Effect of 12-Week Resistance Exercise Program on Body Composition, Muscle Strength, Physical Function, and Glucose Metabolism in Healthy, Insulin-Resistant, and Diabetic Elderly Icelanders

O. G. Geirsdottir,1,2 A. Arnarson,1 K. Briem,3 A. Ramel,1 P. V. Jonsson,2,4 and I. Thorsdottir1

1Unit for Nutrition Research, Landspitali National University Hospital and Faculty of Food Science and Nutrition, University of Iceland, Reykjavik, Iceland.
2The Icelandic Gerontological Research Center, Reykjavik, Iceland.
3Department of Physical Therapy, University of Iceland, Reykjavik, Iceland.
4Department of Geriatrics, Landspitali National University Hospital, Faculty of Medicine, University of Iceland, Reykjavik, Iceland.

Address correspondence to Olof Gudny Geirsdottir, PhD, Unit for Nutrition Research, Eiriksgata 29, Landspitali National University Hospital, IS-101 Reykjavik, Iceland. Email: olofgg@landspitali.is

Background. Insulin is a stimulator of skeletal muscle protein anabolism and insulin resistance might therefore negatively affect muscle protein metabolism. We investigated muscle mass and physical function before and after a resistance exercise program in participants with prediabetes or type 2 diabetes mellitus (T2DM) in comparison to healthy controls.

Methods. This was a secondary analysis of a randomized controlled intervention designed to investigate resistance training among older adults. Glucose metabolism status was not a selection criteria for the trial, and group designation was done retrospectively. Participants (N = 237, 73.7 ± 5.7 y, 58.2% women) participated in a 12-week resistance exercise program (3 times/week; three sets, six to eight repetitions at 75%–80% of the one-repetition maximum), designed to increase strength and muscle mass of major muscle groups. Body composition, muscular strength, timed up and go test, 6-minute walk for distance, and blood chemical variables were measured at baseline and endpoint.

Results. Participants completing the study (n = 213) experienced significant changes in muscle strength or muscle function, which did not differ significantly between healthy (n = 198), prediabetic (n = 20), and T2DM participants (n = 17). Changes in serum glucose during the intervention differed by group: only glucose improved significantly in the prediabetic group, glucose and triacylglycerol improved significantly in the healthy group, whereas no serum parameter improved significantly in the T2DM group.

Conclusions. A 12-week resistance exercise program improves muscle strength and muscle function to a similar extent in healthy, prediabetic, and T2DM elderly people. However, according to our data, T2DM participants do not experience favorable changes in fasting glucose or HbA1C.

Key Words: Elderly—Diabetes mellitus type 2—Intervention.

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The efficacy of primary diabetes prevention in people with impaired glucose tolerance is well known, and there is strong evidence that progression to T2DM can be delayed or prevented. It has been shown that early lifestyle modifications, particularly those relating to beneficial changes in dietary intake, physical activity, and body composition, can be an effective way to avoid later diabetes and its complications later in life (1,2).

Both genetic and environmental factors are involved in the development of T2DM (2) as well as obesity and physical inactivity (3). Exercise, in addition to diet modification and medication, has been recommended as one of the three main components of diabetic therapy (4). Muscle mass seems particularly important when it comes to blood glucose homeostasis. The importance of muscle mass is well underlined by a recent study which found higher fasting blood glucose and insulin levels to be associated with lower muscle mass in people without diabetes (5). Diabetes has also been found to be associated with low muscle mass (6). However, the importance of increased muscle mass has been questioned by studies suggesting that changes in glucose metabolism are rather the consequence of internal alterations in the muscle during resistance training rather than changes in muscle size (7,8).

Resistance training has known benefits in older patients with impaired glucose (6,9). In general, resistance training
can increase muscle mass and consequently the muscle volume available for the uptake of glucose from blood (10). In T2DM patients, resistance exercise reduces insulin resistance and glycosylated hemoglobin (HbA1c; [11]).

Insulin is a potent stimulator of skeletal muscle protein anabolism, the specific mechanism by which insulin exerts its effects in human skeletal muscle is controversial. For example, several studies have reported insulin to have an inhibitory effect on muscle protein breakdown (12), whereas others have shown insulin to have a direct stimulatory effect on muscle protein synthesis (13). Insulin resistance might therefore negatively affect muscle protein metabolism if insulin signaling is compromised. Studies that addressed skeletal muscle amino acid metabolism in patients with T2DM showed mixed results, some reported that whole-body protein turnover was not impaired (14), whereas others showed that whole-body proteolysis is significantly elevated in patients with T2DM (15).

