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REVIEW ARTICLE

The impact of different modes of exercise training on GLP-1: a systematic review and meta-analysis research

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Abstract

Background The impact of exercise training on glucagon-like peptide 1 (GLP-1) of people with type 2 diabetes has been investigated and it has been found that it can improve their levels of blood glucose; however, the effect of exercise intervention mode on GLP-1 levels is still controversial.

Objective The purpose of this study was to investigate the duration, mode, and intensity of exercise intervention effect on the levels of GLP-1 by a systematic review and meta-analysis.

Data sources By March 29, 2020, Google Scholar, PubMed, Medline, Scopus database, Science Direct, and reference lists of articles had been randomly dealing with the subject matter with the purpose of investigating the effect of different variables of duration and short-term and long-term exercise training on GLP-1 through pre-test and post-tests. Thus, to strengthen the outcome of the present study, sixteen studies with 1562 subjects were included.

Results In the present study, we found a significant change on GLP-1 levels in both types of duration exercise intervention groups (MD: − 1.60 pmol/l; 95% CI [− 2.20, − 1.01]; $p < 0.00001$). Separately investigated, the level of GLP-1 in short-term training was MD − 1.26 pmol/l, 95% CI (− 1.79, − 0.73), $p < 0.00001$, and in long-term training, it was −2.76 pmol/l, 95% CI (− 5.10, − 0.43), $p = 0.02$. The intensity of short-term training was between 55 and 65% max HR, and for the long-term-training, it was 65–85% max HR.

Conclusion In this meta-analysis, it was found that the levels of GLP-1 could be affected by short-term and long-term training with different modes and intensity. As a result, current evidence shows that it may be a good choice for patients with type 2 diabetes to control their blood glucose. The mechanism of this GLP-1 increase has not yet been fully discovered. Further longitudinal studies and exploration into mechanisms of action are required in order to determine the precise role of GLP-1 in insulin responses to an exercise intervention.

Keywords GLP-1 · Exercise training · Short-term training · Long-term training · Meta-analysis

Introduction

Over the past three decades, the number of people with type 2 diabetes (T2DM) has more than doubled globally, making it one of the most important public health challenges for all nations [1]. The progress of T2DM is characterized by insulin resistance and insulin secretion from beta cells in the pancreas [2–4]. On the one hand, the cell membranes via the glucose transport (GLUT) allow insulin to bring glucose into the cells; on the other hand, insulin by the Akt substrate of 160 kDa (AS160) pathway has increased the regulation of GLUTs [5]. It has been observed that the other receptors can act like insulin receptors and change the blood glucose levels [6]. In this regard, glucagon-like peptide-1 (GLP-1) is a gastric hormone and plays an important role in responding to the increase of blood glucose after meal ingestion [4, 7], and GLP-1 receptors (GLP-1Rs) represent a unique approach to the treatment of diabetes with benefits extending outside

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glucose control and including positive effects on weight, blood pressure, cholesterol levels, and beta cell functions [8]. A little amplification of GLP-1 can improve beta cells and their function to increase insulin secretion and glucagon suppression [9] where binding GLP-1 to GLP-1Rs can bring about cell proliferation via distinct intracellular signaling pathway and can improve glycemic control with similar mechanisms of glucose-dependent insulin secretion from the beta cells. GLP-1Rs act like the insulin receptor and GLP-1 binds the specific G-proteins, increasing intracellular Ca2+ and adenylate cyclase. It activates PKC (protein kinase c) and PI3k (phosphoinositide 3-kinase) and conveyors GLUT towards the membranes to reduce the blood glucose [2, 10]. It has also been shown that GLP-1Rs preserve and improve the markers of beta cell function [11]. Thus, it is suggested that therapy with the addition of a short-acting GLP-1Rs be incorporated into the programs to bring about some advantages such as the effects on slowing gastric emptying [11]. Slower gastric delivery of meal contents leads to smaller glucose response excursion [12] since glucose and energy intakes are closely related [13]. Therefore, the effect of exercise training on energy intake to reduce the glucose levels can be impressive [4]. In line with this, there is plenty of research on exercise which shows that it reduces the blood glucose and it has proved to be healthier than the other ways in controlling diabetes. Thus, it is becoming increasingly clear that exercise and any kind of physical activity can be a therapeutic tool in a variety of ways for patients with or at the risk of diabetes, though the regulation of GLP-1 and insulin secretion through an exercise program for T2DM patients is still under investigation and question [4, 14, 15]. Nevertheless, according to some articles, the expression of GLP-1 from L-distal ileum has been proven to increase by an exercise program and it can improve pancreatic beta cell function [2, 7]. In the same way, some systematic reviews have measured the efficacy of duration of the exercise training [16], and the mechanism pathways to influence glucose uptake in short-term training versus long-term training have been shown to be different [17].

