

Resistance Training in the Treatment of Diabetes and Obesity

MECHANISMS AND OUTCOMES

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■ Resistance exercise training (RET) is gaining broad acceptance as a complement to endurance exercise in the treatment of cardiovascular risk factors. This article reviews the most current and reliable literature regarding the biological mechanisms and potential clinical effectiveness of RET in the treatment of 2 major cardiovascular risk factors, diabetes and obesity, obtained from human subject studies found by querying MEDLINE Plus/Ovid literature search system for the years 1950–2008. RET appears to enhance insulin sensitivity and improve glucose tolerance in a wide range of study groups. In addition, studies have shown that improved glucose uptake is not a mere consequence of the typical increase in fat-free mass associated with RET but is likely a result of qualitative changes in resistance-trained muscle. There is also substantial evidence that regular RET can effectively alter body composition in both men and women. It has been shown to increase total fat-free mass, muscular strength, and resting metabolic rate, and preferentially mobilize the visceral and subcutaneous adipose tissue in the abdominal region. The studies presented in this review demonstrate that RET should remain an important focus of translational research, where clinical trials of RET encourage the performance of mechanistic studies and where mechanistic studies lead to further clinical trials.

K E Y W O R D S

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Cardiovascular disease is the leading cause of death worldwide for both men and women. According to the World Health Organization, it is now responsible for approximately 17.5 million deaths annually, accounting for 30% of global deaths.¹ Although most forms of cardiovascular disease are potentially life threatening, some are reasonably preventable and treatable by managing risk factors with diet, exercise, cardioprotective drugs, and the cessation of smoking. Nonetheless, the prevalence of 2 important risk factors, obesity and diabetes, is increasing in the United States² and throughout the developed and developing world.^{3,4} The benefits of endurance exercise training (EET), also known as aerobic exercise training, in reducing the risks of cardiovascular disease, including diabetes and obesity, have been well documented for decades.⁵ However, the effectiveness of resistance exercise training (RET), also known as strength, or

weight training, in reducing cardiovascular risk factors remains less certain.

The American Heart Association, the American College of Sports Medicine, and the American Association of Cardiovascular and Pulmonary Rehabilitation now recommend RET as part of a comprehensive exercise program designed for the prevention of cardiovascular disease in individuals at high risk and the rehabilitation of those with established heart disease.^{5–8} While these recommendations are primarily based on the effects of RET on muscular strength, they do acknowledge emerging data that suggest beneficial effects of RET in modifying cardiovascular risk factors and emphasize that this mode of exercise warrants further investigation. Therefore, this article will review the most current and reliable literature to evaluate the biological mechanisms and potential clinical effectiveness of RET in the treatment

of 2 major cardiovascular risk factors, diabetes and obesity.

METHODS

The studies included for this review were obtained by evaluating human-subject studies found by querying MEDLINE Plus/Ovid literature search system for the years 1950–2008 by using the key words *resistance exercise, resistance training, weightlifting, weight training, strength training, cardiovascular risk, cardiovascular rehabilitation, cardiovascular disease, obesity, hypertension, dyslipidemia, insulin resistance, diabetes*, and by cross-referencing.

Insulin Resistance, Glucose Intolerance, and Diabetes

Abnormalities in glucose metabolism such as insulin resistance, glucose intolerance, and diabetes mellitus are central features of the metabolic syndrome and generally arise when there is limited availability of insulin or impaired response to available insulin. The elevated blood glucose levels and increased levels of glycated hemoglobin observed with these disorders are known to increase the risk of microvascular and macrovascular complications that can cause a variety of other health issues, from hypertension and blindness to kidney failure and heart disease.^{9,10} The importance of maintaining low blood glucose levels is further evidenced by the findings of Khaw et al,¹¹ which estimate that a 1-unit (ie, 1%) increase in glycated hemoglobin (HbA_{1c}) among study subjects with HbA_{1c} values 5% to 6.9% is associated with a 28% increase in the risk of death independent of age, blood pressure, serum cholesterol, and body mass index (BMI).

