Original Article

Effect of Strength Training on Plasma Levels of Homocysteine in Patients with Type 2 Diabetes

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Abstract

Background: The objective of this study was to analyze the effects of strength training on plasma homocysteine levels and cardiovascular risk factors in patients with type 2 diabetes. **Methods:** The sample consisted of 14 diabetic women with a mean age of 68 ± 6 years. Biochemical evaluations and anthropometric measurements were taken before and after training. Training sessions lasted 50 min and comprised three sets of 8–12 repetitions each. The established load was 60% of 1 repetition maximum. **Results:** After the training program, it was observed that the levels of homocysteine (average before 13.4 ± 2.9 and after 12.8 ± 3.3, P = 0.40), very low-density lipoprotein (LDL) (average before 41.9 ± 17.0 and after 36.2 ± 11.8, P = 0.47), total cholesterol (average before 214.4 ± 60.6 and after 190.2 ± 62.3, P = 0.09), triglycerides (average before 209.3 ± 85.4 and after 181.5 ± 59.2, P = 0.47), and blood glucose (average before 123.5 ± 30.4 and after 110.1 ± 24.7, P = 0.26) showed no significant changes, but the LDL (average before 129.1 ± 63.4 and after 95.7 ± 53.3, P = 0.04), high-density lipoprotein (average before 43.2 ± 12.0 and after 58.2 ± 15.6, P = 0.01), lean mass (average before 41.1 ± 5.7 and after 42.8 ± 5.4, P = 0.008), fat mass (average before 31.4 ± 8.8 and after 29.7 ± 8.5, P = 0.001), and percentage fat (average before 42.6 ± 4.0 and after 40.3 ± 4.6, P = 0.000) showed significant changes. **Conclusions:** This study concluded that strength training does not improve homocysteine levels, but help to improve the lipoprotein profile in type 2 diabetic patients.

Keywords: *Cholesterol, glucose, hyperhomocysteinemia, obesity, strength exercise*

Introduction

Type 2 diabetes is a metabolic disorder associated with high blood glucose levels due to decreased binding of insulin to its receptor and reduced insulin production.[1] Type 2 diabetes is one of the major risk factors for atherosclerosis, a chronic disease that leads to the formation of atherosclerotic plaques within blood vessels. This leads to obstruction and loss of blood vessel elasticity. In the literature, a relationship between diabetes and the formation of fatty plaques, contributing to the risk of myocardial infarction, stroke, and peripheral vascular disease, can be observed. Moreover, atherosclerosis can lead to hypertension and heart failure by increasing peripheral resistance.[2] Strength training promotes an increase in muscle mass[3] and increase in basal metabolic rate.[4] It has been reported that a strength training program can have good results in controlling diabetes and reducing atherosclerosis and is likely to have positive effects on glucose metabolism. Training can lead to decreased levels of low-density lipoprotein (LDL), decreased very LDL (VLDL) production, and an increase in high-density lipoprotein (HDL) cholesterol levels after the intervention[5] Strength training has also been shown to reduce blood glucose levels, body fat percentage, and abdominal fat.[6,7] Control of these factors is important to reduce cardiovascular risk.[8]

However, the influence of strength training on homocysteine levels is rarely discussed in the literature. Homocysteine is synthesized in the liver from methionine. It is strongly related to atherosclerotic plaque formation, and therefore it is considered an important indicator of cardiovascular disease risk.[9,10] Thus, analyzing the influence of a strength training program on homocysteine levels is important for assessing its contribution to the control of cardiovascular risks and the prevention of atherosclerosis in individuals with type 2 diabetes.[10] With this in mind, the objective of this study was to analyze the effects of strength training on plasma homocysteine levels and cardiovascular risk factors in patients with type 2 diabetes.

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Methods

Design and subjects

This longitudinal, quantitative study included 14 women with a mean age of 68 ± 6 years, with a diagnosis of type 2 diabetes. Patients were assessed before and after the training program. Patients were not permitted to perform any additional training during the study. They were instructed to diet by a nutrition professional; however, the diet was not controlled. The patients used metformin two to three times/day.

