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Effects of single bout resistance exercise on glucose levels, insulin action, and cardiovascular risk in type 2 diabetes: A narrative review

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ABSTRACT

Aims: Previous studies have reported beneficial effects of chronic resistance exercise in the prevention and treatment of type 2 diabetes. To clarify potential modulators of acute responses to resistance exercise, we reviewed the literature to determine the effects of a single bout of resistance exercise on cardiometabolic risk factors in type 2 diabetes.
Methods: Pubmed and Embase were searched for studies investigating the effects of single bouts of resistance exercise on glucose and insulin levels, and cardiovascular disease risk in people with diabetes. Fourteen reports were identified and reviewed to formulate evidence-based resistance exercise prescription recommendations.
Results: Glucose and insulin levels appear to decrease with resistance exercise with effects lasting up to 24 and 18 h, respectively. Bouts of resistance exercise may outperform aerobic exercise in reducing ambulatory blood pressure, with effects lasting up to 24 h. Moreover, resistance exercise after rather than before a meal may be more effective in reducing glucose, insulin, and triacylglycerol levels. However, reducing injectable insulin dosage prior to resistance exercise may blunt its favorable effects on glucose levels.
Conclusions: This review suggests that a single bout of resistance exercise may be effective for acutely improving cardiometabolic markers in people with diabetes.

1. Introduction

Diabetes is associated with an increased risk of cardiovascular disease (CVD) morbidity and mortality.[1] In 2015, diabetes prevalence in the U.S. was estimated at 9.4% of the population, with up to 95% being type 2 diabetes (T2D).[2] T2D is associated with pathological changes to the cardiovascular system including micro- and macrovascular abnormalities.[3] Microvascular complications involve damaged capillaries which reduce glucose and insulin delivery to skeletal muscle, thereby impairing glucose uptake. Macrovascular damage affects the larger blood vessels, and is manifested through impaired endothelial function, increased arterial stiffness, elevated resting blood pressure (BP), abnormal blood-lipid profiles, reduced oxygen delivery to tissues, and, oftentimes, resulting myocardial ischemia.

Regular aerobic exercise (AE),[4,5] resistance exercise (RE),[4–6] or combinations[5,7,8] thereof, are effective interventions to prevent or delay many of the macrovascular complications of T2D such as myocardial and cerebral infarction,[9] through beneficial effects on glucose levels,[4,7] insulin sensitivity/resistance,[7] and CVD risk factors including blood lipids/lipoproteins,[5] BP,[6] and endothelial function.[8] Although the effects of AE and RE on T2D are overwhelmingly beneficial,[4,5,7,8,10] previous research has primarily focused on AE,[4] which is characterized by sustained, dynamic large muscle group activity such as walking, running, cycling and swimming. In contrast, RE involves contraction of skeletal muscles against an external resistance to increase muscular strength, endurance, and power, using either one's body weight, free weights, machine weights, kettlebells, and/or resistance bands. As a physiological stimulus, RE differs from AE in several ways. RE involves lower energy expenditure and predominantly anaerobic energy metabolism, without sustained skeletal muscle contractions or the need for adequate oxygenation of working muscles over time.[11] In the presence of peripheral arterial disease and/or CVD, musculoskeletal dysfunction is common in those with T2D due to vascular complications and contributes to the associated reduced exercise tolerance.[12] Since RE typically involves intermittent, brief work/rest bouts, it is often better tolerated than continuous AE in individuals with T2D.[12]

Single bouts of AE and RE each evoke acute metabolic and cardiovascular responses.[13] When these exercise bouts are repeated over time, physiological and metabolic responses become more pronounced with

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each subsequent exercise bout, chronic adaptations occur, and this is known as the training effect.[13] To achieve a training effect, the minimum duration for clinically meaningful reduction when using AE is 4 weeks for BP,[14] and, when using AE or RE, is 6 weeks for blood lipids,[15,16] and 8–10 weeks for insulin sensitivity[17,18] and glycemic control.[17,18] Clarifying the relationship between acute and chronic effects of AE and RE has implications for prescribing exercise frequency. Reports on the chronic effects of RE in T2D suggest that it is comparable to AE for improving insulin resistance,[19] glycemic control,[20] BP,[21] and blood lipids,[21] and superior to AE for enhancing muscle strength, endurance, and morphology,[6,20] and basal metabolic rate.[22] However, it is important to consider the effects of a single bout of RE when tailoring exercise prescriptions to individuals with T2D, specifically in relation to optimal reduction of glucose and insulin levels, and CVD risk. Clinically relevant investigations can provide information on when to exercise relative to meal timing, modifying insulin doses prior to RE, age, sex, race/ethnicity modulators, and body habitus differences in response to RE, as well as the most effective program characteristics (e.g., intensity and sets) to optimize these outcomes. These studies could be used to favorably modify the design of longer training studies and, in turn, better inform clinicians and patients on specific, individualized guidelines for RE in those with T2D.