Very few studies have investigated the effects of resistance exercise on muscle mass and muscle function in patients with impaired glucose metabolism (16,17), particularly in comparison with healthy elderly controls (11). Blunted anabolic response of muscle to insulin is considered to be associated with lower skeletal muscle mass during aging (18). Therefore, patients with impaired glucose metabolism may gain less muscle mass, muscle strength, and muscle function during a resistance exercise program than healthy elderly controls.

Previously, our group investigated the effects of a 12-week resistance exercise program on body composition, muscle strength, and functional outcomes in Icelandic elderly participants (19). The resistance training program had a positive effect on muscle strength and led to a significant improvement in physical function and health-related quality of life.

The present study focused on the associations between impaired glucose metabolism, muscle strength, physical function, and resistance exercise in elderly Icelanders. The aims were (i) to investigate whether impaired glucose metabolism at baseline predicts changes in glucose metabolism during a 12-week resistance exercise program and (ii) to investigate whether impaired glucose metabolism at baseline predicts changes in muscle strength or physical function during a 12-week resistance exercise program.

**Methods**

**Subjects**

Participants (N = 237) were recruited by advertisements posted in the Reykjavik area (19). Exclusion criteria were age younger than 65 years, low cognitive function (Mini-Mental State Examination ≤ 19 points; [20]), evidence of uncontrolled coronary heart disease, major musculoskeletal disease, and pharmacological interventions with exogenous testosterone or other drugs known to influence muscle mass. Furthermore, participants had to be free of other disorders that could affect their ability to complete the training and testing. Enrolled participants were apparently healthy, although some had milder forms of hypertension, hyperlipidemia, T2DM, or other diseases associated with age. When cardiovascular disease symptoms were detected during screening, participants were encouraged to contact their physician for medical clearance. The study was approved by the Icelandic National Bioethics Committee (VSNb2008060007/03-15), and informed written consent was obtained from all participants.

**Study design and intervention.**—The current study is a part of a randomized and controlled dietary intervention study originally designed to investigate the effects of different dietary supplement drinks on the efficacy of resistance training among older adults. The 12-week resistance exercise program was designed to increase strength and muscle mass of all major muscle groups. All data were obtained at baseline and again at the end of the study period. Glucose metabolism status was not a selection criteria for the weight training trial, and the group designation used in the analyses conducted in the current article was not part of the original study.

Participants exercised for three nonconsecutive days per week for 12 weeks in groups of 20–30 individuals. Each session was supervised by study staff, an athletic trainer, and occasionally a physical therapist. Ten different exercises were performed in weight machines during each training session; seated leg extension, seated leg curl, seated leg press, seated chest fly, seated row, seated pull-down, seated biceps curl, seated triceps curl, seated lower back extension, and seated abdominal curl. Before the intervention started, 1-repetition maximum (1-RM) was assessed using weight machines and by progressively increasing the weight lifted until the participant failed to lift the weight. Prior to the 1-RM test, most of the participants were not familiar with the weight machine equipment. The first week of the 12-week training period was used to teach correct exercise techniques at lower loads (60% of 1-RM). Thereafter, resistance training involved three sets, where each exercise was repeated six to eight times, at 75%–80% of their 1-RM. The training load was systematically increased by 5%–10% each week in order to keep the number of repetitions per set between six and eight. Each exercise session started with a moderate, 10- to 15-minute aerobic warm-up on a treadmill or a stationary exercise bicycle, after which resistance training with weight machines was performed. Stretching exercises were performed at the end of each session.

Participants were randomly assigned to one of three different dietary supplements that were consumed after each training session. The dietary supplements were (i) a whey protein drink (20 g whey protein isolate + 20 g carbohydrates), (ii) a milk protein drink (20 g milk protein isolate...
Methods

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in patients with T2DM (15).

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EFFECT OF 12-WEEK RESISTANCE EXERCISE PROGRAM

M ethods

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Biochemical Measurements

Participants were instructed to avoid strenuous exercise and alcohol consumption the day before the drawing of fasting blood samples at baseline and endpoint. The blood samples were centrifuged and the serum was stored at −80°C for subsequent analysis of blood glucose (mmol/L), insulin (mIU/L), HbA1c (%), and plasma triacylglycerol (mmol/L).

Insulin was measured with electrochemiluminescence immunoassay on a Modular Analytics E170 system from Roche Diagnostics (Manheim, Germany). Plasma triacylglycerol and glucose were analyzed using an enzymatic colorimetric assay and an automated analyzer (Hitachi 911; Roche Diagnostics). HbA1c was measured using a chromatographic–spectrophotometric assay.

