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Exercise in aging: its important role in mortality, obesity and insulin resistance

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Abstract

The prevalence of overweight and obesity has increased dramatically over the last several decades. Obesity and physical inactivity increase the risk for cardiovascular disease, Type 2 diabetes mellitus, hypertension, dyslipidemia and certain cancers. Obesity and low levels of physical fitness are also associated with increased risk of all-cause and cardiovascular mortality. Central and total obesity, insulin resistance and inactivity increase with age. Exercise training and increased fitness promote positive changes in body composition and improve insulin sensitivity. This article will describe the effects of exercise training, both aerobic and resistive, on body composition and obesity as well as review studies investigating the effects of exercise training on glucose metabolism and insulin sensitivity in older adults. Adopting a physically active lifestyle should be emphasized in overweight and obese individuals with insulin resistance to reduce the risk for cardiovascular events in the aging population.

Keywords

aging; body composition; exercise; insulin sensitivity

Obesity

Definition & current trends

Overweight and obesity are defined by BMI, a measure of an individual's weight in relation to their height. A BMI between 25 and 29 kg/m² defines overweight in adults, whereas obesity is defined as a BMI of more than 30 kg/m². BMI for obesity can be further classified as Class I obesity (BMI: 30.0–34.9 kg/m²), Class II obesity (35.0–39.9 kg/m²), and Class III or morbid obesity (BMI >40 kg/m²). Evidence provided by epidemiology studies supports these criteria owing to the observed associations between BMIs above 25 kg/m² and an increased incidence of cardiovascular disease (CVD), Type 2 diabetes mellitus, hypertension and dyslipidemia that affect mortality and morbidity. Of note, BMI does not distinguish between differences in fat mass, lean tissue or percentage of body fat. BMI may also be of limited value in the elderly since it does not indicate the amount of muscle and other

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changes in body composition that occur with aging. However, the use of BMI is valuable in large epidemiologic studies, field work and comparisons across nations.

The National Center for Health Statistics examined the prevalence and trends of overweight US adults from 1960–2000 via the National Health Examination Survey (NHES I) and National Health and Nutrition Examination Surveys (NHANES I, II, III, continuous) [1]. The prevalence of overweight and obesity increased significantly over the 40-year period, from 43% in 1960–1962 to 64.5% in 1999–2000. Most of this increase was attributable to a dramatic rise in the prevalence of obesity that remained stable at approximately 15% for the first three survey periods (1960–1980), and then rose dramatically to 30.5% in 1999–2000. The increased prevalence of overweight and obesity in adults during this time period was evident in both genders, across all races and ethnicities, and across all age groups. The most recent NHANES data report examined trends in obesity from 1999 through 2008 [2]. The study showed that the prevalence of overweight and obesity combined was 68% overall, 72% among men and 64% among women. The prevalence of obesity varies by age, racial and ethnic groups for both men and women. In particular, the likelihood of being obese was significantly higher in men and women aged 40–59 years as well as in the age group 60 years or older, compared with the 20–39 years age group. Of interest is that the authors concluded that the prevalence of obesity did not appear to be growing at the same rate as it had over the last 10 years for women and probably for men. This might suggest that women in particular may be adhering to current recommendations for important lifestyle changes to combat obesity.