The criteria for exclusion of patients with type 2 diabetes were as follows: hypertension, stroke, heart attack, smoking habit, and a change in medication during the training period. Inclusion criteria were sufficient clinical fitness to participate in a strength training program and a sedentary lifestyle for the 12 months prior to starting training. All the study participants signed an informed consent form, explaining the aims of the research and all the risks and benefits to which they may be exposed during the research. The study was approved by the Committee of Ethics and Research from Centro Universitário de Itajubá (protocol no. 139).

Instruments

For analysis of total cholesterol, HDL, LDL, VLDL, and glucose, the following equipment was used: spectrophotometer (Biospectro Benfer SP-22, Brazil) (reading 505 nm), cholesterol kit-PP–Cat. 460 (Labtest, Brazil), glucose PAP Liquiform kit (Labtest, Brazil), centrifuge (Benfer–BMC macro centrífuga, Brazil), and bath (Quimis 021/4, Brazil), using a confidence interval of 95%.[11] The homocysteine analysis was performed with high-performance liquid chromatography (HPLC), which was chosen for its high sensitivity and reliability (coefficient of variation = 5%).[12]

The height was verified by means of a stadiometer (mark Seca®, Alemanha) made of rigid material with a retractable wall-mounted metal measuring tape with range 0–220 cm and 0.1-cm resolution. Weight was measured with Filizola®-branded scales (Filizola, Brazil) with capacity up to 180 kg and 100-g fractions.[13] A metallic tape measure (Cescorf®, Brazil) 2 m in length and 6 mm in width was used to measure waist and hip circumferences.[14] Skinfold thickness was measured using a scientific compass (Cescorf®, Brazil) with constant pressure of 10G/mm² and reading accuracy of 0.1 mm.[15] Blood pressure was measured with a sphygmomanometer (Aneroid Sphygmomanometer HICO HM-1001®, Alemanha) and a stethoscope (Nurse Type Professional Stethoscope-HICO HM-3005®, Alemanha).[11] In assessing initial strength to set the limitations of the strength training, and for the training itself, the following systems and equipment were used: table bench, upright row, low rowing machine, leg curl, leg extension, leg press, triceps pulley bars, dumbbells, and barbells (Movement®, Brazil).[16]

Procedures

Biochemical analysis

Tests were carried out at the beginning and at the end of the training program. Twelve-hour fasting blood samples of 10 mL were collected by venipuncture from the antecubital vein. Enzyme end-point reaction was used for analysis of cholesterol, HDL, LDL, VLDL, and glucose levels. After collection, samples were separated into plasma and serum. Sera were used for measuring concentrations of cholesterol, HDL, LDL, VLDL, and triglyceride levels, and plasma fluoride was used for measuring glucose levels.[11] The samples were separated into test tubes containing ethylenediaminetetraacetic acid for evaluation of homocysteine plasma levels by HPLC. Plasma was separated immediately after collection and frozen at −4°F until analysis. DPC-Medlab reagents with an analytical sensitivity of 0.5 μM/l for values between 5.0 and 15.0 μM/l were used. Plasma and serum levels were interpreted through quantitative analysis of the peak area of the chromatograms.[12]

Blood pressure measurement

Blood pressure was measured through auscultation with the research subjects in the seated position, resting for 5 min before the measurement.[11]

Anthropometric measurements

Body mass index (BMI) was calculated using the formula: weight/height². Individuals were weighed wearing light clothing and without shoes.[13,15] To calculate the waist-hip ratio, waist circumference was measured with a measuring tape below the ribs and above the navel. The hip perimeter was measured with the tape positioned in the area of the greatest gluteal protuberance, and the waist-hip ratio was calculated by dividing the waist circumference by the hip measurement. This procedure has a reliability coefficient of 0.91.[14] Body fat percentage was calculated using the Durnin and Womersley prediction equations with four skinfolds (subscapular, triceps, suprailiac, and biceps).[17]

Strength evaluation

Individuals had two familiarization sessions for each exercise, performing two sets of ten repetitions with no resistance applied. Evaluation of the dynamic strength of the muscles involved in training was performed on the third visit. Three attempts were made to reach the value of 1 repetition maximum (RM), with a rest period of 5 min between each trial.[16] The assessment of the maximum force was made in order to define the loads used in the strength training program and as a means of ensuring that the patients completed the training.