Scientifically speaking, it has been observed that the blood glucose plays an important role in acute training and decreases rapidly after 15–45 min, depending on the workload. These feedback signals can affect the levels of GLP-1 [18], and in patients with T2DM, for example, it is characterized by a reduced incretin effect. Seemingly, a single bout of exercise can bring about a remarkable development in the plasma levels of GLP-1 to reduce energy intake through AS160 pathway, so it can be the cornerstone as the diabetes management [7, 19]. A study recommended a 90-min free weight lifting session followed by a 6.5-h rest period in a 12-repetition round of resistance training and a 60-min running speed required to elicit 70% maximum heart rate. It should be followed by a 7-h rest period with aerobic exercise that can eventually regulate GLP-1 and increase GLUTs in the cell membrane [20]. How long this effect can last has not yet been examined [17].

In the same line, it was observed that weekly exercise volume was positively related with the improvement of T2DM status [21]. The findings showed statistically and clinically significant improvement of glycemic control on the diabetic patients [22]. Respectively, research studies have compared either type of exercise with the control group [19]. On the other hand, not much research has been devoted to the effect of long-term or short-term training on GLP-1 [20]. Although previous findings from aerobic training studies indicated the exercise intensity, they found that structured exercise duration of more than 150 min/week was associated with a decrease in blood glucose and increase in GLP-1 in type 2 diabetes patients [19, 23]. Thus, it seems that the short-term training can bring about more advantages, but since the research of long-term training on GLP-1 is limited, the aim of this study was set to systematically review the literature on the effect of exercise and find out about the best methods that are used in exercise training on GLP-1 and insulin sensitivity in people with T2DM.

Methods

Data sources and searches

We searched and utilized the database in English language on PubMed, CINAHL, Google Scholar, Medline, and Scopus. Pre-specified search terms were GLP-1, incretin, insulin and insulin resistance, blood glucose, aerobic training, long-terms, and acute training. We precisely searched titles, abstracts, subjects, headings, and the contents, and employed the Boolean search terms (AND, OR, or NOT) to create the search strategy. Meta-analyses, systematic reviews, and all references were included. This thorough search was conducted in a time limit of March 29, 2020.

Study selection

The long-term group of exercise training in these analyses was randomly assigned to pre-test and post-test of ≥ 12-week duration and one session of acute training. In our meta-analyses, exercise training included resistance exercise (including full-body training with machine or weight-bearing including at least 6 movements in the upper and lower body), aerobic exercise (including walking, running, and aerobic training), and concurrent exercise (resistance + aerobic). Two authors validated the studies, treatment guidelines, titles, summaries, and full-texts of the appropriate articles to gain qualified analyses.

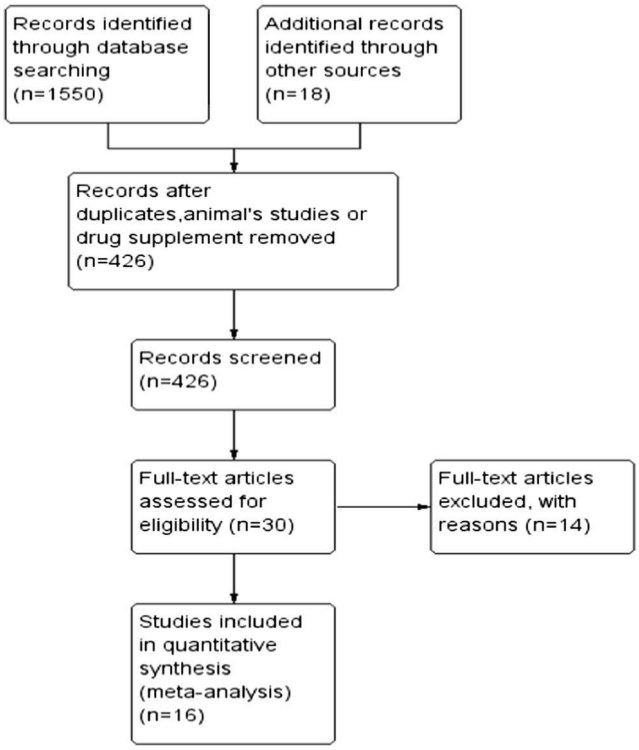

Fig. 1 PRISMA flow diagram

Inclusion/exclusion criteria

In these studies, the following criteria were employed for identification and selection: average age between 35 and 60 years old, T2DM for more than 1 year (fasting blood glucose greater than 126 mg/dl or 7 mmol/l, 2-h plasma glucose equal to or greater than 200 Mg/dl, glycosylated hemoglobin 6.5% or higher). The subjects did not take insulin; rather, they only took their daily requirements like metformin during the treatment period. In this review research, the study protocols used were aerobic, resistance, and concurrent training with an intervention period of ≥ 6 months by a pre-post-test design compared to the control group. Some systematic review articles, conferences, abstracts, and study protocols, as well as studies in which the subjects took part in an exercise regimen during the last 6 months, were excluded.