The vast majority of studies on the effect of exercise training on glucose regulation have used EET as the exercise modality of choice in their methods. Several of these studies have shown that EET can improve insulin-stimulated glucose uptake 2- to 3-fold in skeletal muscle¹² and that increased daily physical activity can improve insulin sensitivity and glucose tolerance as well as prevent the onset of type 2 diabetes in subjects,^{13,14} regardless of whether or not the subjects were obese or had impaired glucose tolerance at baseline.¹⁵ Several of the adaptations that are responsible for improvements in glucose regulation seen after EET include increases in capillary density, glucose transporter isoform 4 (GLUT-4) content, protein kinase B content, and glycogen synthase activity; a shift from low-oxidative type 2b muscle fibers to moderate-oxidative, more insulin-sensitive type 2a muscle fibers; possible changes in the phospholipid composition of the sarcolemma; and increas-

es in oxidative and nonoxidative enzymatic activity.^{12,16–19} GLUT-4 is an insulin-sensitive glucose transporter abundant in skeletal muscle and adipose tissue. Many GLUT-4 proteins are located in intracellular vesicles that attach to the cell membrane when insulin binds to the insulin receptor.²⁰ The content of GLUT-4 has also been shown to increase linearly with contractile stimuli alone in the absence of insulin.^{21–23} Glycogen synthase is the enzyme responsible for catalyzing the $\alpha(1\rightarrow4)$ linkage in the formation of glycogen. Protein kinase B is a kinase involved in the insulin-signaling pathway to glycogen synthase. It may also be important to the regulation of insulin-mediated GLUT-4 translocation from intracellular vesicles to the cell surface.¹⁷

Resistance exercise training has also been shown to produce improvements in glucose regulation similar to those seen with EET. Although there is little scientific evidence that RET alone prevents type 2 diabetes,^{9,24} resistance exercise training has been shown to enhance insulin action in skeletal muscle,^{17,24–26} improve glucose tolerance,²⁶ and decrease glycated hemoglobin concentrations.^{9,27} What remains uncertain is whether the mechanisms by which RET improves glucose regulation are the same as those that affect an improvement after EET. Because certain RET regimens can promote significant skeletal muscle growth and because body sensitivity to insulin is directly proportional to muscle mass and inversely related to adiposity, several studies have attributed the increased glucose uptake observed after RET solely to the increase in muscle mass.^{28,29} In an effort to adjust for this increase in muscle mass and uncover any qualitative changes in resistance-trained muscle, several subsequent studies have expressed their data relative to fat-free mass (FFM).^{12,17,24,30} Results from these studies have shown that insulin-stimulated whole-body glucose uptake does increase with RET, even when differences in fat mass (FM) are taken into account, or where there is no variation in body composition between study groups.^{12,24,30,31} These prospective RET studies involved healthy subjects,^{12,17,25,26,30} subjects with impaired glucose tolerance,³² subjects with type 1 diabetes mellitus,²⁷ and subjects with type 2 diabetes mellitus.^{17,24} Using various methods and techniques, they looked for RET-induced changes in blood flow, capillary density, plasma insulin levels, glucose uptake, as well as the content and/or activity of GLUT-4, glycogen synthase, protein kinase B, and insulin receptor. The findings of these studies are summarized in Table 1.

Holten et al¹⁷ recruited 10 type 2 diabetic subjects and 7 healthy men and had them resistance train one leg at no more than 20% 1-RM (where 1-RM is the maximum load that an individual can lift once) for

Table 1 • SUMMARY OF THE EFFECTS OF VARIOUS RESISTANCE EXERCISE TRAINING REGIMENS ON MEASURES OF INSULIN RESISTANCE AND GLUCOSE INTOLERANCE

