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Original Research

Effect of Aerobic and Resistance Exercise on Glycemic Control in Adults With Type 1 Diabetes

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Key Messages

- Resistance training may improve glycemic control in adults with type 1 diabetes.
- Glucose levels tend to decline less during bouts of resistance training compared with bouts of aerobic exercise.
- Resistance training may result in a decreased mean glucose level and increased time in range during the 24 h after exercise.

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ABSTRACT

Objectives: Physical exercise is recommended for individuals with type 1 diabetes, yet the effects of exercise on glycemic control are not well established. We evaluated the impact of different modes of exercise on glycemic control in people with type 1 diabetes.
Methods: In a 3-week randomized crossover trial, 10 adults with type 1 diabetes (4 men and 6 women, aged 33±6 years; duration of diabetes, 18±10 years; glycated hemoglobin level, 7.4%±1%) were assigned to 3 weeks of intervention: aerobic exercise (treadmill at 60% of maximum volume of oxygen utilization), resistance training (8 to 12 repetitions of 5 upper and lower body exercises at 60% to 80% of 1 repetition maximum) or no exercise (control). During each exercise week, participants completed 2 monitored 45 min exercise sessions. For each week of the study, we analyzed participants' insulin pump data, sensor glucose data and meal intake using a custom smart-phone application. The primary outcome was the percentage of time in range (glucose >3.9 mmol/L and ≤10 mmol/L) for the 24 h after each bout of exercise or rest during the control week. The study was registered on ClinicalTrials.gov (NCT:02687893).
Results: Aerobic exercise caused a mean glucose reduction during exercise of 3.94±2.67 mmol/L, whereas the reduction during resistance training was 1.33±1.78 mmol/L (p=0.007). The mean percentage time in range for the 24 h after resistance training was significantly greater than that during the control period (70% vs. 56%, p=0.013) but not after aerobic exercise (60%).
Conclusions: The results indicate that when various confounders are considered, resistance training could improve glycemic control in this population.

RÉSUMÉ

Objectifs : L'exercice physique est recommandé aux individus atteints du diabète de type 1, toutefois, on connaît mal les effets de l'exercice sur la régulation de la glycémie. Nous avons évalué les répercussions de différents types d'exercices sur la régulation glycémique des personnes atteintes du diabète de type 1.
Méthodes : Dans un essai croisé, à répartition aléatoire, de 3 semaines, nous avons assigné 10 adultes atteints du diabète de type 1 (4 hommes et 6 femmes, de 33±6 ans [durée du diabète, de 18±10 ans;

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concentration de l'hémoglobine glyquée, de 7,4 %±1 %) à 3 semaines d'interventions : exercice aérobique (tapis roulant à 60 % du volume maximal d'oxygène), entraînement musculaire (de 8 à 12 répétitions de 5 exercices du haut et du bas du corps de 60 % à 80 % de la charge maximale en 1 seule fois) ou aucun exercice (période témoin). Chaque semaine d'exercices, les participants ont accompli 2 séances d'exercices supervisés de 45 minutes. Chaque semaine de l'étude, nous avons analysé les données de la pompe à insuline, les données des capteurs de glucose et l'apport alimentaire des participants à l'aide d'une application personnalisée pour téléphone intelligent. Le critère de jugement principal était le pourcentage du temps dans la fourchette (glycémie>3,9 mmol/L et≤10 mmol/L) dans les 24 heures après chaque période d'exercices ou de repos durant la semaine témoin. Nous avons enregistré l'étude sur le site ClinicalTrials.gov (NCT02687893).

Résultats : L'exercice aérobique a entraîné une diminution moyenne de la glycémie durant l'exercice de 3,94±2,67 mmol/L, tandis que la réduction durant l'entraînement musculaire a été de 1,33±1,78 mmol/L (p=0,007). Le temps moyen en pourcentage dans la fourchette dans les 24 heures après l'entraînement musculaire a été significativement plus grand que durant la période témoin (70 % vs. 56 %, p=0,013), mais non après l'exercice aérobique (60 %).

Conclusions : Les résultats montrent que lorsque nous considérons les divers facteurs de confusion, l'entraînement musculaire peut améliorer la régulation de la glycémie dans cette population.

Introduction

In the coming decades, the number of patients with type 1 diabetes is expected to triple (1).

Less than a third of adults with type 1 diabetes achieve the target glycated hemoglobin (A1C) level of <7.0% (2), and a majority are overweight or obese (3,4). Bohn et al have recently shown that less than a fifth of adults with type 1 diabetes manage to meet physical activity recommendations (5). Overweight and obese weight status in individuals with type 1 diabetes is higher than that in the general population, and the prevalence is rising; this appears to be unrelated to aging and instead is related to a lack of physical activity and other clinical factors (6). Currently, it is recommended that adults living with type 1 diabetes perform 150 min of moderate aerobic exercise (AE), 75 min of vigorous AE, or a combination thereof, along with resistance training (RT) on 2 days each week with no more than 2 consecutive days of no activity (7). Regular physical activity in individuals with type 1 diabetes provides many physiological and psychological benefits including improved body composition, increased cardiorespiratory fitness, improved endothelial function and improved blood lipid profile (8–10). In addition, exercise also reduces total daily insulin requirements, stress and depression while improving the overall sense of well-being and quality of life (11–14).

Physical activity has long been associated with improvements in glycemic control in adults with type 2 diabetes (15). These improvements have been shown to be modest when the physical activity is either AE or RT, but a combination of the 2 modalities has demonstrated the greatest improvement in glycemic control in adults with type 2 diabetes (16). However, in individuals with type 1 diabetes, the effects of physical activity on glycemic control are not clear (11,12,17). Individuals with type 1 diabetes routinely experience rapid changes in glucose levels during and immediately after physical activity, leading to loss of control and fear of hypoglycemia (12,14,17,18).

Without advance planning, these glucose changes are challenging to manage. Nocturnal hypoglycemia is common after an individual with type 1 diabetes has engaged in physical activity during the day (19). Optimizing insulin dosage before exercise is challenging for many people with type 1 diabetes who engage in physical activity. Insulin dosage changes must be made up to 90 min before the start of exercise (14,20), and depending on the modality (AE/RT) and intensity of exercise (level of exertion), altering insulin dosing may not result in appropriate glycemic control (14,20). Another strategy adopted by many individuals to prevent hypoglycemia is to keep blood glucose levels higher during and after exercise by increasing the consumption of carbohydrates (21,22). Although many groups of researchers have highlighted the acute challenges faced by people with type 1 diabetes during various types of exercise, to date, no study has shown how exercise affects glycemic control during longer periods after exercise is performed (23–25). In this study we examine the impact of AE and RT and related energy expenditure (EE) on glycemic control. We further examine how exercise affects both insulin dosing requirements and the amount of dietary intake in a period of 24 h after a bout of exercise. We hypothesized that glycemic control during a period of 24 h after exercise would be improved.

