



# The effect of physical activity on total homocysteine concentrations and cardiovascular risk in older Brazilian adults with type 2 diabetes

José Jonas de Oliveira<sup>1,2</sup> · Alexandre de Souza e Silva<sup>2</sup> · Anna Gabriela Silva Vilela Ribeiro<sup>1</sup> · Carolina Gabriela Reis Barbosa<sup>1</sup> · Jasielle Aparecida de Oliveira Silva<sup>2</sup> · Annie Guimarães Pontes<sup>2</sup> · João Paulo Estevam Batista<sup>2</sup> · Adriana Pertille<sup>1</sup>

Received: 26 November 2020 / Accepted: 1 February 2021 / Published online: 22 February 2021  
© Springer Nature Switzerland AG 2021

## Abstract

A low level of physical activity has a potential association with high levels of homocysteine, which implies an increased chance of older adults with type 2 diabetes mellitus developing cardiovascular disease (CVD). However, the effects of physical activity on homocysteine levels have been poorly explored in the literature. Therefore, this study compared homocysteine levels and cardiovascular risk among physically active and inactive older women with type 2 diabetes mellitus. Fifty-nine women with type 2 diabetes mellitus, between 60 and 91 years old, were evaluated. The level of physical activity was assessed using the International Physical Activity Questionnaire (IPAQ) long version to identify active and inactive older women. Blood samples were collected and anthropometric, body composition, and blood pressure measurements were performed to determine homocysteine levels and cardiovascular risk. The results demonstrated that active older women with type 2 diabetes mellitus have lower homocysteine values ( $F = 17.79$ ,  $p < 0.001$ ,  $\eta p^2 = 0.238$ ), cardiovascular risk scores ( $F = 15.84$ ,  $p = p < 0.001$ ,  $\eta p^2 = 0.217$ ), and waist circumferences ( $F = 2.95$ ,  $p = 0.013$ ,  $\eta p^2 = 0.049$ ) when compared with inactive older women. It was concluded that there was a difference in the levels of homocysteine, cardiovascular risk, and waist circumference between active and inactive older women with type 2 diabetes. Active older women are less likely to have cardiovascular risk than inactive older women.

**Keywords** Atherosclerosis · Cardiac risk · Cardiovascular diseases · Diabetes · Homocysteine · Physical inactivity

## Introduction

Type 2 diabetes mellitus is associated with reduced sensitivity of insulin receptors, making glucose uptake difficult [1]. In addition, individuals with type 2 diabetes mellitus have a

higher prevalence of cardiovascular disease (CVD) [2], which is considered the main cause of mortality worldwide [3]. Approximately 32.2% of individuals with type 2 diabetes mellitus are affected by CVD, with a higher incidence of strokes and coronary artery disease [2].

---

✉ Alexandre de Souza e Silva  
alexprofms@yahoo.com.br

José Jonas de Oliveira  
joliveira63@gmail.com

Anna Gabriela Silva Vilela Ribeiro  
annagsvr@hotmail.com

Carolina Gabriela Reis Barbosa  
carolgrb@yahoo.com.br

Jasielle Aparecida de Oliveira Silva  
jasielle\_oliveira@yahoo.com.br

Annie Guimarães Pontes  
annie\_gpontes@hotmail.com

João Paulo Estevam Batista  
joao.paulo.edf.01@gmail.com

Adriana Pertille  
pertille.adri@gmail.com

<sup>1</sup> Post-graduate Program in Human Movement Sciences, Universidade Metodista de Piracicaba, São Paulo, Brazil

<sup>2</sup> Physical Education Department, Centro Universitário de Itajubá – FEPI, Av. Dr. Antônio Braga Filho, 687 – Bairro Varginha, Itajubá 37501-002, Brazil

Physical inactivity, in turn, is associated with the development and worsening of diseases such as type 2 diabetes mellitus and CVD [4], in addition to being considered one of the main causes of premature mortality worldwide [5, 6]. Several studies have reported a high percentage of physical inactivity in older populations [7–10]. Population-wide estimates indicate that if physical inactivity were eliminated, on average, life expectancy would increase by 0.68 (range, 0.41–0.95) years worldwide [11]. And, specifically, in the older adults Brazilian, the fifth largest elderly population in the world [12], if physical inactivity were eliminated, approximately 5.53% of cases CVD, 6.85% of diabetes mellitus 2 and 8.91% of mortality from all causes would be avoided [13].

In this sense, the regular practice of physical activity has numerous health benefits, as it prevents the development of chronic non-communicable diseases (NCDs) and consequently reduces the risk of premature mortality [6]. In addition, regular physical activity is associated with a decrease in CVD-related biomarkers, such as homocysteine [14–16].

According to Neves et al. [17], homocysteine is an essential amino acid synthesized in the liver by demethylation, is associated with fasting, or due to methionine overload via transsulfuration. At higher levels in the bloodstream, it generates a condition called hyperhomocysteinemia (above 15  $\mu\text{mol/L}$ ), directly contributing to the increased incidence of CVD [18].

Hyperhomocysteinemia is considered an independent risk factor for vascular, cerebral, coronary, and peripheral arterial disease [19, 20], and is a predictor of mortality, regardless of the risk factors [21]. According to a meta-analysis of prospective studies, an increase of 5  $\mu\text{mol/L}$  in circulating levels of homocysteine raise the risk of all-cause mortality by 33.6% [22]. Thus, controlling homocysteine levels is important to reduce the risk of thrombogenesis and atherogenesis [21].

Physical inactivity has been linked with higher homocysteine values [15, 23], but the effect of regular physical activity is little explored and is not well understood in the literature. To this end, the current study compared serum levels of homocysteine and cardiovascular risk factors among physically active and inactive older women with type 2 diabetes mellitus. This information is essential to confirm the benefits of regular physical activity on serum levels of homocysteine and cardiovascular risk factors, since hyperhomocysteinemia is independently linked to the development of CVD.

## Methods

### Study design, participants and eligibility criteria

For the primary and quantitative cross-sectional study, 80 older women with type 2 diabetes mellitus, aged between 60

and 91 years, were assessed for eligibility. The study was conducted in the city of Itajubá, in the state of Minas Gerais, which is located in the southeastern region of Brazil (Latitude 22°25'37"/Longitude 45°27'11"), occupying a territorial area of 294,825 km<sup>2</sup>. In 2010, the estimated population was 96,869 inhabitants, the demographic density 307.49 inhabitants per km<sup>2</sup>, with a human development index of 0.787.