Data extraction

Three authors collected the data from the articles included in the review. The data were inclusive of subjects' characteristics (age, gender, body mass index [BMI]), the number of subjects, exercise intervention features (frequency, intensity, duration, and mode of exercise), methods and procedures of measuring the levels of GLP-1, authors, year of publication, study design, mean, standard deviation (SD) of continuous outcomes, and details of the biomarker evaluation methodology.

Data synthesis

In contrast to all studies, we extracted the effect size for any findings by measuring the mean difference between the pre- and post-tests. All the results were reported separately and were analyzed by using the same methods of reporting techniques for the findings. The mean difference for GLP-1 (pmol L^{-1}) in pre- and post-test conditions, sample size, participant characteristics, blood analytical methods, and exercise treatment information was the

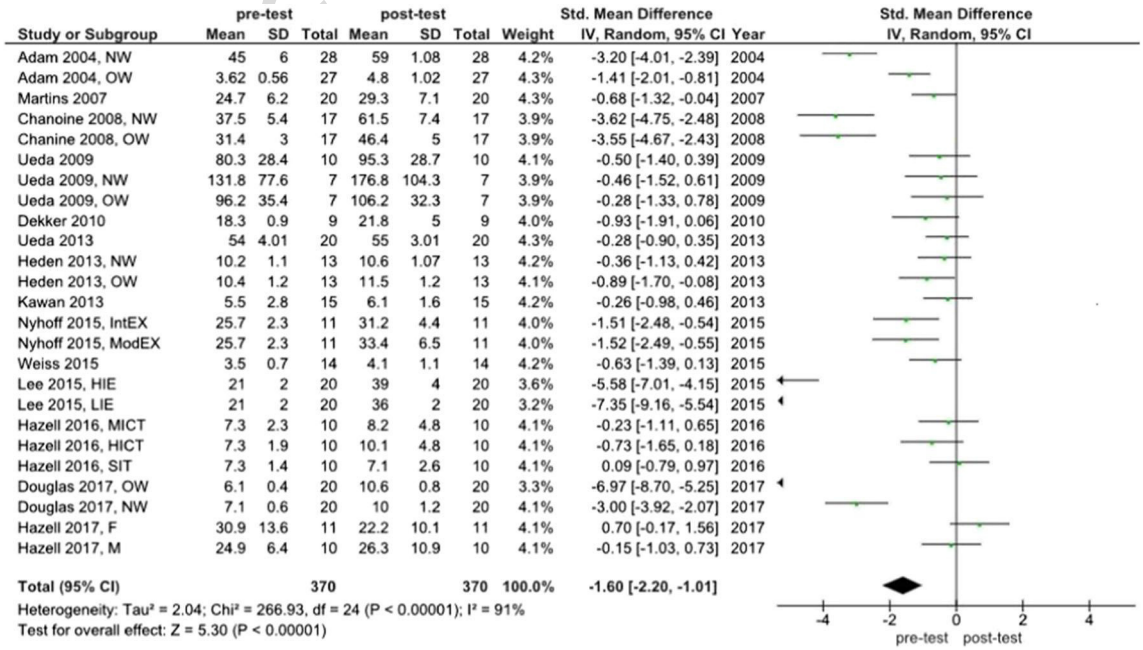

Fig. 2 Forest plot on levels of GLP-1 in exercise intervention

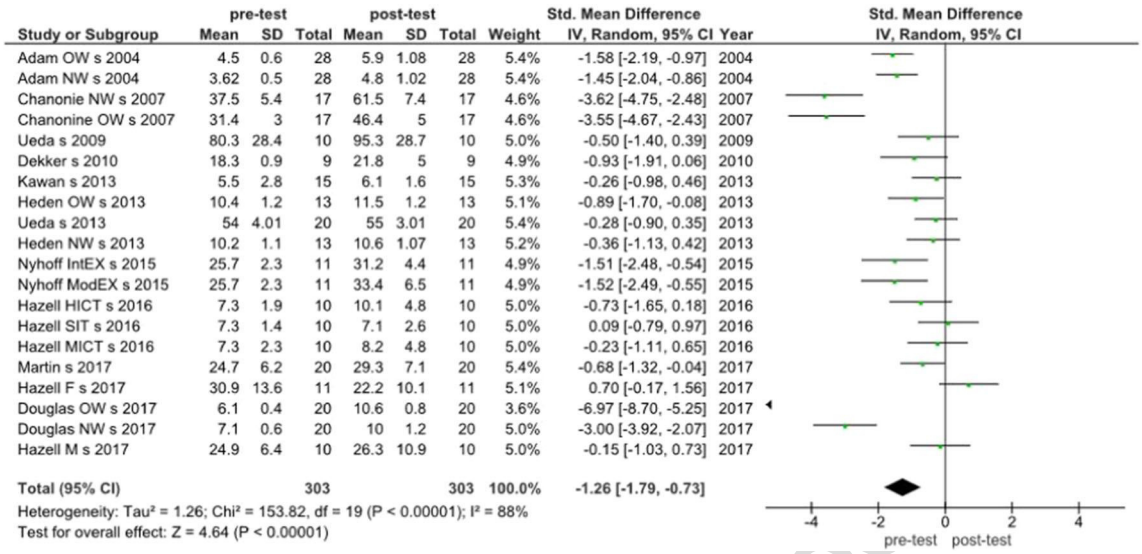

Fig. 3 Forest plot on levels of GLP-1 in short-term training

measures applied. The analysis was done by using the Review Manager 5.3 (The Nordic Cochrane Center, Copenhagen, Denmark). The post-test mean was subtracted from the pre-test mean, and the standard error of means (SEM) value was changed to standard deviation values. If any data was not shown in the texts or tables and we were unable to reach the authors, the data displayed in figures was extracted by employing the TA TechTip and GetData Graph Digitizer software. Where a subject was included in the control group or in more than one intervention group, we reported each group separately and fitted the sample size to the number of other groups. Therefore, heterogeneity was calculated as Cochrane's Q and I^2 index and it was > 50%. Eventually, we presented a 5% level of significance for the forest plot to describe the results.

Study quality

To describe the quality of the studies, we evaluated the data by using the fifteen-point tool in exercise reporting (TESTEX) scales. Two reviewers (RN and MMR) performed the quality control of the studies and reported the assessment.

Results

Study and subject characteristics

One thousand five hundred sixty-two articles were investigated having been searched in the major databases (Google Scholar, PubMed, Scopus, Science Direct, and hand searching). We eliminated animal studies, drug intervention, and duplicate titles. Four hundred twenty-six full-text articles were screened, and after eliminating the irrelevant records, excluded through reading titles and abstracts, we first chose 30 studies and finally 16 articles were selected for the moderator variables through the inclusion and exclusion criteria (PRISMA flow diagram; Fig. 1). Through these 16 studies, 370 subjects had been investigated through a pre-test/post-test design.

Intervention details

The time period during which the selected studies had been conducted ranged from 24 h to 12 weeks. Accordingly, the short-term training interventions ranged from 30 to 60 min at an intensity of 60–85% VO_{2max}, and in the long-term training, it ranged from 45 to 80% VO_{2max}. These findings came out