When prescribing RE to individuals with T2D, medication use should be considered. In addition to antihyperglycemic medications, it is common for antihypertensive drugs and statins to be prescribed in T2D.[23,24] Certain antihyperglycemic diabetes medications may cause hypoglycemia during or after exercise.[25] Although many of the commonly prescribed diabetes medications such as metformin, glucagon-like peptide-1 (GLP-1) analogs, and sodium glucose cotransporter 2 (SGLT-2) inhibitors, carry a low risk for inducing hypoglycemia, others, including sulfonylureas and exogenous insulin, are more likely to result in hypoglycemia when taken 1–2 h before engaging in AE. Insulin therapy is often initiated in later stages of T2D, but can be effective for achieving glycemic control during any stage of the disease.[26] Given the current use of insulin therapy in T2D treatment and the high risk of exercise-induced hypoglycemia, there remains the need for additional investigations regarding the effects of reduced insulin dosage prior to RE. The combination of exercise with other common T2D medications may also have deleterious effects. For example, SGLT-2 may increase fasting blood glucose and attenuate increases in insulin sensitivity following AE in overweight and obese participants[27]; β-blockers, a hypertensive medication, may decrease fatty acid metabolism during AE[24]; and metformin when combined with AE may attenuate beneficial exercise effects on glucose regulation, insulin sensitivity, BP, inflammation, and non-esterified fatty acids in T2D.[28] Statins when combined with AE and RE or AE alone, however, may potentiate the favorable effects of exercise on insulin sensitivity and inflammation with no additive effect on blood lipids.[23] Furthermore, the effects of combining AE with GLP-1 agonists in T2D are unclear as studies have shown mixed results.[29,30] More studies investigating the effects of combining RT with commonly used T2D medications are warranted.

In the 2010 joint American College of Sports Medicine (ACSM) and American Diabetes Association (ADA) position statement on exercise and T2D,[31] the effects of a single bout of RE in those with T2D on insulin action and glucose levels were not addressed, largely due to the limited relevant data. Similarly, the effects of single bouts of RE on blood lipids were not addressed, although both AE and RE were suggested as effective interventions to lower BP, with AE being slightly more effective. In the 2016 ADA position statement on physical activity/exercise and diabetes,[32] only one study addressed managing injectable insulin dosage prior to a RE bout to prevent hyperglycemia.[33] Given the cardiometabolic and musculoskeletal profiles of individuals with T2D, a better understanding of the effects of a single bout of RE in those with T2D can provide safe and effective exercise prescriptions for this escalating patient population. The present clinical review was undertaken to clarify the effects of a single bout of RE on glucose levels, insulin action, and CVD risk in individuals with T2D.

2. Methods

2.1. Literature search

Pubmed and Embase databases were searched. MeSH keywords for Pubmed included “resistance training” AND “Diabetes Mellitus, Type 2.” For Embase, keywords “resistance training” OR “weight training” AND “type 2 diabetes” were used. Only studies published in English were included, and there was no restriction on date published. Studies investigating glucose levels, insulin action, and CVD risk outcomes of a single RE bout in participants with T2D were included, as were RE studies involving circuit training[34,35] and interval RE.[36] A total of 923 studies were initially identified, duplicates were deleted, and titles, abstracts, and in some cases full-text reports were reviewed to exclude nonrelevant studies. Studies were excluded due to inappropriate study design (e.g., systematic review), stage of disease (e.g., prediabetes), population (e.g., family history of diabetes), no RE condition, or animal studies. A total of 14 studies that met the inclusion criteria are included herein.[33–46]

3. Results and discussion

3.1. Preliminary results

Study participant characteristics are displayed in Supplementary Table 1. Participants included middle-aged and older men and women with T2D who were generally inactive at the time of enrollment. Most were not insulin-dependent,[34–39,41–45] and there was considerable variability (years) since T2D was diagnosed and in baseline glycated hemoglobin (HbA_{1c}) values, a marker of average blood glucose levels. Participants were taking a range of antihyperglycemic, hypertension, and statin medications. RE protocol characteristics and study design also varied substantially and are presented in Table 1 and Supplementary Table 2, respectively.

3.2. Glucose levels during and after RE

Circuit training involves multiple exercise stations that an individual rotates through for specified amounts of time, and is different from conventional RE in that lower intensities, higher repetitions, and shorter rest periods are involved. Single bouts of conventional RE training may lower 24-h interstitial (−10.4%, not using insulin therapy; −12%, using insulin therapy)[47] and postprandial blood glucose (−11% to 30%, during exercise; −14.5%, after exercise)[38,39,42] in those with T2D. This beneficial effect may occur to a greater extent with circuit RE as compared to circuit AE[48] with lower circuit RE intensities (−13.9%) being more effective than moderate intensities (−7.8%) in lowering postprandial blood glucose.[34] However, conflicting results have been reported, and comparative AE versus RE outcomes are presented in Table 2.

