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Effects of high-intensity training on glycemic metabolism in type 2 diabetes mellitus

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ABSTRACT

Background: With the exponential increase in hours of exposure in sedentary behavior, associated with greater availability of pre-prepared foods, there is an incidence and prevalence of chronic non-communicable diseases. **Objective:** This review was to analyze the possible effects of high-intensity training on the glycemic metabolism in Type 2 Diabetics in the last 10 years. **Methods:** Searches were carried out between February and April 2022 in the following databases: National Library Of Medicine (PUBMED), Medical Literature Analysis and Retrieval System Online (MEDLINE), Scientific Electronic Library Online (SciELO), Latin American Literature and of the Caribbean in Health Sciences (LILACS), using Medical Subject Heading (MeSH), together with the relevant Entry Terms and Boolean operators (AND and OR). The search key was built using the PICOS strategy (Population, Intervention, Comparator, Outcome and Type of Study). Inclusion criteria were randomized clinical trials; population aged ≤ 65 years and diagnosed with Type 2 Diabetes Mellitus; high-intensity exercise as an intervention; glycemia as one of the outcomes; published in English, Spanish and/or Portuguese between 2012 and 2022 and available in full text. **Results:** After the searches, 85 scientific articles were identified. Of these, 7 studies were selected because they met the proposed objective and criteria. Sample sizes ranged from 7-52 participants, with a mean of 24.17 ± 12.33 . All studies were conducted with adults. With regard to the period of intervention, it was observed that high-intensity training was performed from a single session to 12 weeks, at a frequency of up to three times a week. **Conclusion:** Studies have shown that after performing high-intensity training, there were significant reductions in glycemic values. Despite high-intensity training having contributed significantly to reducing glycemic values, the results of this systematic review must be interpreted with caution, due to the small number of articles included and their respective methodological limitations.

Keywords: High intensity exercises; type 2 diabetes Mellitus

BACKGROUND

With the exponential increase in hours of exposure in sedentary behavior, associated with greater availability of pre-prepared foods, there is an incidence and prevalence of chronic non-communicable diseases⁽¹⁾. Having type 2 Diabetes Mellitus (T2DM) as one of the main ones, whose excessive food consumption, low quality of life, stress, hormonal factors and physical activity levels, become crucial factors for the development of this dyslipidemia^(2, 3).

In recent years there has been a high growth of occurrences in relation to the number of new cases. For Brazil, an estimate of 15.7 million adults (20 to 79 years old) with diabetes was calculated in the year 2021, ranking sixth among the 10 countries or territories with adults between 20 and 79 years old with diabetes in 2021⁽⁴⁾, and projected to 20.3 million by 2045⁽⁵⁾.

T2DM is a chronic disease characterized by insufficient production of insulin by the pancreas, or by the body's inability to use the insulin produced efficiently, raising blood glucose levels⁽⁶⁾, which can lead to several consequences, such as vision loss, dysfunctions in the central nervous system, dysfunctions in blood circulation and cardiac complications⁽⁷⁾.

Among the types of diabetes, T2DM is the most common, accounting for about 90% of cases of diabetes⁽⁸⁾. Currently, T2DM is regarded as a worrying Chronic Non-Transmissible Diseases (CNCD), both in

relation to its aggressiveness towards the patient, and for the coffers of the Unified Health System, generating enormous expenses with hospitalizations and treatment⁽⁹⁾.

T2DM treatment is given through medication and non-medication. The latter involves individual care, such as dietary control and regular physical exercise^(8, 10). Studies point to the adoption of physical exercise as a great ally in the treatment of T2DM, with exercise being responsible for increasing insulin sensitivity, increasing capillarization of muscle fibers, and improving mitochondrial function^(11, 12).

Among the most studied exercise protocols to emphasize the reduction of glycemic levels, high-intensity has been shown to be effective in glycemic control, reduction of HbA1c and fasting glycemia, postprandial glycemia, glycemic variability⁽¹³⁾; increase in insulin sensitivity⁽¹⁴⁾, improvement in maximal oxygen uptake (VO₂ max), Improvement in body weight, reduction in blood pressure⁽¹⁵⁾.

