highly dependent on multiple factors related to training, such as training frequency, length of the training sessions, and type of training, e.g., velocity of muscle action, duration, repetition of the activity and rest intervals. Several basic principals have been related to physical adaptation. First, the overload principle means that an exercise overload specific to the activity must be applied to enhance physiological improvement and bring about the training response (Kraemer et al. 2002b; McArdle et al. 1996). Second, the specificity principle states that specific exercises elicits specific adaptations and creates specific adaptations (McArdle et al. 1996). Third, training benefits are optimized when training programs are planned to meet the individual needs and capacities (Heck et al. 2004). The fourth, the reversibility principle, is that the beneficial effects of exercise are transient and reversible (Coyle et al. 1984).

### **2.4.1 Effects of endurance training on physical fitness**

Endurance training brings about several metabolic and physiologic adaptations which lead to enhanced aerobic performance. Prolonged sessions of moderate intensity exercise (e.g.  $\geq 1$ h at 65% of peak oxygen uptake) performed repeatedly for several weeks increase mitochondrial size and number, as well as capilla-

rization of the trained muscles. Also, activity of several aerobic enzymes improves with exercise and oxidation of lipids and carbohydrates enhances (Gollnick et al. 1973).

Chronic adaptations are likely to be the result of the cumulative effects of repeated bouts of exercise, but the initial signaling responses leading to such adaptation occur after each training session (Widegren et al. 2001). These acute responses in skeletal muscles that occur in response to a single training session include cellular alterations, such as activation of the mitogen-activated protein kinase signaling cascade (Widegren et al. 2001).

Endurance training is also associated with an increase in the activities of enzymes in the mitochondrial electron transport chain and a concomitant increase in mitochondrial protein concentration (Hawley 2002). The increase in mitochondrial content seems to occur relatively early, only after 1-2 weeks of training (Burgomaster et al. 2007; Burgomaster et al. 2008; Gibala et al. 2006).

Morphological changes in muscle produced by endurance training include increases in a capillary supply to skeletal muscle. In trained muscles, diffusion distances for substrates and gases are therefore reduced (Hawley 2002).

The functional and dimensional changes in the cardiovascular system include decreases in resting and submaximal heart rate, enhanced stroke volume and cardiac output and an expanded a-vO<sub>2</sub> difference (McArdle et al. 1996). An increase in maximal cardiac output is the most significant change in cardiovascular function with aerobic training. This change results from an increased internal ventricular volume and possibly enhanced ventricular contractility (Seals et al. 1994), as well as from increased plasma volume (Convertino 1991).

Endurance training reduces the production, uptake and oxidation of plasma glucose during moderate and intense exercise (Coggan et al. 1990; Coggan et al. 1995). The decreased carbohydrate utilization in the trained state is compensated by a proportional increase in fat oxidation (Coggan et al. 1995). The mechanisms behind this glycogen sparing effect are somewhat unclear, but they have been explained by improved muscle respiratory capacity, a greater supply of fat due to an increase in intramuscular triglyceride concentration (Hurley et al. 1986), and a greater recruitment of muscle mass (Coyle 1995).

The above mentioned physiological changes result in enhanced aerobic performance. Both young and older adults elicit the same 10-30% increases in VO<sub>2</sub>max with prolonged endurance training (Hagberg et al. 1989; Pollock et al. 1975). The magnitude of the increases is a function of training intensity, with light-intensity training eliciting minimal or no changes (Seals et al. 1984).

Endurance training also results in modest increases in muscle strength, especially in untrained subjects. The mode of the endurance exercise may play a role in the development of muscle strength. It seems that cycling is superior to walking or treadmill endurance training for an individual with the goal of developing strength in a lower body multijoint movement (i.e. leg press or squat) (Gergley 2009). The reason may be that cycling more closely mimics the biomechanical movement of these exercises (Gergley 2009).

#### 2.4.2 Effects of strength training on physical fitness

Strength training has been shown to be the most effective method to increase muscle strength. Trainable fitness characteristics include muscle strength, power, and local muscular endurance, which can be described as the ability to resist muscular fatigue, particularly when using a submaximal resistance.

In the first phase of training (first two weeks), a rapid improvement occurs in the ability to perform a training exercise, such as lifting weight. This is mainly the result of a learning effect, which is mediated by changes in motor skill coordination and level of motivation.

In the second phase (3-4 weeks), the increases in muscle strength are obtained without a matching increase in muscle mass (Moritani and deVries 1979). This improvement can be explained by neural factors and by increases in high-energy phosphate (Deschenes and Kraemer 2002). Neural adaptations include many elements, such as an increased activation of prime mover muscles (increased number of activated motor units, increased firing rate and/or improved synchronization), and a better coordination of synergistic and antagonistic muscles (Häkkinen et al. 2001a; Moritani and deVries 1980; Sale 1988).

During the third phase of adaptation to strength training (>6 weeks), both size and strength of the trained muscles increase. Hunter et al. (2004) reviewed that numerous studies have reported myofibre hypertrophy from 10 to 72% following a typical 2-3 days per week training programme after 9-52 weeks of training. The total amount of muscle mass gained in response to resistance training is also related to the amount of myofibers present in muscle. Increases in overall muscle size caused by strength training have been measured by using various techniques, such as US, MRI and CT (Abe et al. 2000; Fielding. 1995; Häkkinen et al. 1998a; Häkkinen et al. 2002). The percent increases in quadriceps femoris CSA following two times per week high-intensity strength training have varied between 2-11% in men and women (Häkkinen et al. 1998; Kraemer et al. 2004; Sallinen et al. 2007).

Most strength training interventions have used 12 to 24 week interventions. There is also a wide variation in strength gains after these interventions. It is well known that training adaptation is highly specific for training mode, progression model, and initial training status (Kraemer et al. 2002a). Exercise effects are also influenced by training frequency, exercise order, and rest periods (Kraemer et al. 2002a). Due to these confounding factors strength gains following resistance training interventions have varied from zero up to more than 100% increases. Typically strength gains have been about 20-40% following a six-month strength training intervention for two times per week (Häkkinen et al. 1998, 2001a, 2003).

During longer training periods strength development is highly dependent on muscle hypertrophy. Therefore, basal concentrations of blood anabolic and catabolic hormones may be of importance for both strength development and training-induced muscle hypertrophy (Häkkinen et al. 2000b, 2001b). Also, growth hormone and IGF-1 are of interest due to their anabolic effects and cor-

tisol is associated with catabolic activity. IGF-1 may have greater prognostic abilities than other biochemical markers and is of increasing importance in studies of health and fitness (Nindl et al. 2010).

A number of studies have also demonstrated significant improvements in power production as a consequence of resistance training (Ferri et al. 2003; Häkkinen et al. 2001a; Kraemer et al. 2001). Gains in power are highly specific to the mode of training. Training programs that include high-velocity contractions induce greater gains (Fielding et al. 2002; Häkkinen et al. 2001a; Kraemer et al. 2001).

Rapid power production is essential for daily function. It, for example, prevents falls. Strength training can be used to enhance speed, balance, coordination, jumping ability, flexibility, and other measures of motor performance (Kraemer et al. 2002a).

### **2.4.3 Training response at different ages**

Age-related changes in body composition, metabolic health, and physical performance are presented in chapter 2.1. Shortly, with increasing age skeletal muscle mass is lost, and this age-related atrophy is accompanied by a reduction in muscle strength and aerobic capacity.

During the last decades, numerous studies have shown that physical training can both prevent and treat age-related muscle loss and decreases in muscle strength. Increased strength and muscle mass has been achieved even in the frail elderly  $\geq 90$  yr old (Fiatarone et al. 1990). Strength training-induced increases in muscle strength in knee extensors (1 repetition maximum) have varied up to 152% (Doherty 2003). Some investigations have made direct comparisons of the magnitude of the increases in muscle strength in older and younger individuals to the same training program. Jozsi et al. (1999) observed similar increases in muscle strength and power in 20 and 60 yr-old subjects in response to the 12-week strength training program. Welle et al. (1996) found that increases in muscle force per CSA in elbow flexion and knee extension were of the same magnitude in young and older individuals following 3 months of strength training, but was more than double in older individuals in knee flexion. Increases in muscle strength are weakly related to training duration, so it is likely to be more dependent on training intensity and initial training status of the subjects.

Also, human muscle tissue maintains its ability to adapt strength training even at older age. The percent increases (6-19%) in muscle CSA after 10 to 24 weeks of strength training have been quite similar in younger and older adults (Ferri et al. 2003; Frontera et al. 1988; Häkkinen et al. 1985; Häkkinen et al. 1998b; Harridge et al. 1999; Jones and Rutherford. 1987; Narici et al. 1996). Some studies that have compared the magnitude of training-induced changes in middle-aged and older subjects in a similar training program have, however, observed impairment in muscle hypertrophy in older subjects, even though improvements in force production were large in all age groups (Häkkinen et al. 2001a). Both fast and slow twitch fibers in young subjects, as well as in older adults,



seem to adapt to strength training with hypertrophy (Frontera et al. 1988; Häkkinen et al. 1998b).

Increased muscle CSA and fiber size is a result of increased net protein balance, which is a sum of protein synthesis and breakdown. There are some controversial results with regard to age-related changes in muscle protein synthesis. According to some studies basal muscle protein synthesis rate can be reduced in older adults compared with younger adults (Volpi et al. 2001; Welle et al. 1993), while others have not observed any reduction with aging (Cuthbertson et al. 2005; Volpi et al. 1998). Kumar et al. (2009) also recently reported that the anabolic response of muscle protein synthesis to an acute bout of strength exercise over a wide range of exercise intensities is approximately ~30% lower in older men than in young men. This reduced anabolic response of muscle protein synthesis in the older muscles may be related to a reduced activation of upstream of mTOR signaling and elevated AMPK activity compared with young muscle after resistance exercise (Drummond et al. 2008). However, there is a paucity of data with regard to research in older adults in this area.

Muscle power has been shown to play a greater role in functional capacity than muscle strength, and the decline in power also seems to be more pronounced with aging (Bean et al. 2002). The aging neuromuscular system is quite capable of adapting to increase strength and power through muscle hypertrophy, increased motor control and firing rate, and reduced antagonist coactivation (Häkkinen et al. 2000a; Macaluso and De Vito. 2004). Although many strength training programs (Fiatarone et al. 1994; Jozsi et al. 1999; Skelton et al. 1995) performed in older adults have also resulted in increases in muscle power, there are only a few studies that have been specifically designed to increase power (Fielding et al. 2002; Häkkinen et al. 2002; LaRoche et al. 2008). Typical strength training programs have resulted in power increases of 10 to 28%, while Fielding et al. (2002) reported as high as 97% increases after high-velocity power training. In a study of Häkkinen et al. (2002), 21 and 22% increases in power were found in older men and women after 21-week heavy resistance/power training and 21 and 32% in younger men and women, respectively. In contrast, an explosive force training program used in a study by La Roche et al. (2008) led to blunted torque development and contractile impulse in older subjects compared to younger ones.

As stated in chapter 2, also aerobic capacity decreases with advancing age. These negative changes result from a decline in peak heart rate, ejection fraction, stroke volume and cardiac index, and an increase with aging in blood pressures and cardiac dilation with exercise. This age-related decline can be minimized by physical training.

Endurance training produces similar gains in aerobic capacity in healthy adults throughout the age range of 20 and 70 years and these adaptations are independent of age, sex, and initial fitness level (Kohrt et al. 1991). The effects of physical training on cardiovascular function are well described in younger subjects. Training-induced improvement in  $\text{VO}_2\text{max}$  is usually associated with an increase in maximal cardiac output.

According to some studies improvements in aerobic fitness can be achieved differently in young and older subjects. For example, Meredith et al. (1989) reported greater increases in muscle oxidative enzyme activities in older subjects compared to younger ones in spite of similar increases in  $\text{VO}_2\text{max}$ . They concluded that peripheral factors may play a greater role in aerobic adaptations in older than in younger subjects (Meredith et al. 1989). However, Stratton et al. (1994) did not find differences in cardiovascular responses among young and elderly subjects after 6 months of endurance training. In both young and older subjects adaptations included improvements in maximal workload and increases in ejection fraction, stroke volume index and cardiovascular index at peak exercise (Stratton et al. 1994).

#### **2.4.4 Special effects of combined endurance and strength training**

##### **The interference effect**

As described in earlier sections, adaptations to exercise are highly dependent on the specific type of training performed. A large number of sport activities, and also the newest guidelines for healthy adults recommended a combination of both endurance and strength type of training for peak performance, as well as for health, well being and functional capacity. In some studies, however, a combination of endurance and strength training have resulted to enhanced or diminished performance or muscle growth compared to a situation when either type of training is performed alone (Nader 2006). This phenomenon related to concurrent training was first described by Robert C. Hickson in 1980 and since then it has been referred to as “the interference effect” (Hickson. 1980).

##### **Possible mechanisms behind the interference**

The interference is usually observed during high training volume or training intensity. It is suggested that limiting factors are associated with physiological, biochemical and molecular mechanisms. Both chronic and acute adaptation mechanisms have been proposed to explain the phenomenon of strength and muscle mass inhibition during concurrent training.

Possible explanations are often related to skeletal muscle. It has been suggested that skeletal muscle may not be able to adapt metabolically or morphologically to both strength and endurance training simultaneously, because of different or even opposing adaptations at the muscle level. Endurance training may directly interfere with adaptation to strength training through activation of the AMPK pathway and inhibition of the insulin-like growth factor 1-AKT-mTOR pathway (Nader 2006).

One possible explanation behind interference may also be an overtraining aspect (Kraemer and Nindl 1998). It is been reported that untrained individuals may be more susceptible to stress than trained people, and that may reduce strength development during combined training (Hunter et al. 1987). Thus, when the overall volume of training is high, simultaneous training for both strength and endurance may be associated with large strength gains during initial weeks of training but with only limited maximal strength and/or explosive

strength development later on (Häkkinen et al. 2003, Izquierdo et al. 2002). The physiological basis for this may be linked to an interaction between an elevated catabolic hormonal state leading to a reduced change in muscle CSA.

It is also possible that the differential endocrine changes to either strength or endurance training may underlie part of the antagonism observed during combined strength and endurance training (Bell 1997, 2000). In general, the net hormone response suggests that strength training may produce an increase in the catabolic/anabolic state while endurance training may do the opposite. Therefore, it has been suggested that the underlying reason for the reduced strength gains with concurrent training partially due to suppressed hypertrophic response in the muscle that may be related to an elevated catabolic state as indicated by higher basal concentrations of cortisol (Kraemer et al. 1995, Bell 1997) combined with no change in the concentration of basal anabolic hormones such as T or GH (Bell 2000).

#### **An overview to combined training studies**

About 30 studies have been done to investigate effects of combined endurance and strength training in healthy adults. These studies differed markedly in a number of design factors, including the mode, frequency, duration, and intensity of training, training history of participants, scheduling training sessions, and variable selection. Investigations about the effects of combined training have typically compared the effects of endurance and strength training only and combined endurance and strength training. Only a few studies have used randomized controlled study designs (Bell et al. 2000; Putman et al. 2004; Shaw and Shaw 2009; Shaw et al. 2009a; Shaw et al. 2009b; Wood et al. 2001).

Typically, both aerobic capacity and muscle strength can be improved simultaneously with combined training. Also, body composition changes have been similar during combined training compared with the effects of endurance (decrease in body fat) or strength training (increase in muscle mass or CSA) only.

Most studies have not found interference in physical fitness or body composition development. In these studies, training has typically been performed with low volume or intensity and the amount of training days in a week has been three or less. In contrast, most training studies that have used multiple training sessions per week (four or more) have observed some interference. In these studies, interference has been found in the development of muscle strength (Dolezal and Potteiger 1998; Hickson. 1980; Hunter et al. 1987; Sale et al. 1990a), explosive strength (Häkkinen et al. 2003) or aerobic capacity (Dolezal and Potteiger 1998; Glowacki et al. 2004; Nelson et al. 1990) development. Interference has also been observed in muscle fibre transitions of fiber size development (Kraemer et al. 1995; Putman et al. 2004). For example, Putman et al. (2004) observed similar increases (16-18%) in the CSA of type IIA fibers, but 2.9 fold greater increases in type I fibers in S compared to SE. However, in two studies interference did not occur during 12 weeks of training despite six training sessions weekly (Bell et al. 1991; Bell et al. 2000). The training response may also differ depending on whether strength and endurance training is performed on



alternate days or on the same days per week. Sale et al. (1990a) found that muscle strength was impeded when strength and endurance training was performed on the same day compared with similar training on alternate days.

### **Length of the training period**

The lengths of the training periods in combined training interventions have varied between 7 and 22 weeks. Interference in the improvement of physical fitness or muscle mass is usually observed only during longer (at least >7-8 weeks) training periods. For example, Hickson (1980) observed interference in strength development after 7 weeks of training and Izquierdo (2003) after 8 weeks of training.

### **Sex of the subjects**

Most of the combined training studies have selected male subjects. Only two studies have been conducted with women (Ferketich et al. 1998; Haykowsky et al. 2005). Ferketich et al. (1998) did not observe interference in 60-75 year-old women during 12 weeks of combined training (3 days a week, 70-80%  $\text{VO}_2$  peak for 30 min on a cycle ergometer). Instead, they found synergistic benefits in submaximal aerobic capacity in the combined group compared to cycling only group. Similarly, Haykowsky et al. (2005) found synergistic benefits in aerobic performance ( $\text{VO}_2$ peak) in the combined training group in healthy older women (68+/-4 years), but increases in overall muscle strength only in the strength trained groups.

Some studies have used both males and females as subjects (Bell et al. 2000; Dudley and Djamil 1985; Gergley 2009; Putman et al. 2004; Sale et al. 1990b). Most of these studies have not found differences in physiological adaptations between genders and, therefore, have pooled the results for analysis.

### **Age of the subjects**

Combined training studies have included both young (Dolezal and Potteiger 1998; Kraemer et al. 1995; Leveritt et al. 2003; Putman et al. 2004; Sale et al. 1990a; Sale et al. 1990b; Shaw and Shaw 2009), middle-aged (Häkkinen et al. 2003; Izquierdo et al. 2005) and older subjects (Ferketich et al. 1998; Haykowsky et al. 2005; Izquierdo et al. 2004; Wood et al. 2001).