The study involved a single meeting, in which the international physical activity questionnaire (IPAQ) was used to classify the participants into physically active and inactive groups. Blood samples were collected to determine the biochemical parameters of interest, and blood pressure was measured. Anthropometric measures, body composition, and information regarding the characteristics of the volunteers were also investigated.

The eligibility criteria adopted were: (I) age  $\geq$  60 years, (II) lives independently in the community, and (III) not engaged in systematic exercise programs.

The non-inclusion criteria were as follows: (I) a recent history of CVD, malignant neoplasms, or surgical procedures, (II) physical limitations (orthopedic) that interfere with body movement, (III) diagnosis of neurodegenerative diseases, (IV) refusal to perform blood collection, and (V) not interested in participating in the research. For the exclusion criteria, the following were adopted: (I) inadequate responses in the IPAQ, and (II) insufficient data.

### Ethical considerations

All individuals in the study signed a free and informed consent form (ICF), accepting that the science of the research and all the benefits and risks would be disclosed during the execution of the study. The study was approved by the Ethics and Research Committee of the Centro Universitário de Itajubá (protocol 139) and is in accordance with the National Health Council.

### Outcome measures

#### Sample characterization

Information regarding age, family income, skin color, education, smoking, and medication (to control blood glucose, cholesterol, and blood pressure) were collected by self-reporting for the purpose of characterizing the sample.

#### International physical activity questionnaire (IPAQ) long version

Physical activity was subjectively measured by the long version of the IPAQ, an instrument validated in older Brazilian women by Benedetti et al. [24]. The IPAQ was administered

in the form of an interview by researchers experienced in the application of this instrument. Participants were asked individually in a separate room as to the frequency and time of moderate, vigorous, and walking activities performed in sessions  $\geq 10$  min at work, at home, as a form of transportation or leisure during a typical week.

The questionnaire classifies the subjects into four different levels: very active, active, irregularly active, and sedentary. However, in the present study, we divided the participants into two groups: active (very active and active) and inactive (irregularly active and sedentary).

Thus, the volunteers who performed one session of  $\geq 20$  min/session vigorous physical activity on three or more days a week, or one session  $\geq 30$  min/session of moderate physical activity and/or walking for at least 5 days a week, or one session of  $\geq 150$  min of moderate to vigorous physical activity and/or walking for at least 5 days a week were classified as physically active. Participants who did not reach this level activity were considered physically inactive.

### Blood collection

The volunteers were subjected to the collection of blood samples by venipuncture (antecubital vein) to determine the concentrations of homocysteine, glycated hemoglobin, glycemia, and total cholesterol, HDL, LDL and VLDL. About 10 mL of blood was collected from each participant after a minimum fast of 12 h. The samples were separated into test tubes with ethylenediaminetetraacetic acid (EDTA) to assess plasma levels of homocysteine and glycated hemoglobin (HbA1c). The plasma was separated immediately after collection and frozen at minus 20 °C until analysis. To determine the concentrations of total cholesterol, HDL, LDL, VLDL, triglycerides, and glycemia, serum and plasma were separated from the samples. Serum was used to measure total cholesterol, HDL, LDL, VLDL, triglycerides, and fluoridated plasma to measure glucose.

### Analysis of homocysteine and glycated hemoglobin

The analysis of homocysteine and HbA1c was measured using high-performance liquid chromatography (HPLC) equipment, which has a high sensitivity and reliability [25–28]. The range considered normal for the level of HbA1c is between 4% and 5.6%, levels between 5.7% and 6.4% indicate pre-diabetes, and levels of 6.5% or more indicate diabetes. The DPC-Medlab reagent was used, with values between 5.0 and 15.0  $\mu\text{M}$  per liter and analytical sensitivity of 0.5  $\mu\text{M}$  per liter as the normal range, considering the quantitative analysis of the peak area expressed in the chromatograms [25–29].

### Analysis of plasma levels of cholesterol, HDL, LDL, VLDL, and glucose

The enzymatic method by end point reaction was used to analyze total cholesterol, HDL, LDL, VLDL, and blood glucose. After collection, samples were screened, and after analysis, no collection was discarded. To analyze the plasma levels of total cholesterol, HDL, LDL, VLDL, and glucose, a spectrophotometer (Biospectro Benfer SP-22®) (reading at 505 nm) and a Cholesterol-PP Kit Cat.460 (Labtest) was used, as well as a PAP Glucose Kit Liquiform (Labtest), centrifuge (Benfer-BMC macro centrifuge), and a water bath (Quimis 021/4®) [30–32].

Each sample was subjected to a technical test according to the manufacturer's procedure, respecting volumes, color reagent sequence, and zeroing the absorbance of white, which is the color reagent. After mixing, the solutions were placed in a water bath for 10 min at 37 °C, as determined by the manufacturer. Then, according to the wavelength of each analyte, the absorbance of the standard and sample of each patient, and the internal control of each analyte were read (total cholesterol wavelength values = 500 nm, HDL = 500 nm, triglycerides = 505 nm and glucose = 505).

After reading the absorbances, the concentration of the samples was calculated by comparing them to the standard. Only when the value of internal control was within the parameters of Levey Jenning were the results of the volunteers released [30–32].

### Systemic blood pressure

Aneroid equipment (Welch-Allyn, USA) and a cuff compatible with the volunteers' arm circumference were used to determine blood pressure. The volunteers remained seated in a chair for approximately 5 min in a quiet and peaceful environment. Then, with the forearm and back of the hand resting on a table, and the cuff at heart level, their blood pressure was measured. The collection was carried out in the morning by the same equipment and evaluator.

### Cardiovascular risk

The Framingham score, proposed by D'Agostino et al. [33], was used to estimate the risk of CVD (heart failure, coronary artery, cerebrovascular, and peripheral artery disease) within 10 years. To determine this score, specific scores were assigned to age, HDL-cholesterol, total cholesterol, systolic blood pressure (treated or untreated), presence of diabetes mellitus, and smoking. The scores obtained for each of these parameters were then summed to obtain a final score. A higher score represented a greater cardiovascular risk.