Participants were grouped according to impairment of glucose metabolism into (i) healthy participants, (ii) participants with prediabetes, and (iii) participants diagnosed with T2DM. Participants with prediabetes were defined as having impaired fasting glucose levels, from 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L; [24]).

Statistical Analysis

The data were entered into the SPSS statistical package, version 18.0 (SPSS, Chicago, IL). Data are described as the mean ± standard deviation. Data were checked for normality, using the Kolmogorov–Smirnov test and nonparametric tests were calculated on data not normally distributed. The independent-samples t test and Mann–Whitney U test were used to calculate the differences between individuals who dropped out and those who completed the study. The paired t test and Wilcoxon test (nonparametric) were used to evaluate differences between the baseline and endpoint. Pearson correlation coefficient r was used to investigate associations between anthropometric changes or gains in strength or function and improvements in glucose metabolism observed after the intervention.

Linear Models

Linear models were used to calculate differences in the outcomes between the three groups. The models included fixed factors (gender, group, physical activity category, and protein drink) and covariates (baseline value of the outcome variable and age). Results from the linear models are shown as parameter estimates, where the healthy and prediabetic participants were compared with the T2DM participants. Additionally, pair wise comparisons were done (estimated marginal means with Bonferroni confidence interval adjustment). The significance level was set at p ≤ .05.
Retrospective power calculations showed that with the numbers of participants in the prediabetic and diabetic group, a difference of 0.5% HbA1c and 0.8 mmol glucose can be detected as significant (power = 0.8, significance level = 0.05).

**RESULTS**

At baseline 237 (male = 98, female = 139, age range = 65–92 y) participants started the 12-week program, and 213 (male = 91 and female = 122) participants completed the study. The dropout rate was 9%, and the reasons for dropping out were illness and falls at home (n = 18); some participants did not like the program (n = 8), whereas others had to quit because of previously diagnosed musculoskeletal problems (n = 3) and two participants did not have all results from the serum analysis and were excluded. Dropouts were significantly older at baseline (p = .001), had less quadriceps strength (p = .002), and grip strength (p = .016), and there was no gender difference. Dropouts had less 6-minute walk for distance (p = .006) and slower timed up and go test (p = .003).

### Table 1. Participants’ Characteristics at Baseline and Endpoint

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Healthy elderly (n = 198)</th>
<th>Prediabetic (n = 20)</th>
<th>T2DM (n = 17)</th>
<th>Between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>p Value*</td>
<td>Mean ± SD</td>
<td>p Value*</td>
</tr>
<tr>
<td>Age (years)</td>
<td>73.15 ± 5.51</td>
<td>76.95 ± 5.26</td>
<td>75.18 ± 6.73</td>
<td>.009</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>28.46 ± 4.79</td>
<td>28.79 ± 4.80 .011</td>
<td>31.69 ± 5.71</td>
<td>.029</td>
</tr>
<tr>
<td>Body fat%</td>
<td>37.67 ± 4.44</td>
<td>37.12 ± 7.20 .001</td>
<td>39.93 ± 5.11</td>
<td>.795</td>
</tr>
<tr>
<td>Lean body mass (kg)</td>
<td>47.05 ± 9.45</td>
<td>48.39 ± 9.73 .001</td>
<td>54.09 ± 11.27</td>
<td>.037</td>
</tr>
<tr>
<td>Absolute quadriceps strength (N)</td>
<td>465.57 ± 119.34</td>
<td>522.92 ± 129.28 .001</td>
<td>429.31 ± 123.50</td>
<td>.403</td>
</tr>
<tr>
<td>Quadriceps strength/lean body mass (N/kg)</td>
<td>10.00 ± 2.08</td>
<td>10.92 ± 2.17 .001</td>
<td>9.49 ± 2.61</td>
<td>.001</td>
</tr>
<tr>
<td>Grip strength (kg)</td>
<td>28.19 ± 8.56</td>
<td>29.91 ± 8.96 .001</td>
<td>30.72 ± 10.47</td>
<td>.556</td>
</tr>
<tr>
<td>Six-minute walking distance (m)</td>
<td>459.66 ± 77.59</td>
<td>501.02 ± 70.46 .001</td>
<td>431.80 ± 80.67</td>
<td>.009</td>
</tr>
<tr>
<td>Timed up and go test (s)†</td>
<td>7.74 ± 1.94</td>
<td>7.02 ± 1.54 .001</td>
<td>8.79 ± 3.53</td>
<td>.044</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.51 ± 0.30</td>
<td>5.57 ± 0.30 .001</td>
<td>5.87 ± 0.39</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Glucose (mmol/L)†</td>
<td>4.63 ± 0.46</td>
<td>4.31 ± 0.86 .006</td>
<td>5.99 ± 0.35</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Insulin (μU/L)</td>
<td>10.25 ± 7.27</td>
<td>11.20 ± 9.80 .648</td>
<td>24.6 ± 22.58</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Triacylglycerol (mmol/L)†</td>
<td>143.47 ± 18.27</td>
<td>142.47 ± 18.11 .680</td>
<td>150.52 ± 24.75</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>150.91 ± 23.00</td>
<td>150.18 ± 32.69 .287</td>
<td>150.18 ± 32.69</td>
<td>.129</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>75.18 ± 6.73</td>
<td>74.34 ± 9.63 .019</td>
<td>76.27 ± 8.65</td>
<td>.778</td>
</tr>
</tbody>
</table>