Effects on disease & mortality

Obesity & mortality

Both obesity and physical inactivity effect disease states and mortality rates. The increase in obesity is associated with increased prevalence of CVD, hypertension, gallbladder disease, osteoarthritis and Type 2 diabetes [3]. In addition, obesity is a well-established risk factor for most common cancers including cancer of the breast (postmenopausal), colorectum, esophagus, liver, gallbladder and uterus, and advanced prostate cancer. There is also evidence that being overweight increases the risk for cancer recurrence and may reduce the likelihood of survival [4-7]. Severe obesity is associated with increased mortality [8]. Numerous studies have examined the association between body weight and mortality. In these studies, the association between body weight and mortality is either not apparent [9], shows a J-shaped curve [10], a U-shaped relationship [11] or a direct association [12,13]. Moreover, weight gain of 10 kg or more after the age of 18 is associated with increased mortality in middle adulthood [14]. In a recent study of two populations including the Danish 1905 Cohort Survey and the Longitudinal Study of Aging of Danish Twins (LSADT), approximately 6400 individuals were followed for 19 years with 72% mortality [15]. Their results indicate that mortality and low BMI are associated with advancing age for both men and women. Furthermore, in men there was a tendency for the association between mortality and high BMI to decrease with advancing age. The authors conclude that the association between BMI and mortality became decreasingly U-shaped in a 70–95-year-old Danish population [15]. These data would suggest that the relationship between BMI and mortality is different in elderly and in younger subjects. In men and women aged 70–75 years of the Health in Men Study and the Australian Longitudinal Study of Women's Health who were followed for 10 years, mortality risk was lowest in those who were overweight with a higher risk of death in normal weight than in obese participants [16]. The authors concur that weight loss would be harmful in this elderly group. A direct association between fat mass and all-cause and CVD death rates in men is also reported [17]. In general, these studies suggest that high BMI is associated with mortality and that the relationship between low BMIs and mortality may differ with age.

Physical activity & mortality

A low level of physical fitness is associated with increased risk of all-cause and CVD mortality [18-21]. It has been shown that men who improve their physical fitness reduce their mortality risk by approximately 44% [22]. In addition, both avoiding obesity and beginning moderately vigorous sports activity are separately associated with lower death rates from all causes and from CVD in middle-aged and older men [10]. All-cause mortality risk is also reduced by physical activity in postmenopausal women [23]. Middle-aged women who maintained a healthy lifestyle by not being overweight, not smoking, exercising moderately or vigorously 30 min/day, and eating a healthy diet, had more than an 80% reduction in the incidence of coronary events compared with those women without these traits [24]. Furthermore, brisk walking and vigorous exercise are associated with considerable and similar risk reductions in the incidence of coronary events among women [25].

Evidence that physical activity is beneficial in the very old was provided through the Jerusalem Longitudinal Cohort Study [26]. In approximately 1900 elderly individuals who were followed, the 8-year mortality was 15 versus 27% in the physically active and sedentary, respectively, at age 70 years and 26 versus 41% at age 78 years, respectively, with 3-year mortality rates at the age of 85 years approximately three-times lower in the physically active. There was also a significant survival benefit that was associated with initiating physical activity between ages 70–78 years and between ages 78–85 years. In addition, continuation of physical activity levels was associated with better survival and function in the very old [26]. This study would suggest that even starting physical activity very late in life is beneficial. 10-year mortality was lower in Mexican–American older adults (of ~75 years) who scored better on a five item frailty index that included measures of physical activity, walking speed, grip strength, weight loss and exhaustion [27]. In a similar manner, walking speed was a better predictor of mortality risk than calf skeletal muscle and fat mass in participants 65 years and older in the InCHIANTI study [28]. The NIH-AARP Diet and Health Study determined all cause-mortality in a very large sample (~185,000) of men and women aged 51–72 years [29]. Mortality risks were lower in normal-weight individuals who were physically active, defined as moderate exercise performed for more than 7 h per week, than normal-weight inactive individuals. Similar findings were reported between morbidly obese active compared with morbidly obese inactive persons. This study also combined physical activity with central adiposity measures to indicate that persons with a normal waist circumference had two-times lower mortality risk than those with high waist circumference [29]. Older women (70–75 years) who were sedentary had twice the mortality risk after 10 years regardless of initial BMI (underweight, normal weight, overweight and obese) indicating that being sedentary increases mortality risk across all levels of BMI [16]. Thus, the evidence from these multiple studies reinforces the concept that physical activity can reduce mortality risk. These studies suggest that significant health benefits may be obtained by performance of regular moderate intensity exercise, a goal that is realistic, safe and attainable for most individuals and provides enormous health benefits.

Exercise training

Exercise training has beneficial effects on individual cardiovascular risk factors including obesity, hypertension, dyslipidemia and glucose intolerance (Box 1). The main focus of this review is the effects of exercise training on obesity and insulin resistance. Readers are encouraged to look elsewhere for additional reviews on exercise and hypertension and dyslipidemia [30-33]. In addition, there are several reviews of the importance of weight loss on obesity and insulin resistance [34-36]. One can also read a review of the mechanisms in the prevention of Type 2 diabetes through lifestyle modifications and pharmacological interventions [37].