## Anthropometric and body composition assessment

Anthropometric and body composition measures were recorded according to the instructions of the International Society for the Advancement of Kinanthropometry [34]. Height was measured using a solid PVC stadiometer (Seca® brand), with a scale from 0 to 2.20 m and a resolution of 0.1 cm. Body mass was obtained using a Filizola® scale (Filizola, Brazil) with a capacity of up to 180 kg and fractions of 100 g, with a plate base and a rubber mat [35]. Based on these parameters, the body mass index (BMI) was calculated using the formula:  $\text{body mass/height}^2$  [35, 36].

Skin folds were determined using a Cescorf® compass. The protocol adopted to verify the fat percentage was the specific equation for older people from Durnin and Womersley with four skin folds (subscapular, tricipital, suprailiac and bicipital). The formula used was as follows:  $\{1.1567 - 0.0717 * \text{Log}_{10} [\Sigma (\text{subscapular, tricipital, suprailiaca, bicipital})]\}$  [37, 38]. Meanwhile, lean mass was determined by weight – fat mass. In addition, a semi-rigid measuring tape from the Cescorf® brand was used to assess waist and hip circumference.

## Sample size

The sample was calculated using the GPower version 3.1.9.2 (Universität Kiel, Germany). The estimation was based on first

20 volunteers homocysteine data (Cohen's  $d = 0.93$ ). It was indicated that 21 subjects per group were needed for a power of 90% ( $1 - \beta$ ), 0.05 alpha value (two-tailed), and an allocation ratio of 1.

## Data analysis

The research data were analyzed using descriptive statistical techniques, including mean, standard deviation, and absolute frequency (percentage). The normality of the data was verified by the Shapiro-Wilk test, and the variance and outliers were analyzed. Frequency (histogram), symmetry, or asymmetry were analyzed to establish whether the data were parametric or nonparametric. The characteristics of the participants were compared using the independent t test and chi-square ( $\chi^2$ ) test.

To compare the dependent variables between the groups, an one-way ANOVA test was used. The partial eta-square ( $\eta^2$ ) method was used to estimate the size of the effect. The effect size was interpreted as small ( $\eta^2 < 0.035$ ), medium ( $\eta^2 \geq 0.035$  or  $< 0.140$ ), or large ( $\eta^2 \geq 0.140$ ) [39]. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 20.0, considering the rejection of the null hypothesis of 5% ( $p < 0.05$ ) for all results.

**Table 1** Descriptive characteristics of the participants ( $n = 59$ )

Group/characteristics <sup>a</sup>	All Participants ( $n = 59$ )	Active ( $n = 21$ )	Inactive ( $n = 38$ )	$p$ value
Continuous variables				
Age (y)	64±3	63±3	64±3	0.095
Height (m)	1.52±0.05	1.52±0.05	1.52±0.05	0.652
Body weight (kg)	69.03±12.83	68.28±9.41	69.44±14.47	0.742
BMI (kg/m <sup>2</sup> )	29.47± 4.93	29.27±3.84	29.57±5.48	0.824
MVPA (min/week)	147.17±95.48	244.10±99.27	92.16±19.19	<b>&lt; 0.001</b>
Categorical variables				
<i>Sociodemographic<sup>b</sup></i>				
F. Income (< 3 minimum wages) – n (%)	51 (86.44)	16 (76.19)	35 (92.10)	0.125
Skin Color (White) – n (%)	50 (84.74)	17 (80.95)	33 (86.84)	0.884
Education >8 years – n (%)	57 (96.61)	20 (95.23)	36 (94.73)	0.964
Smoking – n (%)	6 (10.16)	2 (9.52)	4 (10.52)	0.536
<i>Medication Use<sup>b</sup></i>				
Antihypertensive – n (%)	54 (91.52)	19 (90.47)	35 (92.10)	0.785
Cholesterol Reduction – n (%)	48 (81.35)	16 (76.19)	32 (84.21)	0.712
Blood Glucose Control – n (%)	59 (100.00)	21 (100.00)	38 (100.00)	1.00

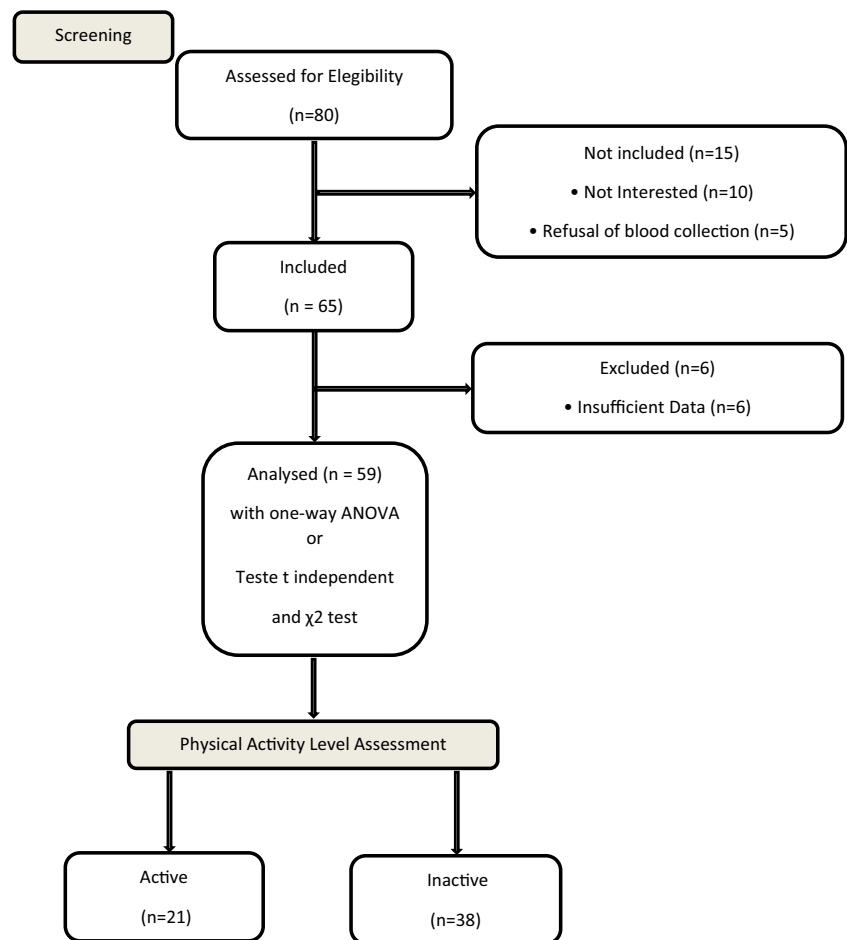
The data are expressed as mean ± SD or absolute number (percentage)