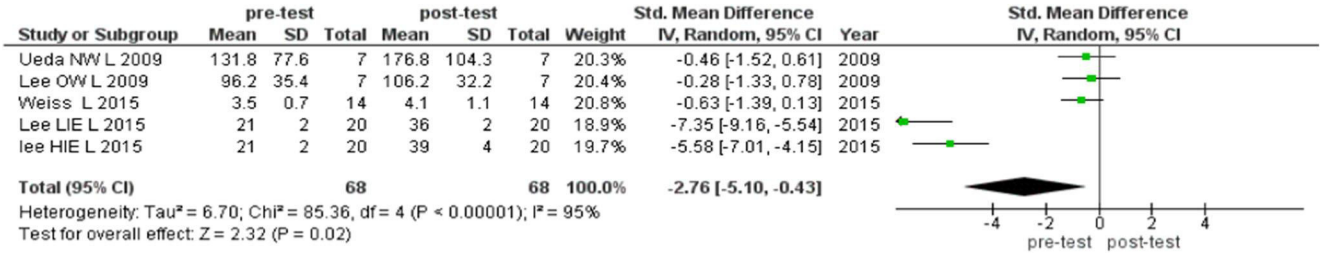

Fig. 4 Forest plot on levels of GLP-1 in long-term training

Q7 **Table 1** Characteristic of included studies in the meta-analysis

Study	Age mean ± SD	BMI mean ± SD	Disease	Gender	*N* E X (CON)	Modes of exercise	Intervention group: frequency and duration	Assessment measure/units
Martins et al. [24]	25.9±4.6	22.0±3.2	None	6 males, 6 females	12 (8)	Short-term aerobic	65% max HR, 60-min interval exercise	GLP-1
Chanoine et al. [15]	15.3±0.2	NW (20.7±0.5) OW (32.4±1.7)	None obese	36 boys	36	Short-term aerobic	5 days aerobic training (1 h/day)	GLP-1
Ueda et al. [4]	23.4±4.3	22.5±1.0	None	10 males	10	Short-term aerobic	3 sessions (75% VO_{2max}) (50% VO_{2max}) and resting session	GLP-1
Lee et al. [25]	15.3±2.2	24.0±3.8	T2DM	Not mention	20	Long-term aerobic	12 weeks (HIE group: ≥ 80% HR, LIE group: ≤ 45% HR)	GLP-1
Ueda et al. [26]	NW (22.4±4.2) OW (22.9±3.4)	NW (22.4±2.4) OW (30.0±3.1)	None obese	Male	7 (7)	Short-term aerobic	2 sessions (50% VO_{2max} for 60 min)	GLP-1
Hazell et al. [27]	30.5±7.9	23.5±2.8	None	27 female	18 (9)	Short-term aerobic	3 sessions (MICT; 65% VO_{2max}), (SIT)	GLP-1
Hazell et al. [28]	M (28.6±5.9) F (30.5 ±7.9)	M (23.7±2.2) F (23.5±2.8)	None	11 female, 10 male	21	Short-term aerobic	3 sessions (MICT: 30 min cycling at 65% VO_{2max}), (SIT; 6×30 s with 4-min recovery	GLP-1
Ueda et al. [29]	49.1±0.8	27.6±0.4	None	28 female	20	Long-term aerobic	12 weeks, 3 times per week(10-m warm-up, 60-m jogging) 65%HR	GLP-1
Heden et al. [30]	NM (26.0±2) OW (25.4±1)	NM (23.0±0.5) OW (34.6±1)	None obese	NM (7 M, 6F) OW (6 M, 7F)	26	Short-term aerobic	1 h of treadmill walking (55–60% $VO_{2\ peak}$)	GLP-1
Hazell et al. [31]	29±6	23.7±2.2	None	Male	10	Short-term aerobic	4 sessions (MICT; 30-m cycling at 65% VO_{2max}), (HICT; 30-m cycling at 85% VO_{2max}), (SIT; 6×30-s cycling)	GLP-1
Adam et al. [32]	NW (F: 35±12.7) OW (47.1±11.9)	NW (22.9±1.4) OW (30.9±2.7)	None obese	NW (F: 16, M: 12) OW (F: 6, M: 21)	NW= 28 OW= 27	Short-term aerobic	60-min cycling at 25% maximal power output	GLP-1
Weiss et al. [33]	EX (56±9) CON (57± 9)	EX (23.1±1.6) CON (25.3±2.3)	None	EX (M: 13, F: 1) CON (M: 13, F: 1)	14 (14)	Long-term aerobic	Balk treadmill test	GLP-1
Dekker et al. [34]	59±2	33.8±1.5	Hypertriacylglycerolemic	Male	9	Short-term aerobic	60 min of treadmill walking (55% VO_2peak)	GLP-1
Nyhoff et al. [35]	24.3±4.6	37.3±7.0	Obese	Female	11	Short-term aerobic	ModEX (55% VO_{2max}), IntEX (4 min (80% VO_{2max})/3 min (50%VO_{2max}))	GLP-1
Douglas et al. [36]	L (37.5±15.2) O (45.0 ±12.4)	L (22.4±1.5) O (29.2±2.9)	Lean obese	Female	40	Short-term aerobic	60-min treadmill (59.4% peak oxygen uptake)	GLP-1