Reference	Intervention	Frequency and duration of training	Outcome
Derave et al ²⁶	Initially 3 sets of 12 reps of single-leg knee extensions (75% 1-RM load), progressing to 5 sets of 12 reps (85% 1-RM load)	2-wk immobilization, followed by RET every other day for 6 wk	GLUT-4 content increased significantly in groups supplemented with creatine (24%) and creatine + protein (33%). Glucose tolerance in group supplemented with creatine ± protein improved a significant 25% (area under glucose curve during OGTT decreased from 232 ± 23 to 170 ± 23 mmol/L/min)
Durak et al ²⁷	3–7 sets of 12 reps for 10 upper-body and 5 lower-body exercises performed with a 12-RM load	3 d/wk for 10 wk	Significant decrease in percentage of glycated hemoglobin (6.9% ± 1.4% to 5.8% ± 0.9%) in training group
Holten et al ¹⁷	During wk 1–2, 3 sets of 10 reps for each of 3 different leg exercises (50% 1-RM load). During wk 3–6, 4 sets of 8–12 reps for each of 3 different leg exercises (70%–80% 1-RM load)	3 d/wk for 6 wk	Trained type II diabetics exhibited significant increase in protein content of GLUT-4 (40%), IR (21% ± 6%), PKB (12% ± 7%), and GS (13% ± 5%), as well as in the total activity of GS (21% ± 4%). Trained healthy controls exhibited significant increases in protein content of IR (19% ± 7%), PKB (22% ± 9%), and GS (12% ± 9%), as well as in the total activity of GS (9% ± 3%)
Ishii et al ²⁴	2 sets of 10–20 reps for 6 upper-body and 3 lower-body exercises (40%–50% 1-RM load)	5 d/wk for 4–6 wk	Significant 48% increase in glucose disposal rate in training group (6.85 ± 1.8 to 10.12 ± 3.15 mg/kg lean body mass-per min)
Tabata et al ²⁵	30 isometric maximal voluntary contractions lasting 3 seconds each, utilizing extensor muscles of the ankle, knee, and hip	Daily for 19 d	Significant 30% increase in GLUT-4 content in training group (510 ± 158 to 663 ± 189 counts/min/μg membrane protein)
Andersen et al ¹²	4–5 sets of 6–15 reps of 4 lower-body and several upper-body exercises using heavy resistance, followed by 90-d detraining	3 d/wk for 90 d, followed by 90-d detraining	Significant decrease (11% ± 4%) in whole-body glucose uptake from the end of training period to the end of detraining
Miller et al ³⁰	1 set of 15 reps for 9 upper-body and 5 lower-body exercises (90% 3-RM load) followed by second set of lower-body exercises	3 d/wk for 16 wk	After training, significant reductions were observed in fasting plasma insulin levels (85 ± 25 to 55 ± 10 pmol/L) and insulin levels during OGTT ($F = 4.9$, $P < .05$). Glucose infusion rates during clamp testing also increase after training by 24% during low insulin infusion and 22% during high insulin infusion. Nonoxidative glucose metabolism also increased by 40% during high insulin infusion
Zachwieja et al ³¹	4 sets of 4–10 reps for 6 upper-body and 3 lower-body exercises (75%–90% 1-RM load)	4 d/wk for 16 wk, sessions alternated between upper- and lower-body exercises	Glucose disappearance rate improved significantly from 3.0 ± 0.3 to 4.0 ± 0.4 mg/100 mL/min, and insulin sensitivity trended toward a significant improvement (6.79 ± 1.14 to 8.42 ± 0.89 = 10 ⁴ per min/[μU/mL], $P = .06$)

Abbreviations: GLUT-4, glucose transporter isoform 4; GS, glycogen synthase; IR, insulin receptor; OGTT, oral glucose tolerance test; PKB, protein kinase B; reps, repetitions; RET, resistance exercise training; RM, repetition maximum.

30 minutes 3 times per week for 6 weeks, while the other leg remained untrained. After the RET period, muscle biopsies were taken, and a hyperinsulinemic-euglycemic clamp combined with arteriofemoral venous catheterization of both legs was carried out. Biopsy results showed an increase in the protein content of GLUT-4, glycogen synthase, protein kinase B, and insulin receptor, as well as an increase in glycogen synthase activity, in the trained legs of both the diabetic and healthy subjects, suggesting that RET may exert an effect on the synthesis of proteins involved further downstream in the insulin-signaling pathway. Capillary density, measured as the number of capillaries per millimeter squared of muscle, was unchanged in the trained and untrained legs of both groups. This finding, in conjunction with the observation that arteriovenous glucose extraction during the clamp did not decrease as leg blood flow increased, suggests an increased capacity for glucose uptake that cannot be attributed solely to an increase in muscle mass. Thus, these observed changes in glucose tolerance may be due to qualitative changes in trained muscle.¹⁷