F. Income familiar income, MVPA moderate to vigorous physical activity

<sup>a</sup> independent t-test

<sup>b</sup> chi-square ( $\chi^2$ ) test

The numbers in bold is the statistical significance ( $p < 0.05$ )

**Fig. 1** Participants group allocation diagram.

## Results

The allocation diagram of the study participants is shown in Fig. 1. Initially, 80 women (age:  $65 \pm 4$  years) were randomly recruited from the community and assessed for eligibility. Fifteen volunteers were not included because they were not interested in participating ( $n = 10$ ) or refused to perform blood collection ( $n = 5$ ). In addition, six older women were excluded due to insufficient data. In this way, 59 volunteers were analyzed, where, following the principles established by IPAQ, 21 participants were allocated to the active group ( $244.10 \pm 99.27$  MVPA), and 38 to the inactive group ( $92.16 \pm 19.19$  MVPA). The average age of the volunteers was 64.3 years, with an average BMI of  $29.47 \text{ kg/m}^2$ . The majority had a family income  $>3$  minimum wages (86.44%), declared to have a white skin color (84.74%), education  $>8$  years (96.61%), not smoking (89.84%), and using medications to control blood pressure (91.52%), cholesterol (81.35%), and blood glucose (100.0%). There were no significant differences in age, height, body mass, BMI, sociodemographic aspects, and medication use between the active and inactive groups (Table 1).

The anthropometric parameters, CVD factors, blood pressure, and diabetes mellitus factors are shown in Table 2. A significant difference was found only for variable waist circumference ( $F = 2.95$ ,  $p = 0.013$ ,  $\eta^2 = 0.049$ ).

Figure 2 shows a comparison of homocysteine levels and cardiovascular risk scores between the active and inactive groups. A significant difference was found for homocysteine, with higher values in the inactive group ( $F = 17.79$ ,  $p < 0.001$ ,  $\eta^2 = 0.238$ ). The same was observed for the cardiovascular risk score, where the active group had a lower score ( $F = 15.84$ ,  $p = p < 0.001$ ,  $\eta^2 = 0.217$ ).

## Discussion

In this study, we aimed to compare serum homocysteine levels and cardiovascular risk factors among physically active and inactive older women with type 2 diabetes mellitus. Our main findings indicate that active older women with type 2 diabetes mellitus have lower serum concentrations of homocysteine, lower cardiovascular risk scores, and a lower waist circumference. This corroborates our initial hypothesis, indicating better

**Table 2** Changes in anthropometric parameters, cardiovascular disease factors, blood pressure, and diabetes factors in the active and inactive groups

Group/characteristics	All Participants (n =59)	Active (n =21)	Inactive (n =38)	F-value	p value	$\eta_p^2$
<i>Anthropometric parameters, mean±SD</i>						
Waist (cm)	97.25 ± 11.79	93.76 ± 8.40	99.18 ± 12.99	2.95	0.013*	0.049
Hip (cm)	104.99 ± 10.05	102.10 ± 8.51	106.57 ± 10.56	2.76	0.102	0.046
WHR	0.92 ± 0.06	0.91 ± 0.05	0.93 ± 0.05	1.56	0.216	0.027
Body fat (%)	40.29 ± 5.23	39.69 ± 4.14	40.62 ± 5.77	0.04	0.518	0.007
Fat body mass, kg	28.32 ± 8.24	27.30 ± 6.13	28.87 ± 9.23	0.48	0.488	0.001
Lean body mass, kg	40.73 ± 5.43	40.96 ± 4.60	40.59 ± 5.88	0.06	0.803	0.008
<i>Cardiovascular disease factors, mg/dL</i>						
Low density lipoprotein	111.99 ± 50.79	104.09 ± 50.61	116.34 ± 51.03	0.78	0.380	0.014
High-density lipoprotein	50.81 ± 14.81	53.80 ± 15.92	49.15 ± 14.09	1.34	0.251	0.023
Triglycerides	172.41 ± 75.31	160.52 ± 67.26	178.97 ± 79.49	0.80	0.372	0.014
Cholesterol	198.14 ± 50.18	192.80 ± 46.70	201.07 ± 52.37	0.36	0.549	0.006
<i>Blood pressure, mean±SD mm Hg</i>						
Systolic	132.12 ± 17.79	130.71 ± 10.98	132.89 ± 20.71	0.20	0.656	0.004
Diastolic	78.14 ± 11.59	76.66 ± 7.30	78.94 ± 13.41	0.51	0.474	0.009
<i>Diabetes factors, mean±SD</i>						
HbA1c%	8.31 ± 1.18	8.51 ± 1.02	8.15 ± 1.27	1.00	0.321	0.019
Fasting glucose, mg/dL	152.10 ± 34.08	149.47 ± 45.80	156.65 ± 25.84	0.59	0.443	0.010

The data are expressed as mean ± SD. Comparison between active and inactive groups one-way ANOVA (\*  $p < 0.05$ )

WHR waist-hip ratio

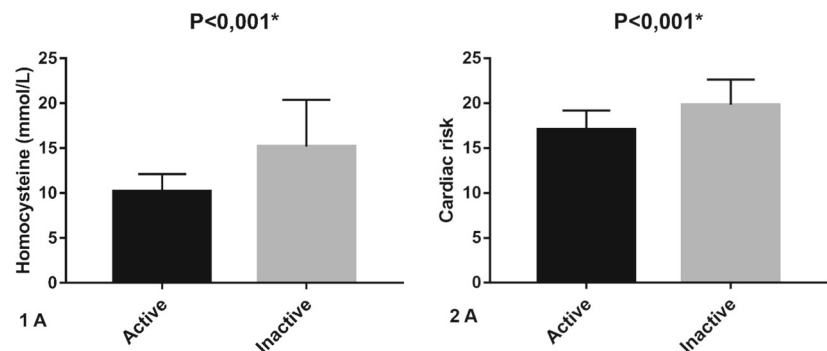
responses in the parameters of homocysteine and cardiovascular risk in the active individuals with type 2 diabetes mellitus active compared to inactive individuals. Our findings on serum homocysteine levels go in the same direction as the results found in the studies by Buckner et al. [40], Hellgren et al. [41], Unt et al. [42], and Loprinzi and Cardinal [43], who analyzed the relationship between physical activity and homocysteine.