Notes: BMI = body mass index; T2DM = type 2 diabetes mellitus.

* p Value between baseline and endpoint within a group (paired t test for data with normal distribution or paired Wilcoxon test for data not with normal distribution).

† p Value between groups according to glucose metabolism, Kruskal–Wallis unparametric test.

‡ Data not with normal distribution; significant difference between baseline and endpoint within a group (paired Wilcoxon test) p value <.05.

§ Timed up and go test is weighed negatively, ie, lower time is better.
A majority (82%) of the participants reported regular physical activity at baseline and two thirds reached the recommended level of 30 minutes per day (25). According to Kruskal–Wallis test, the distribution of physical activity (min/week) was equal across groups ($p = .790$). Reported physical activity was primarily moderate aerobic exercise, and only three male participants had engaged in resistance exercise in the year prior to the start of the study.

At baseline, 7.2% of participants had T2DM ($n = 17$; male $= 9$, female $= 8$), and additional 8.4% of participants were prediabetic ($n = 20$; male $= 9$, female $= 11$). No difference was found in gender, Mini-Mental State Examination, or in sociodemographic factors between diabetic elderly participants and prediabetic or healthy participants at baseline. The characteristics of the three groups are shown in Table 1.

After the intervention, all groups exhibited significant changes in muscle strength and physical function (Table 1). According to linear models, no difference was found in the degree of changes seen in muscle strength or physical function (Table 2) between healthy participants and participants with prediabetes or T2DM.

According to bivariate analysis, only glucose improved significantly in the prediabetic group; glucose and triacylglycerol improved significantly in the healthy group; whereas no serum parameter improved significantly in the T2DM group (Table 1). According to the linear models, healthy and prediabetic participants had (borderline) significantly lower endpoint HbA1c and glucose (both corrected for baseline values) than T2DM participants (Table 3). Differences in insulin and triacylglycerol were not significant between groups (model not shown).

No association was found between increased muscle mass, quadriceps strength, or physical function and improved glucose control during the intervention (data not shown).

**DISCUSSION**

In the present study, we investigated the effects of resistance training on muscle mass, muscle strength, physical function, and glucose metabolism in three groups of healthy, prediabetic, and T2DM older people.

The most important finding of our study is that the participants of the three groups increased muscle mass, muscle strength, and physical function to a similar degree after the intervention. Although studies have reported that resistance training improves muscular outcomes in diabetic older adults (16,17,26), a recently published study indicated that individuals with T2DM gain less strength than non-T2DM participants (11). The authors explained this difference with impairment in the basal hypothalamic-pituitary-adrenal axis function as a limiting factor in strength development in older T2DM adults (11). However, in the study by Holten and colleagues (7), participants in 6-week strength training program, the increase in maximal leg muscle strength were similar between the T2DM and healthy older men, which is in line with our result. In general, muscle weakness in T2DM has been explained by anabolic resistance due to insulin resistance or neuropathy (18,27). Our results do not support a negative effect of impaired glucose metabolism on training efficacy in older adults.

According to bivariate analysis, there were some significant changes in blood variables after the 12-week intervention, ie, glucose (prediabetic and healthy participants) and triacylglycerol (healthy participants). No significant changes in serum parameters were seen in the T2DM group. According to the linear models, healthy and prediabetic participants had (or tended to have) lower glucose and HbA1c compared with T2DM participants. All participants in the T2DM group were taking either oral hypoglycemic medication or insulin during the intervention, resulting into fasting glucose at baseline below 8 mmol/L, which can explain why we did not see any effects of the intervention on parameters.