Training program

The strength training program lasted 16 weeks. It consisted of two training sessions a week (total = 32 sessions), with

initial load of 60% of 1 RM. Each training session lasted 50 min and consisted of three sets of 8–12 repetitions of each exercise, with 1 min 30 s rest between each. When the individual was able to perform 12 repetitions completely, the load was increased by 5 pounds. The exercises performed were bench press, upright row, low row, leg curl, leg extension, leg press, and triceps and biceps curl.[16]

Statistical analysis

The study was designed to determine the influence of strength training on plasma homocysteine levels in individuals with type 2 diabetes. The minimum number of the sample was calculated using the program BioEstat 5.3® (MCT, Belém, Pará, Brazil)**,** the minimum number being defined by means of the differences (before and after) and standard deviation (SD) of the differences. The power of the established test was 0.9 and the alpha level was 0.05. For the strength training program, the minimum number defined was 14 individuals, already considering 10% required to reduce the sample error. The survey data were analyzed quantitatively by using descriptive statistics (mean and SD). Normality was assessed using the Shapiro–Wilk test to analyze the variance and outliers. For parametric data, we used paired Student's *t*-test. For nonparametric data, we used the Wilcoxon matched-pair signed-rank test. Effect sizes were interpreted according to Cohen's effect size index.[18] Statistical analysis was performed using SPSS Statistics 20.0® (IBM®), and the level of significance for the results of 1 RM was $P < 0.01$. Statistical significance for the other results was defined as $P < 0.05$.

Results

The mean values (±SD) of the sample characteristics obtained before and after the exercise program are shown in Table 1. From the analysis of values in Table 1, it is clear that strength training did not influence the characteristics of the sample. Figure 1 shows that strength training did not influence plasma levels of homocysteine. Levels of VLDL, triglycerides, total cholesterol, and glucose showed no significant differences after training. We noticed that the LDL and HDL levels showed significant differences between the pre- and posttest measurements, according to Table 2. Table 3 shows that the percentage of fat and fat mass decreased and lean body mass increased significantly after strength training. Skinfold thickness of the triceps, supra iliac, pectoral, abdomen, thigh, axillary, and biceps showed a significant decrease in the mean, but the subscapular skinfold thickness showed no significant difference pre- and posttest. The 1 RM measurements are shown in Table 4. The results of the test showed significant differences pre- and posttest for the bench press, high stroke, low row, leg curl, leg extension, leg press, triceps, and curl.

Discussion

The study examined the effects of strength training on plasma homocysteine levels in individuals with type 2 diabetes. Plasma homocysteine level was not significantly different after strength training. The results differed from those obtained by Vincent *et al*.,[19] which showed that 24 weeks of strength training decreased homocysteine levels. In this study, the differences in homocysteine levels were monitored before and after 6 months of low- or high-intensity strength training.[20] These differences in results may be due to differences in the samples.

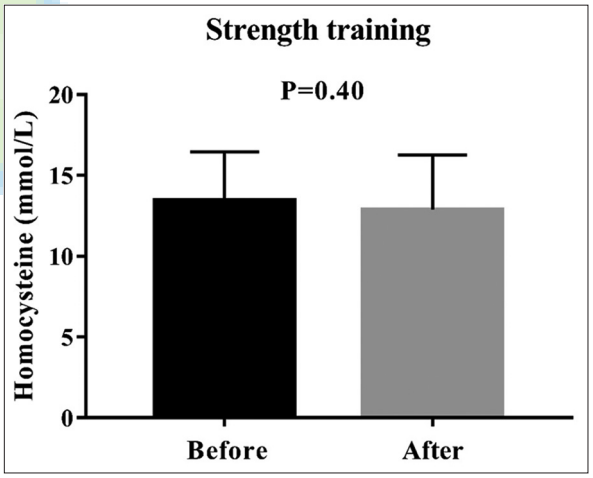

Figure 1: Effect of strength training on plasma levels of homocysteine (average before 13.4 ± 2.9 and after 12.8 ± 3.3; Δ% −4.4 and effect size 0.19)