Studies including older males and females have used low training volume (2-3 days per week) and interference has not been observed. In middle-aged subjects 2 times per week (1+1) combined training did not inhibit increases in muscle CSA but resulted in smaller increases in muscle strength than two times per week strength training only (Izquierdo et al. 2005). In another study in middle-aged subjects, combining endurance training two times per week with strength training two times per week resulted in interference in explosive strength development (Häkkinen et al. 2003). Several studies in young subjects have resulted in interference in strength or muscle mass development (Dolezal and Potteiger 1998; Kraemer et al. 1995; Putman et al. 2004; Sale et al. 1990a). These studies have, however, also used higher training volumes (3 to 6 days per week) and intensities than studies in older subjects.

**Interference in muscle mass**

Combined training studies conducted in healthy adults have mostly concentrated on adaptations in physical fitness development. Several studies have reported muscle adaptations at the muscle fiber level (Kraemer et al. 1995; Putman et al. 2004; Sale et al. 1990a; Sale et al. 1990b) and in CSA of the quadriceps femoris as measured by MRI or CT (Häkkinen et al. 2003; Izquierdo et al. 2003; Izquierdo et al. 2005; McCarthy et al. 2002). Results have been variable. Bell et al. (2000) suggested that combined training can suppress some of the adaptations to strength training, but, on the other hand, augment some aspects of capillarization in skeletal muscle. In another study, concurrent training resulted in greater fast-to-slow fibre type transitions and attenuated hypertrophy of the type I fibres compared with strength training alone (Putman et al. 2004). Thus, it is possible that combining endurance training with strength training may inhibit muscle growth in type I fibers, but not in type IIA fibers (Kraemer et al. 1995). The mechanisms are, however, still unclear.

**Combined training and metabolic risk factors**

Some combined training studies have also reported adaptations in body composition, mostly in %fat, during training (Glowacki et al. 2004; Häkkinen et al. 2003; McCarthy et al. 2002; Shaw and Shaw 2009). These studies have reported either 1) no changes in body fat, 2) similar decreases in all training groups (Dolezal and Potteiger 1998; Shaw and Shaw 2009), 3) similar increases in endurance trained groups (Ghahramanloo et al. 2009), or 4) greater decrease in %fat caused by combined training (Häkkinen et al. 2003). Only a few studies that have compared effects of combined training and endurance and strength only have been focused on adaptations in health parameters. One study including a 10 week training period compared effects of combined training and endurance and strength training only on basal metabolic rate (BMR) (Dolezal and Potteiger 1998). They found that BMR was increased in S and SE and decreased in E during training. In the two studies investigating the effects of combined training on blood lipids and lipoprotein, positive changes were observed in LDL-C in endurance trained groups (E and SE) (Ghahramanloo et al. 2009; Shaw et al. 2009b). Ghahramanloo et al. (2009) also reported positive effects on HDL-C in E and SE and in all training groups in total cholesterol and triglycerides. However, in that study the training period was only 8 weeks long.

Benefits of both endurance and strength training can be shared during combined training. The decrease in body fat caused by endurance training and an increase in fat free mass caused by strength training will in theory lead to greater health outcomes in body composition and various health benefits. However, as yet, there are no studies that have compared the effects of endurance, strength, and combined training on several physiological and health parameters in healthy, non-obese subjects. More research, and especially with randomized controlled designs are needed to find out the effects of combined training on health.

### **3 PURPOSE OF THE STUDY**

This work contains data from two large training studies conducted during 2005 and 2006. The overall purpose of this thesis was to investigate effects of the 21-week endurance, strength and combined training period on body composition, metabolic health, and physical fitness in healthy 39-77-year-old men and women who were normal or slightly overweight. The specific aims of the present studies were as follows:

1. To investigate the training-induced changes in body fat and lean mass during endurance, strength and combined training by using different methods.
2. To compare the effects of different training programs on metabolic health indicators in healthy men and women.
3. To analyze training-specific changes in physical fitness during a prolonged period of training and to find out the possible interference in muscle mass or neuromuscular and aerobic performance development during combined training.
4. To estimate effects of confounding factors (age, sex, nutrition, basal hormones, baseline health status) on training-induced changes in body composition, metabolic health and physical fitness.
5. To examine the effects of endurance, strength and combined training on health-related quality life.

## 4 RESEARCH METHODS

### 4.1 Subjects

Middle-aged and older (39-77 years) men (n=113) and women (n=102) living in the Jyväskylä city region volunteered as subjects. After baseline physical examination, subjects who fulfilled the inclusion criteria were randomized with stratification for age, BMI and menopausal status (pre or post menopausal) into three training groups and a control group.

**The exclusion criteria** included 1) diabetes, cardiovascular disease, cancer, and any other systemic diseases (e.g. rheumatoid arthritis) that could affect the ability to perform strength or endurance training and testing, 2) medications known to influence physical fitness or interpretation of the findings and 3) systematic (moderate to high-intensity) endurance or strength training more than once a week during the last year. Characteristics of the endurance training group (E, n=26 men, 26 women), strength training group (S, n=31 men, 27 women), combined strength and endurance training group (SE, n=33 men, 28 women) and control group (C, n=23 men, 21 women) in different papers are presented in Table 1. In men, DXA measurements (n=53) and oral glucose test (n=63) were performed only by a smaller subsample due to financial limitations. To avoid heterogeneity, we selected only subjects between the ages of 40 and 65 years and a BMI <28 kg/m<sup>2</sup>. Moreover in women, only subjects between the ages of 39 to 64 and a BMI <28 kg/m<sup>2</sup> were selected for DXA measurements and oral glucose tolerance tests in order to compare results between men and women.

## 4.2 Study design

This study used a randomized controlled pre- and post-intervention treatment design (Figure 1). The experimental variables were assessed before and after 21 weeks of physical training. During the intervention period, both endurance and strength training groups trained two times a week. The combined group trained four times a week, performing strength and endurance training protocols on different days.

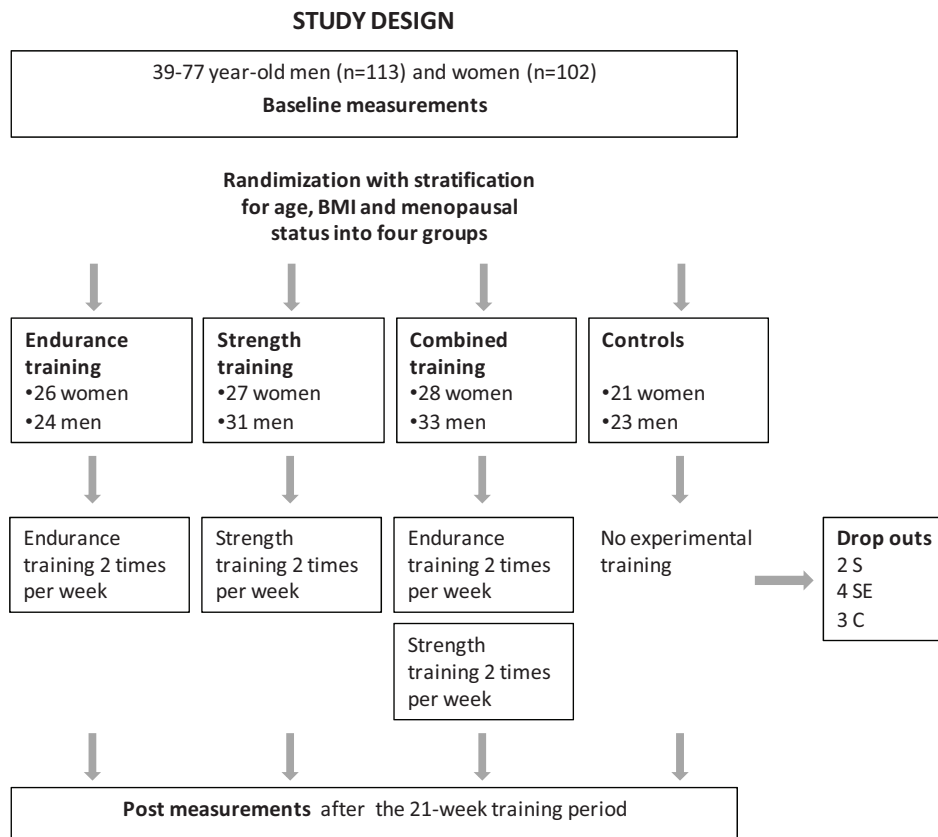


FIGURE 1 Study design. BMI, body mass index, S, Strength, SE, Combined, C, controls.

One to three resting days were provided between the similar types of training sessions. All training sessions were supervised by experienced research personnel. Missed workouts were made up, so that each subject achieved 98-100% of the prescribed number of training sessions assigned. All subjects, including controls, were instructed to continue their habitual physical activities as before (i.e. housework, walking, low-intensity skiing or Nordic walking).

The data is presented in five different articles. Selection criteria for the different articles are presented in Figure 2.

**INCLUSION CRITERIA FOR DIFFERENT PAPERS:**

<b>STUDY I</b>	<b>STUDY II</b>	<b>STUDY III</b>	<b>STUDY IV</b>	<b>STUDY V</b>
40-65 year-old men (n=53) DXA-measurements done	40-65 year-old men (n=63) BMI <28 kg/m <sup>2</sup> OGTT done, no impaired glucose tolerance or diabetes	39-64 year-old women (n=64) BMI <28 kg/m <sup>2</sup> DXA and OGTT done, no impaired glucose tolerance or diabetes	39-64 year-old women (n=79) Nutrition diary at baseline and DXA measurements done	39-77 year-old men (n=108) and women (n=96) RAND-36 done

FIGURE 2 Inclusion criteria. DXA, dual-energy X-ray absorptiometry, BMI, Body mass index, OGTT, oral glucose tolerance test.

### 4.3 Training protocols

#### 4.3.1 Endurance training protocol

The endurance training program was performed on a cycle ergometer. The intensity of cycle training was based on the subject's aerobic and anaerobic thresholds which were determined during the maximal aerobic performance tests (Aunola and Rusko 1986) and controlled by heart rate monitoring. Aerobic and anaerobic thresholds were determined from respiratory gas analysis and blood lactate values (Aunola and Rusko 1986). Blood samples were taken from the fingertip and analyzed with Lactate Pro LT-1710 analyzer (Arkray Inc., Kyoto, Japan).

Endurance training was periodized into three 7-week training cycles. During the first training weeks the training intensity was under the level of their aerobic threshold and training sessions lasted 30 min. During weeks 5 to 7 subjects also performed a few 10 min periods with a training intensity between the aerobic and anaerobic thresholds to become accustomed to higher intensities. Between weeks 8 to 14 the training intensity and volume was progressively increased so that in every other session the training intensity was under the aerobic threshold (60 min) and every second session included 45 min cycling with intensities varying from under the aerobic threshold to over the anaerobic threshold. During the last training weeks, every other training session included 75-90 min of cycling at a steady pace under the aerobic threshold and every other session 50-60 min of cycling with intensities varying from under the aerobic threshold to over the anaerobic threshold.

### 4.3.2 Strength training protocol

The present 21-week periodized training program was a progressive total body program for the lower and upper extremities and trunk. Each training session included two exercises for the leg extensor muscles (leg press and knee extension), one exercise for bilateral or unilateral knee flexion and four to five other exercises for the other main muscle groups of the body (bench press, triceps pushdown, or lateral pull-down exercise for the upper body; sit-up exercise for the trunk flexors or another exercise for the trunk extensors; and bilateral/unilateral elbow flexion exercise or leg adduction/abduction exercise). The number of sets per session for each exercise was 3-4 during the 21-week training period. The rest periods between sets and exercises ranged from 1 to 3 minutes with longer rest used for heavier resistances.

The training program was periodized into three specific training cycles of seven weeks in duration. The individual loads of strength training were determined based on the strength tests performed at baseline and in the middle of the training period. Training loads were also monitored throughout the training period by using the 10 repetition maximum (10RM) method. The role of the first training cycle was to act as a general preparation phase to develop toleration to the resistive exercise stress, verify proper exercise techniques, and to accustom the subjects to strength training, while stimulating the initial expected gains in strength and local muscular endurance. During the first cycle (weeks 1-7) training loads were 40-60% of the 1RM and the number of repetitions per set ranged from 15-20. The focus of the second cycle was to produce muscle hypertrophy and to increase the total muscle mass/fat ratio (loads of 60-80% of 1RM, repetitions 10-12). During the third cycle the goal was to optimize gains in strength of the trained muscles with higher training loads (70-90% of 1RM) and a lower number of repetitions per set (6-8). Each session included also 5-min warm up and recovery by bicycle, and some dynamic stretching exercises. The supervised training sessions averaged from 60 to 90 min in length.

## 4.4 Measurements

### 4.4.1 Body composition

Body composition measurements were performed in the postabsorptive state after a 12-hour overnight fast and the day preceding the measurement day was a rest day from intensive exercise. All body composition measurements were performed by the same investigator throughout the study period.

#### **Anthropometry**

Height was measured by an inelastic plastic tape measure with the subjects standing barefoot. Body weight was measured with the calibrated electrical scale (Model 708 [d=0.1kg], Seca, Germany) with the subjects in their same un-



dergarment apparel at each time point. BMI was calculated by dividing weight in kilograms by the square of height in meters ( $\text{kg}/\text{m}^2$ ).

#### **Dual-energy X-ray absorptiometry**

Total body fat and lean mass, as well as fat and lean mass in different subregions was estimated by Dual energy X-ray absorptiometry (DXA, LUNAR Prodigy, GE Medical systems). The system software was enCORE 2005, version 9.30, which provides the mass of lean soft tissue, fat, and bone mineral for the whole body and specific regions (Kim et al. 2002). Appendages were isolated from the trunk and head by using DXA regional computer-generated default lines with manual adjustments. Body composition was analyzed by using estimated fat mass and lean mass of soft tissue without bone.

#### **Bioelectrical impedance analysis (BIA)**

Percentage of body fat was recorded by the eight-polar bioimpedance method using multifrequency current (InBody 3.0, Biospace Co., Seoul, Korea).

#### **Skin fold measurements**

Percentage of body fat was estimated by measuring skin fold thickness at four different sites according to Durnin and Womersley (1974). The average of three measurements was used in the calculations.

#### **Muscle thickness (ultrasound)**

The muscle thickness of the right upper (triceps brachii) and lower (vastus lateralis and vastus intermedius) extremities were measured with a compound ultrasonic scanner (Aloka SSD280) (Häkkinen et al. 2006). The scanning head was coated with water-soluble transmission gel to provide acoustic contact without depressing the dermal surface. The distance between the subcutaneous adipose tissue-muscle interface and intramuscular interface was defined as muscle thickness. The same investigator made all the measurements.

#### **Circumferences**

Waist circumference was measured mid-way between the lateral lower ribs and the iliac crest. Thigh circumference was measured at the mid-point between trochanter major and the joint space of the knee. The circumference of the right upper arm was measured at the mid-point between the tip of the shoulder and the tip of the elbow (olecranon process and the acromion). An average of three measurements was used in all calculations.

### **4.4.2 Metabolic health indicators**

#### **Blood sampling**

All blood samples were taken after a 12 h fast between 7:00 and 9:00 A.M. The preceding day was a rest day from any strenuous physical activity and the participants were asked to rest at least eight hours during the previous night. All blood samples were drawn from the antecubital vein and handled according to

standardized laboratory practice. Serum samples were stored frozen at  $-80^{\circ}\text{C}$  until analyzed.

#### **Glucose and insulin tests**

Glucose metabolism was assessed with an oral glucose tolerance test (OGTT). Samples for glucose and insulin were taken while fasting at 0 min and 60 and 120 min after a glucose load (75g). Blood glucose samples were analyzed with the Hemocue Glucose Analyzer (B-Glucose Photometer, HemoCue AB, Ängelholm Sweden). Insulin concentrations were assayed using TR-IFMA (time-resolved immuno-fluorometric assays, B080-101) and an AutoDELFIA fluorometer (Wallac, Turku, Finland). Glucose and insulin areas under the curve (AUC) were calculated using a trapezoid model. Glucose tolerance was defined by the WHO 1999 criteria. Impaired fasting glycemia was defined as fasting plasma glucose concentrations  $\geq 6.1$  mmol/l but  $< 7.0$  mmol/l, impaired glucose tolerance as fasting plasma glucose  $< 7.0$  mmol/l and 2-h plasma glucose 7.8 – 11.0 mmol/l and diabetes mellitus as fasting plasma glucose  $\geq 7.0$  mmol/l or 2-h plasma glucose  $> 11.0$  mmol/l or a previous diagnosis of diabetes treated by diet, oral hypoglycemic medication, or insulin (Sacks et al. 2002).

In paper II **the metabolic syndrome** was defined according to the National Cholesterol Education Program (NCEP) criteria: fasting plasma glucose levels  $6.0 \geq$  mmol/l, triglycerides  $1.7 \geq$  mmol/l, HDL-C  $< 1.0$  mmol/l, blood pressure  $\geq 130/85$  mmHg, waist girth  $> 102$  cm (Expert panel 1998).

#### **Serum lipids and lipoproteins**

Total cholesterol, HDL-C and triglycerides were measured by using Vitros DT60 dry chemistry system (Ortho-Clinical Diagnostics, Inc., USA). LDL-C (mmol/L) was estimated using the Friedewald (1972) equation:  $\text{LDL-C} = \text{total cholesterol} - \text{HDL-C} - (\text{triglycerides}/2.2)$ .

#### **Resting blood pressure**

SBP and DBP were taken as the lower of two measurements in the supine position after a rest of 5 minutes using an automatic sphygmomanometer (Omron, model HEM-705C, Omron Corporation, Hamburg, Germany). Resting heart rate was registered after 15 min rest as the lower of two measurements.

#### **4.4.3 Muscle strength**

##### **Leg press, one-repetition maximum**

A David 210 dynamometer (David Fitness and Medical, Outokumpu, Finland) was used to measure maximal bilateral concentric force production of the leg extensors (hip, knee, and ankle extensors) in a horizontal leg press exercise (Häkkinen et al. 1998a). The subject was in a seated position so that the hip angle was  $110^{\circ}$ . On verbal command, the subject performed a concentric leg extension starting from a flexed position of  $70^{\circ}$ , to a full extension of  $180^{\circ}$  against the resistance determined by the loads chosen on the weight stack. In the testing of

the maximal load, separate 1RM contractions were performed. After each repetition, the load was increased until the subject was unable to extend the legs to the required position.