**Table 2. Parameter Estimates From a Linear Model for the Prediction of Normalized Quadriceps Strength and Physical Function (endpoint)**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Healthy elderly participants</th>
<th>Prediabetic elderly participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>95% CI</td>
<td>$p$ Value</td>
</tr>
<tr>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Normalized Quadriceps Strength</td>
<td>$-0.058$</td>
<td>$-0.717$</td>
</tr>
<tr>
<td>6MWD</td>
<td>$-0.320$</td>
<td>$-1.153$</td>
</tr>
<tr>
<td>TUG*</td>
<td>$-0.320$</td>
<td>$-1.153$</td>
</tr>
</tbody>
</table>

Notes: Model adjusted for gender, age, baseline value of the outcome, physical activity, and drink. CI = confidence interval; 6MWD = 6-minute walk for distance; TUG = timed up and go test.

*Lower time indicates better physical function.

†Compared with DM2 participants. Difference between healthy and prediabetic elderly participants was not significant.

**Table 3. Parameter Estimates From Linear Models for the Prediction of Glucose (mg/dL) and HbA1c (%) at Endpoint**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Glucose</th>
<th>HbA1c</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>95% CI</td>
</tr>
<tr>
<td>Healthy elderly participants</td>
<td>$-1.011$</td>
<td>$-2.023$</td>
</tr>
<tr>
<td>Prediabetic elderly participants</td>
<td>$-1.055$</td>
<td>$-1.916$</td>
</tr>
</tbody>
</table>

Notes: $R^2 = .413$; $R^2 = .498$. Model adjusted for gender, age, baseline value of the outcome, and drink. CI = confidence interval.

*Compared with DM2 participants. Differences between healthy and prediabetic elderly participants were not significant.
of glucose metabolism. In a similar study in T2DM participants, a 29% decrease in fasting glucose was observed after 4 months of resistance exercise (compared with baseline). Although the patients received drug therapy, their baseline glucose was more than 11 mmol/L, which possibly explains the huge improvements after training (28). Other studies using a combination of resistance and endurance exercise have also reported improvements in fasting glucose after training in T2DM participants with baseline fasting glucose of 9.2 and 12.0 mmol/L (29,30).

Several studies (16,31), although not all (32), have shown a decline in HbA1c in patients with T2DM after resistance exercise spanning from several weeks to several months. A recent meta-analysis done by Strasser and colleagues (33) showed that the greatest improvements in glycomic control occurred when HbA1c was more than 8.0% at baseline. This is higher than the average HbA1c in our T2DM group (6.8% at baseline) and could explain why no effect was seen on HbA1c among T2DM participants after the intervention.

Our data showed no association between increased muscle mass, quadriceps strength, or physical function and improved glucose control during the intervention. A possible reason is that improvement in glycomic control is not dependent upon change in muscle mass. On the contrary, changes in glucose metabolism are rather the consequence of internal alterations in the muscle than changes in muscle size (7,8).

**Limitation**

The study participants were well-functioning older people who were more physically active and healthier than the average older individual and thus not representative of the general population of this age. Furthermore, the study period was only 12 weeks, which may have limited the participants’ ability to demonstrate larger gains in muscle mass. The number of prediabetic and T2DM participants was low, which limited statistical power to detect statistically significant differences. However, according to the linear models, our study still detected significant differences in blood parameters between the groups but not in muscular strength or physical function, where the actual endpoint differences between groups were small and did not seem clinically relevant, ie, 0.2 seconds for timed up and go test, 6 m in 6-minute walk for distance, and 0.3 N/kg in quadriceps strength/lean body mass.

**Conclusions**

A 12-week resistance exercise program can improve strength and physical function in healthy, prediabetic, and T2DM elderly participants to a similar degree. However, according to our data, T2DM participants do not experience favorable changes in fasting glucose or HbA1c.

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**Conflict of Interest**

The authors declare that they have no competing interests. All authors are responsible for the reported research. O.G.G. worked on study design, project planning, and the statistical analysis and wrote the first draft of the manuscript. A.A., K.B., P.V.J., and A.R. participated in designing the study and project planning. A.R. worked on data analysis and in drafting the article. I.T. was the project leader and participated in all parts of the work. All authors provided critical revision of the article and read and approved the final manuscript.

**Acknowledgments**

This study does not necessarily reflect the views of the sponsors, and the sponsors in no way anticipate future policy in this area. The trial is registered at the US National Library of Medicine (Nr. NCT01074879).

**References**