Table 1: Mean values (±standard deviation) of variables of sample characterizing before (pretest) and after (posttest) the intervention

Variables	Pretest	Posttest	*P*<0.05	Δ%	Effect size
Weight (kg)	72.6±14.1	72.5±13.3	0.93	−0.1	0.007
Height (m)	1.5±0.0	1.5±0.0	-	-	-
BMI (kg/m^2)	30.2±5.4	30.9±5.2	0.38	2.3	−0.13
Waist (cm)	103.3±10.8	102.4±10.7	0.15	−0.8	0.08
Hips (cm)	107.5±10.0	105.8±10.0	0.12	−1.5	0.17
Waist and hip ratio	0.9±0.0	0.9±0.0	0.78	-	-
Systolic blood pressure (mmHg)	137.1±20.5	129.2±21.2	0.11	−5.7	0.37
Diastolic blood pressure (mmHg)	80.0±6.7	77.1±9.9	0.35	−3.6	0.34

BMI=Body mass index

Table 2: Mean values (±standard deviation) of biochemical variables before (pretest) and after (posttest) the intervention

Variables	Pretest	Posttest	*P*<0.05	Δ%	Effect size
LDL (mg/dL)	129.1±63.4	95.7±53.3	0.04*	−25.8	0.57
HDL (mg/dL)	43.2±12.0	58.2±15.6	0.01*	34.7	−1.07
VLDL (mg/dL)	41.9±17.0	36.2±11.8	0.47	−13.6	0.38
Triglyceride (mg/dL)	209.3±85.4	181.5±59.2	0.47	−13.2	0.37
Total cholesterol (mg/dL)	214.4±60.6	190.2±62.3	0.09	−11.2	0.39
Glucose (mg/dL)	123.5±30.4	110.1±24.7	0.26	−10.8	0.48

*Significant difference. LDL=Low-density lipoprotein, HDL=High-density lipoprotein, VLDL=Very low-density lipoprotein

Table 3: Mean values (±standard deviation) of anthropometric variables before (pretest) and after (posttest) the intervention

Variables	Pretest	Posttest	*P*<0.05	Δ%	Effect size
Total fat (%)	42.6±4.0	40.3±4.6	0.000*	−5.3	0.53
Lean mass (kg)	41.1±5.7	42.8±5.4	0.008*	4.1	−0.30
Fat mass (kg)	31.4±8.8	29.7±8.5	0.001*	−5.4	0.19
Triceps (mm)	28.4±8.4	23.9±8.5	0.000*	−15.8	0.53
Suprailiac (mm)	44.9±14.5	38.5±15.5	0.001*	−14.2	0.42
Subscapular (mm)	37.9±8.0	34.7±10.5	0.09	−8.4	0.34
Bicipital (mm)	24.6±8.3	20.4±6.6	0.008*	−17.0	0.56
Pectoral (mm)	37.3±10.3	28.2±7.7	0.004*	−24.3	1.00
Abdominal (mm)	57.7±17.4	47.1±12.1	0.001*	−18.3	0.70
Thigh (mm)	40.8±17.8	31.0±16.3	0.000*	−24.0	0.57
Axillary-average (mm)	38.1±9.5	34.2±10.5	0.01*	−10.2	0.38

*Significant difference

Table 4: Mean values (±standard deviation) of 1 repetition maximum test (kg) before (pretest) and after (posttest) intervention