Box 1. Outcomes of exercise training interventions

Athletes vs controls

<Bodyweight[†]
 <Waist circumference[†]
 >FFM and muscle area
 <Fat mass
 <Visceral fat
 <Subcutaneous abdominal fat
 >Insulin sensitivity

Aerobic exercise

↓ or ↔ bodyweight[†]
 ↓ Visceral fat
 ↓ Subcutaneous abdominal fat
 ↑ or ↔ FFM and muscle area[†]
 ↑ Insulin sensitivity
 ↓ TG, ↓ BP, ↑ HDL

Resistive exercise

↔ Bodyweight
 ↔ Fat mass
 ↑ FFM and muscle area
 ↓ or ↔ visceral fat[†]
 ↓ or ↔ subcutaneous abdominal fat[†]
 ↑ Insulin sensitivity
 ↔ TG, ↔ BP, ↔ HDL

[†]May be related to the duration, frequency and intensity of training and age of subjects.

BP: Blood pressure; FFM: Fat-free mass; HDL: High-density lipoprotein; TG: Triglyceride.

Exercise & obesity

Studies in athletes—In order to examine the influence of physical activity on body fat, studies have been conducted examining body composition in athletes and changes in body composition with exercise training. Body fat is generally determined by dual-energy x-ray absorptiometry (DXA) and visceral and subcutaneous abdominal fat by computed tomography (CT) or MRI. Women athletes between 18 and 69 years of age have lower percent body fat, fat mass, visceral and subcutaneous abdominal fat than normal BMI age-matched controls [38]. Visceral fat of the older controls was more than double that of the older athletes. In addition, only visceral fat increased with age in athletes, but total body fat and subcutaneous abdominal fat were not different between young and older athletes,

suggesting that high levels of endurance training enabled the older athletes to maintain a low body fat despite their age [38]. In the only study of male athletes that examined visceral fat, we showed that older former football players had 26% ($p < 0.01$) lower visceral fat than age-, BMI-, race- and current physical activity level-matched men [39]. This reduced adiposity was accompanied by a 26% ($p < 0.001$) lower total body fat and a 13% ($p < 0.01$) higher muscle mass than male controls, suggesting that the high levels of exercise in young adulthood conferred benefits later in life [39]. In contrast to our study where body fat did not differ between young and older women athletes [38], it has been reported that young male athletes have lower percent body fat than middle-aged and older athletes [40]. In a comparison of groups of older men, the endurance-trained athletes have smaller waist circumference than lean male controls; however, body weight, BMI and percent body fat were similar [41]. When different types of athletes are compared, endurance-trained athletes have lower body weight and fat mass than untrained men and resistance-trained athletes [42]. Resistance-trained athletes have greater fat-free mass (FFM) than untrained men [42] and greater lean mass than endurance trained athletes [42,43]. Therefore, athletes tend to have less adiposity and more muscle than controls.

Endurance training studies

Endurance training alone can have beneficial effects on adiposity in obese individuals [44-47]. A meta-analysis of 40 studies where body fat changes were measured in obese adults after approximately 20 weeks of endurance training, indicated that an average loss of 3 kg of body fat occurs with the exercise programs [48]. Others contend that exercise training may not result in weight loss in obese subjects or if exercise training does reduce body mass and fat mass, the changes are relatively small [49]. In another meta-analysis, Ballor and Keeseey used 53 aerobic exercise training studies published between 1950 and 1988 and showed that for both males and females, initial body fat levels accounted for a large portion of the variance associated with changes in weight, fat mass and percent fat [50]. In their analyses, the reduction in fat mass averaged 1.5 kg and occurred with a 1.7% reduction in percent body fat [50]. Thus, these studies would suggest that normal-weight individuals may either not lose body fat with endurance exercise or, if they do, these changes may be negligible.