Another study by Ishii et al²⁴ enrolled 2 groups of nonobese patients with type 2 diabetes mellitus. One group was assigned to exercise, while the other group remained sedentary. A moderate-intensity, high-volume, whole-body RET protocol was used. The training program consisted of 2 sets of 9 exercises with 10 to 20 repetitions using weight equivalent to 40% to 50% 1-RM. Subjects trained 5 times per week for 4 to 6 weeks. Using the hyperinsulinemic-euglycemic clamp technique, the researchers found a significant increase in the rate of glucose uptake among the subjects in the resistance-trained group. They attributed this change largely to possible changes in muscle fiber type. They postulated that the moderate-intensity, high-volume exercise protocol used in their study may have induced adaptations similar to those seen in EET studies where an increase in the conversion of low-oxidative type 2b fibers to moderate-oxidative type 2a fibers has been observed. Type 2a fibers have a greater capillary density and a higher concentration of GLUT-4, and they exhibit a greater response to insulin than do type 2b fibers.^{18,33}

In a separate study, Tabata et al²⁵ sought to determine the effects of inactivity as well as RET on GLUT-4 content in healthy young men. They randomly assigned 4 subjects to a control group and 5 subjects to a training group. The control group remained in head-down bed rest for 19 days, getting up only every other day to shower. The training group also remained in head-down bed rest for 19 days, getting up daily to perform a protocol of isometric resistance exercises and also every other day to shower. The training protocol consisted of 30 isometric maximal

voluntary contractions lasting 3 seconds each, with no more than 3 seconds rest between each contraction. In total, each training session lasted 3 minutes and involved the recruitment of the extensor muscles of the ankle, knee, and hip. Biopsies of the vastus lateralis were taken before and after the 19 days of head-down bed rest and analyzed for GLUT-4 content. The results showed a significant decrease in GLUT-4 content in the inactive control group and a significant increase in GLUT-4 content in the training group.

In another study that sought to examine the effect of inactivity on glucose metabolism, Andersen et al¹² trained 7 young healthy men 3 times per week for 90 days and then had them return to their everyday lifestyle with no sports activities, EET, or RET for 90 days. The training protocol included 4 to 5 sets of each of the following resistance exercises: hack squat, incline leg press, knee extensions, and hamstring curl. Each set ranged from 6 to 15 repetitions with 2 to 3 minutes rest between each 2 sets. The number of repetitions gradually decreased as resistance was progressively increased over the 90-day training period. Biopsies of the vastus lateralis were taken, and hyperinsulinemic-euglycemic clamps combined with arteriovenous catheterization of the right leg were carried out after 90 days of heavy RET and again after 90 days of de-training. Although analysis of the muscle biopsies did not show significant changes in capillary density or the mRNA content of GLUT-4, glycolytic, lipolytic, or glyconeogenic enzymes, the hyperinsulinemic-euglycemic clamp data revealed an 11% decrease in whole-body glucose uptake after the 90-day detraining period. Indirect calorimetric calculations suggested that the differences in glucose uptake rates were likely due to a decrease in cellular nonoxidative glucose metabolism (or anaerobic glycolysis) after detraining. Using magnetic resonance imaging to measure midthigh muscle mass, measures of insulin-mediated glucose uptake rates were calculated per unit of skeletal muscle. No significant correlation was found between leg glucose uptake rates and changes in muscle mass, providing further evidence that the effect of RET cannot be attributed solely to an increase in FFM.

Despite the lack of conclusive evidence to confirm that RET prevents type 2 diabetes, the fact that RET appears to improve insulin sensitivity and glucose tolerance is very encouraging. In addition to decreasing blood glucose and glycated hemoglobin levels, improvements in insulin sensitivity and glucose tolerance should reduce the amount of insulin necessary to achieve the clearance of any given amount of glucose. Because insulin has an inhibitory effect on β -oxidation, the elevated levels of insulin seen with insulin resistance may limit the utilization of fat stores

and promote weight gain or make weight loss more difficult. Thus, improving insulin sensitivity should allow for a more balanced utilization of both glucose and fatty acids as energy. It should be noted, however, that Holten et al¹⁷ found higher concentrations of free fatty acids in type 2 diabetic subjects than in normal controls. They therefore postulated that insulin resistance may also impair the normal inhibitory response that insulin exerts on fat metabolism.