However, there are relatively few scientific studies evaluating the effects of high-intensity exercise in T2DM, mainly associated with acute glycemic effects. Thus, the present study aims to analyze the possible effects of high-intensity training on glycemic metabolism in acute and chronic T2DM in the last 10 years among adults aged 19 to 64 years.

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METHODS

This is a systematic review, carried out in accordance with the methodological guidelines for the preparation of a systematic review and meta-analysis of randomized clinical trials, reported in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, which had as its point starting with the research question: Is high-intensity training capable of reducing blood glucose levels in T2DM adults?

Search strategy

The systematic search for articles was carried out in April 2022, in four electronic databases: National Library Of Medicine (PUBMED), Medical Literature Analysis and Retrieval System Online (MEDLINE), Scientific Electronic Library Online (SciELO), Literature Latino -American and Caribbean Association in Health Sciences (LILACS), using Medical Subject Heading (MeSH), along with relevant Entry Terms and Boolean operators (AND and OR). The search key was built using the PICOS strategy (Population, Intervention, Comparator, Outcome and Type of Study).

For population, the following terms were used: Adults 19 to 44 years; Middle aged 45 to 64 years; T2DM; for the outcome: blood glucose. In the intervention the terms high-intensity resistance training; high intensity exercise; for comparators it was defined as all types of exercises and/or control group, for the outcome the effects of the intervention, studies of randomized clinical trials were sought.

Selection criteria and data extraction

The selection of studies was carried out by two reviewers simultaneously and independently and in case of doubts, a third experienced reviewer would be consulted, which was not the case. The study followed four stages: analysis of duplicates; reading of titles and abstracts; reading the articles in full and extracting the main information, synthesizing them in a spreadsheet.

Study selection criteria

The study inclusion criteria were: randomized clinical trials; with a population diagnosed with T2DM (glycemia ≥ 126 mmHg and ≤ 200 mmHg) aged between 19 and 65 years; use of high-intensity training (any type of exercise as an intervention); glycemia as one of the outcomes; published in English, Spanish or Portuguese, between the years 2012-2022 and available in full text. Articles that were repeated in two or more databases were computed only once.

RESULTS

In the first selection of articles, 13 publications were extracted from the PUBMED database, 70 publications from the MEDLINE database, 2 publications from the LILACS database; no publication was found in the SciELO database. The terms used to search for references were: (Adults) AND (Middle aged) AND (Diabetes Mellitus, Type 2) AND (Blood Glucose) AND (High-Intensity Interval Training); they were chosen according to their meanings provided by DeCS/MeSH.

From the mentioned descriptors, 85 publications emerged. These were submitted to the evaluation of duplicates, remaining for reading the titles and abstracts of 73 articles. After reading the titles and abstracts of 73 publications, only 19 met all the selection criteria. Of these excluded articles, the population consisted of non-diabetic type 2 (n=7); did not use high-intensity training as an intervention (n=10); had no effect on blood glucose as endpoint (n=32). Thus, in this review, 24 studies were included for analysis, which met the objective of the study (Figure 1).