Kawano et al. [37]	24.4±1.7	22.1±2.0	None	Male	15	Short-term aerobic	Rope skipping (3 sets × 10 m with 5-m interval), bicycle ergometer (3 sets × 10 m with 5-m interval)	GLP-1

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from the aerobic training investigations and there is no study for resistance training on GLP-1 concentration.

GLP-1 assessment

All the studies reported hormone values in pmol/l. If any study reported them otherwise, we converted them to pmol/l.

Outcome measures

Change in GLP-1

Sixteen studies in which a total of 370 subjects had been investigated through 25 pre-test- and post-test-reported changes in GLP-1 levels. We mixed the outcomes to make use of random-effect model and revealed a significant change in GLP-1 after post-test exercise intervention (MD: − 1.60 pmol/l; 95% CI [− 2.20, − 1.01]; $p < 0.00001$); Fig.2).

Analysis of the mode of exercise training

We examined the duration of short-term and long-term training intervention for the levels of GLP-1. These analyses revealed that GLP-1 increased significantly in both types of interventions compared to the values gained through the pre-tests. The results obtained were MD − 1.26 pmol/l, 95% CI (− 1.79, − 0.73), $p < 0.00001$, for the short-term intervention training, and MD −2.76 pmol/l, 95% CI (− 5.10, − 0.43), $p = 0.02$, for the long- term intervention; however, the levels of GLP-1 grew in the two types (Figs. 3 and 4).

Analysis of intensity of exercise training

In all the studies that examined the intensity of short-term training, the value was between 55 and 65% max HR, and for the long-term training, it was 65–85% max HR (Table 1).

Heterogeneity and publication bias

Publication bias was utilized by the funnel plot as described in the subgroup analysis; however, we distributed the mean ES cause of random sampling error if there was no study bias (Fig. 5).

Study quality

The quality of all the studies was judged to be moderate to good, with an average TESTEX score of 10 (ranging between 7 and 12) of a maximum score of 15 (Table 2). Each one of the criteria of monitoring the physical activity was met in all the studies, with the intention-to-treat analysis in 5 studies and relative exercise intensity in 11 studies. The criteria of assessor blinding were also met in 4 studies; however, the criteria of allocation concealment were met in only 3 studies. The other TESTEX criteria were each met in at least 50% of trials.

Discussion

As exercise intolerance is well recognized in patients with type 2 diabetes, the main purpose of this review was to perform a meta-analysis to investigate the impact of duration, mode, and intensity of exercise intervention on the levels of GLP-1 of the subjects.