Methods

Study participants

Ten adults (6 women and 4 men) with type 1 diabetes who were sufficiently active and physically fit were recruited to participate in this randomized, 3-treatment, open, single-center crossover study. Participants' characteristics, expressed as mean±standard deviation (SD), are as follows: age, 33±6 years; body mass index, 24.4±2.1 kg/m^2; duration of diabetes, 18±10 years; A1C level, 7.4%±1%; maximum volume of oxygen utilization [VO_{2max}], 46.8±11.55 mL/kg/min; and fat mass, 30%±7%. The inclusion criteria for this study were as follows: diagnosis of type 1 diabetes present for >1 year; age 21 to 45 years, an age range chosen to limit exposure to unknown cardiovascular risk during exercise as recommended by Mozaffarian et al (26); body mass index <30 kg/m^2; physically active; currently using an insulin pump. Sufficiently active was defined as participating in at least 150 min of aerobic activity at moderate intensity each week for the last 6 months based on the guideline by the American College of Sports Medicine (27). Participants in this study were active at moderate intensity for 7.3±4 h/week. The exclusion criteria were cardiovascular disease, renal dysfunction or any condition that would preclude exercise.

The Institutional Review Board at the Oregon Health and Science University approved the study protocol and consent form. The present paper is a secondary analysis of the data collected during a study to examine the effect of exercise on sleep in adults with type 1 diabetes (19). The study was registered on ClinicalTrials.gov (NCT:02687893). Informed consent was obtained from every participant.

Study design

In this pilot study, we performed a secondary analysis on data that were previously published by Reddy et al (19), a study that demonstrated that exercise affected sleep on nights after exercise. A paired-means power analysis was used to carry out sample size power analysis. A total sample size of 10 achieved 90% power to

detect a mean of paired differences of 30 min in sleep loss. This is with an estimated SD of differences of 25 and a significance level (alpha) of 0.05 with use of a 2-sided paired *t* test comparing sleep loss during the weeks of exercise interventions with the week without any explicit exercise. In the present analysis, we hypothesized that glycemic control during a period of 24 h after exercise would be improved. The primary outcome was the percentage of time in a target glucose range of 3.9 to 10 mmol/L during the 24 h after exercise. Participants' glucose levels, physical activity, insulin dosage, food intake and sleep were continuously measured over the course of 4 consecutive weeks. Glucose levels were tracked using a continuous glucose monitor (CGM) (Dexcom G4 or G4 Share; Dexcom, San Diego, California, United States). Participants were blinded to the sensor glucose readings. Physical activity and sleep were monitored by means of an activity monitor (ActiGraph wGT3X-BT; ActiGraph, Pensacola, Florida, United States). Participants managed their own insulin dosage using their personal insulin pump and a capillary blood glucose meter (Contour Next glucose meter; Ascensia Diabetes Care, New Jersey, United States). Food intake was measured by means of a custom-built food-tracking Android smartphone application. A smartphone (Galaxy S4; Samsung, Los Angeles, California, United States) loaded with this application was distributed to the participants. The first week of the study was a run-in week during which participants became accustomed to the wearable sensors. After the run-in week, participants performed in-clinic AE twice weekly for 1 week, in-clinic RT twice weekly for 1 week and no structured exercise for 1 control week. The order of the AE, RT and control weeks was randomized for each participant. Block randomisation (size of 6) with a 1:1:1 ratio was computer generated for the sequence of the interventions. One of the study coordinators carried out the randomization and the allocations were revealed at the start of the admission visit.

Study protocol

All participants completed a screening visit, training visit and 4 structured exercise sessions. During the screening visit, baseline examinations included an assessment of anthropometric data, physical status and a VO_{2max} test according to the Bruce protocol on a Medtrack ST 55 treadmill (Quinton, Washington, United States). Oxygen consumption was measured during the VO_{2max} test. Each participant wore an airtight mask (Hans Rudolph Inc, Shawnee, Kansas, United States), which had a gas sensor (Cosmed, Rome, Italy) attached to it. Their heart rate was monitored with a Polar Electro T61 chest heart rate monitor (Polar Inc, Lake Success, New York, United States). The Bruce protocol was used to determine VO_{2max}. Body composition was estimated by means of a dual x-ray absorptiometry scan using a Hologic Discovery Wi bone densitometer (Hologic, Bedford, Massachusetts, United States, Apex 4.0 software).

Participants returned on a separate day for the training visit to learn how to use the CGM, how to use the activity monitor and how to accurately record food intake. Participants performed a 1-repetition maximum (1-RM) test for bench press, leg press and seated row during this visit. This was performed to set the exercise intensity (i.e. weight lifted) for RT sessions. We chose not to conduct 1-RM tests on leg extension and flexion exercises because they are single joint movements and, according to recommended guidelines, should be avoided in favor of multi-joint movements to minimize injury risk during maximal testing. Rather, we estimated training loads for single joint exercises using the multiple RM approach to determine each participant's 8-RM workload (28). Participants replaced the CGM each week (at least a day before the exercise visit) and calibrated the sensor at least twice daily using the capillary blood glucose meter. Although participants were blinded to CGM values, for safety, glucose alerts were set at 3.1 mmol/L and 16.67 mmol/L.