Nonetheless, the studies detailed above and those listed in Table 1 support previous findings that RET does have a positive effect on glucose metabolism. In addition, several of these studies suggest that RET can elicit these metabolic benefits with low-to-moderate-intensity, low-volume protocols. This has potential advantage for engaging sedentary individuals, who might otherwise be reluctant to participate in more strenuous activities such as EET or high-intensity RET. Moreover, the benefits induced by RET begin to manifest themselves within a short period of time. This observation may serve as another incentive for these individuals to initiate and maintain such programs. Finally, it seems reasonable that untrained, obese, and frail individuals would be less likely to sustain injuries while performing a low-to-moderate-intensity, low-volume RET program than they would while performing a high-intensity, high-volume RET or EET program.

Obesity

Obesity is an important risk factor for the development of cardiovascular disease. The relationship between obesity and cardiovascular disease in both men and women has been well documented since the mid-1980s.³⁴ Nevertheless, over the past several decades, obesity has grown to be a serious public health epidemic in the United States, and it is now estimated that roughly 65% to 66% of adult Americans aged 20 to 74 years are overweight (BMI \geq 25) and 30% to 32% are obese (BMI \geq 30). This reflects an increase of 75% since 1991.³⁵⁻³⁷ Data from the National Health and Nutrition Examination Survey also reveal that nearly 32% of American children and adolescents aged 2 to 19 are at or above the 85th percentile on the 2000 sex-specific Centers for Disease Control and Prevention BMI-for-age growth chart, perhaps foretelling that this problem is likely to continue into the next generation.³⁸ This astonishing rise in the number of overweight and obese Americans can be attributed to a variety of hormonal, behavioral, and environmental factors. However, the most prevalent reasons for this trend appear to be advancing age of the population as a whole, diets high in fat and calories, and a sedentary lifestyle. Regardless of the cause, weight gain from the storage of excess adipose tissue is most directly a consequence of a positive

energy balance created by a disproportion between the number of calories consumed and the number of calories expended during a certain time frame.

The physical and metabolic changes that typically occur during the normal aging process generally result in the diminution of FFM (ie, bone mass, skeletal muscle mass, and body water), resting metabolic rate (RMR), and the ability to maintain whole-body energy balance. Without appropriate dietary and lifestyle adjustments, these alterations can lead to further accumulation of excess adipose tissue and to further losses of FFM.^{39,40} Excess adipose tissue, in particular abdominal and visceral adipose tissue (VAT), has been linked to the development of the metabolic syndrome and several of its characteristic disorders including hypertension, insulin resistance, glucose intolerance, diabetes mellitus, and dyslipidemia.^{9,41} In contrast, excess adiposity in the periphery does not appear to increase the risk of developing cardiovascular disease.^{42,43} VAT is thought to alter normal plasma concentrations of glucose, insulin, lipids, and lipoproteins by decreasing insulin-receptor sensitivity and promoting the secretion of free fatty acids.^{34,44} The resultant abnormal concentrations then contribute to the development of atherosclerosis and higher rates of diabetes mellitus, ischemic heart disease, and stroke.⁴⁴

Fortunately, weight loss in obese individuals has been shown to improve or prevent many of the aforementioned conditions and also improve left ventricular diastolic function.^{36,45} Furthermore, these beneficial modifications begin to manifest with as little as a 5% drop in body weight, and they continue to improve with further weight loss.³⁶ Thus, the identification of feasible and effective interventions to prevent and reverse the accumulation of abdominal adipose tissue and VAT associated with aging, diets high in fat, and a sedentary lifestyle would likely have a very positive impact in preventing cardiovascular disease in the short and long terms.