#### **Bilateral isometric leg extension**

An electromechanical dynamometer was used to measure maximal isometric force of the bilateral leg extension action at a knee angle of 107° (Häkkinen and Häkkinen 1995; Häkkinen et al. 1998a). A minimum of three trials was completed for each subject and the best performance trial with regard to maximal peak force was used for the subsequent statistical analysis. The force signal was recorded and analyzed with a Micro1401 data acquisition unit and Signal software (Cambridge Electronic Design, Cambridge, UK). Maximal peak force was defined as the highest value of the force (N) recorded during the bilateral isometric leg extension.

#### **Unilateral isometric knee extension**

A David 200 dynamometer modified for strength testing (Häkkinen and Pakarinen 1993; Häkkinen et al. 1998a) was used to measure maximal isometric unilateral force of the right knee extensors. The subject was in a seated position so that the hip and knee joints were 70° and 90° flexion, respectively. On verbal command subjects were instructed to exert their maximal force as fast as possible during a period of 2.5-4.0 s. A minimum of three maximal actions was recorded, and maximal peak force was defined as the highest value of force recorded during maximal isometric knee extension (N).

#### **Isometric bench press**

A modified David 200 dynamometer was applied for the recording of the bilateral isometric force of the bench press action (including triceps brachii, anterior deltoid and pectoralis major muscles) (Häkkinen et al. 1998c). Subjects sat on the dynamometer and pushed with their upper arms against a horizontal bar with their elbows at 90°.

### **4.4.4 Aerobic performance**

#### **Maximal oxygen uptake**

The graded exercise test was carried out by using the Monark E839 (Monark Oy, Sweden) bicycle ergometer to determine maximal oxygen uptake, as well as aerobic and anaerobic thresholds. Oxygen uptake was measured breath-by-breath continuously (SensorMedics® Vmax229).  $\dot{V}O_2$ max was determined as the highest one-minute average of  $\dot{V}O_2$  during the test. Heart rate and continuous electrocardiogram (ECG) were monitored during the test, as well as blood pressure every 2<sup>nd</sup> min by the manual sphygmomanometer (Gamma G-5, Heine, Germany). A physician supervised the maximal test. The subjects were encouraged by the testers to continue cycling until exhaustion. In a few subjects the test was interrupted by a physician for medical reasons (pathological changes in blood pressure or ECG).

### Maximal cycling power

Maximal cycling power was measured during a graded cycling test using the Monark E839 (Monark Oy, Sweden) bicycle ergometer. Heart rate and continuous ECG were monitored and blood pressure was measured every 2<sup>nd</sup> min with a manual sphygmomanometer (Gamma G-5, Heine, Germany). A physician supervised the test. The subjects were encouraged by the testers to continue cycling until exhaustion. Maximal cycling power ( $W_{\max}$ ) was calculated as:  $W_{\max} = W_{\text{com}} + t/120 \text{ DP}$ , in which  $W_{\text{com}}$  is the last cycling load completed,  $t$  is the time in seconds the non-completed load was maintained and DP is the increment in watts (Kuipers et al. 1985).

#### 4.4.5 Serum basal hormone concentrations

Prior to blood sampling subjects were instructed to perform no exercise for 24 hours. The blood samples were obtained after an overnight fast and at the same time of day via venipuncture by a trained laboratorian twice before (weeks -1 and 0) and after 21 weeks of training. The mean of the -1 and 0 week value were used as the baseline value.

Whole blood was collected and centrifuged at 3500 rpm for 10 min at 4°C. The resulting serum and plasma was aliquoted and stored at -80 °C until subsequent analysis. Serum testosterone (T), cortisol, insulin-like growth factor 1 (IGF-1), sex-hormone binding globulin (SHBG) and dehydroepiandrosterone-sulfate (DHEAS) concentrations were analyzed using an immunometric chemiluminescence method (Immulite® 1000, DPC, Los Angeles, USA). The assay sensitivities for T, cortisol and IGF-1 were 0.5nmol/L, 5.5nmol/L and 2.6 nmol/L and for SHBG and DHEAS 0.2nmol/L and 0.08µmol/L. Intra-assay coefficients of variation were 16.4% (T), 10.0% (cortisol), 6.1% (IGF-1), 6.9% (SHBG) and 7.6% (DHEAS).

#### 4.4.6 Dietary intake

The food intake was analyzed by food diaries for three workdays and one weekend day in the beginning and at the end of the study period. Both verbal and written instructions were given to the subjects on how to write down all the foods and drinks they consumed, including portion sizes as household measures, preparation techniques and brand names. The food diaries were analyzed by nutrient analysis software (Nutrica® 3.11, The Social Insurance Institution of Finland). Also a short nutrition counseling session was provided for the training groups before the study. This session included both verbal and written instructions, which were based on the Finnish nutrition recommendations. The main purpose was to provide guidance on a healthy diet sufficient for exercise requirements. The subjects did not use pre- or post- workout protein or other supplements during the study.

#### 4.4.7 Health-related quality of life (HRQoL)

HRQoL was assessed using the self-rating questionnaire RAND-36-Item Health Survey. A Finnish version of Short form 36 (SF-36), RAND-36, is a valid and reliable method to measure HRQoL among the Finnish adult population (Aalto et al. 1999).

RAND-36 estimates HRQoL in eight separate dimensions related to physical, emotional and social well being. The eight dimensions are General Health, Physical Functioning, Mental Health, Social Functioning, Vitality, Bodily Pain, Role Physical and Role Emotional. Scores for each dimension ranged from 0-100, with a higher score reflecting a better quality of life.

The eight scales of the RAND-36 questionnaire were aggregated into two summary measures. The physical component summary included scores of general health, physical functioning, bodily pain and role physical. The mental component summary included scores of mental health, social functioning, vitality and role emotional.

## 4.5 Statistical methods

In the text and tables data are presented as means with standard deviation (SD) (II-V) or 95% confidence interval (I). In figures, data are presented as means with SD (I-IV) or standard error (SE) (V). Analysis of covariance (ANCOVA) corrected with baseline values or scores were used to study differences between groups (I, III-V). If necessary, data were transformed logarithmically to fulfil the criteria of normal distribution. In paper II, the changes in study variables between the groups were compared with multivariate analysis of covariance (MANCOVA) for repeated measures using the baseline values (week 0) as the covariate.

When there were no group effects, the time-effect was analyzed in the total group of trained subjects using multivariate analysis of variances (MANOVA). Within group analyses were performed by paired samples T-tests. The relationship between study variables were assessed with Pearson product-moment correlation coefficients and the relationship between the changes in variables during the intervention were studied using partial correlation analysis with adjustment for group. An alpha of  $P < 0.05$  was selected as a level of statistical significance in within and between groups analysis.

Glucose and insulin AUCs during the OGTT were measured with the following equation:  $AUC = [(baseline\ 0-h + 1-h\ concentrations)/2 + (1-h\ concentrations + 2-h\ concentrations)/2]$ .

Reproducibility of %fat analysis by BIA, circumferences, skin fold thicknesses and muscle thickness measurements by ultrasound were tested by comparing the two control period measurements (at week -1 and week 0) (I). The reproducibility was assessed by one-way random model of intraclass correlation coefficient (ICC) (Weir 2005).

## **4.6 Study approval**

The study design was approved by the Ethics Committee of the Central Finland Health Care District. All subjects were carefully instructed about the possible risks and discomforts related to the study, and they signed a written consent form before participation.

## 5 RESULTS

### 5.1 Subject characteristics

At baseline mean (SD) weights (range) were  $81.3\pm 11.3$  kg (53.6-113.8) in men and  $66.3\pm 9.0$  kg (44.1-86.2) in women. Mean body heights were  $176.8\pm 6.8$ cm (158.1-195.5) in men and  $163.8\pm 6.5$ cm (147.3-178.1) in women. Mean BMIs were  $26.0\pm 3.1$ kg/m<sup>2</sup> (17.5-33.9) and  $24.6\pm 2.8$  kg/m<sup>2</sup> (17.6-29.7), in men and in women respectively. Men were on average  $56.3\pm 8.2$  (40-77) and women  $51.6\pm 7.4$  (39-64) years old. Baseline subject characteristics in different articles and training groups are presented in table 1.

### 5.2 Drop-outs and compliance to experimental training

115 men and 102 women volunteered for the study. During the baseline measurements one man quit because of a complication in muscle biopsy measurements. During the intervention period six men and four women dropped out the study. Two men (C, S) and one woman (C) withdrew due to medical reasons (not related to training or testing) and three women (2SE, S) and three men (2SE, C) due to personal reasons.

A total of 99 women and 108 men performed the intervention as planned. Any missed workouts were made up, so that each subject achieved 98-100% of the prescribed number of training sessions assigned.



TABLE 1 Subject characteristics at baseline.

	Group	n (M/W)	Age mean (SD)	Height mean (SD)	Weight mean (SD)	Body mass index mean (SD)
paper I	E	14/-	54 (8)	179 (6)	76 (9)	24 (2)
	S	13/-	55 (6)	177 (7)	79 (5)	25 (2)
	SE	15/-	56 (7)	176 (9)	77 (13)	25 (3)
	C	10/-	53 (8)	177 (6)	77 (7)	25 (1)
paper II	E	17/-	53 (8)	178 (6)	76 (8)	24 (2)
	S	15/-	54 (6)	180 (7)	80 (5)	25 (2)
	SE	15/-	56 (7)	176 (9)	77 (13)	25 (3)
	C	15/-	54 (8)	177 (5)	77 (6)	25 (1)
paper III	E	-/15	52 (7)	162 (7)	63 (7)	24 (2)
	S	-/17	51 (8)	164 (8)	61 (9)	23 (2)
	SE	-/18	49 (7)	164 (6)	62 (8)	23 (2)
	C	-/12	51 (8)	166 (7)	64 (7)	23 (2)
paper IV	E	-/21	53 (8)	162 (2)	66 (9)	25 (3)
	S	-/27	52 (8)	164 (7)	67 (11)	25 (3)
	SE	-/22	51 (7)	163 (7)	66 (8)	25 (3)
	C	-/9	53 (8)	167 (7)	66 (8)	23 (2)
paper V	E	24/26	54 (8)	170 (9)	73 (12)	25 (3)
	S	29/30	54 (8)	171 (10)	76 (13)	26 (3)
	SE	25/31	54 (8)	171 (10)	75 (14)	25 (3)
	C	18/21	55 (9)	171 (8)	73 (10)	25 (2)

M, men, W, women, SD, standard deviation. E, Endurance, S, Strength, SE, Combined, C, controls.

### 5.3 Body composition

After 21 weeks of training, %fat measured by DXA, decreased in all training groups in men and in the endurance trained groups in women (Figure 3). In contrast, as measured by BIA, %fat decreased only in E in men (summary of the body composition changes in Table 2). Concurrently, in men total body lean mass increased in SE and in women in E and SE. In both genders muscle thickness measured by ultrasound in VL+VI increased in all training groups. In women, legs lean mass increased significantly also in all training groups, but in men only in S. More detailed results are presented in the following sections.

TABLE 2 Summary of the body composition changes in the subject groups during the 21-week training period.

Variable	Sex	Difference between groups	E	S	SE	C	paper
Body weight (kg)	M	n.s.	↓	↔	↔	↔	I
	W	n.s.	↓	↔	↔	↓	III
BMI (kg/m <sup>2</sup> )	M	n.s.	↓	↔	↔	↔	I
	W	n.s.	↓	↔	↓	↓	IV
Percentage of fat (DXA)	M	n.s.	↓	↓	↓	↔	I
	W	n.s.	↓	↔	↓	↔	III
Percentage of fat (BIA)	M	n.s.	↓	↔	↔	↔	I
	W	n.s.	↔	↔	↔	↔	
Percentage of fat (skinfolds)	M	n.s.	↓	↓	↓	↓	I
	W	n.s.	↔	↓	↔	↔	
Total body lean mass (DXA)	M	0.040	↔	↔	↑	↔	I
	W	n.s.	↑	↔	↑	↔	III
Lean mass of the legs (DXA)	M	0.027	↔	↑	↔	↔	I
	W	n.s.	↑	↑	↑	↔	III
VL+VI muscle thickness (US)	M	<0.001	↑	↑	↑	↔	I
	W	<0.001	↑	↑	↑	↔	
Lean mass of the arms (DXA)	M	n.s.	↔	↑	↔	↔	I
	W	0.015	↔	↔	↑	↔	III
Triceps muscle thickness (US)	M	0.005	↔	↑	↑	↔	I
	W	0.003	↑	↑	↑	↔	

M, men, W, women, E, Endurance, S, Strength, SE, Combined, C, controls. BMI, Body mass index, DXA, dual-energy X-ray absorptiometry, BIA, Bioimpedance, VL+VI, vastus lateralis + vastus intermedius, US, ultrasound.

### 5.3.1 Body weight and BMI

In men, body weight decreased by 1.5kg and BMI by 0.5 kg/m<sup>2</sup> in E during the 21-week period, and in women body weight decreased in E (-1.0±1.7 kg, p=0.038) and C (-0.4±0.6 kg, p=0.033), but not in the other groups (I,II). The

changes in body weight or BMI did not differ between the groups in men or in women during the 21-week training period (I,II).

### 5.3.2 Total body fat

Percentage of fat measured by DXA decreased significantly by 5.2 – 8.3% in all three training groups in men and in E (-5.9%,  $p=0.002$ ) and SE (-4.8%,  $p<0.001$ ) in women (men and women in Figure 3) (I,III). The between groups differences in percent body fat tended to be significant in men ( $p=0.081$ ) and in women ( $p=0.095$ ) as measured by DXA, but not by skin folds ( $p=0.62$  and  $p=0.50$ ) or BIA (0.78 and 0.94) (I, III).

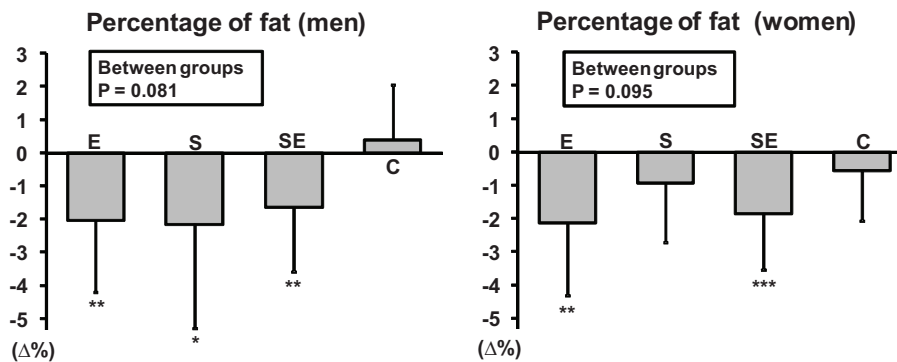


FIGURE 3 Mean (SD) changes in percentage of fat as measured by DXA during the 21-week training period in men (I) and women (III). E, Endurance, S, Strength, SE, Combined, C, control. \* $p<0.05$ , \*\* $p<0.01$ , \*\*\* $p<0.001$  significant difference within group from week 0 to week 21.

### 5.3.3 Abdominal fat

In women, waist circumference and trunk fat mass decreased significantly only in E and SE (Figure 4). Waist circumference decreased by -1.9 cm ( $p=0.003$ ) in E and by -1.6 cm ( $p=0.007$ ) in SE. Trunk fat mass decreased by  $-5.9\pm 9.0\%$  ( $p=0.048$ ) in E and  $-3.5\pm 7.0\%$  ( $p=0.049$ ) in SE, respectively. Waist circumference decreased on average by 1.7 to 2.9 cm in all three training groups in men ( $p=0.001-0.007$ ) and also trunk fat mass decreased in all training groups significantly, but not in C. The decreases in the fat mass of the trunk were  $-12.0\pm 16.6\%$  ( $p=0.003$ ) in E,  $-6.1\pm 25.2\%$  ( $p=0.031$ ) in S and  $-8.2\pm 11.5\%$  ( $p=0.009$ ) in SE. The changes in waist circumference or fat mass of the trunk, measured by DXA, did not differ between groups during the training period in men or in women (II, III).

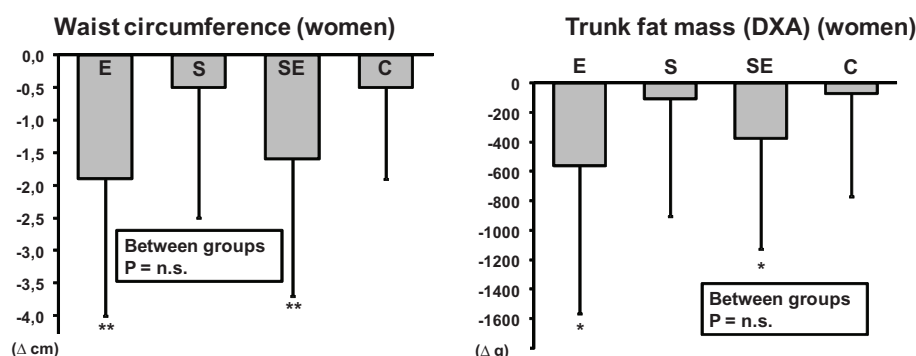


FIGURE 4 Mean (SD) changes in abdominal fat as measured by waist circumference and trunk fat mass (DXA) during training in women. E, Endurance, S, Strength, SE, Combined, C, Control. \* $p < 0.05$ , \*\* $p < 0.01$  significant difference within group from week 0 to week 21.

### 5.3.4 Body lean mass and muscle thickness

In men, the increases in total body lean mass were of the same magnitude in S ( $1.8 \pm 2.9\%$ ) and SE ( $1.6 \pm 2.4\%$ ), but the within group change was statistically significant only in SE ( $p = 0.019$ ). In women, the within group increases were significant in E ( $2.0 \pm 2.8\%$ ,  $p = 0.019$ ) and in SE ( $1.8 \pm 2.7\%$ ,  $p = 0.024$ ). During training, the changes in the total body lean mass differed between groups in men ( $p = 0.040$ ), but not in women ( $p = 0.17$ ) (I, II) (Figure 5).