Some studies found that single bouts of RE did not affect post-exercise postprandial glucose tolerance,[41,45] whereas others showed that postprandial glucose levels were reduced during RE (−11%)[38] and 12–24 h after a bout of RE (−14.5%).[42] Fig. 1 presents the time course for beneficial effects of cardiometablic risk factors following a single RE bout. Fluckey and colleagues[41] compared the effects of a bout of RE on postprandial glucose tolerance between older adults with T2D and younger healthy controls. Disappointingly, glucose tolerance remained unchanged in those with T2D. In contrast, Fenicchia and associates[42] found that 4-h area under the curve (AUC) integrated postprandial glucose concentration lowered (−14.5%) 12–24 h after a single bout of RE in the T2D group. The disparate findings may be related to differences in the RE protocols used. Fenicchia et al.[42] included three

Table 1
Resistance exercise protocol characteristics.

Study	Intensity (% of 1RM unless otherwise indicated)	Repetitions per set (#)	Sets per exercise (#)	Exercises	Modality (elastic bands, machines, free weights, body weight)	Rest intervals (sec unless otherwise indicated)
Bacchi, 2012	70–80	10–12	3	Major muscle groups, alternating lower body, upper body, and core exercises	Machine and free weights	60 between sets
Fenicchia, 2004	80% of 3RM; to failure	8–12	3	Chest press, shoulder press, lat pull-down, leg curl, leg extension, leg press, triceps extension, bicep curl	Machines and body weight; unclear if bicep curl was free weight	90 between sets
Fluckey, 1994	50, 75, 100% of 10RM	8–10	3	Leg extension, seated leg curl, torso arm, pullover, arm cross, triceps, biceps	Machines	70 between sets, 120 between exercises
Francois, 2016	RPE of 5 "hard"	37 ± 12 reps/min	7	Leg press, leg extension, hamstring curl	Machines, one free weight and ab crunches	60 between sets
Gordon, 2013a	45, 60 and 75	10	3	Bench press, 45-degree leg press, shoulder press, 45-degree calf raises, lat pull-down	Machines and free weights	NR
Gordon, 2013b	70	8–10	3	Bench press, 45-degree leg press, lat pull-down, unilateral leg extension, seated row, and unilateral leg curl	Machines and free weights	60–90 between sets
Gordon, 2016	70	8–10	3	Bench press, 45-degree leg press, lat pull-down, unilateral leg extension, seated row, and unilateral leg curl	Machines and free weights	60–90 between sets
Heden, 2015	50, 100, 100% of 10RM	10	3	Leg press, seated calf raises, seated chest flies, seated back flies, back extensions, shoulder raises, leg curls, and abdominal crunches.	Machines and body weight	60–120 between sets
Heden, 2018	50, 100, 100% of 10RM	10	3	Leg press, seated calf raises, seated chest flies, seated back flies, back extensions, shoulder raises, leg curls, and abdominal crunches	Machines and body weight	60–120 between sets
Kanaley, 2001	80% of 3RM to failure	8–12	3	Leg extension, lat pull-down, leg curl, chest press, leg press, shoulder press, biceps curl, triceps press down and abdominal crunches.	Machines and body weight; unclear if bicep curl was free weight or machine	NR
Morais Junior, 2017	NR; intensity based on heart rate reserve (60–70%)	NR; 40 seconds of work	3	Standing row, sit and stand chair, bench press, deadlift, bicep curl, squat with ball, tricep curl, overhead squat	Theraband, body weight, free weights, gym ball, stick	20 between stations, 60 between sets
Morais, 2011	70	8	3	Leg extensions, bench press, leg press, seated pulley, leg curls, and rowing machine	Machines	60 between sets, 40 between exercises
Moreira, 2012	LI group = 23%; MI group = 43%	LI group = 30; MI group = 16	3	Leg extension, bench press, leg press, lat pull-down, leg curl, and seated row	Machines	LI group = 15–20 between exercises, 120 between sets; MI group = 45–50 between exercises, 120 between sets
Van Dijk, 2012	55%, 65%, 75%, 75% and 75% of 1RM	10	5	Press, lat pull-down, leg curl, and seated row	Machines	120 between sets

RM = repetition maximum; RPE = rating of perceived exertion; NR = not reported; LI = low intensity; MI = moderate intensity; sec = seconds.