Studies have also reported changes in regional adiposity with exercise training. An aerobic exercise program of 13 weeks duration induced a reduction in visceral fat and subcutaneous abdominal fat without a change in body weight in obese men with and without Type 2 diabetes [47]. It has also been suggested that a 9-month exercise program representing approximately 20 miles/week at 65–80% peak VO_2 (described as high amount of vigorous exercise) is necessary to significantly decrease visceral and subcutaneous abdominal fat, despite a lack of significant weight loss [51]. Thus, abdominal fat can be reduced with aerobic exercise training, even without a change in body weight.

Individuals with the greatest adiposity may lose more body fat with endurance training. Moreover, the duration of the exercise (min per session) and weeks of training were significant predictors of the change in percent fat in females [50]. This was confirmed in a review of aerobic training studies in older adults, which indicated that losses of fat mass were related to the duration of the exercise program (e.g., total number of sessions) [52]. In a more recent review of exercise training effects on adiposity, Elder *et al.* concluded that aerobic training without a dietary change conferred a loss of body fat [53]. Furthermore, there was a greater reduction in body fat with an increase in energy expenditure in both men and women. Therefore, the amount of exercise performed is an important determinant of the changes in body composition with aerobic training and needs consideration in the comparison of endurance training studies and changes in fat mass.

Ross *et al.* reported that when an exercise-induced weight loss of 2–3 kg occurs with exercise training, there is a small reduction of approximately 2 cm in the waist circumference [54]. In addition, the literature would suggest that aerobic exercise training without significant weight loss does not result in a decrease in waist circumference [54,55]. However, other changes in abdominal obesity, such as losses of visceral fat and subcutaneous abdominal fat, occur with moderate aerobic exercise and minimal weight loss [56,57].

Resistive training studies

In general, resistive training in older individuals does not result in a loss of body weight or total body fat [58,59], although a decrease in visceral fat after resistive training was reported in older women [60]. However, total body FFM and thigh muscle area increase after resistive training in postmenopausal women and middle-aged and older men [58,59]. Moreover, absolute increases in muscle volume after a 9-week leg extension strength program of the dominant leg are greater in older men than older women [61]. These increases in muscle volume were followed by a greater absolute loss of muscle volume in the men after 31 weeks of detraining [61]. In a study of 10 weeks of unilateral strength training, muscle volume increased in men and women aged 50–85 years of age without changes in inter-muscular fat or midthigh subcutaneous fat [62]. As a follow-up to this study, the same investigative team had the men and women who were over 65 years of age complete a 12-week program of whole-body strength training and reported significant increases in FFM [63]. Taking the muscle analyses further, Melnyk *et al.* reported increased proximal, middle and distal quadriceps muscle areas of the thigh after a 9-week one-legged strength training program in older (65–75 years) men and women suggesting that the increases in muscle area occur across the entire thigh muscle [64]. A total of 6 months of progressive whole-body resistive training resulted in an increase in lean tissue mass in older men (aged 65–74 years) but did not change lean mass in older women [65]. Although the sample size was small, midthigh muscle area did not change significantly after a 6-month resistive training program in overweight and obese older men (50–79 years of age) [66].

There are several randomized controlled trials that also emphasize the benefits of resistance training in the elderly. A 3-month progressive resistance training program that followed an aerobic exercise training intervention increased total body FFM by approximately 1 kg but did not change visceral fat or subcutaneous abdominal fat in community dwelling frail elderly men and women (>78 years of age) [67]. In a randomized control trial of almost 250 elderly community living women, Kemmler *et al.* showed that appendicular skeletal muscle mass and total lean body mass increased after an 18-month high-intensity exercise program that consisted of aerobic dance, balance exercises and a dynamic and static strength component [68]. In addition, there were significant reductions in abdominal and total body fat measured by DXA. Compared with an active control group of men 55–80 years of age, the men who were randomized to a 1-year resistance training program had a significant 1.5% increase in lean body mass [69]. By contrast, in a meta-analysis of nine studies, body composition changes were not significantly different with progressive resistive exercise compared with no exercise in individuals with Type 2 diabetes [70]. Thus, in contrast to aerobic exercise that results in minimal changes in FFM, resistive training may increase total body and regional muscle mass, but the population studied may be important with respect to body composition results.