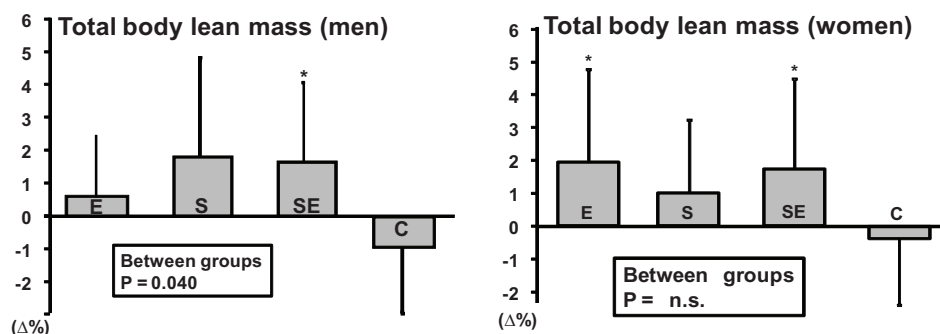


FIGURE 5 Mean (SD) changes in total body lean mass during the 21-week training period in men (I) and in women (II). E, Endurance, S, Strength, SE, Combined, C, Control. \*  $p < 0.05$  significant difference within group from week 0 to week 21.

In men during the 21-week training period, muscle thickness in VL+VI increased significantly by 0.26 to 0.36 cm in all three training groups (all  $p < 0.001$ ), but as measured by DXA, lean mass of the legs increased significantly only in S ( $2.0 \pm 1.5\%$ ,  $p < 0.001$ ) (I) (Figure 6). In contrast, in women the VL+VI thickness increased more in SE ( $10.9 \pm 6.8\%$ ,  $p < 0.001$ ) than in S ( $7.5 \pm 5.2\%$ ), E ( $5.8 \pm 5.6\%$ ) or C ( $3.5 \pm 8.0\%$ ) (all  $p < 0.001$ ). Also, lean mass of the legs measured by DXA in-

creased significantly ( $P=0.010-0.004$ ) by 1.9 to 3.5% in all three training groups in women (III).

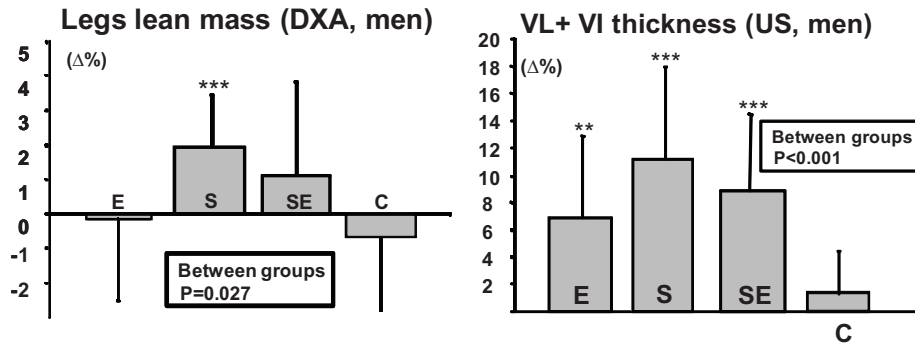


FIGURE 6 Relative changes (mean and SD) in lean mass of the legs and VL+VI muscle thickness during the 21-week training period in men (I). E, Endurance, S, Strength, SE, Combined, C, Control. \*\*\*  $p<0.001$ , \*\*  $p<0.01$  significant difference within group from week 0 to week 21.

A significant increase was found during the training period in lean mass of the arms in S ( $3.2\pm 3.6\%$ ,  $p=0.006$ ) in men and in SE ( $1.8\pm 3.9\%$ ,  $p=0.021$ ) in women (women in Figure 7). The changes between groups during training in lean mass of the arms were significant in women ( $p=0.015$ ), but not in men ( $p=0.15$ ) (I,III).

In men, triceps brachii muscle thickness increased in the strength trained groups;  $22\pm 16\%$ ,  $p<0.001$  in S and  $20\pm 19\%$ ,  $p<0.001$  in SE, but not in E or C (between groups  $p=0.005$ ) (I). In women, increases in triceps brachii thickness were observed in E ( $3.4\pm 5.8\%$ ,  $p=0.011$ ), S ( $6.6\pm 6.3\%$ ,  $p<0.001$ ) and SE ( $5.0\pm 4.5\%$ ,  $p<0.001$ ), but not in C (between groups  $p=0.003$ ) (Figure 7).

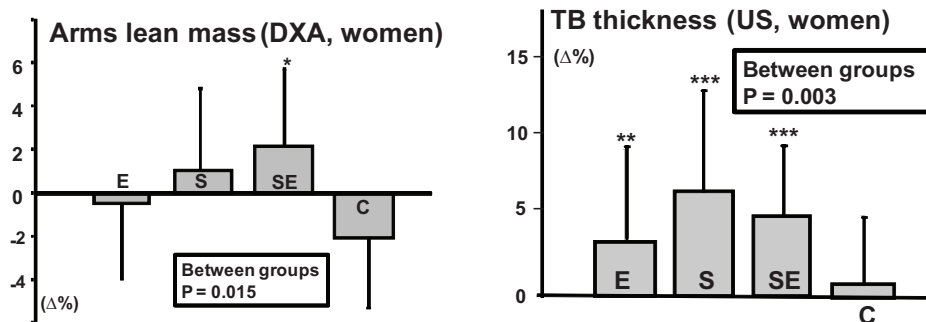


FIGURE 7 Relative changes (mean and SD) in the lean mass of the arms (III) and TB muscle thickness during the 21-week training period in women. E, Endurance, S, Strength, SE, Combined, C, Control. \* $p<0.05$ , \*\* $p<0.01$ , \*\*\*  $p<0.001$  significant difference within group from week 0 to week 21.

### 5.3.5 Reproducibility of different body composition methods

Reproducibility of different body composition methods was very high among percent fat analysis (BIA, skin folds) and waist circumference and rather high among muscle thickness measurements (Table 3).

TABLE 3 Intraclass correlation coefficient (ICC) of selected body composition analyses for the two control period measurements (I)

Variable	ICC (95% CI)
Fat% (BIA)	0.98 (0.96 to 0.99)
Fat% (skin folds)	0.98 (0.97 to 0.99)
Waist circumference	0.98 (0.96 to 0.99)
Muscle thickness TB	0.95 (0.91 to 0.97)
Muscle thickness VL+VI	0.92 (0.86 to 0.95)

CI confidence interval, Fat%, percentage of fat, BIA, bioimpedance analysis, TB triceps brachii, VL+VI vastus lateralis + intermedius

### 5.3.6 Relationships between different body composition methods

At baseline, in the total group of subjects, the %fat measured by DXA correlated with BIA ( $r=0.90$ ,  $p<0.001$ ), %fat measured by skin fold thicknesses ( $r=0.80$ ,  $p<0.001$ ) and waist circumference ( $r=0.84$ ,  $p<0.001$ ) (I). In the total group of trained subjects, the change in DXA during the training period correlated with the changes in BIA ( $r=0.66$ ,  $p<0.001$ ), skin fold thicknesses ( $r=0.78$ ,  $p<0.001$ ) and waist circumference ( $r=0.74$ ,  $p<0.001$ ). The changes in leg lean mass (DXA) and in the (US) thicknesses of VL+VI were related in the trained subjects ( $r=0.31$ ,  $p=0.045$ ).

## 5.4 Metabolic health indicators

The 21-week training period resulted in decreases in abdominal fat, as measured by waist circumference, in all training groups except in S in women (Table 5). Resting blood pressure decreased only in E and S in men. Some changes occurred in glucose and lipid metabolism. Detailed results are presented in the following sections.

### 5.4.1 Glucose and insulin metabolism

In the endurance-trained men serum fasting insulin decreased significantly ( $-17\pm 27\%$ ,  $p=0.013$ ), while the other groups did not show statistically significant changes. In E, serum insulin concentration at post 2-h ( $-16\pm 47\%$ ,  $p=0.027$ ) de-

creased significantly during training, but the difference between the groups was not statistically significant. In women, serum fasting insulin decreased in E ( $-11.1\pm 22.4\%$ ), S ( $-9.3\pm 16.0\%$ ) and SE ( $-5.6\pm 24.0\%$ ), but changes were significant only in S ( $p=0.049$ ), and SE ( $p=0.042$ ). The difference between the groups in the change of serum fasting insulin values was not statistically significant in women, but approached statistical significance ( $p=0.054$ ) in men (Figure 8) (II, III).

During the OGTT in men, fasting glucose decreased by  $-2.8\pm 5.0\%$  ( $p=0.046$ ) in S, and 1-h glucose concentration increased by  $14\pm 18\%$  ( $p=0.008$ ) in C, during the intervention period (Figure 9). In women, in S serum glucose 2-h concentration decreased significantly during training ( $p=0.038$ ). There were no differences between the groups in the changes of serum fasting glucose or 1-h and 2-h concentrations.

Insulin area under the curve (AUC) did not change significantly in any of the groups. In men, glucose AUC increased only in C by  $0.9\pm 1.3$  mU/ml ( $p=0.017$ ), while all female and male training groups showed nonsignificant changes. There were no differences between the groups in the change of glucose and insulin AUCs during the training period (II, III).

### Serum insulin

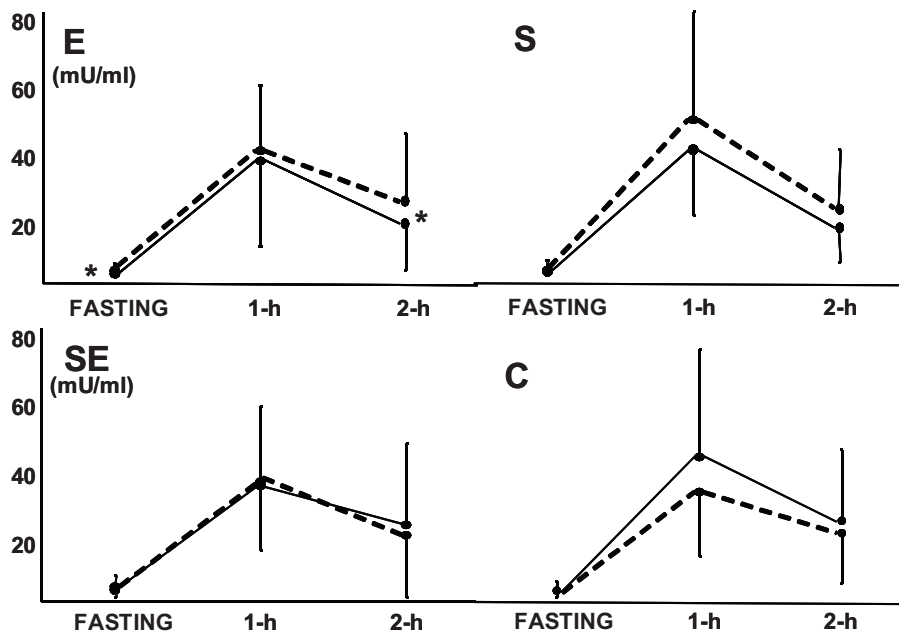


FIGURE 8 Serum insulin levels (mean and SD) during oral glucose tolerance test before (dashed line) and after the intervention (solid line) in men (II). E, Endurance ( $n=17$ ), S, Strength ( $n=15$ ), SE, Combined ( $n=15$ ), C, Control ( $n=15$ ). \*  $p<0.05$  significant difference within the group from week 0 to week 21.



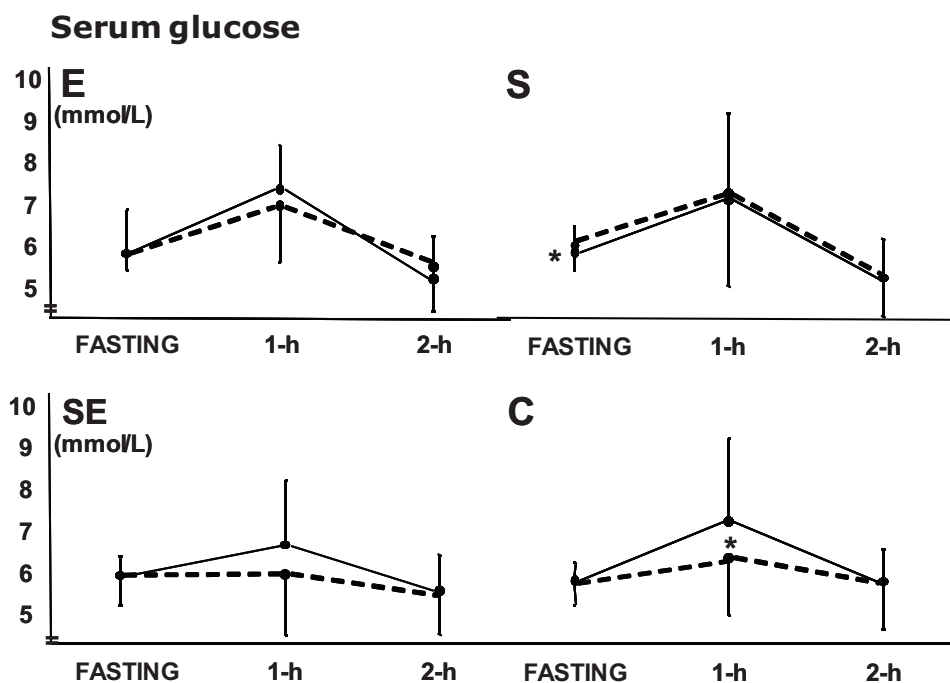


FIGURE 9 Serum glucose levels (mean and SD) during oral glucose tolerance test before (dashed line) and after the intervention (solid line) in men (II). E, Endurance (n=17), S, Strength (n=15), SE, Combined (n=15), C, Control (n=15). \* p<0.05 significant difference within the group from week 0 to week 21.

#### 5.4.2 Lipid and lipoprotein metabolism

After training, the HDL-C levels in men were significantly lower than before training in S (by  $-0.12 \pm 0.20$  mmol/L,  $p=0.029$ ) and C (by  $-0.09 \pm 0.12$  mmol/L,  $p=0.014$ ), while E and SE showed no changes. In women, E showed decreases in total cholesterol ( $-0.2 \pm 0.3$  mmol/l,  $p=0.003$ ) and LDL-C ( $-0.3 \pm 0.4$  mmol/l,  $p=0.010$ ) and an increase in HDL-C ( $0.1 \pm 0.2$  mmol/l,  $p=0.045$ ) after training. There were no differences between the groups in the changes in blood lipids or lipoproteins during the training period (II, III) (Table 4).

TABLE 4 Blood lipids and lipoproteins and their changes with training in men and in women in different subject groups (II, III).

	Sex	Group	Baseline	Post training	Change ( $\Delta$ mmol/L) 0-21 weeks	Between groups p-value
<b>Total cholesterol (mmol/L)</b>	M	E	5.3 (1.0)	5.0 (1.0)	-0.3 (0.6)	0.38
		S	5.0 (0.9)	5.0 (1.0)	0.0 (0.8)	
		S+E	4.9 (0.6)	5.1 (0.6)	0.2 (0.4)	
		C	5.2 (0.8)	5.2 (0.8)	-0.1 (0.5)	
	W	E	5.0 (0.6)	4.7 (0.6)	-0.2 (0.3)**	0.43
		S	5.3 (0.7)	5.2 (0.7)	-0.1 (0.6)	
		S+E	4.9 (0.6)	4.8 (0.6)	-0.1 (0.5)	
		C	5.4 (0.9)	5.2 (0.6)	-0.2 (0.4)	
<b>LDL-C (mmol/L)</b>	M	E	3.7 (0.9)	3.5 (1.0)	-0.2 (0.5)	0.35
		S	3.4 (0.9)	3.6 (0.7)	0.2 (0.8)	
		S+E	3.2 (0.3)	3.4 (0.5)	0.2 (0.4)	
		C	3.7 (0.7)	3.8 (0.8)	0.0 (0.4)	
	W	E	2.9 (0.4)	2.6 (0.6)	-0.3 (0.4)*	0.21
		S	3.2 (0.6)	3.1 (0.6)	-0.1 (0.5)	
		S+E	2.9 (0.5)	2.8 (0.6)	0.0 (0.4)	
		C	3.2 (0.7)	3.0 (0.6)	-0.2 (0.3)	
<b>HDL-C (mmol/L)</b>	M	E	1.1 (0.3)	1.1 (0.3)	0.0 (0.2)	0.21
		S	1.1 (0.3)	0.9 (0.3)	-0.1 (0.2)*	
		S+E	1.2 (0.4)	1.1 (0.4)	-0.1 (0.2)	
		C	1.0 (0.2)	0.9 (0.2)	-0.1 (0.1)*	
	W	E	1.6 (0.4)	1.7 (0.3)	0.1 (0.2)*	0.31
		S	1.7 (0.3)	1.7 (0.3)	0.0 (0.2)	
		S+E	1.5 (0.4)	1.6 (0.3)	0.0 (0.2)	
		C	1.8 (0.3)	1.7 (0.2)	-0.1 (0.3)	
<b>Triglycerides (mmol/L)</b>	M	E	1.0 (0.3)	0.9 (0.3)	-0.1 (0.4)	0.38
		S	1.2 (0.4)	1.1 (0.4)	-0.1 (0.4)	
		S+E	1.2 (0.7)	1.2 (0.7)	0.0 (0.7)	
		C	1.0 (0.5)	1.0 (0.4)	-0.1 (0.4)	
	W	E	0.9 (0.3)	0.8 (0.4)	-0.1 (0.4)	0.14
		S	0.8 (0.3)	0.8 (0.2)	0.0 (0.2)	
		S+E	1.1 (0.8)	0.9 (0.5)	-0.2 (0.5)	
		C	0.9 (0.2)	1.0 (0.3)	0.1 (0.2)	

Values are means (SD), M, men, W, women E, Endurance (n=15 women, 16 men), S, Strength (n=17 women, 15 men), SE=Combined (n=18 women, 15 men), C=Control (n=12 women, 15 men). \* p<0.05, \*\*p<0.01 significant difference within group from week 0 to week 21.

### 5.4.3 Blood pressure

Mean (SD) SBP decreased in both E ( $-6\pm 8$  mmHg,  $p=0.008$ ) and S ( $-9\pm 7$  mmHg,  $p<0.001$ ). Also, DBP decreased in both E ( $-4\pm 6$  mmHg,  $p=0.020$ ) and S ( $-5\pm 7$  mmHg,  $p=0.018$ ). There was a significant difference between the groups in the changes of SBP ( $p=0.003$ ), but not in the changes in DBP ( $p=0.073$ ) during the 21-week training period in men (II) (Figure 10). In women, no differences occurred in resting blood pressure in any of the groups during training (III).