sets of 8–12 repetitions to failure, whereas Fluckey et al.[41] included a total of three sets at 50, 75, and 100% of 10 RM each, suggesting that only one set was completed to failure (100% of 10 RM). It may be that having only one set rather than three sets to failure may be insufficient to reduce blood glucose concentrations.[49] Additionally, Fenicchia et al.[42] employed eight RE movements, including four multi-joint (chest press, shoulder press, lat pull-down, and leg press) and four single-joint exercises (leg curl, leg extension, tricep extension, and bicep curl), whereas, Fluckey et al.[41] employed only seven single-joint exercises (Table 1). Multi-joint exercises, such as back squats, involve the movement of more than one joint (i.e., hip, knee, and ankle joints), while single-joint movements, such as leg extensions, involve the movement of a single joint (i.e., knee joint). Given that multi-joint exercises recruit adjoining muscle groups compared to single-joint movements,[50] it appears that more pronounced glucose lowering may result from greater muscle mass and fiber being involved in the exercise.[51]

In single-bout RE studies that employed continuous glucose monitoring (CGM), which uses interstitial rather than venous glucose to assess glucose levels, RE reduced 24-hour interstitial glucose levels (−10.4%, not using insulin therapy; −12%, using insulin therapy),[46] but the effects may have depended on meal timing.[38] Contrasting findings are reported. For example, one investigation found AE reduced postprandial interstitial glucose AUC during (−12%) and after exercise (−30%) compared to control with no change in the RE condition,[43] while another study demonstrated that single bouts of AE or RE similarly reduced hyperglycemia (−35%, RE; −33%, AE) and postprandial interstitial glucose (−10.4%, RE; −10.4%, AE) up to 24 h after exercise.[46] The difference in findings between the two studies may be related to the number of sets employed and the exercises used. The former study used 3 sets of each exercise at intensities between 70 and 80% of 1 RM, but did not specify which exercises were used, whereas, the latter included 5 sets at 55, 65, 75, 75, and 75% of 1RM using primarily multi-joint exercises. In another report, RE performed 45 min after a meal did not

Table 2
Summary of resistance exercise main study findings.

Study	Findings
Bacchi, 2012[a]	*Interstitial glucose during exercise:* RE = no change, AE = decrease *Interstitial glucose during nocturnal period after exercise:* RE = no change, AE = decrease *Interstitial glucose 24 h after exercise:* RE = no change, AE = no change *Hypoglycemia during nocturnal period after exercise:* RE = no change, AE = increase *Hypoglycemia 24 h after exercise:* RE = no change, AE = no change
Fenicchia, 2004	*Integrated glucose concentration after exercise:* RE = decrease 12–24 h, control = no change *Insulin concentrations after exercise:* RE = no change up to 24 h, control = no change up to 24 h
Fluckey, 1994	*Integrated glucose concentration after RE:* T2D = no change, age-matched control = no change, young control = no change; *Insulin concentrations after exercise:* T2D = decreased, age-matched control = no change, young control = decreased
Francois, 2016[a]	*Brachial artery FMD% after RE interval:* T2D = increased immediately, 1 h, and 2 h after RE *Brachial artery FMD% after AE interval:* T2D = unchanged immediately, increased 1 h, and no change 2 h after AE *Absolute FMD after RE interval:* T2D = increased immediately after exercise *Absolute FMD after AE interval:* T2D = no change *Dbase-adjusted FMD after RE interval:* T2D = increased immediately and 1 h after exercise, higher than AE interval at 1 h *MAP after RE interval:* T2D = decreased 1 and 2 h after RE interval *MAP after AE interval:* T2D = unchanged
Gordon, 2013a	*Insulin sensitivity after RE:* T2D = no change 24–78 h
Gordon, 2013b[a]	*Interstitial glucose concentrations after RE:* T2D = increase in glucose AUC in 1st 24 h, decrease from 24 to 72 h to pre-exercise levels *Interstitial glucose concentrations after AE:* T2D = no change *Duration of hyperglycemia after RE:* T2D = increased up to 24 h; duration of hyperglycemia after AE: no change
Gordon, 2016[a]	*Interstitial glucose concentrations after RE:* T2D = no change *Interstitial glucose concentrations after AE:* T2D = no change *Incidence of hyperglycemia after RE:* T2D = no change *Incidence of hyperglycemia after AE:* T2D = no change
Heden, 2015	*TAG iAUC concentrations after postdinner RE:* T2D = decrease *TAG iAUC concentrations after predinner RE:* T2D = no change *Postprandial glucose iAUC concentrations after postdinner RE:* T2D = decrease *Postprandial glucose iAUC concentrations after predinner RE:* T2D = decrease *Insulin iAUC concentrations after postdinner RE:* T2D = decrease *Insulin iAUC concentrations after predinner RE:* T2D = decrease
Heden, 2018	*Venous glucose during RE:* T2D = 11% lower compared to no-exercise; 23% lower than interstitial glucose *Interstitial glucose during RE:* T2D = no change
Kanaley, 2001	*Fasting glucose 24 h after RE:* T2D = no change *Fasting insulin 24 h after RE:* T2D = no change
Morais, 2011[a]	*Ambulatory systolic BP after RE compared to control:* T2D = decreased 0–2, 6–8, and 18–20 h after RE *Ambulatory systolic BP after AE compared to control:* T2D = no change *Ambulatory diastolic BP after RE compared to control:* T2D = decreased 0–2, 6–8, and 14–16 h after RE *Ambulatory diastolic BP after AE compared to control:* T2D = no change *Ambulatory MAP after RE compared to control:* T2D = decreased 0–2, 14–16, and 18–20 h after RE *Ambulatory systolic BP after AE compared to control:* T2D = decreased 16–18 and 18–20 h after AE
Morais Junior, 2017[a]	*Venous glucose after exercise:* T2D = greater decrease after RE circuit compared to guided walking
Moreira, 2012	*AUC glucose during and after exercise:* T2D = decreased, with greater reduction in low intensity circuit condition; nondiabetic = decreased, with greater reduction in low intensity circuit condition
Van Dijk, 2012[a]	*24 h Interstitial glucose concentrations following RE:* IGT = decrease, T2D groups = decrease *24 h Interstitial glucose concentrations following AE:* IGT = decrease, T2D groups = decrease *24 h hyperglycemia prevalence following RE:* IGT = decrease, T2D groups = decrease *24 h hyperglycemia prevalence following AE:* IGT = decrease, T2D groups = decrease