Exercise & glucose metabolism

Insulin resistance is defined as the change in glucose disposal rate elicited by a unit change in insulin concentration [71]. Insulin sensitivity quantifies a dose–response relationship such that the response, or change in glucose concentration, changes the dose or insulin

concentration. An increase in insulin sensitivity is defined as a reduction in the insulin concentration needed to produce one half of the maximal response [72]. Methods exist for the measurement of insulin sensitivity [73], including the glucose clamp [74] and the minimal model technique [75]. Both methods have been used in the study of the effect of exercise on glucose metabolism.

Cross-sectional studies

Cross-sectional studies consistently demonstrate the benefits of exercise on glucose homeostasis. In a large population of elderly men and women, physical activity, measured by self-administered questionnaire, decreased with increasing glucose intolerance and persisted after adjustment for age, BMI, waist:hip ratio, family history of diabetes and smoking [76]. Research in athletes concurs the benefits of exercise on glucose metabolism such that endurance-trained athletes have higher insulin sensitivity [77-79] and increased rates of glucose disposal [80,81]. In a small sample of male master athletes, the EC_{50} , the half-maximal increase in glucose disposal during a three-step hyperinsulinemic–euglycemic clamp, was approximately 40% lower than age- and body fat-matched sedentary men indicating an enhanced insulin sensitivity in aerobically trained older athletes [82]. In another study of male athletes, both young and middle-aged cyclists had higher insulin sensitivity by the minimal model than young and middle-aged sedentary men [83]. We showed for the first time that β -cell sensitivity to glucose and peripheral tissue sensitivity to insulin using a newly devised sequential hyperglycemic–euglycemic clamp was preserved in women athletes (swimmers, runners and tri-athletes) as a function of age [81]. Furthermore, athletes were compared with normal-weight controls and the results indicated that older sedentary women had a 70% greater first-phase and 103% greater second-phase insulin response during hyperglycemia than the athletes (Figure 1A) [81]. Furthermore, older athletes utilized approximately 30% more glucose than similarly aged sedentary women (Figure 1B); thus, results from both the hyperglycemic and the euglycemic parts of the combined clamp indicate increased insulin sensitivity in older athletes [81]. This was confirmed in a similar recent study where insulin sensitivity by a euglycemic clamp was not different in younger men and women athletes versus older endurance-trained athletes [84]. In addition, younger versus older normal-weight subjects, and young versus older obese subjects have similar insulin sensitivity, suggesting that the obesity and physical inactivity are more important in insulin resistance than aging *per se* [84]. To understand the influence of various sports on insulin resistance, it is necessary to examine the literature that reports this in young subjects. Insulin sensitivity as estimated by the homeostatic metabolic assessment for insulin resistance (HOMA-IR) was determined in over 750 athletes representing 33 different sports [85]. Those athletes with the lowest HOMA-IR values were rowers and short-distance track athletes, whereas archery and field-throwing athletes had higher HOMA-IR values than the control group. A comparison of weight lifters, endurance athletes and sedentary men indicated that glucose uptake by the hyper-insulinemic–euglycemic clamp was higher only in endurance athletes whereas glucose uptake was not significantly different between weight lifters and sedentary men [86]. These results might suggest that the weight-lifting athletes do not confer the same metabolic benefits in terms of glucose metabolism as aerobically trained athletes. Studies in older athletes are necessary to make this statement in the elderly.

Aerobic training studies

In some early longitudinal aerobic exercise training studies of varying duration, glucose metabolism by oral glucose tolerance tests or glucose clamps improved by between 11 and 36% [87-90]. Studies in patients with Type 2 diabetes yielded similar results, with improvements in insulin action ranging from 20 to 30% [91-93]. The results suggested that the increase in insulin-mediated glucose disposal was similar to that observed in healthy

subjects but exercise training does not completely reverse the insulin resistance observed in Type 2 diabetes. The enhanced insulin action is the result of regularly repeated exercise bouts (i.e., training), and was not the result of the last exercise bout since in many studies, which indicate improvements in glucose metabolism after aerobic training [91-93], the hyperinsulinemic–euglycemic clamps were performed 16 h–6 days after the last bout of exercise. In a study to test whether the effects of exercise training were long-lasting, DiPietro *et al.* performed glucose clamps 72 h after the last training session in older (~73 years) women after 9 months of endurance training [94]. Insulin sensitivity increased by approximately 20% suggesting that the exercise training effects on glucose metabolism are prolonged.