In-clinic exercise sessions

Each participant completed 2 sessions of monitored AE during the AE week and 2 sessions of monitored RT during the RT week. Participants arrived at the laboratory at 4:00 PM for each of the exercise sessions. For both the AE and RT weeks, the same exercises were performed on 2 separate days with 1 day in between during which participants were instructed not to exercise (e.g. RT sessions on Tuesday and Thursday). There were at least 48 h between the exercise visits. Participants were instructed to refrain from formal exercise 24 h before and 24 h after their scheduled exercise. Actigraph data collected during this time were used to confirm that participants complied with this instruction. A study coordinator also contacted participants on the day after the in-clinic exercise session and asked questions about compliance during this phone call. The days of the week on which exercise sessions were conducted were identical for each participant across weeks. Between each intervention week there were at least 4 days. All exercise sessions were conducted on weekdays excluding Friday. During each exercise session, participants were outfitted with a Zephyr Biopatch (Zephyr Technology, Annapolis, Virginia, United States) that included a 2-lead electrocardiogram-based heart rate monitor to continuously monitor heart rate. RT sessions, after a brief warm-up period, included 3 sets of 8 to 12 repetitions at 60% to 80% of 1-RM of 5 different exercises (leg press, bench press, leg extension, leg flexion and seated row) with a 90 s rest period between exercises and sets (total duration of 45 min). The exercises were chosen to recruit similar volumes of upper and lower body muscle mass; machine-based exercises, rather than equal numbers of exercises per group, were used for control of movement and safety. Although we allowed participants some flexibility in doing 8 to12 repetitions to allow for a tolerable workout, participants generally did not change their weight load or number of repetitions during a session. The Borg perceived exertion scale was used to estimate fatigue and to maintain a moderate intensity rating of 12 to 14 for each exercise performed. The duration of each set of exercises and the duration of the rest period were closely tracked using an electronic data capture tool—Research Electronic Data Capture (REDCap), a secure Web-based data capture application hosted at Oregon Health and Science University (29). AE consisted of 45 min of treadmill exercise. Based on the VO_{2max} value obtained during the first visit, the heart rate at 60% of VO_{2max} was calculated and used during the AE visits. During each exercise training visit, heart rate was closely monitored, and treadmill speed and grade were adjusted to keep each participant's work rate at 60% of VO_{2max}. The duration of the exercise intervention was kept consistent between the 2 types of exercise, but the EE between these 2 types of exercises was not controlled for in this study. The capillary glucose level was checked before the start of the exercise period and immediately after exercise or if a participant experienced any symptoms of hypoglycemia. Each exercise session was followed by 60 min of monitored recovery. Participants were provided with a preselected standardized meal of 540 calories (23% protein, 47% carbohydrate and 30% fat) to eat during the recovery period; the identical meal was provided during all in-clinic exercise sessions.

Exercise EE

EE during the exercise period was estimated to determine the differences between the 2 types of exercise interventions. The data collected during the VO_{2max} test were used to show a relationship (ordinary least-squares linear regression) between oxygen uptake and heart rate data. We used this equation to estimate the amount of oxygen uptake based on the heart rate data obtained during each in-clinic session. EE during continuous AE was estimated by the cumulative oxygen uptake during the exercise period and converting the oxygen uptake to kilocalories using the standard 1 L of

oxygen to 5.0 kcal (30,31). To estimate EE during RT, we used the nonsteady-state model proposed by Reis and Scott (32) and Vezina et al (33) by considering the oxygen uptake not only during each bout of exercise (~30 s) but also during the recovery periods (~90 s) in between each bout of RT. Both the recorded exercise EE and recovery EE were converted to kilocalories. The EE values during exercise were calculated using the standard conversion of 1 L of oxygen to 5.0 kcal, whereas the EE values during recovery were calculated using the nonsteady-state conversion of 1 L of oxygen to 4.7 kcal.

Nutritional assessment

All participants were verified to be experienced in carbohydrate counting before this study; they were asked whether they used carbohydrate counting techniques and had recently been educated about them. Each participant was provided with an Android study phone preloaded with a custom food meal photography application. All participants were trained in the use of the application and were instructed to take pictures of all meals consumed during the study. Participants were provided with a ruler to be included in the photograph to provide an approximate size measure for the meal. The custom application allowed each participant to enter the estimated carbohydrate amount, his or her capillary blood glucose value at the time of the meal, the type of meal (breakfast, lunch, dinner, snack or hypoglycemic treatment) and an optional text description of the meal. Each entry was uploaded to the study database with the date and time recorded. A trained dietitian analyzed all meals for each participant on the day of the in-clinic exercise visit and the day after each exercise visit to estimate the content and quantity of each meal. The dietitian also analyzed meal data during matched days of the control week. The energy and macronutrient composition of meals was analyzed with ESHA Food Processor SQL Software (ESHA Research, Salem, Oregon, United States) (34).

Statistical analysis

Meal intake, exogenous insulin delivery and glycemic control metrics were calculated over the 24 h period from the end of exercise to the same time on the next day. One participant failed to report any meal intake on multiple study days, and therefore dietary records were only analyzed for 9 subjects, and they were included in all of the food analyses. We performed the Shapiro-Wilk test to evaluate the assumption of normality, and for the normally distributed values, we analyzed the relationship between each outcome and the intervention using a randomized mixed-effects regression model with a random intercept to account for correlation between observations on the same participant. Because 2 interventions were compared against a single control, significance was adjusted to 0.025. We included an effect for the day to control for possible carryover effects. The Wilcoxon rank-sum test was used to assess differences in the non-normally distributed duration of hypoglycemia. Data are presented as mean±SD or mean (95% confidence interval [CI]); data that are non-normally distributed are presented as median and interquartile range (IQR). All statistical analyses were conducted in R (version 3.4.2) (35).

Results

Results are described in 2 sections with regard to 2 endpoints: first during the in-clinic exercise period and second for the 24 h period after exercise.

Ten adults (6 women and 4 men) with type 1 diabetes had the following baseline characteristics: age, 33±6 years; body mass index, 24.4±2.1 kg/m^2; duration of diabetes, 18±10 years; A1C level, 7.4%±1%; VO_{2max}, 46.8±11.55 mL/kg/min; fat, 30%±7%; total daily insulin dose, 40.99±7.26 units; resting heart rate, 62.8±7 beats/min; daily time in moderate to vigorous physical activity, 1.1±0.7 h/day.