[a] Indicates a study comparison of resistance and aerobic exercise; T2D = group with type 2 diabetes; group with IGT = impaired glucose tolerance; AE = aerobic exercise; RE = resistance exercise; FMD = flow-mediated dilation; MAP = mean arterial pressure; LW = light walking; BP = blood pressure; AUC = area under the curve; iAUC = incremental area under the curve; Dbase = baseline diameter.

change interstitial glucose but decreased venous blood glucose.[38] Additionally, this was the only study using CGM that included sets to failure. While some have attributed improvements in glycemic control (0.6% reduction in HbA_{1c}) to increased muscle mass following prolonged RE training,[52] others[42] suggest that glucose uptake is increased after a single bout of RE, independent of increased muscle mass. This is in agreement with a meta-analysis of RE studies lasting at least eight weeks in older adults with T2D that showed a reduction of 0.50% in HbA_{1c}, with no change in lean body mass.[53] There is some evidence that RE may reduce post-exercise interstitial postprandial glucose similarly to AE. Future studies should report specific exercises used in RE protocols in order to determine effective program characteristics. Additionally, in studies that found beneficial of effects of RE on postprandial glucose levels, the analysis periods only extended up to 24 h post-exercise. Future studies should monitor glucose levels over longer time periods to determine the maximum duration of beneficial effects of RE.

When using RE to reduce postprandial glucose levels in T2D, completing at least two sets to failure may be necessary.[38,39,42] Prescribing sets comprised of 8–12 repetitions, primarily multi-joint exercises, and rest periods of 60–120 s between sets with longer rest periods when using multi-joint exercises may be optimal for reducing blood glucose levels. There is ample evidence to support the use of RE for immediate reductions in postprandial glucose levels, and clinicians can follow the recommendations for improvement in T2D risk factors presented in Table 3 which also includes warm-up and cool-down strategies consistent with ACSM[54] and National Strength and Conditioning Association[55] guidelines.

3.3. Insulin action during and after RE

Single bouts of RE may be effective in reducing insulin levels (−21% to 48%),[39,41] but conflicting data are reported.[39,41,42,44,45] For example, the baseline insulin response measured by oral glucose tolerance testing (OGTT) decreased 18 h after RE in one report (−21%),[41] but remained unchanged 12 h after exercise in another.[42] Fluckey et al.[41] investigated