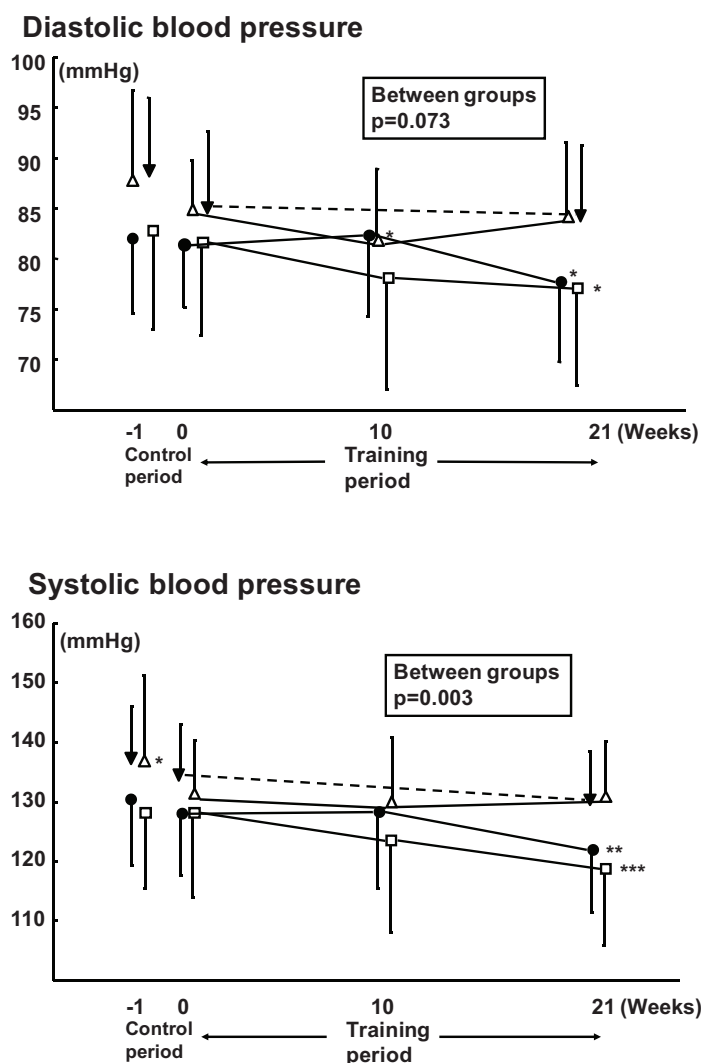


FIGURE 10 Changes in mean (SD) in systolic and diastolic blood pressure during the 1-week control period and 21-week training period in men (II). ● = Endurance, □ = Strength, Δ = Combined and ▼ = control. \*\*\*  $p<0.001$ , \*\*  $p<0.01$ , \*  $p<0.05$  significant difference within the group from week 0 value.

TABLE 5 Summary of the changes in metabolic health indicators in the groups during the 21-week training period.

Variable	Sex	Difference between groups	E	S	SE	C	paper
Waist circumference	M	n.s.	↓	↓	↓	↔	II
	W	n.s.	↓	↔	↓	↔	III
Systolic blood pressure	M	0.003	↓	↓	↔	↔	II
	W	n.s.	↔	↔	↔	↔	III
Diastolic blood pressure	M	n.s.	↓	↓	↔	↔	II
	W	n.s.	↔	↔	↔	↔	III
Fasting glucose	M	n.s.	↔	↓	↔	↔	II
	W	n.s.	↔	↔	↔	↔	III
Post 1-h glucose	M	n.s.	↔	↔	↔	↑	II
	W	n.s.	↔	↔	↔	↔	III
Post 2-h glucose	M	n.s.	↔	↔	↔	↔	II
	W	n.s.	↔	↑	↔	↔	III
Fasting insulin	M	n.s.	↓	↔	↔	↔	II
	W	n.s.	↔	↓	↓	↔	III
Post 1-h insulin	M	n.s.	↔	↔	↔	↔	II
	W	n.s.	↔	↔	↔	↔	III
Post 2-h insulin	M	n.s.	↓	↔	↔	↔	II
	W	n.s.	↔	↔	↔	↔	III
Glucose AUC	M	n.s.	↔	↔	↔	↑	II
	W	n.s.	↔	↔	↔	↔	
Insulin AUC	M	n.s.	↔	↔	↔	↔	II
	W	n.s.	↔	↔	↔	↔	
Total cholesterol	M	n.s.	↔	↔	↔	↔	II
	W	n.s.	↓	↔	↔	↔	III
LDL cholesterol	M	n.s.	↔	↔	↔	↔	II
	W	n.s.	↓	↔	↔	↔	III
HDL cholesterol	M	n.s.	↔	↓	↔	↓	II
	W	n.s.	↑	↔	↔	↔	III
Triglycerides	M	n.s.	↔	↔	↔	↔	II
	W	n.s.	↔	↔	↔	↔	III

M, men, W, women, AUC, area under the curve, LDL, low-density lipoprotein, HDL, high-density lipoprotein E, Endurance, S, Strength, SE, Combined, C, Control.

#### 5.4.4 Relationships between body composition and metabolic health indicators

At baseline, in men, serum fasting glucose and insulin levels correlated with BMI ( $r=0.27$ ,  $p=0.034$  and  $r=0.48$ ,  $p<0.001$ ), waist circumference ( $r=0.28$ ,  $p=0.028$  and  $r=0.51$ ,  $p<0.001$ ) and % fat ( $r=0.34$ ,  $p=0.008$  and  $r=0.38$ ,  $p=0.003$ ) (II). In men, HDL-C levels also correlated negatively with body weight ( $r=-0.39$ ,  $p=0.002$ ), BMI ( $r=-0.43$ ,  $p=0.001$ ), waist circumference ( $r=-0.40$ ,  $p=0.001$ ) and %fat ( $r=-0.37$ ,  $p=0.004$ ) at baseline. At baseline in women HDL-C ( $r=-0.29$ ,  $p=0.024$ ) and triglycerides ( $r=0.28$ ,  $p=0.025$ ) correlated with waist circumference in the total group of subjects ( $n=62$ ) (III).

During training, in the total group of trained subjects, the change in HDL-C levels correlated negatively with the change in waist circumference ( $r=-0.31$ ,  $p=0.036$ ) and the change in %fat ( $r=-0.30$ ,  $p=0.040$ ) (III). During training, in women, the individual changes in triglycerides correlated with the changes in body weight ( $r=0.35$ ,  $p=0.013$ ) and %fat ( $r=0.32$ ,  $p=0.026$ ) in the total group of trained subjects ( $n=47$ ) (III).

## 5.5 Physical performance

Supervised 21-week strength and endurance training led to training-specific improvements in physical performance. Combined strength and endurance training led to similar increases in muscle strength and aerobic performance as each training method alone. Adaptations in physical performance are presented in the following sections.

### Leg press, one-repetition maximum

The differences in the changes in leg extension between the groups were significant both in men ( $p<0.001$ ) and in women ( $p=0.001$ ) (I, III) (Figure 11). In within-group analyses, women showed significant increases in leg extension strength in S by  $9\pm 8\%$  ( $p<0.001$ ) and in SE by  $12\pm 8\%$  ( $p<0.001$ ). The corresponding increases in men were  $22\pm 8\%$  ( $p<0.001$ ) in S and  $23\pm 9\%$  ( $p<0.001$ ) in SE. Both in men ( $7\pm 5\%$ ,  $p=0.001$ ) and in women ( $3\pm 4\%$ ,  $p=0.036$ ) E showed smaller, but significant increases in leg extension, while C showed no changes.

### Isometric leg extension strength

A significant difference between the groups in the change of isometric leg extension strength ( $p=0.010$ ) was observed in men. After the 21-week training period significant increases were found in leg strength in S  $15\pm 11\%$  ( $p=0.001$ ), SE  $17\pm 15\%$  ( $p<0.001$ ) and E  $8\pm 9\%$  ( $p=0.002$ ), but not in C (II).

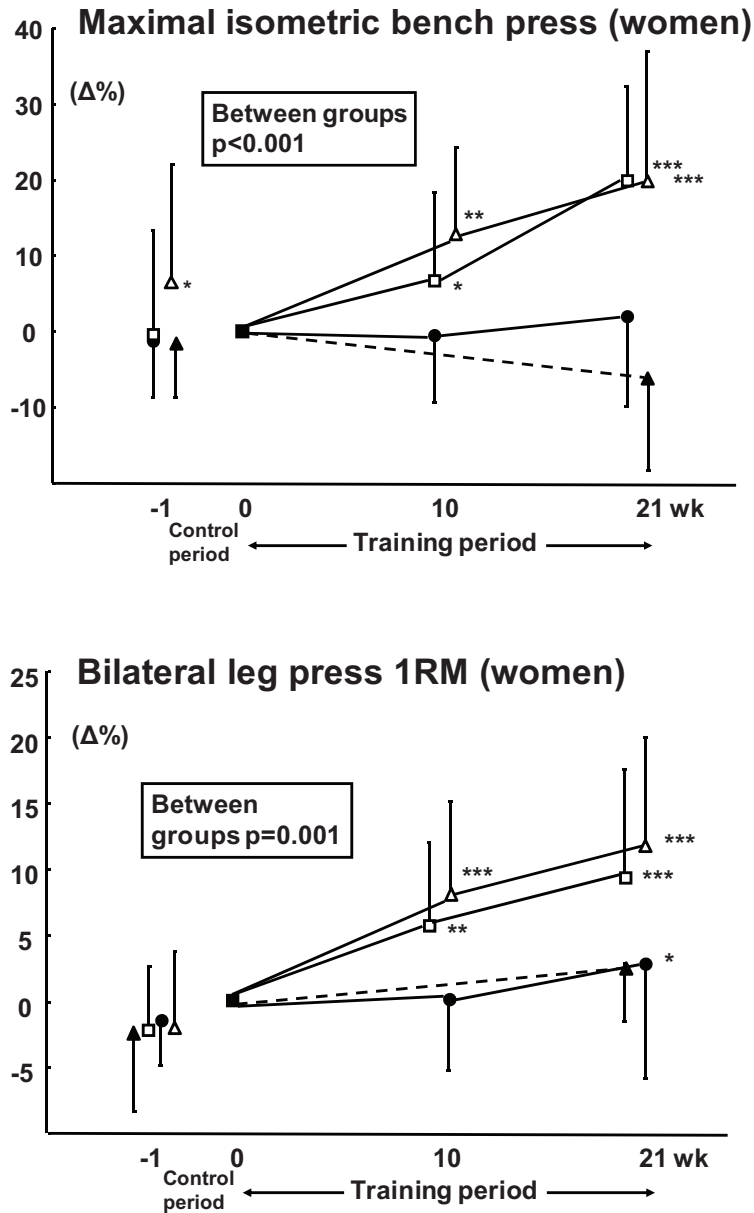


FIGURE 11 Relative changes (mean and SD) in maximal leg extension strength (1RM, one repetition maximum) and maximal isometric bench press during the 1-week control period and the 21-week training period in women (III). ● Endurance training group, □ strength training group, Δ combined training group, ▲ control group. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$  significant difference within the group from the value at week 0.

### **Isometric bench press**

The differences in the changes in isometric bench press between the groups were significant both in men ( $p=0.002$ ) and in women ( $p<0.001$ ) (I, III) (women in Figure 11). In men, isometric bench press strength increased by  $13\pm 8\%$  ( $p<0.001$ ) in S and by  $14\pm 10\%$  ( $p<0.001$ ) in SE respectively. Also E showed increases in bench press ( $6\pm 9\%$ ,  $p=0.044$ ), but the changes in C were not significant. In women, the increases in the isometric bench press ( $\sim 20\%$ ) were significant in both strength training groups ( $p<0.001$ ), but not in E or C.

#### **5.5.1 Aerobic performance**

In both men and in women, E ( $11\pm 11\%$ ,  $p=0.001$  and  $23\pm 18\%$ ,  $p<0.001$ ) and SE ( $11\pm 11\%$ ,  $p=0.002$  and  $16\pm 12\%$ ,  $p<0.001$ ) increased their  $VO_2\max$  during the training period, whereas no significant changes occurred in S or C (I, II, III) (between groups  $p=0.006$ - $<0.001$ ) (men in Figure 12).

Maximal cycling power increased significantly in all training groups in men and women, but not in the controls. The increases in power were significantly higher in E ( $14\pm 10\%$  men,  $16\pm 8\%$  women) and SE ( $13\pm 7\%$  men,  $17\pm 9\%$  women) than in S ( $7\pm 7\%$  men,  $8\pm 9\%$  women) (all  $p<0.001$ , between groups  $p<0.001$ ) (IV) (men in Figure 12).

#### **5.5.2 Relationships between metabolic health indicators and physical fitness**

At baseline, in the total group of subjects, triglycerides correlated negatively with  $VO_2\max$  ( $r=-0.35$ ,  $p=0.006$ ).  $VO_2\max$  also correlated with serum insulin 1-h and 2-h concentrations ( $r=-0.39$ ,  $p=0.002$  and  $r=-0.43$ ,  $p=0.001$ ) and 1-h glucose concentration ( $r=-0.32$ ,  $p=0.013$ ). During training, the change in HDL-C levels in the trained subjects correlated with the change in  $VO_2\max$  ( $r=0.30$ ,  $p=0.042$ ).



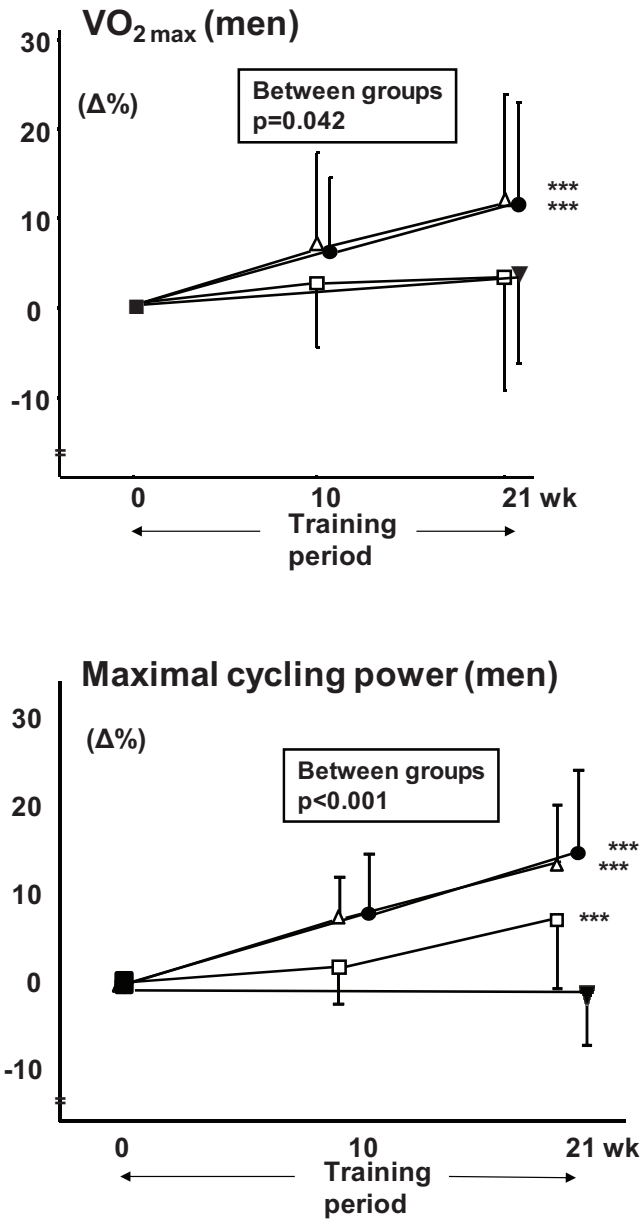


FIGURE 12 Relative changes (mean and SD) in maximal oxygen uptake (I) and maximal cycling power in men during the 21-week training period. ●= Endurance training group, □ = Strength training group, Δ= Combined strength and endurance training group and ▼= Control group. \*\*\* p<0.001, \*\* p<0.01, \* p<0.05 significant difference between groups from week 0 to week 21.

## 5.6 Nutrition intake

In women, the food intake was similar in all four groups at baseline (IV). Average energy intake (mean from weeks 0 and 21) varied between 7.0 and 7.3 MJ in all groups. In female subjects, the average food intake during training was  $47 \pm 6$  E% for carbohydrates,  $19 \pm 3$  E% for proteins and  $32 \pm 4$  E% for fat. Protein intake (g/kg) was of the same magnitude in all groups 1.2-1.3 g/kg and decreased slightly during training only in E (-7.6%,  $p=0.038$ ). There were no other changes within or between groups in food intake during training.

## 5.7 Basal hormone concentrations

Basal hormone concentrations were measured only in women (IV). There were no differences between the groups in the changes of serum T, cortisol, DHEAS or SHBG during training (Table 6). Serum T increased significantly in S (29%,  $p=0.003$ ) and SE (29%,  $p=0.011$ ) during training and serum cortisol increased significantly in all training groups (33-35%,  $p=0.002-0.027$ ). Serum DHEAS decreased significantly in C (-12.2%,  $p=0.015$ ).

There was a significant difference between groups in the changes of serum IGF-1 during training ( $p=0.028$ ). Moreover, a negative correlation between individual IGF-1 baseline levels and individual IGF-1 changes ( $r=-0.67$ ,  $p<0.001$ ) was observed in S. IGF-1 at week 0 and percent change in IGF-1 during training correlated significantly also in SE ( $r=-0.48$ ,  $p=0.023$ ). Only in S a positive correlation was found between individual IGF-1 levels at baseline and individual changes in the lean mass of the total body ( $r=0.44$ ,  $p=0.028$ ), legs (0.46,  $p=0.019$ ) and arms ( $r=0.42$ ,  $p=0.039$ ).

TABLE 6 Changes in basal hormone concentrations before and after the 21-week training period in the female subject groups.