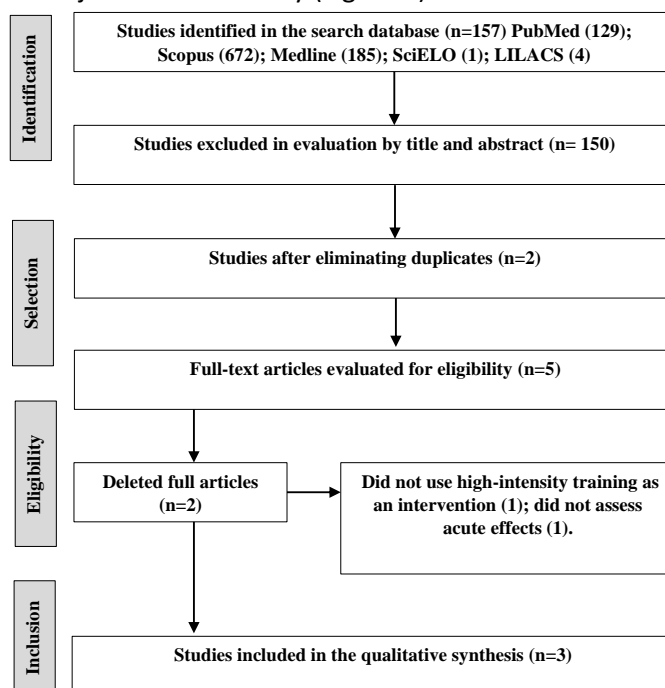


Figure 1. Article identification and selection process

DISCUSSION

This systematic review sought answers about the effects that high-intensity exercise promotes on the glycemic metabolism of adults with T2DM.

After rigorous analysis of the results found, it is pointed out that high-intensity exercise is a safe practice with proven benefits. For example, Gillen et al., 2012⁽¹⁶⁾, studied seven adults with T2DM and examined the 24 hour continuous glycemic response (CGM) after a high-intensity interval Training (HIT) session of cycling effort



of 10 repetitions of 60 seconds, at an intensity of 90% of the maximum heart rate, interspersed with 60 s of rest. They underwent 24-hour CGM on two occasions under standard dietary conditions, after acute HIT and on a no-exercise control (CTL) day. Resulting in a reduction in hyperglycemia measured as the proportion of time spent above 10 mmol/l (HIT: 4.5 ± 4.4 vs. CTL: $15.2 \pm 12.3\%$, $p = 0.04$). Postprandial hyperglycemia, measured as the sum of the postmeal areas under the glucose curve, was also lower after HIT vs. CTL (728 ± 331 vs. 1142 ± 556 mmol/l•9 h, $p = 0.01$). These findings highlight the potential of high-intensity exercise for glycemic control in T2DM.

In a chronic study, Fex et al., 2015⁽¹⁷⁾ examined the impact on metabolic risk factors and body composition of 16 participants with pre-diabetes ($n=8$) and type 2 ($n=8$), involving HIT with a frequency of 3 times a week for 12 weeks. Where they had measured fasting blood glucose, HbA1c, anthropometric measurements, body composition dual X-ray absorptiometry (DXA), blood pressure, resting heart rate, VO₂ max and dietary factors, total energy expenditure and physical activity. After intervention, the study indicated that elliptical HIT appears to improve metabolic risk factors and body composition in patients with pre and T2DM, significantly improving fasting blood glucose, waist and hip circumference, appendicular fat mass, leg lean body mass and appendicular lean body mass, systolic blood pressure, resting heart rate, and VO₂ max ($p < 0.05$).

Corroborating the previously mentioned results, we can observe the study by Madsen et al., 2015⁽¹⁸⁾. Where there were significant reductions in glycated hemoglobin ($p = 0.04$), mean fasting venous glucose

concentration ($p = 0.04$) and oral glucose tolerance test (OGTT) of 2 hours ($p = 0.04$). The research was carried out with ten non-active T2DM patients ($56 \text{ years} \pm 2$) paired with thirteen healthy control participants ($52 \text{ years} \pm 2$), in which blood pressure was measured at rest, performed on a separate day, followed by an increase in VO₂ max cycle ergometer test. Finally, whole-body DXA was performed. Repeating the same after 8 weeks of training. The exercise protocol was performed 3 times (10×60 sec. HIT) per week over a period of 8 weeks on a cycle ergometer.