In-clinic exercise visits

At the start of the exercise bouts, there was no difference between the glucose levels (AE: 8.78±3.22 mmol/L vs. RT: 8.72±3.5 mmol/L), but the decrease in glucose levels during exercise was significantly different between the 2 exercise types. AE caused a precipitous reduction in sensor glucose value over the exercise period with a mean glucose reduction of 3.94±2.67 mmol/L, whereas the reduction in sensor glucose value was smaller during RT with a mean glucose reduction of 1.33±1.78 mmol/L (p=0.007). By the end of the recovery period (60 min after exercise), the sensor glucose levels were not statistically different. CGM glucose values during the exercise and recovery periods are shown in Figure 1A. The mean heart rate during the AE bout was 144.6±8 beats/min, and the mean heart rate during the RT bout was 112.3±11 beats/min. Additional RT information is provided in

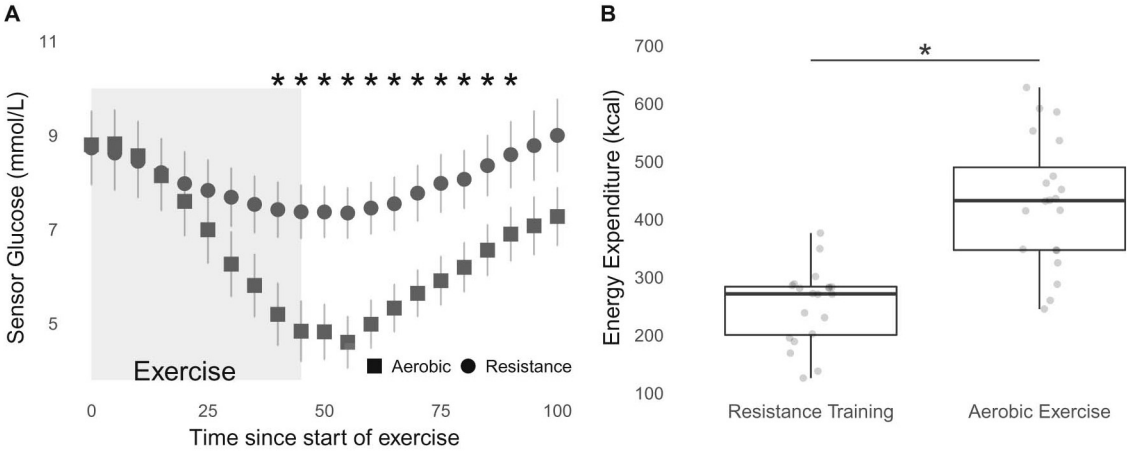

Figure 1. A, Glycemic response during the in-clinic exercise visits. Sensor glucose data are represented as mean±standard error during exercise (represented by box) and 60 min of recovery: ■ resistance training, ●, aerobic exercise. Asterisk indicates the statistically significant difference between the 2 interventions based on the paired-sample *t* tests (p<0.05). B, Box plots with individual points indicating the estimated energy expenditure in kilocalories during the in-clinic exercise sessions. Energy expenditure between the visits was significantly different between the interventions. Asterisk indicates the statistically significant difference between the energy expenditure during the 2 types of interventions based on the paired-sample *t* test (p<0.05).

Supplementary Table 1. The EE during the AE visits was significantly higher than that during the RT visits, with the EE during the AE visits being 429±111 kcal and the EE during the RT visits being 252±65 kcal (p<0.001). The EE values during the in-clinic visits are shown in Figure 1B. On average, the participants had similar glucose and insulin levels on board at the start of the exercise interventions. The average insulin level on board at the start of the AE intervention was 4.56±1 units, and the average insulin level on board at the start of the RT bout was 4.68±1 units.

Twenty-four–hour postexercise in-home glycemic control

The mean glucose value for the 24 h period was lowest after RT visits (8.01±1.94 mmol/L) as compared with AE visits (8.80±2.17 mmol/L), and during the control week it was 9.5±2.7 mmol/L. The mean glucose value for the 24 h after the RT visit was 1.39 mmol/L lower than the mean glucose value for the 24 h during the matched control week (95% CI −2.25 to −0.55, p=0.002, Z=−3.29). However, the mean glucose value for the 24 h after the AE visits was only 0.66 mmol/L lower than the 24 h during the matched control week, and the difference was not significant (95% CI −1.51 to −0.19, p=0.134, Z=−1.53). Adjusting for the total insulin dosage within the random-effects model, we observed a mean glucose value during the 24 h period after RT exercise that was 1.03 mmol/L lower than that in the control week (95% CI −1.90 to −0.17, p=0.024).

However, when the same adjustment was made for total insulin dosage, the mean glucose value during the 24 h period after AE visits was lower than that during the control week by only 0.40 mmol/L, and again, the difference was not significant (95% CI −1.24 to 0.45, p=0.39). When controlling for food intake, the mean glucose value was still lower during the 24 h period after RT than that during the control week by 0.96 mmol/L (95% CI −1.82 to −0.10, p=0.036). When controlling for food intake, the drop in mean glucose after AE was smaller at 0.06 mmol/L and not significantly different than that during the control week (95% CI −0.98 to 0.86, p=0.903). After adjusting for either insulin dosage or meal intake, the mean glucose value was significantly lower after RT, but there was no difference from the control value after AE visits.

The time in range (defined as percentage of time with sensor glucose between 3.9 mmol/L and 10 mmol/L) over the 24 h period after the RT visits was 70.3%±15%, whereas the time in range over the 24 h period after the AE visits was 60.5%±22%. During the control week, the time in range was 55.7%±27%. We observed a statistically significant improvement in time in range of 14.61% (95% CI 3.50–25.71, p=0.013, Z=2.6) for the RT visit compared with the control week, whereas the increased time in range after the AE visits was only 4.72% compared with the control week, and the change was not significant (95% CI −6.38–15.83, p=0.41, Z=0.8).

During the 24 h period after the RT visits, the time in hyperglycemia (defined as percentage of time with sensor glucose >10 mmol/L) was 23.1%±17%, and after the AE visits, it was 32.9%±25%. Participants spent 39.1%±28% of the time in hyperglycemia during the same period in the control week of the study. We observed a significant reduction in the time in hyperglycemia by −16% (95% CI −26.69 to −5.32, p=0.005, Z=−2.94) for the 24 h period after RT visits compared with the control week. The reduced time in hyperglycemia after the AE visits was only −6.25% (95% CI −16.94 to 4.43, p=0.258, Z=−1.15) compared with the control week.

The median time in hypoglycemia (percentage of time with sensor glucose ≤3.9 mmol/L) over the 24 h period was 3.72% (IQR, 9.83%) after the AE visits and 3.63% (IQR, 6.07%) after the RT visits, whereas during the control week, the median time in hypoglycemia was 1.86% (IQR, 7.15%). Participants did not experience statistically significant differences in time in hypoglycemia after either AE or RT visits as compared with the control week of the study.