	Group	Baseline* Mean (SD)	Post training Mean (SD)	Change (%) Mean (SD)	Between groups p-value
<b>Testosterone</b> (nmol/L)	E	1.2 (0.6)	1.4 (0.8)	17.7 (39.9)	0.28
	S	1.5 (0.8)	1.9 (1.2)	29.1 (41.9)**	
	SE	1.2 (0.5)	1.5 (0.8)	29.2 (44.6)*	
	C	1.6 (0.7)	1.6 (0.6)	6.5 (21.5)	
<b>Cortisol</b> (nmol/L)	E	375 (128)	486 (208)	32.7 (51.3)**	0.14
	S	405 (130)	500 (186)	33.1 (52.5)*	
	SE	380 (111)	483 (168)	35.0 (42.8)**	
	C	348 (47)	462 (228)	14.8 (25.5)	
<b>DHEAS</b> ( $\mu$ mol/L)	E	2.8 (1.8)	2.6 (1.6)	-4.1 (17.0)	0.32
	S	3.2 (1.5)	3.1 (1.4)	-2.7 (14.9)	
	SE	2.5 (1.2)	2.6 (1.3)	-1.7 (12.8)	
	C	2.5 (1.1)	2.4 (1.1)	-12.2 (12.1)*	
<b>SHBG</b> (nmol/L)	E	59 (21)	58 (26)	-1.9 (19.7)	0.96
	S	72 (32)	72 (36)	3.8 (40.2)	
	SE	53 (31)	51 (40.5)	-4.1 (14.1)	
	C	62 (22)	61 (17)	6.0 (19.3)	
<b>IGF-1</b> (ng/mL)	E	150 (36)	144 (38)	-3.7 (12.6)	0.028
	S	152 (62)	145 (50)	-1.2 (14.0)	
	SE	150 (36)	155 (39)	7.6 (15.6)	
	C	149 (29)	146 (38)	-7.1 (8.8)	

SD, standard deviation. M, men, W, women, E, Endurance, S, Strength, SE, Combined, C, Control. \*Baseline values are means of week -1 and 0. DHEAS, dehydroepiandrosteronesulfate, SHBG, sex hormone-binding globulin, IGF-1, insulin-like growth-factor I.

## 5.8 Health-related quality of life

The eight dimensions of HRQoL at week 0 for three training groups and controls are shown in Figure 12. A significant difference was observed between the groups ( $p=0.038$ ) in the changes of vitality dimension of HRQoL, characterized by a  $7\pm 2\%$  increase in the combined group ( $p<0.001$ ) and no change in other training groups or controls (Figure 14) (IV). Moreover, the dimensions of general ( $5\pm 2\%$ ,  $p<0.05$ ) and mental health ( $4\pm 1\%$ ,  $p<0.01$ ) improved significantly in SE during training. Also, in E, the dimensions of general health ( $4\pm 2\%$ ), bodily pain ( $5\pm 2\%$ ), and role physical ( $6\pm 2\%$ ) improved significantly during training (all  $p<0.05$ ). In S bodily pain dimension deteriorated ( $-5\pm 2\%$ ,  $p=0.005$ ).

At baseline, summary scores were on average  $349 \pm 36$  for physical component and  $330 \pm 37$  for mental component. Physical component summary scores improved only in E ( $5 \pm 10\%$ ,  $p=0.002$ ), and mental component summary scores only in S ( $6 \pm 17\%$ ,  $p=0.032$ ) during training. Moreover, changes in physical component summary and  $VO_{2max}$  correlated significantly in E ( $r=0.41$ ,  $p=0.016$ ).

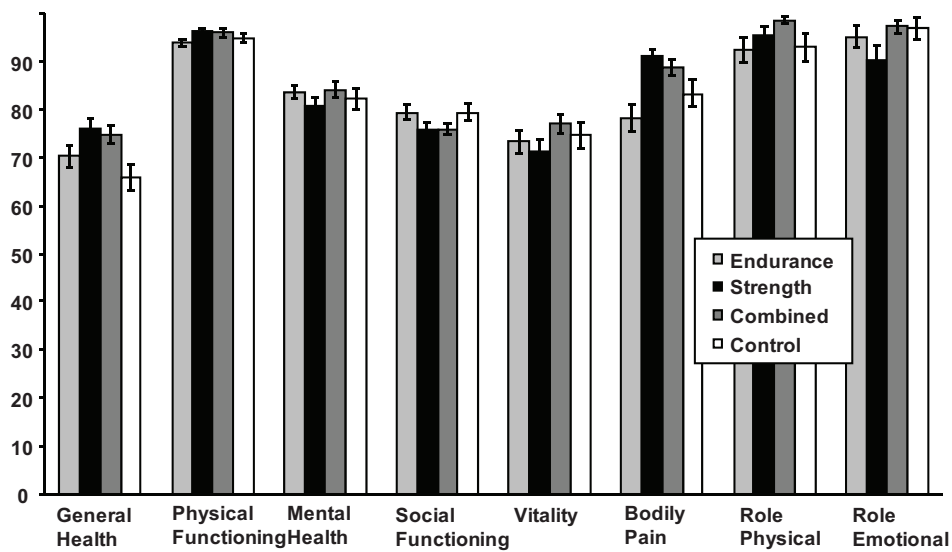


FIGURE 13 Baseline scores of RAND-36 dimensions in the subject groups (mean and SE).

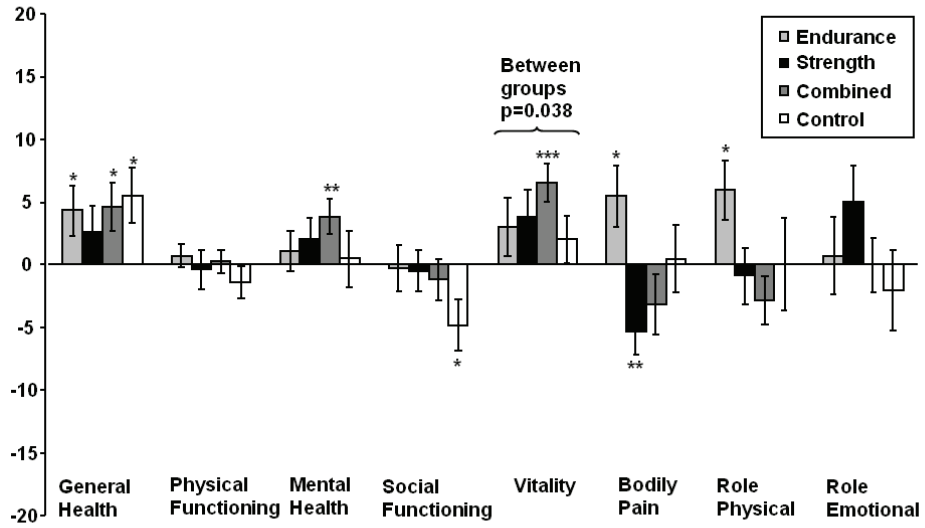


FIGURE 14 Changes in RAND-36 subscales during training in the subject groups (mean and SE). Significant difference within group during the 21-week follow-up \*p<0.05, \*\*p<0.01, \*\*\*p<0.001.

## 6 DISCUSSION

### 6.1 Changes in body fat and fat distribution during training

Aging is associated with reduced lean body mass and accumulation of fat into the visceral depot (Kuk et al. 2009), which predicts cardiovascular risk and risk for type 2 diabetes, also in lean subjects (Goodpaster et al. 2005; Rexrode et al. 1998; Shen et al. 2006). Due to the age-related changes in body composition and function the metabolic syndrome, deteriorating glucose tolerance, type 2 diabetes and cardiovascular disease become increasingly common during middle-age. Regular exercise training may ameliorate body composition by decreasing total and abdominal fat (mainly endurance training) and increasing lean mass (mainly strength training). Therefore, exercise training interventions are of high interest also in healthy normal and slightly overweight middle-aged and older adults.

We observed that both combined training and endurance and strength training alone caused changes in body composition during the 21-week intervention period. Both endurance and strength training were effective in decreasing the %fat in men as measured by DXA. In women, total body fat decreased only in the endurance trained groups. Decreases in body fat by 5-8% were related to concomitant increases in lean body mass. Thus, body weight decreased slightly only in the endurance trained groups in men (-1.5kg) and in women (-1.0kg). The present findings are in line with previous training studies showing that endurance training has resulted in decreases in body fat and in increases in training-induced energy consumption. In contrast, high-intensity strength training mainly results both in decreases in body fat and at same time in increases in lean body mass with little or no change in body weight (Cauza et al. 2005; Dunstan et al. 2002; Hunter et al. 2000; Treuth et al. 1994; Treuth et al. 1995). There are fewer studies that have investigated the effects of combined training on body composition. Similarly to our study Ghahramanloo et al. (2009) observed significant decreases in body fat and concurrent increases in lean body mass in their combined training group. The favorable changes in body composi-

tion in S and SE may be of high value, thus increases in lean body mass also increases resting metabolic rate and, therefore, prevents weight gain during aging. Moreover, from health risk perspective, skeletal muscle is also the primary target organ for glucose and triglyceride disposal.

It is complicated to objectively estimate changes in body composition during intervention studies, at least, if the intervention does not include weight loss. Very few analyzing methods can measure small changes that typically occur during a training intervention of a couple of months. Moreover, the methods are not directly comparable with each other. In this study, at baseline, percent body fat values measured by BIA were systematically lower than those measured by DXA, on average 6.4%, although a high correlation existed between these methods ( $r=0.90$ ). A similar systematic difference in %fat analysis has been reported earlier between DXA and bioimpedance (Bolanowski and Nilsson 2001). In contrast, %fat estimated by skin fold thicknesses were of the same magnitude than those measured with DXA, and the correlation between DXA and skin fold thicknesses was also high ( $r=0.80$ ).

During the training period, the decrease in percent body fat as measured by skin folds and BIA was of a similar magnitude as that measured by DXA. However, the correlations of the change in percent body fat measured by skin folds and BIA with that measured by DXA were weaker than the cross-sectional correlations. We conclude that the use of especially BIA to assess changes in body composition with training requires further study and should be used with caution. It has to be noted also that it is very difficult to generalize results concerning DXA and BIA, because results can differ depending on the software, hardware and company.

Body weight and the high amount of total body fat are important health risks at the population level. Many studies, however, have reported that central obesity and especially visceral adipose tissue has an even stronger connection to the development of dyslipidemia, hypertension, insulin resistance and cardiovascular diseases (Hurley and Roth 2000; Shen et al. 2006).

In this study the decreases in body fat were evident also in the abdominal area in all training groups in men and in endurance trained groups in women. As measured by waist circumference decreases were on average from 2 to 3 cm in both men and women. The changes in waist circumference were also in line with the changes in trunk fat as measured by DXA. Neither waist circumference nor trunk fat measured by DXA can distinguish visceral and subcutaneous fat in the abdominal area. It has been shown, however, that these measures correlate well with disease risk also in lean subjects (Goodpaster et al. 2005; Rexrode et al. 1998; Shen et al. 2006).

Interestingly, the correlation of waist circumference, which is a crude index of body fat distribution, with the %fat measured by DXA at baseline was quite high ( $r=0.84$ ), as was the correlation between their respective changes with training ( $r=0.74$ ). Based on the present study observations, skin fold thicknesses, and waist circumference are more sensitive methods than eight-polar



BIA and body weight to evaluate training-induced changes in body composition when DXA was used as the reference method.

Although some previous studies suggest that training volume affects changes abdominal fat (Slentz et al. 2005; Slentz et al. 2009), we did not observe differences between double volume combined training compared to endurance or strength training alone. There are, however, several limitations in studies that have tried to establish whether reduction of visceral fat by aerobic exercise has a dose-response relationship. The most important limiting factors are related to the amount of energy consumption of exercise; in most studies definitions are unclear. Moreover, the influence of several confounding factors, such as metabolic-related disorders, gender, and duration of the intervention remains unclear (Ohkawara et al. 2007). It is also very difficult to compare the volume of the strength training to endurance training, and thus, these training modalities are totally different in nature.

In women, the decreases in abdominal fat seems to be more related to aerobic training, which is supported by a large number of training studies in different populations (Giannopoulou et al. 2005; Irwin et al. 2003; Lee et al. 2005). Some previous studies suggest that visceral fat is used more quickly as an energy resource than subcutaneous fat during aerobic exercise induced weight loss (Numao et al. 2006). In this study, the greatest losses in abdominal fat were found in E, which also showed concurrent decreases in body weight in women. This finding is also in line with a previous review showing that the change in body weight is related to changes in visceral fat, especially in people without metabolic disorders (Ohkawara et al. 2007). A decrease in visceral fat may, however, occur even without a corresponding decrease in body weight. Typical gender differences also occur between men and women. Although women generally store more fat relative to body weight than men, different fat distribution may also affect on training response. It is possible that men are more prone to lose visceral fat because men tend to have more abdominal obesity (Ohkawara et al. 2007). Moreover, initial values of total and visceral fat could contribute to the amount of fat lost during an intervention and in this thesis our male subjects tended to be more overweight.

In addition to metabolic consequences, age-related changes in body composition may affect physical and functional performance. Progressive reduction in skeletal muscle mass and strength, i.e., sarcopenia, contributes to impaired functional performance that is also associated with increased risk of frailty, falls and fractures. The mechanisms behind sarcopenia and decreased neuromuscular performance include deficient production of androgens, growth hormone and IGF-1, reduced physical activity, inadequate nutrition (i.e. protein or energy intake), upregulation of catabolic cytokines, and loss of  $\alpha$ -motoneurons in the spinal cord (Kraemer et al. 1998). Reductions in lean body mass and physical performance can be minimized by regular physical training. Especially periodized heavy resistance strength training has been shown to lead to increases in muscle mass and strength both in older men and women (Frontera et al. 1988;

Häkkinen et al. 1998a; Häkkinen et al. 2002; Häkkinen et al. 2001; Kraemer et al. 2004; Nindl et al. 2000).

In this study, DXA was used as the reference method. DXA also proved to be the most powerful method for detecting changes in body composition among the groups. DXA is considered to be a valid technique for fat and muscle tissue assessment, and also the most sensitive method for assessing small changes in body composition (Houtkooper et al. 2000).

The 21-week high intensity endurance, strength, and combined training periods did not result in differences between groups in the changes of serum basal T, DHEAS, SHBG and cortisol in women. However, the changes in serum IGF-1 differed significantly between groups, characterized mainly by an increase of 7.6% in SE ( $p=0.097$ ) and a decrease of 7.1% ( $p=0.074$ ) in the control group. Typically, during the aging process serum anabolic hormones such as T, estrogen, DHEAS and growth hormone decline (Lamberts et al. 1997). A single strength training session can acutely stimulate an increase in these anabolic hormones (Häkkinen and Pakarinen 1993; Häkkinen et al. 1998c; Häkkinen et al. 2001b; Kraemer et al. 1991; Schwab et al. 1993), but long term changes in basal hormone levels following strength or endurance training have been variable (Consitt et al. 2002; Izquierdo et al. 2006; Kraemer and Ratamess 2005; Vale et al. 2009).

Decreased IGF-1 in C can occur due to negative energy balance (Nemet et al. 2004; Smith et al. 1995). A decline in IGF-1 has also been observed with increased physical activity while maintaining energy balance (Rarick et al. 2007). However, most other studies have found no effect of either strength training (Ibañez et al. 2008; Izquierdo et al. 2006; Starkweather 2007) or endurance training (Vale et al. 2009; Vitiello et al. 1997) on basal IGF-1 concentrations. Instead, one previous study showed that IGF-1 has a moderate association with physical activity-induced increases in FFM accretion in young, healthy women (Nindl et al. 2010). The association with increased FFM and circulating bioavailable IGF was even greater than that observed for total IGF-1 (Nindl et al. 2010).

A couple of previous combined training studies have suggested that reduced gains in muscle strength and mass reported during high-intensity combined training may be related to an elevated catabolic state, as indicated by higher concentrations of cortisol and no change in anabolic hormones such as T and growth hormone (Kraemer et al. 1995, Bell 2000). In this thesis we did not observe any differences between the combined female group, and the other training groups, in term of increased catabolic state, due to very high individual variation in serum cortisol. However, a small but significant increase in serum T was observed both in S and SE suggest that high-intensity strength training alone and combined with endurance training may stimulate an increase in serum basal T in 39-65 year-old women.

## 6.2 Training effects on metabolic health indicators

Combined endurance and strength training seems to be especially effective in improving body composition and cardiorespiratory and neuromuscular fitness in middle-aged and older men and women. However, based on the results of this study, combined training did not produce complementary benefits on metabolic health indicators over endurance or strength training only. In addition to abdominal obesity, training effects on serum lipids and lipoproteins, blood pressure, and glucose and insulin metabolism were also investigated.

### **Blood glucose and insulin**

Aging is often accompanied by a reduction in lean body mass and an increase in fat mass, especially in the visceral depot (Pascot et al. 1999), worsening insulin resistance and glucose tolerance, dyslipidemia, and hypertension. In women these changes occur particularly rapidly after menopause (Kotani et al. 1994), and increase the risk for type 2 diabetes and cardiovascular disease (Shen et al. 2006). Most middle-aged adults are glucose tolerant and do not have the metabolic syndrome. However, over this age range the metabolic syndrome, deteriorating glucose tolerance, and cardiovascular disease become increasingly common. Knowledge of the impact of strength and endurance training on metabolic risk factors in adults with relatively few risk factors is, therefore, important from the perspective of public health and prevention of the metabolic syndrome and its consequences (Lakka and Laaksonen 2007).

Physical training is a cornerstone in the prevention of the metabolic syndrome and type 2 diabetes (Laaksonen et al. 2005; Lakka and Laaksonen 2007). However, the optimal type and intensity of physical exercise that should be used to maximize health benefits of exercise in decreasing metabolic risk factors is unclear (Johnson et al. 2007; Lakka and Laaksonen 2007). To our knowledge, this is the first study comparing strength and endurance training alone and together on body composition, physical fitness, and metabolic health in middle-aged and older generally healthy, non-obese adults. The main findings of this study were that both high intensity endurance and heavy resistance strength training can cause minor, but statistically significant improvements in glucose and insulin metabolism even in relatively lean older men and women with normal glucose tolerance. A combination of strength and endurance training did not produce complementary benefits over strength or endurance training only. However, a combination of these two training methods was effective in improving both aerobic and neuromuscular performance and body composition, which may be of benefit in preventing the adverse changes in body composition and metabolic risk factors that occur with aging.

The long-term adaptive responses to endurance and resistance training are divergent in nature. Endurance training improves insulin sensitivity and glucose uptake, especially in people with insulin resistance (Anderssen et al. 2007; Boule et al. 2001; Kahn et al. 1990; Kirwan et al. 1993; Lakka and Laaksonen

2007; Rockl et al. 2008). Enhanced glucose homeostasis is likely related to the reductions in body fat and to exercise-induced improvements in muscle oxidative capacity, decreases in muscle lipid content, and increases in whole-body rates of fat oxidation and turnover (Bruce and Hawley 2004). The mechanisms behind these improvements are most likely related to activation of AMP-activated protein kinase, upregulation of glucose transporter 4 and glycogen synthase, changes in muscle fibre type, and increased muscle capillarisation (Hawley and Lessard 2008; Rockl et al. 2008).