Different types of aerobic exercise training programs have been implemented to examine changes in glucose metabolism with varying duration, mode and intensities. A 6-week exercise training intervention of stair climbing increased glucose uptake by about 20% in insulin-resistant adults [95]. In addition, glycogen synthesis increased by almost 100% in these individuals. In a randomized controlled trial comparing aerobic exercise of different intensity and amount of exercise, Studies of a Targeted Risk Reduction Intervention through Defined Exercise (STRRIDE) investigators reported beneficial effects of exercise on insulin sensitivity in middle-aged overweight/obese adults [96]. Specifically, insulin sensitivity index, SI, by the minimal model technique decreased in the control group over time and increased to a similar degree with a range of intensity (40–80% peak VO_2) and training volume per week (12–20 miles/week). Yet, the changes in SI were greater in the higher weekly training duration groups. These results suggested that moderate-intensity exercise was as beneficial as vigorous exercise training. In younger men (<45 years of age), 24 weeks of either moderate-intensity or high-intensity aerobic exercise reduced insulin resistance by HOMA and decreased fasting insulin with no difference between the exercise intensities [97]. Together, these studies would suggest that improvement in insulin sensitivity occurs with exercise training regardless of intensity in workloads that are moderate or high. Comparisons of different exercise intensities on insulin sensitivity in the elderly are lacking.

Resistive training studies

Owing to the deterioration in glucose metabolism with aging, strength training or resistive training has also been studied as a mode of exercise to improve glucose homeostasis. In general, resistive training does not change fasting plasma glucose in young and older subjects [98-100]. This is true regardless of age or sex [98]. Yet, resistive training does improve glucose metabolism in men and women [98-102]. A total of 4 months of resistive training improved glucose tolerance, significantly lowered the insulin responses to an oral glucose tolerance test and increased insulin sensitivity by 33% during a hyperinsulinemic–euglycemic clamp in adult men [99]. Moreover, resistive training for 4 months alone, or in combination with weight loss, increased insulin action and reduced hyperinsulinemia as assessed by hyperglycemic clamps in postmenopausal women with no difference between groups [102]. More than a decade later, Brochu *et al.* conducted a randomized clinical trial of a similar group of postmenopausal women and reported that the change in glucose disposal was significantly increased after either weight loss alone or weight loss and resistive training with no difference between the interventions [103]. However, these changes were significant only when expressed in mg/kg and not when glucose disposal was expressed in ml/kg/min. Only when the weight loss and resistive training group was subdivided into those women who had more than 80% compliance was there a significant increase in glucose disposal. Therefore, this study would confirm our results that resistive training can be beneficial in terms of glucose metabolism. In older insulin-resistant adults, a 6-month resistive training program tended to improve insulin action and the change in glucose utilization was a function of initial glucose utilization [100]. More studies are

needed to further delineate whether resistive training can be effective in improving glucose metabolism in the elderly with comorbidities (e.g., stroke and cancer).

Combined intervention strategies

Studies have also combined resistive training with aerobic exercise or have directly compared the two types of exercise to examine changes in glucose metabolism [66,104,105]. When resistive training (4 months) was added to an existing aerobic program, insulin area measured by an oral glucose tolerance test decreased by 25% in older overweight men but did not change significantly in the men who maintained their aerobic exercise program [104]. When we studied older, overweight and obese men assigned to aerobic exercise or resistive training for 6 months, whole-body glucose utilization by hyperinsulinemic–euglycemic clamp increased comparably by 20–25% after the interventions (Figure 2) [66]. Changes in muscle metabolism were also examined in this study. The results indicated that the increase in vastus lateralis glycogen synthase fractional activity in response to the hyperinsulinemia was significantly higher after the aerobic exercise compared with the resistive exercise. In a randomized controlled trial comparing changes in insulin resistance by hyperinsulinemic–euglycemic clamp after exercise interventions, Davidson *et al.* reported that the combination of resistance and aerobic exercise improved glucose utilization more than the resistance exercise alone or control groups [105]. Although insulin resistance improved after aerobic exercise alone, the combination of the two exercise programs was recommended as the optimal strategy to improve glucose metabolism [105].