Contradicting some findings, Ruffino et al., 2017⁽¹⁹⁾ studied sixteen men with T2DM (mean \pm SD age: 55 ± 5 years, body mass index: $30.6 \pm 2.8 \text{ kg} \cdot \text{m}^{-2}$, maximum aerobic capacity: $27 \pm 4 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) during 8 weeks of reduced-effort high-intensity interval training (REHIT) (three 10 min/week low-intensity cycling sessions with two 10-20 s all-out sprints) plus 8 weeks of walking of moderate intensity (five sessions of 30 min/week at an intensity corresponding to 40%-55% of the heart rate reserve), respecting a wash-out period of 2 months between interventions. After the intervention, the study showed that none of the interventions were efficient in reducing OGTT of insulin sensitivity, glycemic control measured using continuous glucose monitors, blood lipid profile or body composition.

However, in addition to the findings mentioned above, other benefits provided by high-intensity exercise were observed, such as: mean and maximum glucose levels of CGM⁽²⁰⁾, reduction of fasting glucose levels^(17, 21-23), reduced HbA1c levels⁽²¹⁻²³⁾, improved insulin resistance⁽¹⁸⁾, improved insulin sensitivity⁽¹⁸⁾. These findings, and other findings, can be seen in Table 1.

Table 1: Studies included in the systematic review and with their respective objectives, study design and results.

Author and year	Objective	Study design	Outcome
Gillen et al., 2012 ⁽¹⁶⁾	To examine the 24 h blood glucose response to a HIT session consisting of cycling efforts.	* 7 patients with T2DM underwent HIT training. *Standards evaluated were glucose measured after HIT and on a CTL day.	* HIT: reduced hyperglycemia measured as a proportion of time spent above 10 mmol/l and postprandial hyperglycemia.
Karstoft et al., 2013 ⁽²⁰⁾	To evaluate the feasibility of walking in T2DM patients and to investigate the effects of interval walking versus continuous walking training on physical fitness, body	* 32 patients with T2DM, divided into 3 groups, control ($n=8$), continuous walking ($n=12$) and interval walking ($n=12$). * The standards evaluated were glycemic control, and others.	* Glycemic control worsened in the control group * Mean and maximum CGM glucose levels





	composition and glycemic control.	*Duration of 4 months.	decreased in the interval walking group.
Mitranun et al., 2014 ⁽²¹⁾	To determine the effects of CON versus aerobic interval training (INT) on glycemic control.	* 43 participants, divided into sedentary, CON and INT groups. *Duration of 12 weeks.	*CON and INT: fasting blood glucose levels decreased. *INT: HbA1c levels decreased.
Fex et al., 2015 ⁽¹⁷⁾	To examine the impact of 12 weeks of HIT on metabolic risk factors and body composition in patients with prediabetes and T2DM.	* 16 participants divided into 2 groups, pre-T2DM (n=8) and T2DM (n=8), underwent HIT training. * Standards evaluated were fasting blood glucose, HbA1c and others. *Duration of 12 weeks.	* HIT: significant improvement for fasting blood glucose.
Madsen et al., 2015 ⁽¹⁸⁾	To investigate glycemic control, pancreatic function, and total fat mass before and after 8 weeks of low-volume HIT on a cycle ergometer in T2DM patients and matched healthy controls.	* 23 participants, 10 patients are sedentary and have T2DM, and 13 are healthy. * HIT training *Standards evaluated were 2-hour OGTT, and others * Intervention lasting 8 weeks.	* In participants with T2DM, the glycemic percentage was significantly reduced. Insulin resistance was significantly improved, same for insulin sensitivity.
Alvarez et al., 2016 ⁽²²⁾	To investigate the effects of low-volume, HIT on cardiometabolic risk and exercise capacity in women with T2DM.	* 23 overweight/obese sedentary women divided into 2 groups, HIT (n=13) and control (CON) (n=10). * Standards assessed were glycemic control, medication use, and others. * Duration of 16 weeks.	* Fasting blood glucose and HbA1c improved in the HIT group. * Reduction in the daily dosage of antihyperglycemic and antihypertensive drugs during the intervention.
Mangiamarchi et al., 2017 ⁽²³⁾	To determine the effects of a 12-week HIT exercise program on cardiometabolic and quality of life variables in patients with T2DM.	* 19 women with T2DM, divided into 2 groups: HIT + nutrition education group (GE): 9 women; and Nutrition education only group (CG): 10 women. * Glycemia and glycated hemoglobin, among others, were evaluated.	* Fasting blood glucose and glycated hemoglobin decreased in the EG group. * There was a significant correlation between the decrease in total fat mass and that of glycated hemoglobin.
Ruffino et al., 2017 ⁽¹⁹⁾	To compare the effects of REHIT and moderate-intensity walking on health markers in patients T2DM in a counterbalanced crossover study.	* 16 men with T2DM underwent REHIT and moderate-intensity walking training, with an interval of 2 months between them. *Standards evaluated were OGTT before and after each intervention, and others. *Duration 8 weeks	* None of the interventions improved OGTT-derived measures of insulin sensitivity, glycemic control.