High levels of homocysteine may be associated with increased body adiposity, inadequate nutrition, sedentary behavior, and physical inactivity itself [44]. Higher serum homocysteine levels in women than in men are due to greater muscle mass and creatine phosphate synthesis in

men, in addition to the estrogen-reducing effect and variations in the rate of synthesis of homocysteine compared to men [45–48]. It is important to note that in older adults, high levels of homocysteine are also related to intestinal malabsorption, a slowing down of the metabolism, impaired renal metabolism, and reduced intake of vitamin B12.

For Dankner et al. [49], physical activity can reduce homocysteine independently of B vitamins, corroborating these findings, the study by Alomari et al. [23] suggests that regular physical activity may be an additional treatment strategy to reduce levels of homocysteine, regardless of lifestyle and B vitamins.

**Fig. 2** Comparison of serum homocysteine (1A) and cardiovascular risk score (2A) between the active and inactive groups



Comparison between active and inactive groups one-way ANOVA (\*  $p < 0.001$ ).

Therefore, the encouragement of doctors and health professionals to partake in the regular practice of physical activity/physical exercise for cardiovascular health is of great importance, since the adoption of healthy lifestyle habits, such as increased physical activity and decreased sedentary behaviors, is able to decrease the risk of diabetes type 2 mellitus, stroke, cardiac events, and CVD [50, 51] improving quality of life and decreasing the risk of death, and be considered a public health intervention [52].

Meta-analyses indicated that individuals who practice the equivalent of 150 min per week of moderate-intensity leisure physical activity have a 15% to 20% lower risk of developing coronary artery disease than those who do not [53, 54]. Our findings add to the findings of the meta-analyses, indicating that physically active older adults with diabetes type 2 mellitus by IPAQ had lower cardiovascular risk compared to inactive individuals.

Our study also found a significant difference in waist circumference between the two groups. Studies indicate that waist circumference is a good parameter for tracking CVD [55]. In a study published by the Scottish Health Survey, carried out between the years 1998 and 2008, an increase of 5 to 10 cm in the waist circumference was observed in both sexes between 50 to 70 years [56], an age equivalent to the volunteers in our study, suggesting an increased risk of CVD. Additionally, the simultaneous presence of excessive sedentary time (> 10 h/day) and noncompliance with recommendations for physical activity (<150 min/week of physical activity of moderate to vigorous intensity MVPA) were related to greater waist circumference by Figueiro et al. [57]. On the other hand, Ribeiro et al. [10] observed the performance of 150 min per week in sessions  $\geq 10$  min was linked to lower chances of older Brazilian adults having a waist circumference above the recommended parameters.

The study by Loureiro et al. [58] recommends the adoption of simple methods such as waist circumference, as they are low-cost and noninvasive. They can be adopted in clinical practice and in epidemiological studies with older adults and adults, and this could contribute to the screening and early identification of risk factors, thus enabling actions and strategies for the prevention and control of CVD.

For Del Pozo-Cruz et al. [59], in a meta-analysis of objective assessment studies, reallocating sedentary time to light physical activities or MVPA can result in reductions in waist circumference. The equal exchange of sedentary behavior with MVPA can lead to further reductions in fasting glucose, all-cause mortality, and increased HDL-c levels. The replacement of sedentary behavior by light physical activities may be a possible alternative intervention strategy, as it is more viable and less challenging than more strenuous activities, therefore recommended for older adults.

In our study, the other anthropometric parameters related to cardiometabolic risk and obesity in individuals with type 2

diabetes mellitus did not show statistical differences between the active and inactive groups. Individuals in the active group did not perform systematic control of their diet. For Carbone et al. [60], physical activity is important in controlling variables related to obesity; however, healthy eating habits and diet control over a long period are necessary. We emphasize that obesity is a multifactorial chronic disease that is related to genetic factors or disturbances in energy metabolism, related to insulin resistance with its receptors, leading to type 2 diabetes mellitus.

There was also no significant difference in the factors of isolated cardiovascular diseases. These findings are also corroborated by studies that used systematic exercise. In the study by Silva et al. [61] and Silva et al. [62], aerobic and strength activities, respectively, were not able to significantly change cardiometabolic risk factors. In both studies, the weekly frequency of activities was low and the intensity was mild. In another study, when we compared active individuals with type 2 diabetes mellitus with the control, we also found no differences in the main cardiometabolic risk variables [63]. Systolic and diastolic blood pressure also did not show statistical differences between the active and inactive groups.

Based on the above findings and understanding the importance and relevance of the subject addressed in this study for quality of life and decreased mortality in the older population with type 2 diabetes mellitus, we propose that activity programs be controlled to control cardiometabolic risk factors systematized and oriented physics, with adjustment of weekly frequency, volume, and intensity of exercises, respecting biological individuality.

In the present study, we emphasize that the isolated analysis of cardiovascular risk factors can lead to misinterpretations due to the responses of each individual to the stimuli applied. On the other hand, when grouping these factors, we see differences in favor of the active group. This finding has great implications for public health, since the score used in this study uses variables commonly investigated in clinical practice and may be a viable alternative for the early detection of cardiovascular risk.

It is observed, in a qualitative analysis, that physical activity tends to decrease in older adults, it also suggests that the results of biochemical parameters and body composition tend to be better with a control of the diet, since, the high values of glycated hemoglobin may be related to an unbalanced diet, the last being a limitation of the study, since nutritional diet was not analyzed and systematized by a professional in the area of nutrition for the inclusion of people in the groups.

The study also has other limitation that need to be emphasized, this was a cross sectional study, therefore, it is not possible to determine the causal action of the event. However, it is emphasized that the variables investigated in the present study have great applicability in primary and secondary healthcare in most diverse populations. There is a need

for studies with nutritional control protocols to analyze the effects of physical activity plus the systematization of the diet in the studied population.

Finally, the study compared serum homocysteine levels and cardiac risk factors between active and inactive elderly people with type 2 diabetes mellitus. It was concluded that active older women with type 2 diabetes mellitus demonstrated a reduction in homocysteine levels and a lower cardiovascular risk score when compared to inactive older women. The analysis of isolated anthropometric and biochemical variables did not show any differences.