The combination of aerobic and resistance training is also beneficial in Type 2 diabetes. Maiorana *et al.* reported a reduction in HbA1c and fasting glucose levels in subjects with Type 2 diabetes after an 8 week combined aerobic and resistance exercise intervention [106]. Likewise, a longer (1 year) combined aerobic and resistance training program in older (~61 years) sedentary men and women with Type 2 diabetes of approximately 10 years duration, reduced fasting plasma glucose and HbA1c [107]. In a randomized controlled trial of subjects with Type 2 diabetes aged 39–70 years, 22 weeks of aerobic exercise, resistive training and aerobic plus resistive training reduced HbA1c compared with controls [108]. However, the combination of aerobic and resistive training was more effective in reducing HbA1c than either intervention alone. In a small group of healthy subjects and subjects with Type 2 diabetes, strength training of the single leg increased insulin-mediated glucose clearance, which involved changes in skeletal muscle insulin action and signaling [109]. Moreover, a meta-analysis of nine resistive training studies in individuals with Type 2 diabetes mellitus indicated that progressive resistive exercise led to a small (0.3%) but significant reduction in HbA1c compared with a no exercise group [70]. The resistive exercise changes were no different to those observed after aerobic exercise training [70]. This review would suggest that resistive training is effective in improving glycemia in Type 2 diabetes. Thus, resistive training may be useful in ameliorating insulin resistance that often occurs with physical inactivity and obesity in adults.

Diabetes prevention trials

Both the US Diabetes Prevention Program and the Finnish Diabetes Prevention Study are in agreement that lifestyle interventions can reduce the risk of diabetes in subjects with impaired glucose tolerance [110,111]. During a mean follow-up of 3–4 years in the Finnish and US Diabetes Prevention Studies, the progression to frank diabetes was almost 60% lower for men and women with impaired glucose tolerance assigned to an intense lifestyle intervention that included regular physical activity, modest weight loss and healthier dietary habits compared with glucose-intolerant men and women in the control group. In the US Diabetes Prevention Program with over 3000 individuals enrolled, the lifestyle intervention

(~150 min/week of moderate-to-vigorous intensity activities) was more effective than metformin or placebo. Furthermore, the advantage of the lifestyle intervention over metformin was greater in older persons and those with a lower BMI than in younger persons and those with a higher BMI. In the Finnish Diabetic Prevention Study, the lifestyle intervention (30 min exercise/day; goal of 5% weight reduction) was most effective among the individuals older than 61 years or the oldest group, such that the relative risk reduction was 64% compared with the control group, suggesting that age was important in the effectiveness. These two trials provide key evidence that adherence to the programs are crucial to success.

Exercise effects on the metabolic syndrome

After the introduction of syndrome X [100,102,112], the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II [ATP III]) reported on the significance of the metabolic syndrome [113]. Others have defined the metabolic syndrome including the WHO [114]. Metabolic syndrome according to ATP III includes having three or more of the following criteria: abdominal obesity or waist circumference more than 102 cm in men and more than 88 cm in women; hypertriglyceridemia as 150 mg/dl or more; low high-density lipoprotein cholesterol as less than 40 mg/dl in men and less than 50 mg/dl in women; high blood pressure as 130/85 mmHg or more; and high fasting glucose as 110 mg/dl or more. Since insulin resistance is a key component of the metabolic syndrome, it is relevant to discuss it in terms of the exercise training.