Calorie restriction diets have long been accepted as effective means for inducing weight loss. However, when employed as a sole intervention, calorie restriction diets have been shown to reduce RMR by as much as 30%, decrease FFM, and actually contribute to gains in adipose tissue subsequent to the intervention.^{34,46} Therefore, to achieve lasting results, it is essential that an intervention include a component that addresses the need to increase or maintain RMR and FFM.^{47,48} Because lean skeletal muscle is known to have an average daily resting energy expenditure of approximately 17.6 kcal/kg and because some types of RET are known to produce substantial increases in lean skeletal muscle, it has been suggested that RET can be utilized as a means to increase or at least maintain RMR and FFM, thereby helping to

slow, stop, or reverse gains in adipose tissue in an aging and sedentary population.^{40,49,50} Several studies have examined the effects of RET on body composition and RMR and have found that RET does in fact promote increases in both FFM and RMR, as well as decreases in total FM (Table 2).^{34,39,42,51-53}

In one such study, Treuth et al⁴² recruited 22 healthy untrained men averaging 60 ± 4 years of age and separated 13 into an exercise group and 9 into a control group. The exercise group performed a RET protocol consisting of 2 abdominal, 7 upper-body, and 5 lower-body exercises on 3 nonconsecutive days per week for 16 weeks. After the completion of 1 set of 15 repetitions at 90% 3-RM for each exercise, each lower-body exercise was repeated in a second set. Using dual-energy x-ray absorptiometry and magnetic resonance imaging, researchers found significant increases in total FFM and significant decreases in total FM. They also observed significant regional increases in the FFM of the arms, legs, and trunk, as well as a corresponding significant decrease in the FM of the same regions. They also measured significant increases in upper- and lower-body strength, significant increases in mid thigh muscle cross-sectional area, and significant decreases in mid thigh fat. None of the measured variables changed significantly in the control group. In a subsequent study, these investigators recruited 14 healthy older women, averaging 67 ± 1 years of age, to perform a whole-body RET routine for 1 hour, 3 times per week for 16 weeks. The routine consisted of 2 sets of 12 repetitions for 1 abdominal, 6 upper-body, and 5 lower-body exercises performed initially at 50% 1-RM and increased to 67% 1-RM by the end of the intervention period. Total body composition and regional body composition were measured before and after the intervention period by hydrodensitometry and computed tomography. After 16 weeks of RET, researchers found significant reductions in VAT, the VAT-to-subcutaneous adipose tissue (SAT) ratio, and mid thigh SAT, as well as a significant increase in mid thigh muscle.³⁹

In another study, Ross and Rissanen⁵¹ investigated the effects of a calorie-restriction diet in combination with either EET or RET on the distribution of adipose tissue in 24 obese women. Ten women completed the diet and EET protocol, while 14 completed the diet and RET protocol. The EET protocol involved 15 minutes, which progressively increased to 60 minutes, of any combination of stationary cycling, treadmill walking, and stair-stepping at 50% to 85% maximum heart rate 5 days per week for 16 weeks. The RET protocol involved 1 set of 8 to 12 repetitions completed to exhaustion for 1 abdomi-

nal, 5 upper-body, and 2 lower-body exercises performed 3 days per week for 16 weeks. Using magnetic resonance imaging, researchers found similar reductions between the 2 groups in body weight, SAT, VAT, and the ratio of VAT to SAT. Further comparisons of the regional mobilization of SAT and VAT also revealed similar reductions in the arms, torso, abdomen, and lower body, with preferential mobilization in the abdominal region. Finally, significant reductions were recorded for both intraperitoneal and extraperitoneal VAT in both groups.

In a subsequent study designed to isolate the effects of EET and RET from the effects of the calorie-restriction diet, Ross et al³⁴ randomized 33 obese men evenly into a diet-only group, a diet plus EET group, or a diet plus RET group. Both the EET and RET protocols were identical to those of the preceding study except for the addition of 1 chest exercise to the RET protocol in the newer study. Measurements of body composition were again taken by magnetic resonance imaging. Results were similar among the study groups. All groups demonstrated significant reductions in body weight, SAT, and VAT. Furthermore, the relative reduction of VAT was larger than that of SAT. For both exercise groups, losses in abdominal SAT were greater than losses in gluteal-femoral SAT. Reductions in VAT were uniform across all 3 groups. Interestingly, lean tissue and skeletal muscle decreased in the upper- and lower-body regions of the diet-only group, while muscular strength increased in the RET group and peak O_2 uptake increased in the EET group.