Støa et al., 2017 ⁽¹⁵⁾	To investigate the effects of HAIT on type A1C glycated hemoglobin, and other parameters among people with T2DM; and compare with moderate intensity training program (MICT).	* 38 subjects with T2DM separated into 2 groups, HAIT (4 × 4 minutes of walking or running uphill at 85-95% of maximum heart rate) and MICT (continuous walking at 70-75% of maximum heart rate.). * Standards evaluated were type A1C glycated hemoglobin (HbA1c), and others. * Duration of 12 weeks.	* HAIT: Reduction in HbA1c; 21% increase in Vo ² Max; Improvement in body weight; Reduction in Blood Pressure;
Fealy et al., 2018 ⁽¹⁴⁾	To determine the effectiveness of high-intensity functional training (F-HIT) to reduce insulin resistance in T2DM. To examine the acute effects of exercise timing on glycemic control during and after exercise in T2DM.	* 13 overweight/obese adults (5 men, 8 women) were evaluated during F-HIT training. * Standard assessed was insulin resistance. *Duration of 6 weeks.	* F-HIT increased insulin sensitivity.
Huang et al., 2018 ⁽²⁴⁾	To determine the acute effects of high-intensity, REHIT on 24-hour blood glucose in male patients with type 2 diabetes	* 26 T2DM patients (14 women and 12 men) who were treated with metformin, then exercised for different times: EX 30 (HIT for 30 min), EX 60 (HIT for 60 min), and EX 90 (HIT for 90 min) * Standards evaluated were glucose, insulin, and others.	* Glucose: decreased after exercise at EX30, EX60 and EX90. * Metformin treatment indicated that glucose declines more after exercise EX30, EX60 and EX90, respectively; insulin decreased more at EX30 and EX60.
Metcalfe et al., 2018 ⁽²⁵⁾	To assess whether HIT with less time commitment may be as effective as resistance training (END) on glycemic control, physical fitness, and body composition in individuals with T2DM.	* 11 homens com T2DM separados em 4 grupos, CON ou sem exercícios, MICT, HIT e REHIT. * Os padrões avaliados foram as medições contínuas de glicose de 24 horas padronizado pela dieta	* 24h glucose: decreased in all 3 exercise groups, being lower in the MICT group than REHIT. * HIT group, glucose was not changed
Winding et al., 2018 ⁽¹³⁾	To compare the acute effects of HIT versus MICT on glycemic control in middle-aged and elderly patients with T2DM.	* 29 subjects with T2DM separated into 3 groups, control or no training, END and HIT. *Standards evaluated were HbA1c, glucose tolerance, and others. * Intervention of 11 weeks	* HIT: decreased HbA1c and fasting blood glucose, postprandial blood glucose, glycemic variability. The reduction in postprandial glucose in the HIT group was primarily driven by a lower rate of exogenous glucose onset.