Table 1
Summary of the average glycemic control, insulin dosage and energy intake for the 24 h period after the exercise visit

	Control	Aerobic exercise	Resistance training
Time in range (%)	55.7±25	60.5±22	70.3±15*
Time in hypoglycemia (%)	1.86 (7.15)	3.71 (9.83)	3.63 (6.07)
Time in hyperglycemia (%)	39.1±28	32.9±25	23.1±17*
Glucose mean (mmol/L)	9.5±2.7	8.80±2.17	8.01±1.94 *
Energy intake (kcal/day)	1,347±606	1,970±630*	1,816±362*
24 h insulin dosage (units)	43.6±9	40.8±9	39.8±9*
24 h bolus insulin dosage (units)	19.2±10	18.3±8	15.7±8*
24 h basal insulin dosage (units)	24.4±6	22.5±5*	24.1±5

Notes: A randomized mixed-effects regression model with a random intercept to account for correlation between observations on the same participant was used to determine the significance of each outcome relative to the intervention. Because 2 interventions were compared against a single control, significance was adjusted to 0.025. Time in hypoglycemia is presented as median (interquartile range).
* p<0.025.

Table 1 shows the summary measures of the 24 h glycemic data. Individual markers of 24 h glycemic control are shown in Figure 2.

Energy and carbohydrate intake

A total of 112 weekdays of meal data were analyzed for this study. Participant-recorded meal data were corroborated with both the insulin pump bolus data and the corresponding glucose sensor data. To account for missing meal data, we removed that day's data from the analysis if either the participant had not reported more than 1 main meal for the day or if the total daily estimated consumption was less than 1,000 kcal. Nine underreported days from 4 different participants met the criteria to be deleted from the analysis, leaving 103 days of nutrient intake. Participants had a significantly greater amount of energy intake during the 24 h after both types of in-clinic exercise visits relative to the control days. The average energy intake was greater after the AE visits and RT visits compared with the control days by 623±158 kcal (p<0.001) and 468±145 kcal (p=0.003), respectively. Controlling for meal intake when looking at mean glucose during the 24 h period after the RT visits, we observed a lower mean glucose value during the 24 h period after RT, which was less than that during the control week by 0.96 mmol/L (95% CI 1.82 to −0.10, p=0.036). Time in range was also higher after RT compared with the control week when controlling for meal intake by 11.74% (p=0.051). When comparing mean glucose after AE vs. the control week while making the same adjustment for meal intake, we found that the mean glucose level was slightly lower during the 24 h period after AE, but the 0.06 mmol/L was smaller and not significant (95% CI −0.98 to 0.86, p=0.903). After controlling for meals, time in range after AE was only slightly higher compared with the control week at 0.77% and was not significant (p=0.9).

There was a greater need for hypoglycemic treatments during the 24 h period after the AE and RT visits compared with control days whereby the total carbohydrate intake was higher than that during the control week by 77±17 g (p<0.001) for AE and 42±19 g (p=0.02) for RT. Figure 3A shows the differences in energy intake during the different weeks of the study.

Twenty-four–hour postexercise activity levels

Participants were instructed to refrain from any structured and formal activity during the 24 h before and 24 h after their scheduled exercise or control period. There were no significant differences in time spent in moderate to vigorous physical activity (MVPA) between the 3 periods. Participants spent 302±118 min in MVPA during the control period, 305±92 min in MVPA during the 24 h period after AE and 275±96 min in MVPA after RT (p=NS).