Our primary analysis shows that the levels of GLP-1 were affected by two types of exercise duration (long-term and short-term training), mode, and intensity. Yet, the effect of short-term training with 55–65% max HR intensity protocol and long-term training with 65–85% max HR might also change GLP-1 concentration.

As the overall analysis of short-term training and GLP-1 shows, the GLP-1 concentration can be enhanced following a bout of exercise session. According to the overall analysis in participants, our short-term training findings differ from the

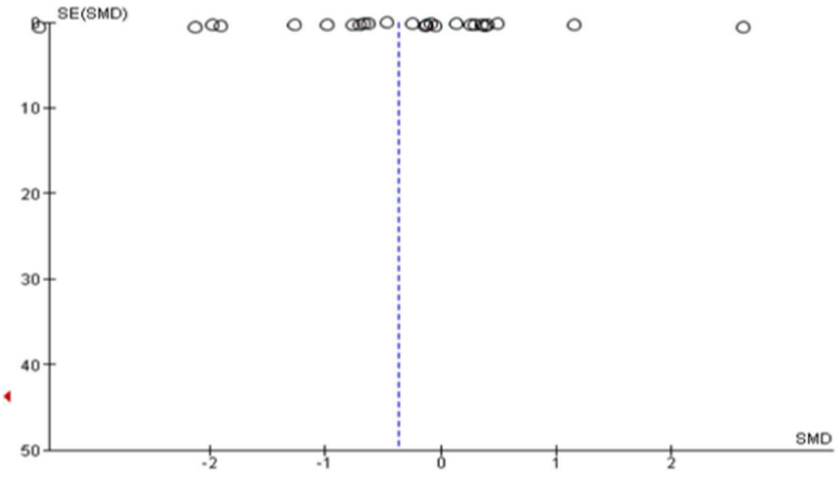

Fig. 5 Funnel plot aerobic and resistance

t2.1 **Table 2** (TESTEX)

t2.2 Study	Eligibility criteria specified	Randomization details specified	Allocation concealed	Groups similar at baseline	Assessors blinded	Outcome measures assessed > 85% participants[#]	Intention to treat analysis	Reporting between group statistical comparison	Point measures and measures of variability	Activity monitoring in control group	Relative exercise intensity constant	Exercise volume and energy expenditure	Overall TESTEX [15]
t2.3 Martin et al.	1	1	0	1	1	3	1	2	1	0	1	0	12
t2.4 Chanoine et al.	1	1	0	1	0	2	0	2	1	0	1	1	10
t2.5 Ueda et al.	1	1	0	1	0	2	0	2	1	0	1	1	10
t2.6 Lee et al.	1	0	0	0	0	1	0	2	1	0	1	1	7
t2.7 Ueda et al.	1	1	0	1	0	3	0	2	1	0	1	1	11
t2.8 Hazell et al.	1	1	0	1	0	2	0	2	1	0	1	1	10
t2.9 Hazell et al.	1	1	1	1	1	2	0	2	1	1	0	1	12
t2.10 Ueda et al.	1	0	0	1	0	1	0	2	1	1	0	1	8
t2.11 Heden et al.	1	0	0	1	1	3	1	2	1	0	1	1	12
t2.12 Hazell et al.	1	1	1	1	0	2	0	2	1	0	0	1	10
t2.13 Adam et al.	1	1	0	1	0	3	1	2	1	0	0	0	10
t2.14 Weiss et al.	1	0	0	0	0	2	0	2	1	0	1	0	7
t2.15 Dekker et al.	1	1	0	1	0	1	0	2	1	0	1	1	9
t2.16 Nyhoff et al.	1	0	0	1	0	2	0	2	1	1	1	1	10
t2.17 Douglas et al.	1	1	1	1	0	2	1	2	1	0	1	1	12
t2.18 Kawan et al.	1	1	0	0	1	2	1	2	1	1	0	0	10

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findings of Heden et al. (2013) who found that 1 h of treadmill walking did not change the GLP-1 concentration between trials [26]. In addition, Ueda et al. (2009) reported that a session of cycling exercise at 50% VO_{2max} significantly did not change the GLP-1 levels [26], which differs from our findings. Our short-term training group analysis indicated a positive effect of exercise training on GLP-1 concentration. According to the findings of Heden et al., exercise training may decrease postprandial insulin levels via reduced pancreatic β cell insulin secretion. Interestingly, the reduction in insulin secretion in the exercise training happened in the face of similar plasma glucose and GLP-1 levels as compared to the control group [30]. They also suggested that GLP-1 concentration is not only modulated by blood glucose, but it is as well impressed by other hormones and nervous system. It is possible that these levels are masked by alterations in the other variables. Yet, care shall be taken in explaining the findings because the short-term training group analysis only contained a small number of studies.

From the clinical research in short-term training group, our findings are close to the findings of Martin et al. (2007) who found that GLP-1 concentration is related with 1 h of 65% HR cycling and it can significantly increase the GLP-1 concentration [24]. In addition, Adams et al. (2004) reported that a 60-min cycling at 25% maximum power output significantly changes the GLP-1 concentration compared with that of the pre-test group.