Mendes et al., 2019 ⁽²⁶⁾	To compare the acute effects of HIT versus MICT on glycemic control in middle-aged and elderly patients with T2DM.	<ul style="list-style-type: none"> * 15 middle-aged and elderly T2DM patients divided into 3 groups: HIT, MIIT and CON. * Capillary blood glucose was evaluated immediately before, during and up to 50 minutes after the experimental conditions. 	<ul style="list-style-type: none"> * HIT and MICT reduced blood glucose levels during exercise and the 50-minute lab recovery period compared to the CON group. * HIT had greater effect than MICT.
Rafiei et al., 2019 ⁽²⁷⁾	To compare the effects of HIT with MICT on improving markers of 24-hour glycemic variability and other biomarkers within a population at high risk of developing T2DM.	<ul style="list-style-type: none"> * 15 overweight or obese inactive women were divided into 2 groups: HIT (n=8) and MICT (n=7). * Fasting blood tests were performed before and three days after training. * Intervention duration: 2 weeks 	<ul style="list-style-type: none"> * HIT and MICT improved glycemic variability, with no difference between them. * Two weeks of HIT or MICT similarly decreased glycemic variability in overweight/obese women at high risk of T2DM.
Savikj et al., 2019 ⁽²⁸⁾	To determine whether exercise training at two different times of the day would have different effects on 24-hour blood glucose levels in men with T2DM.	<ul style="list-style-type: none"> * 11 men with T2DM separated into 2 HIT morning and HIT afternoon groups. * Assessed glucose using CGM, and others. * Intervention lasting 2 weeks. 	<ul style="list-style-type: none"> * Morning HIT: increased glucose concentration. * HIT late: reduced glucose concentration.
Banitalebi et al., 2021 ⁽²⁹⁾	To examine the effects of interval sprint (SIT) and combined aerobic + resistance training (COMB) on HbA1C and (primary outcome) in participants with T2DM.	<ul style="list-style-type: none"> * 52 overweight women with T2DM were divided into 3 groups: SIT (n=17), COMB (n=17), control (n=18). * Type A1C glyated hemoglobin (HbA1c) and others were evaluated. * The intervention lasted 10 weeks. 	<ul style="list-style-type: none"> * HbA1c had a significant reduction in the SIT and COMB groups; showing effective results in overweight women with T2DM regardless of changes in body mass.
Li et al., 2022 ⁽³⁰⁾	To compare the effects of different exercise intensities, HIT and MICT, on body composition, heart and lung fitness, blood glucose and blood pressure indices in patients with T2DM, in use of power cycle.	<ul style="list-style-type: none"> * 37 men with T2DM were divided into 3 groups: HIT, MICT and CON. * The indicators of blood glucose (FBG), type A1C glyated hemoglobin (HbA1c); and other indicators. * The intervention lasted 12 weeks. 	<ul style="list-style-type: none"> * FBG indicators were different between MICT and CON groups. * HbA1c was statistically different between the HIT and MICT groups after the intervention. In the HIT Group, there was a difference in the results before and after the intervention.

CONCLUSION

T2DM as it is a worldwide disease, which affects men and women without distinction, especially those who have sedentary behaviors and/or are overweight/obese. Having as one of the strategies to improve the quality of life, is the adherence to physical activity programs in their daily lives. However, this activity must consider some factors such as the duration, intensity and types of exercises, and the use of medications, for example.

Thus, it is noted that HIT presents encouraging results, especially in terms of comparison with other types of training. Since, in most studies, the practice of high-intensity exercise proved to be effective in reducing glucose levels in men and women aged between 19 and 65 years diagnosed with T2DM. Another point that can be observed was the reduction in the dosage of antihyperglycemic drugs in those who adhered to HIT. Having seen these factors, HIT seems to constitute an interesting strategy for the treatment of T2DM, increasing the quality of life of those who practice it.

Authors' contribution: Santos. JWC e Cunha. RM are the main investigators, the first as author and the second as supervisor. Both conceived the study, led the development of proposal and protocol. De Sousa. GS contributed to the development of the proposal. All authors read, approved and agreed with the publication of the definitive manuscript. All named authors adhere to the Essays authorship guidelines.

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