We observed that both in men (-17%) and women (-12%) high-intensity endurance training by cycling led to improvements in serum fasting insulin levels, but the decrease was statistically significant only in men ( $p=0.013$ ). There was also a borderline significant change ( $p=0.054$ ) in men in fasting insulin levels between the groups during the training period. Moreover, in endurance trained men, insulin responses during the OGTT decreased by 16% ( $p=0.027$ ) in the 2-hour sample. However, due to very high individual variation in the changes of insulin, the statistical differences between and within groups were very difficult to detect. Glucose and insulin levels were related to fat% and waist circumference at baseline, which is supported by a large number of cross-sectional studies and which emphasizes the importance of concomitant training-induced changes in body composition in the prevention and treatment of metabolic risk factors.

Strength training may offer additional or complementary benefits over endurance training alone (Praet and van Loon 2007). Age-related loss of muscle mass is associated with a decline in muscle strength and a reduction in blood glucose disposal capacity (Park et al. 2006), which may increase metabolic risk (Dela and Kjaer 2006). Regular strength training can minimize this age-related loss of muscle mass and function by promoting substantial gains in skeletal muscle mass, and thereby improving also whole body glucose disposal capacity (Fenicchia et al. 2004). In addition to increases muscle mass, strength training may also enhance insulin signaling (Braith and Stewart 2006; Holten et al. 2004). In the present studies, there were no differences between the groups in glucose metabolism during the training period in men or in women. This may be expected, because our subjects were healthy non-obese middle-aged and older adults without diabetes or pronounced features of the metabolic syndrome. However, in the male strength training group fasting glucose decreased significantly by -2.8% during the training period. This small improvement may be explained by substantial gains in lean mass of the legs and arms during training. Previous studies in type 2 diabetic individuals have shown that strength training can improve glycemic control both acutely (Fenicchia et al. 2004) and in the long term (Castaneda et al. 2002), and that high-intensity strength training for 16 weeks seems to be especially effective (Castaneda et al. 2002; Dunstan et al. 2002). Findings in non-diabetic individuals have, however, been inconsistent (Fenicchia et al. 2004).

In this study, combined training with higher training volume and frequency (2 times endurance and 2 times strength) did not produce synergistic

benefits over 2 times a week endurance or strength training alone, even though total workload and energy output were much higher during the present combined training than E or S only. Due to different mechanisms, combined endurance and strength training could be expected to have synergistic benefits compared with either method alone. A recent study found that in type 2 diabetic patients both aerobic and resistance training led to improvements in glycemic control and that the effects of combined training were greater than either method alone, especially among patients with poor glycemic control at baseline (Sigal et al. 2007).

Overall, in these studies the effects of strength and endurance training on metabolic risk factors were modest, probably because the men and women in these studies were non-obese with relatively few features of the metabolic syndrome. In previous studies, the impact of endurance and strength training has generally been greater in those with more pronounced risk factors at baseline (Cornelissen and Fagard 2005a; Laaksonen et al. 2000; Lakka and Laaksonen 2007). Even in overweight individuals with impaired glucose tolerance, indirect evidence suggests that increased physical activity may be more effective at preventing worsening of impaired glucose tolerance rather than improving it (Laaksonen et al. 2007). With longer training periods, changes in body composition may be greater, which could more favorably affect glucose and insulin metabolism. Nonetheless, the large improvements in cardiorespiratory fitness and muscle strength and more modest improvement in body composition obtained by endurance and combined training in this study may be of importance in preventing the development of the metabolic syndrome and its consequences, especially type 2 diabetes and cardiovascular disease (Jurca et al. 2005; Laaksonen et al. 2002; Lakka and Laaksonen 2007).

### **Blood lipids and lipoproteins**

In women after 21 weeks of training, only E showed decreases in TC and LDL-C and increases in HDL-C. Concurrently only E showed decreases in body weight after training. Improvements in blood lipid profile due to physical training may be dependent on concomitant loss of total and abdominal fat (Leon and Sanchez 2001). Also in this study, higher body weight and higher amount of total and abdominal fat were associated with higher blood triglyceride levels and lower HDL-C levels at baseline. In the total group of subjects in women, individual changes in triglycerides were also weakly, but significantly related to changes in weight ( $r=0.35$ ) and fat% ( $r=0.32$ ), and in men changes in HDL-C were related to changes in waist circumference ( $r=-0.31$ ) and fat% ( $r=-0.31$ ).

As might be expected, the training-induced changes in serum lipids and lipoproteins were slight in these non-obese and quite healthy men and women. These minor improvements in blood lipids and lipoproteins were related to aerobic training. Interestingly, significant decreases in total cholesterol and LDL-C, and increases in HDL-C that were observed in the endurance trained men after 10 weeks of training and in the endurance trained women after 21 weeks of training were not evident in the combined training groups (II).



Although the results regarding the training effects have been inconsistent mostly aerobic training has been shown to produce improvements in serum lipid and lipoproteins, mainly increases in HDL-C and secondary decreases in TC, TG and LDL-C (Tambalis et al. 2009). In contrast, the effects of strength and combined training studies are very difficult to review due to differences between exercise programs and study designs (Tambalis et al. 2009). Some studies, however, suggest that resistance training may improve dyslipidemia, at least in early postmenopausal women (Asikainen et al. 2004).

The changes in serum lipids may also be dependent on to the improvements in physical fitness. In line with these observations, the results of this thesis showed that the minor improvements in blood lipids and lipoproteins were related to changes in  $VO_2\max$ . In addition to aerobic component and concomitant body compositions changes, training intensity may also be the factor that explains the conflicting changes in blood lipid and lipoprotein changes after exercise interventions. According to a recent meta-analysis favorable alterations seem to be especially related to high-intensity aerobic training ( $VO_2\max > 60\%$  or heart rate reserve  $> 60\%$  or maximal heart rate  $> 60\%$ ) (Tambalis et al. 2009).

Combined training did not produce synergistic benefits in serum lipids and lipoproteins over endurance training only despite the larger training volume (four vs. two training sessions per week). Previous results regarding the influences of training volume have also been inconsistent, especially in women (Durstine et al. 2001). Durstine et al. (2001) concluded in their review that regular aerobic exercise can increase HDL-C and decrease triglyceride level, but there seems to be a threshold at training volumes of 24 to 32 km per week of brisk walking or jogging which elicit  $\geq 1200$  kcal/wk increase in energy expenditure before noticeable differences in serum lipids occur.

Minor positive changes in the endurance trained groups, lack of changes in combined training groups, and decreases in HDL-C both in S and C in men after the 21-week training period can be explained by several other factors than physical training. Age, genetics, sex, training background, diet, and seasonal variations may have influenced the results. Baseline cholesterol levels were on average at the normal level in our healthy subjects. More favorable changes in response to training usually occur in those with more pronounced dyslipidemia at baseline (Laaksonen et al. 2000), which in part explains the minor changes in blood lipids and lipoproteins in our subjects.

The seasonal effects that may have affected to these results could include changes in physiological functions due to changes in light and temperature or due to qualitative changes in diet, for example, in the amount of saturated fat and dietary cholesterol. Moreover, leisure-time physical activity or the amount of inactive periods may vary between the winter and summer time. However, these several confounding factors are unlikely to differ between the groups, and also diet and the amount of leisure-time physical activity were controlled by diaries. No changes were observed in the amount of leisure-time physical activity. Moreover, there were no differences among groups in the changes of energy substances or in total energy intake before and after training in women (IV).

### **Blood Pressure**

One of the major risk factor for metabolic syndrome, type 2 diabetes and cardiovascular diseases is hypertension. Hypertension is a multifactorial disease, which is influenced by age and several lifestyle and genetic factors. One of the lifestyle factors related to hypertension is physical inactivity. Physical training has been recommended as a treatment especially for prehypertensive subjects (i.e. SBP 120-139 mmHg or DBP 80-89 mmHg) (Chobanian et al. 2003).

In this thesis, reductions in BP were quite high in E (-6/-4 mmHg) and in S (-9/-5 mmHg) in men with blood pressure on average high normal (SBP 120-139 mmHg and DBP 80-89 mmHg). However, no changes occurred in SBP or DBP in our lean 40-65 year-old women with normal BP at baseline (mean SBP 119-127 mmHg, mean DBP 71-77 mmHg in intervention groups) after 21 weeks of endurance and/or strength training. In meta-analyses, both endurance and resistance training have been shown to produce on average 2-3 mmHg decreases in SBP and DBP (Cornelissen and Fagard 2005b; Kelley and Kelley 2000; Kelley et al. 2001). Training-induced decreases have been more pronounced in hypertensive subjects and also concomitant decreases in body weight have been shown to intensify decreases in BP (Cornelissen and Fagard 2005b). Interestingly, combined endurance and strength training did not produce improvements in BP. The DBP transiently decreased after 10 weeks, but returned to baseline level after 21 weeks. We may hypothesize that prolonged high intensity training 4 times per week was too stressful for some of the older previously untrained individuals.

### **6.3 Changes in aerobic performance and muscle strength and mass during training**

The present 21 weeks of endurance and strength training led to large training specific improvements aerobic performance and muscle strength. In line with previous studies (Ferketich et al. 1998; Hagberg et al. 1989; Häkkinen et al. 2003; Izquierdo et al. 2004), 21 weeks of high-intensity endurance and combined endurance and strength training improved  $\text{VO}_2\text{max}$  by 11% both in E and SE in men and by 23% and 16% in E and SE in women, respectively. Increases in aerobic performance were also seen in maximal power output during cycling test. In women, the increases were 16% in E and 17% in SE. Moreover, also S increased cycling power (8%), but the increase was smaller than in the endurance trained groups. Also, other studies have observed that high-intensity strength training may also enhance aerobic work capacity (Izquierdo et al. 2005), even though strength training usually does not improve  $\text{VO}_2\text{max}$ .

Two times per week strength training resulted in large increases in dynamic and isometric muscle strength in lower extremities as well as to significant improvements in upper body isometric strength both in men and in women. In men, two times per week total body strength training for 21 weeks with



progressive training loads resulted in 22% increases in leg press (I), 13% increases in isometric leg extension (II) and 13% increases in isometric bench press (I). In women, the corresponding increases in S were 9% in leg press (III), 7% in isometric leg extension (IV) and 20% in bench press (III). These results are in line with previous studies investigating effects of high-intensity periodized strength training two times per week in middle-aged and older individuals (Häkkinen and Pakarinen 1993; Häkkinen et al. 2001a; Häkkinen et al. 2002; Sallinen et al. 2006; Sallinen et al. 2007).

In the present study, training effects were investigated in middle-aged and older men and women who were rather active, but did not have background in systematic physical training prior the study. Two times per week endurance training plus two times per week strength training with progressively increasing training volume and intensity and individually regulated training loads were used. Four times per week training did not interfere with development of maximal strength. Combined training may diminish training-specific improvements in muscle strength and mass or  $\text{VO}_2\text{max}$  (Dolezal and Potteiger 1998; Hickson. 1980; Kraemer et al. 1995; Putman et al. 2004). This effect, referred as the interference effect, holds true when the training intensity or volume is too high for subjects' individual capacities. Our results are in line with previous combined training studies performed in older adults (Ferketich et al. 1998; Haykowsky et al. 2005; Izquierdo et al. 2004; Izquierdo et al. 2005; Wood et al. 2001). However, these studies have used lower training volumes i.e. training 2-3 times per week. Only a few studies (Häkkinen et al. 2003, Hunter et al. 1987) have used four times per week training. Hunter et al. (1987) observed interference in strength development in the combined training group. This interference was, however, found only in previously untrained subjects and the other combined group with a background in aerobic training did not show any interference. Häkkinen et al. (2003) did not find interference in strength development, but an interference effect was observed in explosive strength development, mediated in part by the limitations of rapid voluntary neural activation of the trained muscles, was observed. However, the subjects were younger than our subjects, with a mean age of less than forty years.

We did not observe statistically significant differences between the groups in the changes of lean mass during the intervention period. Both in men and in women combined training was effective in increasing total body lean mass. In women, also endurance training resulted in increases in total body lean mass, in spite of slightly negative energy balance.

Muscle thickness measured by US increased in all training groups both in upper and lower extremities. DXA measured lean mass of the legs and arms, however, increased only in the strength training group during training, which may indicate possible interference during longer training periods (>21 weeks) or higher training volumes. A couple of studies have also reported that combining endurance training to strength training may inhibit gains in muscle mass, at least when the amount of training is as high as 6-8 sessions per week (Kraemer et al. 1995; Putman et al. 2004). However, combined training studies performed

in middle-aged and older subjects have used a lower amount of training session per week. According to our knowledge our study is the first which investigated effects of 2+2 times per combined training in older adults.

Interestingly, in women, the results were slightly different. In addition to strength training, also endurance training performed by cycling was effective in increasing lean mass of the legs from 1.9 to 3.5% in all training groups. We hypothesize that gender differences in muscle mass development shown by DXA resulted from lower baseline strength levels in women. Therefore, two times per high-intensity bicycle training was a sufficient stimulus for muscle hypertrophy in the legs in women. In general, training load is significantly lower in bicycle training than in strength training, but the high amount of repetitions and high intensity of cycling with rather high loads has been shown to cause some hypertrophy in knee extensors (McCarthy et al. 2002). Izquierdo et al. (2005) have also reported increases of a similar magnitude in quadriceps femoris CSA caused by endurance, strength or combined training in middle-aged men, when high-load cycling was used for endurance training. However, typical aerobic training such as walking or jogging, which is recommended to improve metabolic health in elderly subjects, does not lead to muscle hypertrophy in the legs (Sipilä and Suominen 1995), although it may improve muscle strength (Gergley 2009).

In this study, training effects on muscle growth at the total body level were evaluated with DXA (lean mass) and at the regional level with DXA and US (muscle thickness). These methods differ significantly, because thigh or arm fat free mass measured by DXA includes skin, as well as the fat free components of adipose tissue (Levine et al. 2000), and with US we measured only muscle thickness at a specific site of the muscle. Skeletal muscle mass measured by DXA in extremities correlate well with CT measured muscle mass, although, DXA systematically overestimates muscle mass (Levine et al. 2000). Compared with gold standard methods in muscle mass analyses, MRI and CT, the advantages of DXA are lower costs and low radiation exposure. Low-cost ultrasound measurements are easily attainable, but measurements can include quite large measurement error, which can be diminished with practice, carefully performed measurements, and high-quality equipment (Miyatani et al. 2002). In this study, intraclass correlation coefficient for US between the baseline and control measurements was 0.95 for TB and 0.92 for VL+VI (I).

The changes in total body lean mass measured by DXA differed significantly between groups in men ( $p=0.040$ ), with a significant increase in SE (1.6%) and a nonsignificant but larger increase in S (1.8%), and no changes in other groups. In contrast in women, there were no differences between groups, but significant increases in lean mass were observed in the endurance (2.0%) and combined training groups (1.8%). The magnitude of the increases in total body lean mass was similar to changes observed in previous studies in younger adults after 24 weeks of strength and endurance training five times per week (Nindl et al. 2000).

## 6.4 Training effects on health-related quality of life

This thesis investigated the effects of 21 weeks of endurance, strength or combined training in healthy 39-77 yr-old subjects, which represented on average higher HRQoL values than the average Finnish population at the baseline level (Aalto et al. 1999). The results showed that intensive endurance training alone or combined with high-intensity strength training increases the sense of energy and well-being even in healthy volunteers. This may indicate that aerobic training is more effective in improving HRQoL in older adults than strength training.

The benefits of regular physical exercise on health are well accepted, but the relationships between exercise type and dose and HRQoL have not been adequately described (Bize et al. 2007). Chronically diseased individuals tend to increase their HRQoL with increased physical training or leisure time physical activity (Rejeski et al. 1996). These results, however, cannot be generalized to healthy populations, because diseased people typically represent a group with poorer physical fitness, individual HRQoL profiles and specific challenges and needs (Bize et al. 2007). In contrast, in healthy adults HRQoL scores tend to cluster in the highest categories and, therefore, the effects of physical activity are more difficult to detect than, for example, in depressed adults.

Much research has been conducted to evaluate the effects of physical activity and fitness on HRQoL. However, most of these studies have used cross-sectional designs (Bize et al. 2007; Lavie and Milani 2000; Rejeski et al. 2006; Sloan et al. 2009). Those studies that have examined the effects of exercise training on HRQoL in a pre- to post-treatment design have used different patient groups as subjects.

Some intervention studies have found improvements in HRQoL after 10 weeks to 1 year of progressive strength training in depressed older adults, and in older community-dwelling adults (Inaba et al. 2008; Singh et al. 1997). In contrast, other studies have not found improvements after 9 months of resistance training or after 8-weeks resistance training utilizing elastic bands in community-dwelling older women (Damush and Damush 1999; de Vreede et al. 2007). Conflicting results related to effects of strength training are possibly explained by the differences in subjects at baseline, study designs, training protocols, and the measurements used in the studies.

In this thesis, combined endurance and strength training especially improved the vitality dimension of the HRQoL over endurance or strength training only. Increased vitality means an increased sense of energy and mental agility, whereas low vitality means persistent tiredness (Aalto et al. 1999). There are a few training studies investigating the effects of certain modes and doses of physical training on HRQoL. Partonen et al. (1998) found that in middle-aged Finnish adults, strenuous aerobic training 2-3 times per week improved the vitality dimension of HRQoL in the training group compared to the control group (13.7 versus 1.3 units). In comparison to that study, the present results showed a smaller increase (6.6) in vitality dimension in the combined group and no

change in E, which trained endurance two times per week. Aurilio (2000) also found a 6.0 increase in vitality scores after 8 weeks of training in middle-aged subjects who performed at least 80% of the requested (72 min or 3 miles) weekly physical activity. In cohort studies, increased leisure-time physical activity has also been associated with increased scores of vitality (Tessier et al. 2007). These results suggest that vitality may be the most sensitive dimension of HRQoL for physical training.

In S, the bodily pain dimension decreased significantly during training, which indicates more perception of bodily pain. These results may be related to strength training-induced muscle soreness, which can last up to 5-7 days after a single high-intensity strength training session in the beginning of an intensive strength training period in previously untrained subjects. Later on, muscle soreness usually becomes milder or disappears, depending on the training protocol used. Interestingly, according to the present results, increased perception of pain related to the first weeks of high-intensity strength training in previously untrained subjects can be prevented by concomitant endurance training. This is especially important among aging people, because strength training is important to counteract the negative effects of aging on muscle strength and mass, functional capacity and independence.