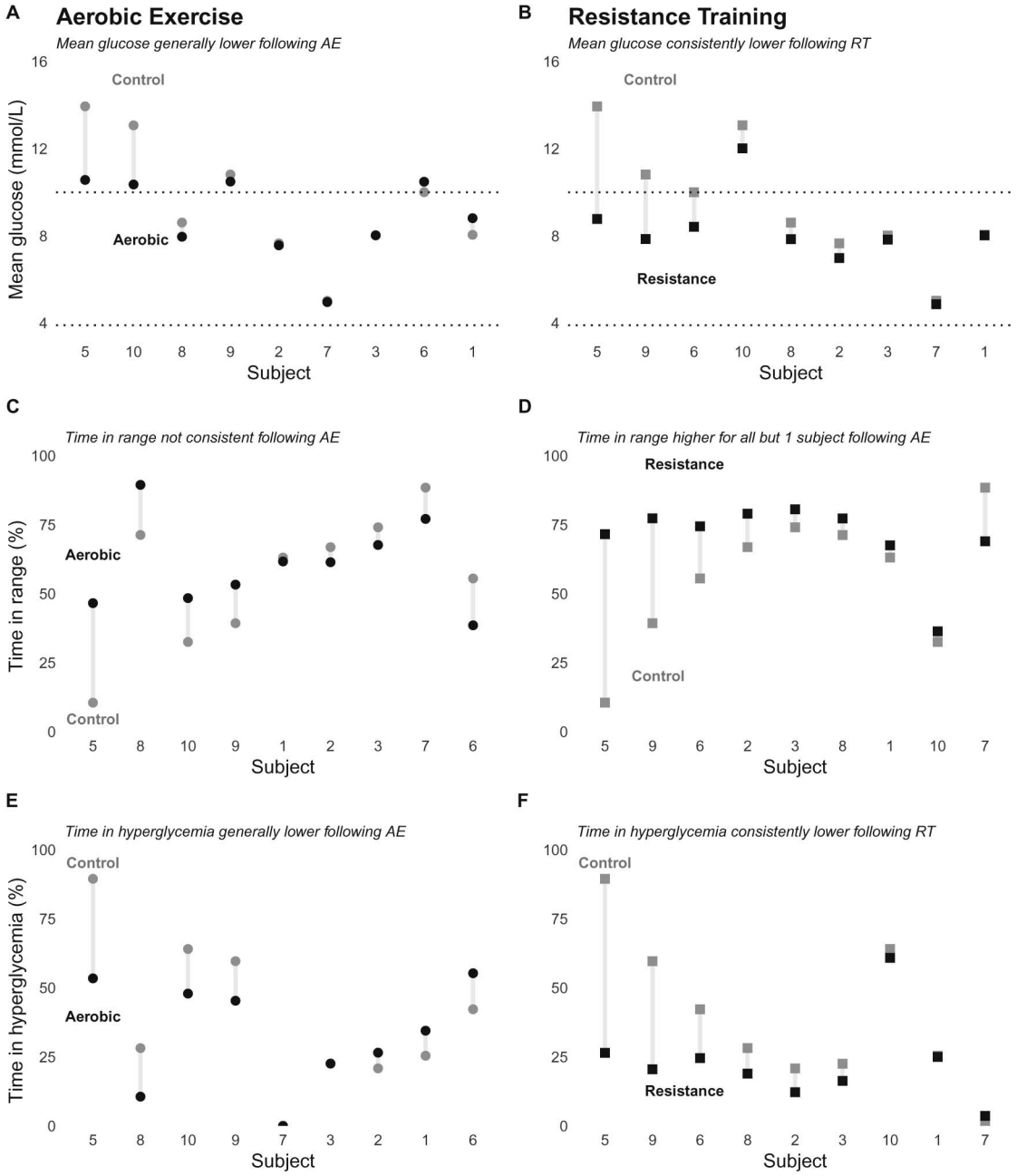

Figure 2. Improvements in glycemic outcomes for each study participant are shown. In the 24 h period after resistance training, all participants experienced positive reductions in mean glucose value, and all but 1 participant experienced reductions in time in hyperglycemia and improvement in time in range compared with the control week. The same outcomes after aerobic exercise are not as consistent. In each panel, data for each participant are shown with ■ indicating resistance training and ● indicating aerobic exercise.

Insulin administration

Insulin dosage data are shown in Table 1. Despite an increase in both energy and carbohydrate intake, the total insulin dosage during the 24 h period was not significantly higher for days after either type of exercise visit as compared with the control days. Rather, basal insulin dosage was significantly lower by 2±0.4 units of insulin after the AE visits ($p<0.001$) as compared with control days. Insulin use was lowered by only 0.4±0.5 units after RT visits compared with the control week ($p=0.3$). Participants injected significantly less bolus insulin after the RT visits, a reduction of 3.5±1.5 units ($p=0.01$) as compared with control days and as opposed to a reduction of only 0.9±2.7 units ($p=0.5$) after the AE visits. Figure 3B shows the differences in total insulin dosage during the different weeks of the study.

Discussion

Physical exercise is a cornerstone of diabetes management, but recent reviews have shown no clear evidence of glycemic benefit from physical activity in adults with type 1 diabetes (11,14,16,36). However, exercise could provide a potential improvement in A1C in children and adolescents (8). The present study highlights that RT is a promising strategy that can lead to improved glycemic control, but for AE, the results are not as significant. In this study we demonstrate that during the 24 h period after either intervention,

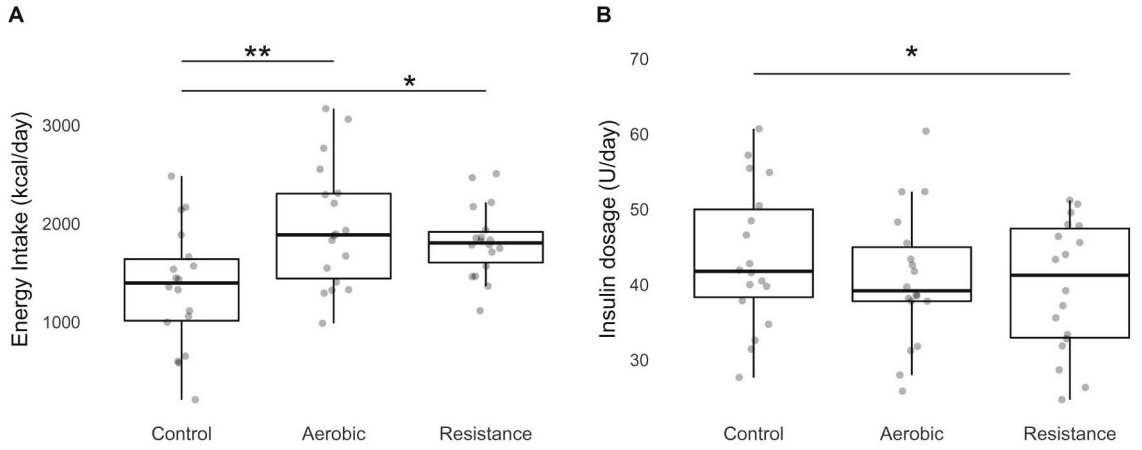

Figure 3. A, Box plots with individual data points indicating nutritionist-estimated energy intake from the meal pictures collected during the 24 h period after the in-clinic exercise visit during each intervention week. The energy intake was significantly higher during the 24 h after the aerobic exercise and resistance training in-clinic sessions, as indicated by the asterisk based on the randomized mixed-effects regression model with a random intercept to account for correlation between observations for the same participant ($p<0.025$). B, Box plots with individual data points indicating the insulin dosage downloaded from the insulin pump during the 24 h period after the in-clinic exercise visit during each intervention week. The total insulin dosage was significantly lower during the 24 h after the resistance training in-clinic sessions, as indicated by the asterisk based on the randomized mixed-effects regression model with a random intercept to account for correlation between observations on the same participant ($p<0.025$).

participants increased meal intake to manage hypoglycemic episodes and increased consumption of after-dinner snacks to prevent nocturnal hypoglycemia, as speculated by Kennedy et al (11). We also show that the participants used less insulin after both AE and RT interventions, with use of significantly less bolus insulin after the RT visits and a significant reduction in basal insulin after the AE visits. The decrease in bolus insulin after RT could be due to either fewer correction boluses or reduced meal-related insulin boluses. We also show that the decrease in glucose during RT is less compared with AE, which confirms prior reports (24). However, we also found that the time spent in hypoglycemia during the 24 h period after a bout of either type of exercise was no different as compared with the control week. Another insight generated by this study was that EE during AE and RT is significantly different, with participants during the RT bout expending less energy compared with AE and then subsequently consuming less food after RT compared with AE.

People with type 1 diabetes find it challenging to dose insulin appropriately for meals, and this becomes more challenging when exercise must also be considered because exercise is known to affect insulin sensitivity for many hours after exercise (36). This study further expands on the published literature by investigating the effects of physical activity (RT and AE) on glycemic control during the 24 h period after the intervention while controlling for total insulin dosed and/or meal intake. These data highlight that individualized physical activity regimens could augment current insulin therapies to achieve optimal glycemic control. The responses to exercise are heterogonous in our subjects, but the most improvement in time in range was experienced by individuals who spent more time in the hyperglycemic range during the control weeks. Engaging in specific strategies to adjust insulin doses and minimize excessive carbohydrate consumption before, during and after exercise could help improve glycemic control and prevent dysglycemia.