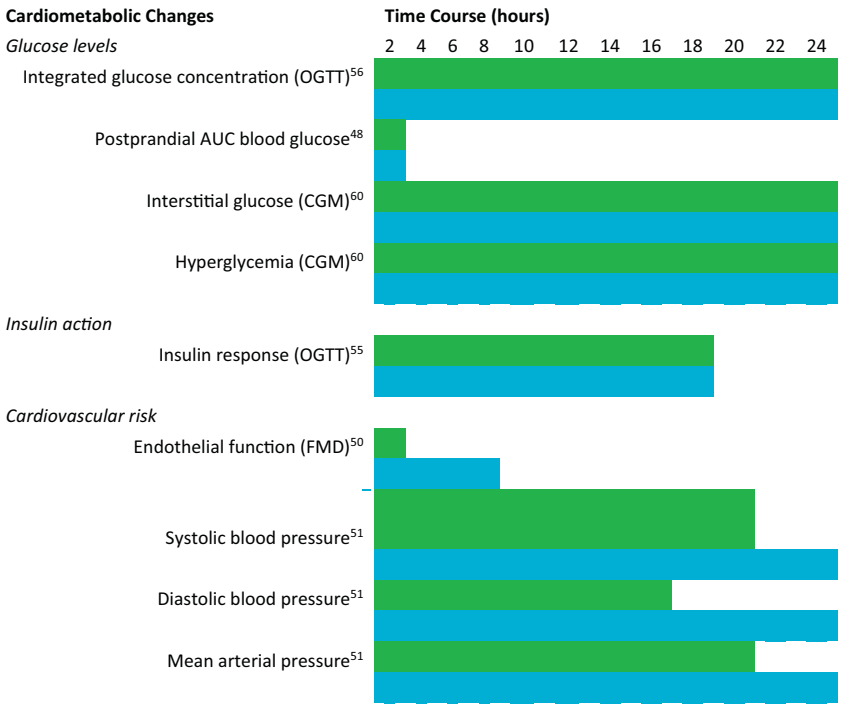

Fig. 1. Time course for beneficial effects after single resistance exercise bout OGTT = oral glucose tolerance test; AUC = area under the curve; CGM = continuous glucose monitoring; FMD = flow-mediated dilation. Green bar indicates the duration of the beneficial effect on the variable; blue bar indicates the post-exercise analysis period.

whether a single bout of RE could lower insulin levels measured by OGTT in older adults with T2D compared to younger healthy controls, and observed a decline in insulin levels 18 h following the RE bout in the younger controls (−22%) and diabetes (−21%) groups. In contrast, Fenicchia et al.[42] using OGTT, found no change in the plasma insulin response 12 to 24 h after RE in females with and without T2D, but with decreased glucose concentrations immediately after exercise (−14.5%). The former study[41] reported decreased insulin with no change in glucose levels, whereas the latter[42] found no change in insulin with decreased glucose levels. This discrepancy may be related to food intake prior to the OGTT. Although Fluckey et al.[41] required participants to ingest a standardized meal plan for 2 days prior to both OGTT assessments, no dietary instructions were provided by Fenicchia et al.[42] Another explanation may be the variability of OGTT in estimating insulin sensitivity as potential confounders such as β-cell function and intestinal glucose absorption rates strongly influence estimates of insulin sensitivity when using this methodology.[59] Additionally, the failure to account for participant characteristics such as HbA_{1c} levels and medication usage limit the interpretation of these findings. Future studies are needed to determine which RE protocols reduce insulin levels after a single bout of RE. The duration of these effects should be monitored using robust measures such as homeostatic model assessment during and after exercise in a fasted state,[60] and over multiple days if exercise is performed in a non-fasting state similar to the approach of others.[44] Studies should employ time periods >18 h post-exercise to determine how long insulin action is improved following RE.

When using RE to reduce insulin levels in T2D, two sets at 50% and 75% of 10 RM with a third set to failure may be sufficient.[39,41] Patients may need to complete between 8 and 10 repetitions with rest periods of 60–120 s between sets and 120 s[41] between exercises. Additional studies are needed to clarify optimal rest periods between exercises and sets for insulin level reduction.

3.4. RE in relation to meal timing

High levels of postprandial glucose[61] and triacylglycerol (TAG) increase the risk for CVD,[62] and performing RE after a meal may acutely reduce these levels.[39] Heden et al.[39] investigated the timing of a single bout of RE relative to having dinner on postprandial glucose, TAG, and insulin in obese individuals with T2D. Performing RE before or after dinner reduced postprandial glucose (−30%, RE after a meal; −18%, RE before a meal) and insulin (−39%, RE after a meal; −31%, RE before a meal), but only exercising after dinner lowered TAG (−92%). The mechanisms for reducing postprandial glucose through RE before and after dinner may differ since the patterns of glucose uptake varied between conditions. While pre-dinner RE resulted in lower postprandial glucose compared to no exercise 1–3 h after eating, post-dinner RE elicited a reduction in glucose during exercise persisting for 45–90 min after eating. These findings are in agreement with studies in those with T2D that reported that AE after a meal results in superior effects on lowering glucose levels compared to AE before a meal[63] or in a fasting state.[64] However, this is the only study that has investigated the effects of meal timing and RE on cardiometabolic outcomes, and the experiment was conducted in the evening. Future studies should investigate the effects of meal timing and RE in the morning as fasted-state moderate intensity AE and high-intensity interval training have been found to lower postprandial interstitial glucose to a greater extent than post-breakfast AE and high-intensity interval training.[60] Additionally, in studies that reported meal timing and dietary instructions, these factors varied substantially across all studies included in this review (Supplementary Table 2) and may have influenced cardiometabolic responses. Given the known relationship between energy deficits and cardiometabolic health, future studies should investigate how energy deficits resulting from RE influences cardiometabolic risk factors.[65] Thus, performing RE 45 min after a meal may lower glucose levels and reduce TAG in individuals with T2D, but additional studies are needed.