Overall, the findings of these studies offer strong support for the use of RET as a means to reduce total and regional adipose tissue, as well as increase FFM, and hence RMR. The results from the 2 Ross et al studies^{34,51} also suggest a potential for low-volume, high-intensity RET protocols to achieve reductions in total and regional adipose tissue comparable to those achieved by high-volume, high-intensity EET protocols when used in conjunction with a calorie-restriction diet; however, this observation requires confirmation by additional studies. In addition to the aforementioned benefits of RET on obesity, a study by Ades et al⁵⁴ demonstrated that the gains in muscular strength from a 12-week RET program can significantly improve submaximal walking time in healthy elderly individuals by as much as 38%. So in addition to increasing RMR, increases in muscular mass and strength can contribute to longer EET sessions, thereby allowing for greater calorie expenditure and further promoting weight loss and weight maintenance in those engaged in comprehensive programs involving both RET and EET.

Table 2 • SUMMARY OF THE EFFECTS OF VARIOUS RESISTANCE EXERCISE TRAINING REGIMENS ON OBESITY

Reference	Intervention	Frequency and duration of training	Outcome
Truth et al ⁴²	1 set of 15 reps performed to exhaustion for 9 upper-body and 5 lower-body exercises, then each lower-body exercise repeated in a second set. Resistance started at 90% 3-RM and was gradually decreased to achieve 15 reps	3 nonconsecutive d/wk for 16 wk	Significant increases in upper-body strength (39% ± 8%), lower-body strength (42% ± 14%), total FFM (62.0 ± 7.1 to 64 ± 7.2 kg), FFM in arms (6.045 ± 0.860 to 6.418 ± 0.803 kg), legs (19.416 ± 2.228 to 20.131 ± 2.303 kg), and trunk (29.229 ± 4.108 to 30.134 ± 4.184 kg), and midhigh muscle cross-sectional area (161 ± 19 to 172 ± 18 cm ²). Statistically significant decreases in total FM (23.8 ± 6.7 to 21.8 ± 6.0 kg), FM in arms (2.383 ± 0.830 to 2.128 ± 0.714 kg), legs (7.583 ± 1.675 to 6.945 ± 1.551 kg), and trunk (12.216 ± 4.143 to 11.281 ± 3.653 kg), and midhigh fat (65 ± 19 to 59 ± 17 cm ²)
Truth et al ³⁹	2 sets of 12 reps performed at 50%–67% 1-RM for 7 upper-body and 5 lower-body exercises	1 h, 3 d/wk for 16 wk	Significant increases in upper-body strength (51%), lower-body strength (65%), and midhigh muscle (52.9 ± 2.6 to 58.0 ± 2.0 cm ²). Significant decreases in VAT (143.9 ± 13.3 to 130.0 ± 12.4 cm ²), the ratio of VAT/SAT (0.48 ± 0.04 to 0.44 ± 0.04), and midhigh SAT (141.7 ± 11.5 to 133.6 ± 10.8 cm ²)
Ross and Rissanen ⁵¹	Diet + EET: 15–60 min stationary cycle, treadmill, and/or stair-stepper at 50%–85% maximum heart rate. Diet + RET: 1 set of 8–12 reps performed to exhaustion for 6 upper-body and 2 lower-body exercises	Diet + EET: 5 d/wk for 16 wk. Diet + RET: 3 d/wk for 16 wk	Diet + EET produced significant reductions in body weight (−10.9 ± 2.7 kg or 11.4%), total SAT (−9.2 ± 2.4 L or 22.6%), VAT (−1.1 ± 0.50 L or 34.4%), intraperitoneal VAT (−0.89 ± 0.42 L or 34.2%), extraperitoneal VAT (−0.22 ± 0.13 L or 33.8%), and the ratio of VAT/SAT (−0.01 ± 0.01 or 12.5%). Diet + RET produced significant reductions in body weight (−10.1 ± 3.0 kg or 11.7%), total SAT (−8.5 ± 2.5 L or 22.6%), VAT (−0.69 ± 0.40 L or 30.0%), intraperitoneal VAT (−0.57 ± 0.34 L or 31.6%), extraperitoneal VAT (−0.10 ± 0.09 L or 20.8%), and the ratio of VAT/SAT (−0.01 ± 0.01 or 16.6%)
Ross et al ³⁴	Diet + EET: 15–60 min on stationary cycle, treadmill, and/or stair-stepper. Diet + RET: 1 set of 8–12 reps performed to exhaustion for 7 upper-body and 2 lower-body exercises. Diet only	Diet + EET: 5 d/wk for 16 wk. Diet + RET: 3 d/wk for 16 wk. Diet only: 16 wk	Diet + EET produced significant reductions in body weight (−11.6 ± 3.7 kg or 11.4%), SAT (+5.9 ± 2.8 L or 22.1%), VAT (−1.8 ± 1.0 L or 39.4%), and the ratio of VAT/SAT. Diet + RET produced significant reductions in body weight (−13.2 ± 4.1 kg or 12.3%), SAT (−8.0 ± 2.8 L or 25.7%), VAT (−1.4 ± 0.7 L or 40.4%), and the ratio of VAT/SAT. Diet only produced significant reductions in body weight (−11.4 ± 3.5 kg or 11.5%), SAT (−6.5 ± 2.1 L or 23.7%), VAT (−1.5 ± 0.8 L or 31.7%), and the ratio of VAT/SAT. Significant increases were observed in muscular strength in the RET group (~20%) and in peak O ₂ uptake in the EET group (~14%). For the EET and RET groups, losses in abdominal SAT (~27%) exceeded losses in gluteal-femoral SAT (~20%). Total lean tissue and skeletal muscle decreased significantly in the diet only group