Three prior studies of people with type 1 diabetes have demonstrated that RT could provide improvements in A1C levels (37–39). However, a recent nonrandomized long-term study conducted with 8 adults with type 1 diabetes who participated in unsupervised recreational training consisting of both AE and RT showed no improvement in A1C levels (40). This inconsistency may have been a result of performing both AE and RT during this study. As we show in the present study, RT resulted in significant improvement in glycemic outcomes but AE did not. The inconsistencies may also be explained by the fact that these studies have not accounted for varying meal and insulin intake during the monitoring period and that metrics beyond A1C level are important to consider (41,42). A regular exercise regimen of RT has been demonstrated to elicit beneficial metabolic responses (reductions in A1C level and increased insulin sensitivity) in individuals with type 2 diabetes as a result of gains in muscle mass and improved mitochondrial oxidative capacity (43,44).

Limited stores of muscle and liver glycogen are used as energy substrates during AE and RT, with the source and relative rate of glycogen depletion dependent on the type and intensity of training (45). The effects of either exercise modality on glycemic control can often last for several hours after exercise completion. As observed in this study, increased energy consumption after both exercise modalities could be a result of needing to replenish glycogen stores. Other studies have shown that glucose uptake by the exercising muscles may be enhanced for many hours and often overnight (25). Although we strived to have participants performing both AE and RT at moderate intensities, it is possible that the relative rates of glycogen depletion and other sources of depletion (e.g. liver vs. muscle) differed between the 2 modalities and could account for some of the variation in glucose dynamics between AE and RT.

This pilot study had a few limitations, including a small sample size. We have plans to replicate this study with a larger number of subjects. Another limitation is that we did not test other exercise modalities, such as intermittent high-intensity interval training or a combination of AE and RT; thus, our findings here should be interpreted accordingly. We plan to investigate alternative exercise modalities in future projects to continue to determine how exercise affects glycemic control. Another limitation of the present study is that although we controlled for the duration and intensity of exercise, we did not control for the differences in EE between the 2 exercise modalities. It is not possible to simultaneously control for duration, intensity and EE, and we chose in this study to control for the first two. In the future, it would be important to determine whether these results hold when EE is maintained at a constant between the exercise modalities. A further limitation was that although more than half of the participants were female, we did not

collect information on the female participants' menstrual cycles, which are known to affect glucose levels.

Conclusions

RT may improve glycemic control in adults with type 1 diabetes, even when adjustments are made for changes in meal intake and changes in insulin dosage after the exercise event. The beneficial effects of AE on glycemic control may be tempered by increased amounts of food consumed during the day after exercise to balance increased EE.

Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Diabetes* at www.canadianjournalofdiabetes.com.

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Author Contributions

RR and PGJ developed the protocol for the study, performed the data analysis and wrote the manuscript. RR and AW contributed to the meal intake data analysis. RR, AW, JEY, KWS, JRC and MG contributed to the data collection and to the manuscript writing. The guarantor of this research is Peter Jacobs, who takes responsibility for the contents of this article.

References

1. Imperatore G, Boyle JP, Thompson TJ, et al. Projections of type 1 and type 2 diabetes burden in the US population aged < 20 years through 2050. Diabetes Care 2012;35:2515–20.
2. Miller KM, Foster NC, Beck RW, et al. Current state of type 1 diabetes treatment in the U.S.: Updated data from the T1D Exchange clinic registry. Diabetes Care 2015;38:971–8.
3. Weinstock RS, Schütz-Fuhrmann I, Connor CG, et al. Type 1 diabetes in older adults: Comparing treatments and chronic complications in the United States T1D Exchange and the German/Austrian DPV registries. Diabetes Res Clin Pract 2016;122:28–37.
4. McKnight JA, Wild SH, Lamb MJE, et al. Glycaemic control of type 1 diabetes in clinical practice early in the 21st century: An international comparison. Diabet Med 2015;32:1036–50.
5. Bohn B, Herbst A, Pfeifer M, et al. Impact of physical activity on glycemic control and prevalence of cardiovascular risk factors in adults with type 1 diabetes: A cross-sectional multicenter study of 18,028 patients. Diabetes Care 2015;38:1536–43.
6. Conway B, Miller RG, Costacou T, et al. Temporal patterns in overweight and obesity in type 1 diabetes. Diabet Med 2010;27:398–404.
7. Colberg SR, Sigal RJ, Yardley JE, et al. Physical activity/exercise and diabetes: A Position Statement of the American Diabetes Association. Diabetes Care 2016;39:2065–79.
8. Quirk H, Blake H, Tennyson R, Randell TL, Glazebrook C. Physical activity interventions in children and young people with type 1 diabetes mellitus: A systematic review with meta-analysis. Diabet Med 2014;31:1163–73.
9. Miller RG, Mahajan HD, Costacou T, Sekikawa A, Anderson SJ, Orchard TJ. A contemporary estimate of total mortality and cardiovascular disease risk in young adults with type 1 diabetes: The Pittsburgh Epidemiology of Diabetes Complications Study. Diabetes Care 2016;39:2296–303.
10. Katz M, Giani E, Laffel L. Challenges and opportunities in the management of cardiovascular risk factors in youth with type 1 diabetes: Lifestyle and beyond. Curr Diab Rep 2015;15:119.
11. Kennedy A, Nirantharakumar K, Chimen M, et al. Does exercise improve glycaemic control in type 1 diabetes? A systematic review and meta-analysis. PLoS ONE 2013;8:e58861.
12. Chimen M, Kennedy A, Nirantharakumar K, Pang TT, Andrews R, Narendran P. What are the health benefits of physical activity in type 1 diabetes mellitus? A literature review. Diabetologia 2012;55:542–51.
13. Zoppini G, Carlini M, Muggeo M. Self-reported exercise and quality of life in young type 1 diabetic subjects. Diabetes Nutr Metab 2003;16:77–80.
14. Riddell MC, Gallen IW, Smart CE, et al. Exercise management in type 1 diabetes: A consensus statement. Lancet Diabetes Endocrinol 2017;5:377–90.
15. Umpierre D, Ribeiro PAB, Kramer CK, et al. Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: A systematic review and meta-analysis. JAMA 2011;305:1790–9.
16. Sigal RJ, Kenny GP, Boulé NG, et al. Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: A randomized trial. Ann Intern Med 2007;147:357–69.
17. Yardley JE, Hay J, Abou-Setta AM, Marks SD, McGavock J. A systematic review and meta-analysis of exercise interventions in adults with type 1 diabetes. Diabetes Res Clin Pract 2014;106:393–400.
18. Jacobs PG, El Youssef J, Reddy R, et al. Randomized trial of a dual-hormone artificial pancreas with dosing adjustment during exercise compared with no adjustment and sensor-augmented pump therapy. Diabetes Obes Metab 2016;18:1110–9.
19. Reddy R, El Youssef J, Winters-Stone K, et al. The effect of exercise on sleep in adults with type 1 diabetes. Diabetes Obes Metab 2018;20:443–7.
20. Zaharieva DP, Riddell MC. Insulin management strategies for exercise in diabetes. Can J Diabetes 2017;41:507–16.
21. Francescato MP, Stel G, Stenner E, Geat M. Prolonged exercise in type 1 diabetes: Performance of a customizable algorithm to estimate the carbohydrate supplements to minimize glycemic imbalances. PLoS ONE 2015;10. e0125220.
22. Ryninks K, Sutton E, Thomas E, Jago R, Shield JPH, Burren CP. Attitudes to exercise and diabetes in young people with type 1 diabetes mellitus: A qualitative analysis. PLoS ONE 2015;10. e0137562.
23. Yardley JE, Kenny GP, Perkins BA, et al. Effects of performing resistance exercise before versus after aerobic exercise on glycemia in type 1 diabetes. Diabetes Care 2012;35:669–75.
24. Yardley JE, Kenny GP, Perkins BA, et al. Resistance versus aerobic exercise: Acute effects on glycemia in type 1 diabetes. Diabetes Care 2013;36:537–42.
25. Iscoe KE, Riddell MC. Continuous moderate-intensity exercise with or without intermittent high-intensity work: Effects on acute and late glycaemia in athletes with type 1 diabetes mellitus. Diabet Med 2011;28:824–32.
26. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics—2015 update: A report from the American Heart Association. Circulation 2015;131:e29–322.
27. American College of Sports Medicine. ACSM's guidelines for exercise testing and prescription. Philadelphia, PA: Lippincott Williams & Wilkins; 2013.
28. Haff GG, Triplett NT. Essentials of strength training and conditioning. 4th edn. Champaign, IL: Human Kinetics; 2015.
29. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–81.
30. di Prampero PE, Ferretti G. The energetics of anaerobic muscle metabolism: A reappraisal of older and recent concepts. Respir Physiol 1999;118:103–15.
31. Vianna JM, Werneck FZ, Coelho EF, Damasceno VO, Reis VM. Oxygen uptake and heart rate kinetics after different types of resistance exercise. J Hum Kinet 2014;42:235–44.
32. Reis VM, Scott CB. Modeling the total energy costs of resistance exercise: A work in progress. Cent Eur J Sport Sci Med 2016;14:5–12. https://doi.org/10.18276/cej.2016.2-01.
33. Vezina JW, Der Ananian CA, Campbell KD, Meckes N, Ainsworth BE. An examination of the differences between two methods of estimating energy expenditure in resistance training activities. J Strength Cond Res 2014;28:1026–31.
34. Ahuja JKC, Moshfegh AJ, Holden JM, Harris E. USDA food and nutrient databases provide the infrastructure for food and nutrition research, policy, and practice. J Nutr 2013;143:241S–9S.
35. R Core Team. R: A Language and Environment for Statistical Computing. Vienna, Austria; 2017.