3.5. Insulin dosage prior to RE

In individuals with T2D who are taking insulin, recommendations typically include reducing insulin dosage or increasing carbohydrate intake prior to exercise in order to prevent hypoglycemia.[66] Only two studies investigated reducing injectable insulin dosage prior to RE, and the results were contradictory.[33,40] Although one study found that

Table 3
Summary of recommendations for resistance training in type 2 diabetes.

Component	Guidelines
Warm-up and cool-down	A general warm-up should include between 5 and 10 min of light aerobic activity like walking or cycling.[54] Additionally, a specific warm-up using dynamic stretching and/or a set(s) of the programmed exercise at light to increasing intensities may improve performance.[55] The cool-down should follow the resistance training session and consist of 5–10 min of light aerobic activity and stretching.
Intensity and repetitions	A range of 8–12 repetitions at intensities of 70% of 1 RM, 80% of 3 RM, or 100% of 10 RM completed to failure may reduce glucose levels,[38,39,42] insulin sensitivity,[39,41] BP control,[37] and reduce postprandial TAG concentrations.[39]
Frequency	While current evidence suggests that daily RE may result in reduced glucose levels,[38,39,42] insulin levels,[39,41] TAG concentrations,[39] and enhanced BP control,[37] this frequency of resistance training may not allow sufficient recovery which could increase the risk of musculoskeletal injuries.[56] Until additional investigations are available, the recommended resistance training frequency should include 2–3 days per week which is based on training studies in T2D.[57]
Exercise selection	The majority of exercises should include multi-joint movements using free weights, machines, one's body weight, or combinations thereof to reduce glucose levels,[38,39,42] insulin levels,[39,41] postprandial TAG concentrations,[39] and BP.[37] Complementary resistance bands along with free weights and body weight exercises may be appropriate when using circuit RE.[35]
Number of sets	Three sets of each exercise are recommended, and at least one set should be completed to failure for reducing insulin levels,[39,41] at least two sets to failure for reducing postprandial TAG concentrations[39] and reduced glucose levels.[38,39,42]
Rest intervals	Rest intervals should include 60–120 s between sets and 40–120 s between exercises for improved BP control,[37] insulin sensitivity,[39,41] glucose levels,[38,39,42] and reduced postprandial TAG concentrations.[39] If the patient is hypertensive, rest between sets should be at least 90 s.[58]

TAG = triacylglycerol; RM = repetition maximum; BP = blood pressure.

lowering insulin dosage (mean dosage not reported) prior to RE resulted in a prolonged hyperglycemic state,[40] another reported that this practice resulted in no adverse hyperglycemic events, but may impair the magnitude of blood glucose lowering (mean morning insulin dosage: Aspart = 30.25 U; Lispro = 36 U; Lispro + Glargine = 6 U; Regular + Glargine = 4 U; Aspart + Glargine = 27.33 U; Human Insulin + Glargine = 20 U).[33] Gordon et al.[33] investigated the post-exercise response on glucose levels in patients with T2D who were taking injectable insulin. Following a reduction in insulin dose, RE and AE resulted in significant, similar increases in interstitial glucose within 2 h post-exercise, with no increase in the 24 h post-exercise value. The rise in interstitial glucose was likely due to either hormonal changes resulting from increased sympathetic stimulation, or to meal ingestion 15 min before each of the exercise bouts. Decreasing injectable insulin dose prior to RE may attenuate the lowering of post-exercise glucose levels, and may not be an effective strategy for improving glucose regulation. Given the limitations of using interstitial blood glucose as a measure of glucose levels and the relationship between meal timing and modulations in blood glucose,[38,67] future studies should investigate the effects of lowering injectable insulin dosages prior to exercise with glycemic measures that utilize plasma glucose at different time intervals after meal ingestion. Therefore, patients with T2D who take injectable insulin should be cautious of adjusting their insulin dosage prior to RE, as this may result in hyperglycemia and impair the beneficial effects of RE on lowering glucose levels.

3.6. Cardiovascular disease risk: Blood pressure, triglycerides, and endothelial function

Two studies examined the effects of a single bout of RE, including interval RE,[36] on BP, and reported that RE may be more effective than AE in lowering BP in those with T2D.[36,37] Morais et al.[37] compared the effects of RE and AE on 24-h BP control in individuals with T2D. Over the 24 h following the RE bout, reductions in systolic BP (~7 mmHg), diastolic BP (~5 mmHg), and mean arterial pressure (MAP) (~3 mmHg) were lower compared to controls including waking and nocturnal periods. Following the AE bout, the only change was a reduction in MAP by ~13 mmHg during the nocturnal period. Thus, the superiority of RE compared to AE in reducing BP values may be related to the higher intensity during the RE bout. Although AE has been the traditional exercise modality recommended for BP control, in a review that investigated ambulatory BP in normotensive and hypertensive individuals, similar reductions in systolic (−12 mmHg) and diastolic (−7 mmHg) BP following a single bout of AE and a single bout of RE were found.[68] However, only five out of the 30 included single bout exercise studies in this review investigated the effects of RE. Although RE appears to be equally or more effective than AE in reducing BP, it has been understudied compared with AE, and would be an important new area of investigation. Additional studies are needed to investigate the BP lowering effects of RE in T2D.