Abbreviations: EET, endurance exercise training; FFM, fat-free mass; FM, fat mass; reps, repetitions; RET, resistance exercise training; RM, repetition maximum; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue.

SUMMARY

The effectiveness of RET in reducing cardiovascular risk will likely depend on many variables including age, sex, race, cardiovascular history, current risk levels, and the type of RET regimen employed. Because of the relatively small number of well-controlled interventional studies that examine the benefits of RET, as well as the large variation in study design among the studies that do exist, it is not possible to broadly extrapolate all of the positive outcomes observed. Nonetheless, it is worthwhile to reiterate the effects of RET on glucose intolerance and obesity. RET appears to enhance insulin sensitivity and improve glucose tolerance in a wide range of study groups. In addition, studies have shown that improved glucose uptake is not a mere consequence of the typical increase in FFM associated with RET, but is likely a result of qualitative changes in resistance-trained muscle. There is also substantial evidence that regular RET can effectively alter body composition in both men and women. It has been shown to increase total FFM, muscular strength, and RMR, as well as reduce total FM with the preferential mobilization of VAT and SAT in the abdominal region. Notably, these reductions have been observed with and without calorie-restriction diets.

While these studies answer many questions, they also serve to demonstrate wide gaps in our understanding of RET. Hence, they provide an important stimulus for many future studies that need to be done. Examples of such studies might include (1) a focus on whether a single standardized RET regimen can provide optimal benefits in glucose tolerance, weight loss, and muscular strength or whether a variety of customized RET regimens are needed to meet the desired effects in a given patient; (2) studies that evaluate the amount of RET needed to increase FFM in a given patient and whether this differs with age, gender, race/ethnicity, anthropomorphic, and other characteristics including genotype, an example of such a study being the one that would assess the effect of higher-intensity (80% 1-RM), moderate-volume RET compared with lower-intensity (40%–60% 1-RM), moderate-volume RET, after an 8-week introductory period of lower-intensity RET to allow for early adaptations; (3) studies that evaluate how to perform RET in patients with morbid obesity who are limited by orthopedic, respiratory, and other comorbidities; and (4) studies that evaluate whether RET alone can prevent or delay the onset of diabetes in patients at high risk for this disease. Importantly, what is clearly needed is a standard for defining the volume of RET performed such that outcomes can be assessed relative to

this measure. Finally, the studies presented in this review demonstrate that RET should remain an important focus of translational research where clinical trials of RET encourage the performance of mechanistic studies and where mechanistic studies lead to further clinical trials.

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