36. Ostman C, Jewiss D, King N, Smart NA. Clinical outcomes to exercise training in type 1 diabetes: A systematic review and meta-analysis. Diabetes Res Clin Pract 2018;139:380–91.
37. Durak EP, Jovanovic-Peterson L, Peterson CM. Randomized crossover study of effect of resistance training on glycemic control, muscular strength, and cholesterol in type I diabetic men. Diabetes Care 1990;13:1039–43.
38. Mosher PE, Nash MS, Perry AC, LaPerriere AR, Goldberg RB. Aerobic circuit exercise training: Effect on adolescents with well-controlled insulin-dependent diabetes mellitus. Arch Phys Med Rehabil 1998;79:652–7.
39. Ramalho AC, de Lourdes Lima M, Nunes F, et al. The effect of resistance versus aerobic training on metabolic control in patients with type-1 diabetes mellitus. Diabetes Res Clin Pract 2006;72:271–6.
40. Rissanen A-PE, Tikkanen HO, Koponen AS, Aho JM, Peltonen JE. One-year unsupervised individualized exercise training intervention enhances cardiorespiratory fitness but not muscle deoxygenation or glycemic control in adults with type 1 diabetes. Appl Physiol Nutr Metab 2018;43:387–96.
41. Wright LA-C, Hirsch IB. Metrics Beyond Hemoglobin A1C in diabetes management: Time in range, hypoglycemia, and other parameters. Diabetes Technol Ther 2017;19:S16–26.
42. Agiostratidou G, Anhalt H, Ball D, et al. Standardizing clinically meaningful outcome measures beyond HbA1c for type 1 diabetes: A consensus report of the American Association of Clinical Endocrinologists, the American Association of Diabetes Educators, the American Diabetes Association, the Endocrine Society, JDRF International, The Leona M. and Harry B. Helmsley Charitable Trust, the Pediatric Endocrine Society, and the T1D Exchange. Diabetes Care 2017;40:1622–30.
43. Pesta DH, Goncalves RLS, Madiraju AK, Strasser B, Sparks LM. Resistance training to improve type 2 diabetes: Working toward a prescription for the future. Nutr Metab 2017;14:24.
44. Mann S, Beedie C, Balducci S, et al. Changes in insulin sensitivity in response to different modalities of exercise: A review of the evidence. Diabetes Metab Res Rev 2014;30:257–68.
45. Egan B, Zierath JR. Exercise metabolism and the molecular regulation of skeletal muscle adaptation. Cell Metab 2013;17:162–84.

Supplementary Material

Supplementary Table 1
Summary of the resistance exercises during the resistance training visits

Resistance Exercise	Weight lifted (Kg)	Perceived Exertion (RPE)	Repetitions (reps)	Sets	% 1-RM
Leg Press	134 ± 43	13 ± 1	12 ± 1	3	68 ± 10
Bench Press	49 ± 17	15 ± 1	12 ± 1	3	67 ± 10
Leg Extension	23 ± 7	13 ± 2	12 ± 0	3	NA
Leg Flexion	11 ± 2	13 ± 1	12 ± 0	3	NA
Seated Row	38 ± 10	15 ± 1	12 ± 1	3	70 ± 10

Note. Data is shown as mean ± standard deviation.