**Abbreviations** CVD, Cardiovascular disease; NCDs, Non-communicable diseases; IPAQ, International physical activity questionnaire; ICF, Informed consent form; HDL, High-density lipoprotein; LDL, Low-density lipoprotein; VLDL, Very-low-density lipoprotein; EDTA, Ethylenediaminetetraacetic acid; HbA1c, Glycated hemoglobin; HPLC, High-performance liquid chromatography; SPSS, Statistical Package for the Social Sciences; BMI, Body mass index; MVPA, Physical activity of moderate to vigorous intensity

**Acknowledgments** The authors would like to thank the volunteers, collaborators of the research, and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior—Brasil (CAPES) for the financial support through scholarships—Finance Code 001.

## Declarations

**Conflict of interest** The authors declare that there is no conflict of interest associated with this manuscript.

## References

1. Chadt A, Al-Hasani H. Glucose transporters in adipose tissue, liver, and skeletal muscle in metabolic health and disease. *Pflugers Arch*. 2020;472(9):1273–98. <https://doi.org/10.1007/s00424-020-02417-x>.
2. Einarson TR, Acs A, Ludwig C, Panton UH. Prevalence of cardiovascular disease in type 2 diabetes: a systematic literature review of scientific evidence from across the world in 2007–2017. *Cardiovasc Diabetol*. 2018;17(1):83. <https://doi.org/10.1186/s12933-018-0728-6>.
3. Collaborators GBDCoD. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the global burden of disease study 2016. *Lancet*. 2017;390(10100):1151–210. [https://doi.org/10.1016/S0140-6736\(17\)32152-9](https://doi.org/10.1016/S0140-6736(17)32152-9).
4. Booth FW, Roberts CK, Laye MJ. Lack of exercise is a major cause of chronic diseases. *Compr Physiol*. 2012;2(2):1143–211. <https://doi.org/10.1002/cphy.c110025>.
5. Booth FW, Roberts CK, Thyfault JP, Rueggsegger GN, Toedebusch RG. Role of inactivity in chronic diseases: evolutionary insight and pathophysiological mechanisms. *Physiol Rev*. 2017;97(4):1351–402. <https://doi.org/10.1152/physrev.00019.2016>.
6. Bull FC, Al-Ansari SS, Biddle S, Borodulin K, Buman MP, Cardon G, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *Br J Sports Med*. 2020;54(24):1451–62. <https://doi.org/10.1136/bjsports-2020-102955>.
7. Jefferis BJ, Sartini C, Lee IM, Choi M, Amuzu A, Gutierrez C, et al. Adherence to physical activity guidelines in older adults, using objectively measured physical activity in a population-based study. *BMC Public Health*. 2014;14:382. <https://doi.org/10.1186/1471-2458-14-382>.
8. Ortlieb S, Gorzelniak L, Nowak D, Strobl R, Grill E, Thorand B, et al. Associations between multiple accelerometry-assessed physical activity parameters and selected health outcomes in elderly people—results from the KORA-age study. *PLoS One*. 2014;9(11):e111206. <https://doi.org/10.1371/journal.pone.0111206>.
9. Dos Santos CES, Manta SW, Maximiano GP, Confortin SC, Benedetti TRB, d'Orsi E, et al. Accelerometer-measured physical activity and sedentary behavior: a cross-sectional study of Brazilian older adults. *J Phys Act Health*. 2018;15(11):811–8. <https://doi.org/10.1123/jpah.2017-0456>.
10. Ribeiro A, Verlengia R, de Oliveira MRM, Oliveira MVA, Pellegrinotti IL, Crisp AH. Compliance of the physical activity guidelines accumulated in bouts  $\geq 10$  min and Nonbouts and its association with body composition and physical function: a cross-sectional study in Brazilian older adults. *J Aging Phys Act*. 2020;22:1–8. <https://doi.org/10.1123/japa.2020-0181>.
11. Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT. Lancet Physical Activity Series Working Group. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet*. 2012;380(9838):219–29. [https://doi.org/10.1016/S0140-6736\(12\)61031-9](https://doi.org/10.1016/S0140-6736(12)61031-9).
12. United Nations. Department of Economic and Social Affairs, population division. World population prospects: the 2015 revision. New York: United Nations; 2015.
13. de Rezende LF, Rabacow FM, Viscondi JY, Luiz Odo C, Matsudo VK, Lee IM. Effect of physical inactivity on major noncommunicable diseases and life expectancy in Brazil. *J Phys Act Health*. 2015;12(3):299–306. <https://doi.org/10.1123/jpah.2013-0241>.
14. Okura T, Rankinen T, Gagnon J, Lussier-Cacan S, Davignon J, Leon AS, et al. Effect of regular exercise on homocysteine concentrations: the HERITAGE family study. *Eur J Appl Physiol*. 2006;98(4):394–401. <https://doi.org/10.1007/s00421-006-0294-6>.
15. Silva ASMM. Effects of physical activity and training programs on plasma homocysteine levels: a systematic review. *Amino Acids*. 2014;46(8):1795–804. <https://doi.org/10.1007/s00726-014-1741-z>.
16. Han L, Liu Y, Wang C, Tang L, Feng X, Astell-Burt T, et al. Determinants of hyperhomocysteinemia in healthy and hypertensive subjects: a population-based study and systematic review. *Clin Nutr*. 2017;36(5):1215–30. <https://doi.org/10.1016/j.clnu.2016.11.011>.
17. Neves LBMD, Lopes AC. Homocisteína. *J Bras Patol Med Lab*. 2004;40:311–20.
18. Rehman T, Shabbir MA, Inam-Ur-Raheem M, Manzoor MF, Ahmad N, Liu ZW, et al. Cysteine and homocysteine as biomarker of various diseases. *Food Sci Nutr*. 2020;8(9):4696–707. <https://doi.org/10.1002/fsn3.1818>.
19. Muniz MT, Siqueira ER, Fonseca RA, D'Almeida V, Hotta JK, dos Santos JE, et al. Evaluation of MTHFR C677T gene polymorphism and homocysteine level in coronary atherosclerotic disease. *Arq Bras Endocrinol Metabol*. 2006;50(6):1059–65. <https://doi.org/10.1590/s0004-27302006000600012>.
20. Wolfgang HOR, Jouma M. Hyperhomocysteinemia and vitamin B-12 deficiency are more striking in Syrians than in Germans - causes and implications. *Atherosclerosis*. 2003;166(1):143–50. [https://doi.org/10.1016/s0021-9150\(02\)00320-9](https://doi.org/10.1016/s0021-9150(02)00320-9).
21. Anderson JL, Muhlestein JB, Home BD, Carlquist JF, Bair TL, Madsen TE, et al. Plasma homocysteine predicts mortality independently of traditional risk factors and C-reactive protein in patients with angiographically defined coronary artery disease. *Circulation*.