BP during a bout of RE can increase to a greater extent than a comparable bout of AE, but the lowering effect after RE training over time may be similar to chronic AE.[68] Higher levels of BP for the duration of a RE bout is not considered a major safety issue unless resting BP is not controlled.[10] Furthermore, the higher intensity of RE and greater muscle mass involved compared to AE may have elicited greater neuromuscular and metabolic stress, triggering a higher release of metabolites, a primary factor in muscle vasodilation. Rest intervals characteristic of RE training may also explain the differences in post-exercise ambulatory hypotension between RE and AE, as pauses in work have been linked to a more sustained hypotensive effect post-exercise.[69] Additional research is needed regarding the acute and chronic effects of RE on BP in T2D.

For BP reduction in T2D, patients may need to complete three sets of 8 repetitions at 70% of 1 RM.[37] Rest periods of 60–90 s between sets and 40 s between exercises,[37,58] and use of primarily multi-joint movements may provide a sufficient stimulus for reducing BP in T2D. Given that RE can evoke high acute BP values,[70] and because hypertension affects 50–75% of people with T2D,[71] the safety of RE in this patient population should be considered. There is currently no evidence that the rise in BP during a bout of RE does any harm in patients with hypertension.[72] When considering patients with T2D, the risk is likely lower to larger arteries compared to small vessels (i.e., in the eye), but this is based only on clinical opinion. Lamotte and colleagues[58] found that the magnitude of the pressure load is optimally reduced when RE is performed for 3 sets of 10 repetitions at 75% of 1RM, at a speed of 1 s during concentric and 1 s during eccentric contractions using rest periods ≥90 s between sets in patients with hypertension.

Only one study investigated the effects of a single bout of interval RE on endothelial function in patients with T2D.[36] Similar to conventional circuit training, interval RE typically involves lower intensities, higher repetitions, and shorter rest periods compared to conventional RE. Francois et al.[36] demonstrated that a single bout of interval RE increased brachial artery endothelial function in older adults with T2D when compared to interval AE. Interval RE acutely increased flow-mediated vasodilation by 4, 2, and 2% immediately, 1 h, and 2 h after exercise, respectively. Patterns of increased shear stress during lower body RE exercises likely contributed to systemic improvements in endothelial function. Since the endothelium plays a key role in vascular homeostasis regulation,[73] additional studies investigating the effects of conventional RE on endothelial function in persons with T2D are needed, as well as the RE program characteristics that most favorably modify these variables. Although patients may improve systemic endothelial function using lower body interval RE

training, this type of exercise alone may not elicit similar musculoskeletal adaptations compared to conventional RE.[56]

One limitation of this literature review and analysis was the use of a narrative approach. Although this methodology allowed for a broader scope in tracking the clinical utility of RE in those with T2D, the subjectivity in study selection by only one author conducting the search may have led to bias. Another limitation was the heterogeneity of the studies selected (e.g., participants, measures of glucose levels and insulin sensitivity, and RE protocols), which precluded any firm conclusions. Lastly, this review was restricted to investigations published in the English language, and may not have captured all of the relevant RE studies that have been previously published.

4. Conclusions

A single bout of RE seems to offer transient benefits to individuals with T2D and differs from AE in several ways. There is ample evidence that RE evokes reductions in glucose levels during exercise,[38] up to 24 h post-exercise,[42] and reduces hyperglycemia prevalence similar to AE, that is, 24 h post-exercise.[46] Since RE lowers glucose levels in patients who have had T2D for a shorter duration or those who have higher baseline HbA_{1c} levels,[74] it is important for these participant characteristics to be reported. There is some evidence that a single bout of RE may decrease insulin levels up to 18 h post-exercise[41] but additional studies are needed in both understanding the role of RE in insulin sensitivity as well as designing RE protocols that may optimally reduce insulin levels. RE following a meal may be more effective in reducing glucose, insulin, and TAG concentrations than performing RE before a meal,[39] and it may not be beneficial to reduce injectable insulin dosage prior to RE.[33,40] Given the varied medications used in conjunction with RE in the included studies and the potential impact of these medications on the exercise response,[23–30] clinicians should interpret these results accordingly. Lastly, RE may be more effective than AE in reducing ambulatory BP in persons with T2D,[37] but more work on how a single bout of RE affects BP and other CVD risk factors is needed. Accordingly, acute RE bouts repeated over time, elicit beneficial chronic adaptations that become the training effect.

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Declaration of competing interest

The authors report no conflicts of interest.

Appendix A. Supplementary data

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