## 6.5 Methodological strengths and limitations

The strengths of the present study included a randomized, controlled pre- and post-treatment design with a long supervised training period, good compliance, and carefully controlled and repeated measurements of body composition, metabolic health factors, aerobic performance, and muscle strength. Control measurements were performed before the baseline measurements to minimize the possible learning effects on physical fitness measurements and to evaluate physiological reproducibility and reliability of several laboratory measurements, body composition analyzing methods, and fitness tests.

The main outcome variables in physical fitness, muscle strength and aerobic performance were measured by using the best measurement techniques available: 1RM testing and  $\text{VO}_2\text{max}$ .  $\text{VO}_2\text{max}$  was measured breath by breath continuously during incremental cycling test until voluntary exhaustion.

Body composition in this study was analyzed by using multiple techniques (DXA, ultrasound, bioimpedance, skin folds, and circumferences). Other methods were compared with DXA, which has been considered a gold standard method for body composition analysis (van der Ploeg et al. 2003). Standardized practices were followed to avoid confounding effects of hydration status, acute exercise, or medications. Moreover, we tried to minimize the measurement error in skin fold and US measurements by marking the anatomical measurement places with tattoo points during the control measurements.

The amount and intensity of training during the 21-week training period were carefully defined and completely supervised by M.Sc. students in the De-

partment of Biology of Physical Activity. Missed training sessions were made up during subsequent training weeks, so that the total required amount of training sessions were reached. Subjects were advised to continue their habitual physical activities as before and the amount of these activities was also monitored regularly by physical activity forms.

The same instructions, time of day, investigator, measurement technique and calibrated measurement equipment were always used to study changes in all the outcome variables of body composition, physical fitness, metabolic health factors, and nutrition etc. Also, the data analysis of different variables was performed by the same investigator, equipment and technique pre- and post-training.

Our design was planned to investigate the possible interference effects in physical performance and muscle mass developments, as well as to detect whether the added strength training produces health benefits over endurance training only. Due to the research questions, the training volume in our combined group was double compared to endurance or strength training only. This of course limits the conclusions, which can be drawn about the effects of training mode per se, for example, on body composition and metabolic health markers. Moreover, in some papers (I, II, III) the amount of subjects was limited, because it was not possible to do all measurements to all subjects due to financial limitations. This may have limited the statistical power in group comparisons and possible correlations, especially in those variables in which individual variations are naturally high (such as blood insulin).

A longer intervention may have produced greater changes in body composition, which could be reflected in more marked improvements in metabolic risk factors. A longer training study would be less feasible economically, however, and more prone to drop-outs and decreased compliance with training.

The subjects were selected by using convenience sampling (i.e. sampling of volunteers). This may have increased the probability of those individuals who feel strongly about the issue in question to become recruited to the study (Sousa et al. 2004). Moreover, strict inclusion and exclusion criteria used in this study compound the selection bias even more. Criteria were, however, essential to confirm that healthy, non-obese and well-motivated subjects were selected due to the nature of the intervention. This source of error in convenience sampling can be determined by comparing the collected data with previous data from a population in terms of average variability (Sousa et al. 2004). For example, at baseline, all dimensions of HRQoL were higher in our voluntary subjects than average HRQoL scores in healthy 18-79-yr-old adults in Finnish population (Aalto et al. 1999). Our subjects were also much leaner than the average middle-aged and older male and female Finnish population (Lahti-Koski 2001). Therefore, our results can be generalized only to healthy, non-obese middle-aged and older subjects. This relatively homogenous group of quite fit older adults may also have reduced our power to detect differences between groups in HRQoL, as well as in metabolic risk factors and body composition.



Finally, the present nutritional data is limited by the dietary assessment methodology i.e. food records. Although the food diary methods are among the most commonly used dietary assessment tools, it can be rather imprecise, and underreporting is an acknowledged problem (Buzzard 1998). We also have problems with missing and incomplete data regarding the nutritional diaries.

## 6.6 Practical applications and suggestion for future research

The present data showed that both high-intensity endurance training and heavy resistance strength training can produce some improvements in metabolic health during the 21-week intervention period, even in relatively lean healthy middle-aged and older adults. The present combined training four times per week did not produce complementary benefits on metabolic health over endurance or strength training only, but was especially effective in improving body composition and both aerobic performance and muscle strength, which may be of high value in preventing worsening metabolic syndrome risk factors, even in low-risk individuals without the metabolic syndrome. It is, however, still unclear what are the minimal and optimal levels of different types of physical training to prevent age-associated negative changes in body composition and metabolic health. Future studies are needed to determine the optimal levels for the amount, type, and frequency of individual training sessions and duration of prolonged endurance, strength, and combined training to improve metabolic health in obese individuals or in individuals with metabolic syndrome.

The modest improvements in blood lipids and lipoproteins and glucose and insulin metabolism caused by physical training were related to concomitant changes in body composition. These improvements in metabolic risk factors and body composition were observed without corresponding changes in nutrient intake. It can be concluded that regular the Finnish diet, which includes 1.2-1.3 g/kg protein intake per day is sufficient to produce large increases in muscle strength and modest increases in lean body mass in 39-64 year old women.

Supervised, high-intensity endurance training by cycling and total body strength training performed mainly with gym equipments were safe training methods even for the older individuals. Training was well tolerated and adherence was extremely high. During longer (>21 weeks) training periods, however, four times per week training with progressive training loads may be too stressful for some individuals, which can be seen in increased blood pressure or as an interference in muscle mass development. Based on current knowledge, it is unsolved whether the interference occurs in the development of muscle mass or strength in older individual during prolonged (>21 weeks) combined training.

## 7 PRIMARY FINDINGS AND CONCLUSIONS

1. Combined strength and endurance training is of greater value than either endurance or strength training alone in optimizing body composition i.e. decreasing body fat and increasing lean mass in older adults. In men, lean mass of the legs and arms increased significantly only in the strength training group, which may indicate possible interference in muscle mass development during 2+2 times per week high-intensity endurance and strength training. However, in women high-intensity endurance training performed by cycling produced some additional benefits for training-induced muscle hypertrophy.
2. Bioimpedance, skin folds, and waist circumference showed good reproducibility in assessing body fat, and these methods correlated well with DXA in the cross-sectional analysis. DXA was able to detect small training-induced changes in lean body mass.
3. Both endurance and strength training may modestly improve metabolic health characterized by abdominal obesity, blood lipids and lipoproteins, glucose and insulin metabolism, and blood pressure, even in healthy normal or slightly overweight men and women. Combined training did not produce synergistic benefits in any of the metabolic health factors over endurance or strength training alone.
4. Changes in basal hormone concentrations following high-intensity endurance and strength training, as well as combined training were rather minor and the groups differed significantly only in the changes in serum IGF-1. The minor increase observed in serum IGF-1 in SE may be a physiological response to high-intensity training and may, in part, contribute to increases in lean mass during the present training period.
5. Twenty-one-weeks of training led to large gains in muscle strength and maximal oxygen uptake in the combined strength and endurance group.



The magnitude of these increases did not differ from the corresponding changes observed in the group that performed either strength or endurance training alone.

6. The improvements in serum lipids and lipoproteins were related to concomitant decreases in total and abdominal obesity and to changes in maximal oxygen uptake. Modest improvements in metabolic health were evident even without changes in dietary intake during training.
7. High-intensity endurance and combined training, which leads to increased aerobic capacity, may increase the sense of energy and well-being in middle-aged and older healthy men and women. Endurance training alone and combined with strength training positively affects some dimensions of HRQoL, and combined training especially improved the vitality dimension of the HRQoL over endurance or strength training only.
8. In 39-77-year-old men and women, combined high-intensity endurance and strength training for 21 weeks leads to great increases both in aerobic performance and muscle strength and to more modest improvements in body composition and metabolic health.

## YHTEENVETO (FINNISH SUMMARY)

Kansanterveyden suurimpia uhkia tulevina vuosina tulevat olemaan väestön ikääntyminen ja lihavuuden ja sen liitännäissairauksien yleistyminen. Ikääntyminen ja fyysinen inaktiivisuus aiheuttavat kehossa terveydelle epäedullisia rakenteellisia ja toiminnallisia muutoksia. Lihasmassan määrä vähenee ja kehon rasvapitoisuus kasvaa ja keskittyy enemmän sisäelinten ympärille. Lisäksi aerobinen suorituskyky heikkenee ja lihasvoima vähenee kaikissa lihasryhmissä ja erityisesti alaraajoissa.

Nämä muutokset edesauttavat myös metabolisten terveyden riskitekijöiden lisääntymistä: verenpaine ja veren kokonaiskolesterolin ja huonon LDL kolesterolin -pitoisuudet nousevat ja hyvän HDL kolesterolin -pitoisuus laskee ja glukoosiaineenvaihdunta häiriintyy. Edellä mainittujen muutosten seurauksena riski sairastua sydän- ja verisuonitauteihin, metaboliseen oireyhtymään ja diabetekseen kasvaa. Terveydelle epäedulliset muutokset kehossa alkavat jo 10-15 vuotta ennen tyypin 2 diabeteksen diagnosoimista. Tämän vuoksi on ensiarvoisen tärkeää pyrkiä ehkäisemään sairastumiselle altistavia tekijöitä jo varhaisessa vaiheessa.

Tämän väitöskirjan tarkoituksena oli tutkia 21 viikon voima- ja kestävyysharjoittelun sekä yhdistetyn voima- ja kestävyysharjoittelun vaikutuksia 39-77-vuotiaiden terveiden miesten (n=113) ja naisten (n=102) kehon koostumukseen, metaboliseen terveyteen, fyysiseen suorituskykyyn ja koettuun elämänlaatuun.

Alkumittausten jälkeen tutkittavat satunnaistettiin kolmeen harjoittelu-ryhmään ja kontrolliryhmään. Voima- ja kestävyysryhmät harjoittelivat ohjatus- ti kaksi kertaa viikossa (koko kehon lihasvoimaharjoittelua kuntosalilla tai kestävyysharjoittelua kuntopyörällä). Yhdistelmäryhmä teki sekä kestävyys- että voimaharjoittelua yhteensä neljänä päivänä viikossa. Tutkittavat suorittivat 98-100%:a suunnitelluista harjoituskerroista.

Fyysisen suorituskyvyn muutoksia tutkittiin uupumukseen asti suoritettulla pyöräilytestillä, jonka aikana mitattiin maksimaalinen hapenottokyky ja polkemisteho. Lihasvoiman muutoksia tutkittiin mittaamalla maksimivoima ylä- ja alaraajoista. Kehon koostumuksen muutoksia seurattiin useilla eri menetelmillä. Kehon kokonaisrasvamäärää mitattiin kaksiennergisen röntgensäteiden absorptiometrialla (DXA), bioimpedanssilla ja ihopoimiumittauksin. Rasvan jakautumista kehon eri osissa tutkittiin DXA-mittauksella ja vyötärön ympärysmittauksella. Lihasmassan muutoksia seurattiin DXA-mittauksella, ultraäänimittauksella ja raajojen ympärysmittoja mittaamalla. Seerumista määritettiin veren kolesteroli- ja hormonipitoisuuksia ja glukoosiaineenvaihduntaa tutkittiin glukositolianssitestillä. Koehenkilöiden ravinnonsaantia arvioitiin ruokapäiväkirjojen avulla ja RAND-36 kyselylomakkeella seurattiin muutoksia terveyteen liittyvässä elämänlaadussa.

Tutkimuksen päätulokset osoittavat, että 21 viikon harjoittelu paransi aerobista suorituskykyä ja lihasvoimaa harjoitteluspesifisti. Yhdistelmäharjoittelulla voitiin samanaikaisesti lisätä sekä aerobista suorituskykyä että lihasvoi-

maa yhtä paljon kuin kummallakin harjoittelumuodolla erikseen. Sekä kestävyys- että yhdistelmäryhmät lisäsivät merkittävästi maksimaalista hapenotto-kykyään harjoittelujakson aikana. Vastaavasti maksimaalinen ala- ja yläraajojen ojennusvoima kasvoi sekä voima- että yhdistelmäryhmillä.

Yhdistelmäharjoittelu johti sekä rasvamäärän vähenemiseen että koko kehon rasvattoman massan määrän nousuun sekä naisilla että miehillä. Yhdistelmäryhmien lisäksi DXA:lla mitattu kehon rasvaprosentti pieneni naisilla myös kestävyysryhmällä ja miehillä sekä voima- että kestävyysryhmällä. Vyötärön ympärysmitta pieneni harjoittelujakson aikana kaikilla harjoitteluryhmillä, paitsi ei voimaharjoitelleilla naisilla.

Koko kehon rasvaton massa (DXA) lisääntyi sekä naisilla että miehillä yhdistelmäryhmällä ja naisilla lisäksi kestävyysryhmällä. Ultraäänimenetelmällä mitattu reisilihaksen paksuus kasvoi kaikilla harjoitteluryhmillä. Vastaavasti DXA:lla mitattu alaraajojen rasvaton massa lisääntyi naisilla kaikilla harjoitteluryhmillä, mutta miehillä ainoastaan voimaryhmällä. Alaraajojen rasvattoman massan määrän pysyminen ennallaan miesten yhdistelmäryhmällä voi johtua samanaikaisen kestävyysharjoittelun aiheuttamasta inhibitiomekanismista, jonka syytä ei vielä täysin tunneta.

Tutkimustulokset osoittivat lisäksi, että sekä voima- että kestävyysharjoittelulla voidaan parantaa metabolisen terveyden osatekijöitä normaali- ja lievästi ylipainoisilla terveillä miehillä ja naisilla. Sekä voima- että kestävyysharjoittelu laskivat systolista ja diastolista verenpainetta miehillä. Naisilla vastaavaa verenpaineen laskua ei havaittu, mikä saattaa johtua alhaisemmasta verenpaineesta lähtötilanteessa. Jollekin koehenkilöille kovatehoinen harjoittelu neljä kertaa viikossa saattaa olla liian rasittavaa, mikä tutkimustuloksissa näkyi miesten yhdistelmäryhmän verenpaineen nousuna harjoittelujakson puolivälin jälkeen. Veren kolesteroli- ja lipoproteiinipitoisuudet paranivat harjoittelun myötä ainoastaan kestävyysharjoitteluryhmän naisilla. Pieniä, mutta tilastollisesti merkittäviä parannuksia voima- ja kestävyysharjoitteluryhmillä havaittiin myös glukoosi- ja insuliinitasoissa. Positiiviset muutokset metabolisissa terveydessä olivat yhteydessä korkeampiin lähtötasoihin, kehon massan ja vyötärön ympäryksen pienenemiseen harjoittelun aikana sekä aerobisen suorituskyvyn paranemiseen.

Sekä pelkkä kestävyysharjoittelu että yhdistelmäharjoittelu paransivat tutkittavien koettua terveyteen liittyvää elämänlaatua. Yhdistelmäharjoitteluryhmän koettu tarmokkuus lisääntyi enemmän kuin muilla harjoitteluryhmillä tai kontrolliryhmällä. Lisäksi koetun terveyden ja psyykkisen hyvinvoinnin osa-alueet paranivat yhdistelmäharjoittelulla. Myös kestävyysryhmän koetun terveyden, kivuttomuuden ja fyysisen roolitoiminnan osa-alueet paranivat. Voimaryhmällä kivun tuntu lisääntyi harjoittelun aikana, mikä saattaa johtua kovaintensiteettisen voimaharjoittelun aiheuttamasta lihasarkuudesta ensimmäisten harjoitteluviikkojen aikana. Samanaikainen kestävyysharjoittelu saattaa vähentää kivun tuntua, sillä yhdistelmäryhmällä tässä ulottuvuudessa ei tapahtunut muutoksia.

Tutkimustulokset osoittavat, että puolen vuoden ohjatulla, systemaattisella kestävyys- tai voimaharjoittelulla kaksi kertaa viikossa voidaan parantaa joko aerobista suorituskykyä tai lihasvoimaa yhtä paljon kuin suorituskyky keskimäärin laskee ikääntymisen myötä 10-15 vuodessa. Suorituskyvyn paranemisen lisäksi harjoittelu vaikuttaa edullisesti kehon koostumukseen. Kestävyysharjoittelu vähensi kehon rasvan määrää erityisesti keskivartalossa ja voimaharjoittelulla voitiin lisätä aineenvaihdunnallisesti aktiivisen lihasmassan määrää.

Sekä voima- että kestävyysharjoittelu vaikuttivat lisäksi edullisesti keski-ikäisten ja ikääntyvien normaali- tai lievästi ylipainoisten, terveiden koehenkilöiden metaboliseen terveyteen, mikä pitkällä tähtäimellä vähentää riskiä sairastua mm. metaboliseen oireyhtymään, tyypin 2 diabetekseen ja sydän- ja verisuonitauteihin. Voimaharjoittelun yhdistäminen kestävyysharjoitteluun ei tuonut merkittävää lisähyötyä metabolisen terveyden osa-alueisiin. Yhdistelmäharjoittelu paransi kuitenkin monipuolisesti sekä kehon koostumusta että aerobista suorituskykyä ja lihasvoimaa, millä voi olla suuri merkitys metabolisen oireyhtymän syntymisen ehkäisyssä. Lisäksi sekä kestävyys- että yhdistetyllä kestävyys- ja voimaharjoittelulla voitiin parantaa 39-77-vuotiaiden miesten ja naisten koettua elämänlaatua.

Tutkimustulokset osoittavat että nousujohteinen, ohjatusti toteutettu yhdistetty kestävyys- ja voimaharjoittelu on turvallinen ja tehokas tapa parantaa monipuolisesti keski-ikäisten ja ikääntyvien miesten ja naisten kehon koostumusta, terveyttä ja suorituskykyä. Sekä kaksi että neljä kertaa viikossa toteutetun harjoittelun toteutuvuus oli erittäin hyvä ja keskeyttäneiden määrä poikkeuksellisen alhainen interventiotutkimukseen. Tutkimustuloksia voidaan hyödyntää suunniteltaessa liikuntainterventioita, joiden tarkoitus on ennaltaehkäistä ikääntymiseen, liikkumattomuuteen tai ylipainoon liittyvien toiminnanvaja-uuksien ja sairauksien syntymisen.

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