- 2000;102(11):1227–32. <https://doi.org/10.1161/01.cir.102.11.1227>.
22. Fan R, Zhang A, Zhong F. Association between Homocysteine levels and all-cause mortality: a dose-response meta-analysis of prospective studies. *Sci Rep.* 2017;7(1):4769. <https://doi.org/10.1038/s41598-017-05205-3>.
  23. Alomari MA, Khabour OF, Gharaibeh MY, Qhatan RA. Effect of physical activity on levels of homocysteine, folate, and vitamin B12 in the elderly. *Phys Sportsmed.* 2016;44(1):68–73. <https://doi.org/10.1080/00913847.2016.1135037>.
  24. Benedetti TM, GZ, de Barros MVG. Aplicação do questionário internacional de atividades físicas para avaliação do nível de atividades física de mulheres idosas: Validade concorrente e reprodutibilidade teste-reteste. *Rev Bras Ciênc Mov.* 2008;12(1):25–34.
  25. Ichinose S, Nakamura M, Maeda M, Ikeda R, Wada M, Nakazato M, et al. A validated HPLC-fluorescence method with a semi-micro column for routine determination of homocysteine, cysteine and cysteamine, and the relation between the thiol derivatives in normal human plasma. *Biomed Chromatogr.* 2009;23(9):935–9. <https://doi.org/10.1002/bmc.1205>.
  26. Ferin R, Pavao ML, Baptista J. Methodology for a rapid and simultaneous determination of total cysteine, homocysteine, cysteinylglycine and glutathione in plasma by isocratic RP-HPLC. *J Chromatogr B Analyt Technol Biomed Life Sci.* 2012;911:15–20. <https://doi.org/10.1016/j.jchromb.2012.10.022>.
  27. Sawula W, Banecka-Majkutewicz Z, Kadzinski L, Jakobkiewicz-Banecka J, Wegrzyn G, Nyka W, et al. Improved HPLC method for total plasma homocysteine detection and quantification. *Acta Biochim Pol.* 2008;55(1):119–25.
  28. Vincent KR, Braith RW, Bottiglieri T, Vincent HK, Lowenthal DT. Homocysteine and lipoprotein levels following resistance training in older adults. *Prev Cardiol.* 2003;6(4):197–203. <https://doi.org/10.1111/j.1520-037x.2003.01723.x>.
  29. Chen SM, Shen FC, Chen JF, Chang WD, Chang NJ. Effects of Resistance Exercise on Glycated Hemoglobin and Functional Performance in Older Patients with Comorbid Diabetes Mellitus and Knee Osteoarthritis: A Randomized Trial. *Int J Environ Res Public Health.* 2019;17(1):224. <https://doi.org/10.3390/ijerph17010224>.
  30. Assmann G, Jabs HU, Kohnert U, Nolte W, Schriewer H. LDL-cholesterol determination in blood serum following precipitation of LDL with polyvinylsulfate. *Clin Chim Acta.* 1984;140(1):77–83. [https://doi.org/10.1016/0009-8981\(84\)90153-0](https://doi.org/10.1016/0009-8981(84)90153-0).
  31. Martins RA, Verissimo MT, Coelho e Silva MJ, Cumming SP, Teixeira AM. Effects of aerobic and strength-based training on metabolic health indicators in older adults. *Lipids Health Dis.* 2010;9:76. <https://doi.org/10.1186/1476-511X-9-76>.
  32. Gabriel R, Saiz C, Susi R, Alonso M, Vega S, Lopez I, et al. Epidemiology of lipid profile of the Spanish elderly population: the EPICARDIAN study. *Med Clin (Barc).* 2004;122(16):605–9. [https://doi.org/10.1016/s0025-7753\(04\)74326-2](https://doi.org/10.1016/s0025-7753(04)74326-2).
  33. D'Agostino RB Sr, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: the Framingham heart study. *Circulation.* 2008;117(6):743–53. <https://doi.org/10.1161/CIRCULATIONAHA.107.699579>.
  34. Stewart A, Marfell-Jones M, Olds T, Ridder H. International standards for anthropometric assessment. International Society for the Advancement of Kinanthropometry: Lower Hutt; 2011.
  35. Orsatti FL, Nahas EA, Nahas-Neto J, Maesta N, Orsatti CL, Fernandes CE. Effects of resistance training and soy isoflavone on body composition in postmenopausal women. *Obstet Gynecol Int.* 2010;2010:156037. <https://doi.org/10.1155/2010/156037>.
  36. Christos Z, Tokmakidis SP, Volaklis KA, Kotsa K, Touvra AM, et al. Lipoprotein profile, glycemic control and physical fitness after strength and aerobic training in post-menopausal women with type 2 diabetes. *Eur J Appl Physiol.* 2009;106:901–7. <https://doi.org/10.1007/s00421-009-1104-8>.
  37. Durnin JV, Womersley J. Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. *Br J Nutr.* 1974;32(1):77–97. <https://doi.org/10.1079/bjn19740060>.
  38. Rech C, Lima LRA, Cordeiro BA, Petroski EL, Vasconcelos FAG. Validity of anthropometric equations for estimating body fat in the elderly in southern Brazil. *Braz J Cineanthropometry Hum Perform.* 2010;12(1):1–7. <https://doi.org/10.5007/1980-0037.2010v12n1p1>.
  39. Sink C, Mvududu NH. Statistical power, sampling, and effect sizes. *Couns Outcome Res Eval.* 2010;1(2):1–18. <https://doi.org/10.1177/2150137810373613>.
  40. Buckner SL, Loenneke JP, Loprinzi PD. Single and combined associations of accelerometer-assessed physical activity and muscle-strengthening activities on plasma homocysteine in a national sample. *Clin Physiol Funct Imaging.* 2017;37(6):669–74. <https://doi.org/10.1111/cpf.12356>.
  41. Hellgren M, Melander A, Ostgren CJ, Rastam L, Lindblad U. Inverse association between plasma homocysteine, sulphonylurea exposure and physical activity: a community-based sample of type 2 diabetes patients in the Skaraborg hypertension and diabetes project. *Diabetes Obes Metab.* 2005;7(4):421–9. <https://doi.org/10.1111/j.1463-1326.2004.00431.x>.
  42. Unt E, Zilmer K, Magi A, Kullisaar T, Kairane C, Zilmer M. Homocysteine status in former top-level male athletes: possible effect of physical activity and physical fitness. *Scand J Med Sci Sports.* 2008;18(3):360–6. <https://doi.org/10.1111/j.1600-0838.2007.00674.x>.
  43. Loprinzi PD, Cardinal BJ. Interrelationships among physical activity, depression, homocysteine, and metabolic syndrome with special considerations by sex. *Prev Med.* 2012;54(6):388–92. <https://doi.org/10.1016/j.ypmed.2012.03.016>.
  44. Venâncio L, Burini RC, Yoshida WB. Dietary treatment of hyperhomocysteinemia in peripheral arterial disease. *J Vasc Bras.* 2010;9(1):28–41. <https://doi.org/10.1590/S1677-54492010000100006>.
  45. Norlund L, Grubb A, Fex G, Leksell H, Nilsson JE, Schenck H, et al. The increase of plasma homocysteine concentrations with age is partly due to the deterioration of renal function as determined by plasma cystatin C. *Clin Chem Lab Med.* 1998;36(3):175–8. <https://doi.org/10.1515/CCLM.1998.032>.
  46. Brosnan JT, Jacobs RL, Stead LM, Brosnan ME. Methylation demand: a key determinant of homocysteine metabolism. *Acta Biochim Pol.* 2004;51(2):405–13.
  47. Malinow MR, Duell PB, Williams MA, Kruger WD, Evans AA, Anderson PH, et al. Short-term folic acid supplementation induces variable and paradoxical changes in plasma homocyst(e)ine concentrations. *Lipids.* 2001;36 Suppl:S27–32. <https://doi.org/10.1007/s11745-001-0678-8>.
  48. Chen KJ, Pan WH, Yang FL, Wei IL, Shaw NS, Lin BF. Association of B vitamins status and homocysteine levels in elderly Taiwanese. *Asia Pac J Clin Nutr.* 2005;14(3):250–5.
  49. Dankner RGG, Farber N, Novikov I, Segev S, Sela BA. Cardiorespiratory fitness and plasma homocysteine levels in adult males and females. *Isr Med Assoc J.* 2009;11(2):78–82.
  50. Biswas A, Oh PI, Faulkner GE, Bajaj RR, Silver MA, Mitchell MS, et al. Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis. *Ann Intern Med.* 2015;162(2):123–32. <https://doi.org/10.7326/M14-1651>.
  51. Baker PR, Costello JT, Dobbins M, Waters EB. The benefits and challenges of conducting an overview of systematic reviews in