The efficacy of exercise training in treating the metabolic syndrome was reported in over 600 participants from the health, risk factors, exercise training and genetics (HERITAGE) Family Study who underwent a 20-week aerobic exercise training program [115]. At baseline, the prevalence of metabolic syndrome was approximately 17%. Notably, approximately 30% of the individuals with metabolic syndrome at baseline were no longer classified as having the metabolic syndrome after the training program. These improvements were evident by decreases in triglyceride concentrations (43% of individuals), blood pressure (38% of individuals) and waist circumference (28% of individuals), and improvements in HDL-cholesterol (16% of individuals) and fasting glucose levels (9% of individuals). Importantly, there were no sex or race differences in the efficacy of the exercise training in treating metabolic syndrome. Later, the same group compared risk factors associated with the metabolic syndrome in women with and without estrogen replacement therapy [116]. They found no difference in the percentage classified as having metabolic syndrome between the two groups. However, when the groups were classified with respect to the number of components of the metabolic syndrome, there were a greater percentage of women not taking hormones who had two or more components of the metabolic syndrome [116]. Furthermore, the 20-week exercise training intervention did not improve the overall metabolic syndrome status of either group. It is unclear why these results contrast with those from their larger study as described earlier.

In another study of hypertensive patients with metabolic syndrome, weight reduction by diet alone and diet plus exercise resulted in improvements of the parameters of metabolic syndrome [117]. There were significant reductions in blood pressure, triglyceride levels, HbA1c levels and waist:hip ratio, with significant increases in HDL-cholesterol. However, the exercise training did not confer any added benefit with respect to the metabolic syndrome components. Yet, importantly, these studies were performed in a rural setting, implicating the general applicability of these interventions to sedentary overweight individuals with metabolic syndrome.

Other work might suggest that exercise training may not confer extra benefits in participants with the metabolic syndrome. In one published study of older adults with a baseline prevalence of metabolic syndrome of 42%, approximately 18% of those who participated in a 6-month aerobic training program no longer had metabolic syndrome compared with a somewhat similar 15% of controls [118]. Thus, some of the controls did not differ in their response with respect to metabolic syndrome when compared with those who exercised. However, a small percentage (~8%) of controls developed metabolic syndrome after the control period. Clearly, more research needs to be conducted in well-designed exercise training studies to examine the implications of exercise training on individuals classified as having metabolic syndrome.

Future perspective

Future research could utilize novel exercise strategies or different types of aerobic exercise to gain insight into what type of exercise provides the greatest improvement in insulin sensitivity. Most studies have utilized traditional modes of exercise (treadmill/walking or cycle exercise) but, given the new interest in nontraditional exercise such as pilates and yoga, these types of exercise could be explored. In addition, direct comparisons of aerobic versus resistive training of similar duration in different groups of elderly populations (e.g., frail elderly vs healthy elderly) or in those with chronic conditions (e.g., stroke survivors), are needed to establish their effects on glucose homeostasis. Furthermore, studies of the different types of exercise (aerobic vs resistive), intensity of exercise and duration of training to elicit changes in classification of the metabolic syndrome are warranted. Adopting a physically active lifestyle should be emphasized in individuals with obesity and insulin resistance to reduce cardiovascular events in this population.

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Figure 1. Glucose metabolism in women athletes and healthy controls

(A) Second-phase (10–60 min) insulin response to hyperglycemia (~11 mmol/l) in the athlete and control groups. Values are means $\pm$ SE. * $p < 0.001$, 18–29-year-old athletes vs 30–39-, 40–49-, 50–69-year-old athletes. ** $p < 0.01$, 40–50-year-old controls vs 40–49-year-old athletes. (B) Glucose R_d during the hyperinsulinemic–euglycemic clamp (R_d 180–240 min) in the athlete and control groups. Values are means $\pm$ SE. * $p < 0.005$, 40–49-year-old athletes vs 40–50-year-old controls.

Data taken from [119].

Figure 2. Nonoxidative and oxidative glucose disposal ($\mu\text{M/kg}_{\text{FFM}}/\text{min}$) in the aerobic ($n = 9$) and resistive ($n = 13$) groups during $480 \text{ pmol/m}^2/\text{min}$ at baseline and after 6 months of exercise training (mean $\pm$ standard error of the mean)

* $p < 0.05$, pre- vs post-exercise).

AEX: Aerobic; RT: Resistive.

Data taken from [120].