Although other articles had reported the positive change in GLP-1 concentration that increases immediately after an acute session, these studies investigated only one session of exercise training effects. In this regard, Chanoine et al. (2008) reported that 5 days of aerobic exercise training increases the GLP-1 concentration [15]. Hazell et al. (2017) reported the sessions of MICT and SIT only increased the GLP-1 concentration in females following MICT training compared to the CTRL group [28].

Compared to the pre-test results, the long-term training group's GLP-1 concentration was highly affected and increased as the post-test results indicated. To explain this, Lee et al. (2015) found that 12 weeks of exercise training with an intensity of ≤ 45 to ≥ 80% significantly increased the GLP-1 concentration in patients with type 2 diabetes [25]. In the same line, Ueda et al. (2013) reported that 12 weeks of exercise training with 65% max HR significantly increased the GLP-1 concentration compared with the findings in the pre-test [29]. However, a cross-sectional study reported that post-exercise GLP-1 levels do not differ between the control group and non-obese control subjects who had higher insulin levels. These findings suggest that the lower levels of insulin in the control group are not mediated by the reduction in GLP-1 concentration. It also reported that lower blood glucose might provide less β cell stimulus for insulin. This stimulus to GLP-1 might be reduced in exercise-trained individuals.

Regarding the GLP-1 function on pancreas, the mechanism pathway by exercise is still unclear. Exercise training including short-term or long-term training has been prescribed for increasing GLP-1 concentration and appears to be one of the safest treatments for the patients with type 2 diabetes. Furthermore, some investigations suggested that the exercise training can prevent blood glucose in patients with type 2 diabetes from increasing [38]. As far as our knowledge allows, this is the first systematic review and meta-analysis to investigate the effect of long-term and short-term training with the mode and intensity suggestions on the GLP-1 concentration. There are, of course, some limitations in our meta-analysis that need to be reported. First of all, some studies have been conducted only on animals and few studies on humans; secondly, some studies have used several types of medicines which limited us; thirdly, the number of the articles that worked on different types of training was limited; and finally, the studies were limited to English language, so we could not extract all the data to obtain all potentially relevant studies.

Conclusion

Through this meta-analysis, we found that short-term and long-term training with different modes and intensities could influence the levels of GLP-1. The mechanism of this increase has not yet fully been discovered and many questions still exist.

Abbreviations GLP-1, Glucagon-like peptide-1; GLP-1Rs, Glucagon-like peptide-1 receptors; T2DM, Type 2 diabetes mellitus; BMI, Body mass index; Vo_{2max}, Maximal oxygen uptake; 1RM, One repetition maximum; Max HR, Maximum heart rate; HIE, High-intensity interval exercise; LIE, Low-intensity interval exercise; MICT, Moderate-intensity continuous training; SIT, Sprint interval training; HICT, High-intensity continuous training; NW, No overweight; OW, Overweight; ModEX, Moderate-intensity aerobic continuous exercise; IntEX, High-intensity aerobic interval exercise; NOEX, No exercise; Vs, Versus; GLUT, Glucose transport; AS160, Akt substrate of 160 kDa; AMPK, 5′ AMP-activated protein kinase; MD, Mean difference; PKC, Protein kinase C; EI, Exercise intensity; PI3K, Phosphoinositide 3-kinase

Data availability The data used to support the findings of this study are available from the corresponding author upon request.

Declarations

Conflict of interest The authors declare no competing interests.

References

1. Chen L, Magliano DJ, Zimmet PZ. The worldwide epidemiology of type 2 diabetes mellitus—present and future perspectives. Nat Rev Endocrinol. 2012;8(4):228–36.