- public health: a focus on physical activity. *J Public Health (Oxf)*. 2014;36(3):517–21. <https://doi.org/10.1093/pubmed/fd0050>.
52. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart disease and stroke Statistics-2016 update: a report from the American Heart Association. *Circulation*. 2016;133(4):e38–360. <https://doi.org/10.1161/CIR.0000000000000350>.
  53. Sattelmair J, Pertman J, Ding EL, Kohl HW 3rd, Haskell W, Lee IM. Dose response between physical activity and risk of coronary heart disease: a meta-analysis. *Circulation*. 2011;124(7):789–95. <https://doi.org/10.1161/CIRCULATIONAHA.110.010710>.
  54. Woodcock J, Franco OH, Orsini N, Roberts I. Non-vigorous physical activity and all-cause mortality: systematic review and meta-analysis of cohort studies. *Int J Epidemiol*. 2011;40(1):121–38. <https://doi.org/10.1093/ije/dyq104>.
  55. Koning L, Merchant AT, Pogue J, Anand SS. Waist circumference and waist-to-hip ratio as predictors of cardiovascular events: meta-regression analysis of prospective studies. *Eur Heart J*. 2007;28(7):850–6. <https://doi.org/10.1093/eurheartj/ehm026>.
  56. Han TS, Tajar A, Lean ME. Obesity and weight management in the elderly. *Br Med Bull*. 2011;97:169–96. <https://doi.org/10.1093/bmb/ldr002>.
  57. Figueiro TH, Arins GCB, Santos C, Cembranel F, Medeiros PA, d'Orsi E, et al. Association of objectively measured sedentary behavior and physical activity with cardiometabolic risk markers in older adults. *PLoS One*. 2019;14(1):e0210861. <https://doi.org/10.1371/journal.pone.0210861>.
  58. Loureiro NSL, Amaral TLM, Amaral CA, Monteiro GTR, Vasconcellos MTL, Bortolini MJS. Relationship between anthropometric indicators and risk factors for cardiovascular disease in adults and older adults of Rio Branco, Acre. *Rev Saude Publica*. 2020;54:24. <https://doi.org/10.11606/s1518-8787.2020054001088>.
  59. Del Pozo-Cruz J, Garcia-Hermoso A, Alfonso-Rosa RM, Alvarez-Barbosa F, Owen N, Chastin S, et al. Replacing sedentary time: meta-analysis of objective-assessment studies. *Am J Prev Med*. 2018;55(3):395–402. <https://doi.org/10.1016/j.amepre.2018.04.042>.
  60. Carbone S, Del Buono MG, Ozemek C, Lavie CJ. Obesity, risk of diabetes and role of physical activity, exercise training and cardio-respiratory fitness. *Prog Cardiovasc Dis*. 2019;62(4):327–33. <https://doi.org/10.1016/j.pcad.2019.08.004>.
  61. Silva ASE, Lacerda FV, da Mota MPG. Effect of strength training on plasma levels of Homocysteine in patients with type 2 diabetes. *Int J Prev Med*. 2019;10:80. [https://doi.org/10.4103/ijpvm.IJPVM\\_313\\_17](https://doi.org/10.4103/ijpvm.IJPVM_313_17).
  62. Silva ASLF, Mota MPG. Effect of aerobic training on homocysteine levels in type 2 diabetic individuals. *Rev Bras Med Esporte*. 2015;21(4):275–8. <https://doi.org/10.1590/1517-869220152104140828>.
  63. Silva A, Lacerda FV, da Mota MPG. The effect of aerobic vs. resistance training on plasma homocysteine in individuals with type 2 diabetes. *J Diabetes Metab Disord*. 2020;19(2):1003–9. <https://doi.org/10.1007/s40200-020-00596-z>.
- Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.