Variables	Pretest	Posttest	*P*<0.01	Δ%	Effect size
Bench press (kg)	13.2±4.4	20.8±3.7	0.001*	57.5	−1.86
Low rowing (kg)	46.0±10.8	65.6±15.0	0.001*	42.6	−1.49
Triceps (kg)	30.7±5.4	40.7±7.5	0.001*	32.5	−1.53
Screw (kg)	26.0±3.4	32.1±3.7	0.000*	23.4	−1.71
High rowing (kg)	28.9±6.5	39.6±5.7	0.001*	37.0	−1.75
Leg extension (kg)	27.8±9.7	45.0±14.8	0.000*	61.8	−1.37
Leg press (kg)	59.8±14.6	101.5±17.0	0.001*	69.7	−2.63
Leg curl (kg)	16.0±6.8	26.7±7.4	0.000*	66.8	−1.50

*Significant difference

Plasma homocysteine level appears to be influenced by several factors, including the state of training and diet composition. According to Dankner *et al.*,[21] when training regimens in the elderly were studied, there is an inverse relationship between homocysteine levels and the level of training. With regard to diet, the ingestion of food rich in protein is associated with higher levels of plasma homocysteine. Protein excess can lead to increased methionine. The catabolism of methionine leads to homocysteine production, high levels of which may lead to thrombogenesis and atherogenesis.[10] Lifestyle, smoking, and Vitamin B deficiency are also factors that may contribute to elevated levels of homocysteine.[10] Although in our study the homocysteine levels were not significantly different with strength training, it showed a tendency to decrease. Considering that the patients in this sample were taking medication and that the values of homocysteine in the pretest were in the high end of the normal range, it seems important to highlight that while this variation is not statistically significant, reductions represent a reduced risk for atherosclerosis with strength training. Although speculative, it seems likely that extending the training period and increased training frequency in the week may have had more significant effects on the levels of homocysteine and eventually in medication decrease. After training, patients also showed no significant difference in the levels of VLDL, triglycerides, and total cholesterol. In the literature, the results are similar to our study, in that after 16 weeks of training, cholesterol values did not show any significant differences.[22] In another study, the metabolic variables also showed no significant difference after training.[23] Strength training with a duration of 6 months of high- or low-intensity training also showed no significant differences in biochemical variables.[20] A 16-week training program of moderate intensity may not be sufficient to control some risk variables. In our study, LDL and HDL levels showed significant differences after strength training. Plasma levels of HDL and LDL also showed similar results in other studies after strength training for 16 weeks.[24] The results show that LDL and HDL levels may be controlled using strength training, contributing to the control of vascular diseases and reducing the risk of atherosclerosis. In vascular disease, oxidized LDL is taken up by macrophages, leading to the formation of atheromatous plaques. It is also important to highlight that the training improves levels of HDL, which contributes to the removal of LDL by transporting it to the liver. In our study, glucose level was not significantly different after strength training. The results from the literature are equivocal on this point, with some studies finding significant differences,[23,25] and other studies finding no difference.[26] Strength training is believed to improve insulin receptor sensitivity. The GLUT4 glucose transporter quantity increases in response to training, allowing the transport of glucose into the cell.[23,25] Although the results were not statistically significant, there was a general decrease in plasma glucose values. The anthropometric

variables of lean mass, fat mass, and percentage fat showed a significant difference after 16 weeks of strength training. Previous studies have demonstrated a decrease in body fat and increased lean body mass in diabetics who undergo weight training. The data show that strength training can help control some anthropometric variables related to cardiovascular risk. Reducing central obesity contributes to the control of risk factors for diabetes and atherosclerosis, including inflammatory issues.[27] The anthropometric variables that signify this such as weight, BMI, waist circumference, hip circumference, and waist hip ratio did not show any differences after training. Previous results are similar, with no difference in these anthropometric variables seen after 20 weeks of training. The increase in lean mass and decrease in fat mass may explain these results.[28] In our study, the results demonstrate a significant increase in strength after 16 weeks of strength training, with an increase in load used during the training program. This is in concordance with previous results.[22]

It was concluded that strength training for 16 weeks is not sufficient to reduce serum homocysteine levels in individuals with type 2 diabetes. This form of training can help to reduce plasma levels of LDL, increase plasma levels of HDL, decrease body fat, and increase muscle mass.

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Conflicts of interest

There are no conflicts of interest.

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