2. Furtado LM, Somwar R, Sweeney G, Niu W, Klip A. Activation of the glucose transporter GLUT4 by insulin. Biochem Cell Biol. 2002;80(5):569–78.
3. Wollheim CB. Beta-cell mitochondria in the regulation of insulin secretion: a new culprit in type II diabetes. Diabetologia. 2000;43(3):265–77.
4. Ueda S-y, Yoshikawa T, Katsura Y, Usui T, Fujimoto S. Comparable effects of moderate intensity exercise on changes in anorectic gut hormone levels and energy intake to high intensity exercise. J Endocrinol. 2009;203(3):357–64.
5. Kramer HF, Witczak CA, Fujii N, Jessen N, Taylor EB, Arnolds DE, et al. Distinct signals regulate AS160 phosphorylation in response to insulin, AICAR, and contraction in mouse skeletal muscle. Diabetes. 2006;55(7):2067–76.
6. Sheikh A. Direct cardiovascular effects of glucagon like peptide-1. Diabetol Metab Syndr. 2013;5(1):47.
7. Kreymann B, Williams G, Ghatei MA, Bloom SR. Glucagon-like peptide-1 7-36: a physiological incretin in man. Lancet. 1987;2(8571):1300–4.
8. Prasad-Reddy L, Isaacs D. A clinical review of GLP-1 receptor agonists: efficacy and safety in diabetes and beyond. Drugs Context. 2015;4:212283.
9. Gupta V. Glucagon-like peptide-1 analogues: an overview. Indian J Endocrinol Metab. 2013;17(3):413–21.
10. Atlas D. International diabetes federation. IDF Diabetes Atlas, 7th edn Brussels, Belgium: International Diabetes Federation. 2015.
11. Balena R, Hensley IE, Miller S, Barnett AH. Combination therapy with GLP-1 receptor agonists and basal insulin: a systematic review of the literature. Diabetes Obes Metab. 2013;15(6):485–502.
12. Chaikomin R, Doran S, Jones KL, Feinle-Bisset C, O'Donovan D, Rayner CK, et al. Initially more rapid small intestinal glucose delivery increases plasma insulin, GIP, and GLP-1 but does not improve overall glycemia in healthy subjects. Am J Physiol Endocrinol Metab. 2005;289(3):E504–E7.
13. Pilichiewicz AN, Chaikomin R, Brennan IM, Wishart JM, Rayner CK, Jones KL, et al. Load-dependent effects of duodenal glucose on glycemia, gastrointestinal hormones, antropyloroduodenal motility, and energy intake in healthy men. Am J Physiol Endocrinol Metab. 2007;293(3):E743–E53.
14. Martins C, Morgan L, Truby H. A review of the effects of exercise on appetite regulation: an obesity perspective. Int J Obes. 2008;32(9):1337–47.
15. Chanoine J-P, Mackelvie KJ, Barr SI, Wong ACK, Meneilly GS, Elahi DH. GLP-1 and appetite responses to a meal in lean and overweight adolescents following exercise. Obesity. 2008;16(1):202–4.
16. Gordon BA, Benson AC, Bird SR, Fraser SF. Resistance training improves metabolic health in type 2 diabetes: a systematic review. Diabetes Res Clin Pract. 2009;83(2):157–75.
17. Kristiansen S, Hargreaves M, Richter E. Exercise-induced increase in glucose transport, GLUT-4, and VAMP-2 in plasma membrane from human muscle. Am J Physiol Endocrinol Metab. 1996;270(1):E197–201.
18. Huda MSB, Wilding JPH, Pinkney JH. Gut peptides and the regulation of appetite. Obes Rev. 2006;7(2):163–82.
19. Umpierre D, Ribeiro PAB, Kramer CK, Leitão CB, Zucatti ATN, Azevedo MJ, et al. Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis. JAMA. 2011;305(17):1790–9.
20. Broom DR, Batterham RL, King JA, Stensel DJ. Influence of resistance and aerobic exercise on hunger, circulating levels of acylated ghrelin, and peptide YY in healthy males. Am J Physiol Regul Integr Comp Physiol. 2009;296(1):R29–35.
21. Umpierre D, Ribeiro P, Schaan B, Ribeiro J. Volume of supervised exercise training impacts glycaemic control in patients with type 2 diabetes: a systematic review with meta-regression analysis. Diabetologia. 2013;56(2):242–51.
22. Zanuso S, Jimenez A, Pugliese G, Corigliano G, Balducci S. Exercise for the management of type 2 diabetes: a review of the evidence. Acta Diabetol. 2010;47(1):15–22.
23. Lee SS, Yoo JH, So YS. Effect of the low- versus high-intensity exercise training on endoplasmic reticulum stress and GLP-1 in adolescents with type 2 diabetes mellitus. J Phys Ther Sci. 2015;27(10):8–3063.
24. Martins C, Morgan LM, Bloom SR, Robertson MD. Effects of exercise on gut peptides, energy intake and appetite. J Endocrinol. 2007;193(2):251–8.
25. Lee SS, Yoo JH, So YS. Effect of the low-versus high-intensity exercise training on endoplasmic reticulum stress and GLP-1 in adolescents with type 2 diabetes mellitus. J Phys Ther Sci. 2015;27(10):3063–8.
26. Ueda S-y, Yoshikawa T, Katsura Y, Usui T, Nakao H, Fujimoto S. Changes in gut hormone levels and negative energy balance during aerobic exercise in obese young males. J Endocrinol. 2009;201(1):151.
27. Hallworth JR, Copeland JL, Doan J, Hazell TJ. The effect of exercise intensity on total PYY and GLP-1 in healthy females: a pilot study. J Nutr Metab. 2017;2017:1–7.
28. Hazell TJ, Townsend LK, Hallworth JR, Doan J, Copeland JL. Sex differences in the response of total PYY and GLP-1 to moderate-intensity continuous and sprint interval cycling exercise. Eur J Appl Physiol. 2017;117(3):431–40.
29. Ueda S-y, Miyamoto T, Nakahara H, Shishido T, Usui T, Katsura Y, et al. Effects of exercise training on gut hormone levels after a single bout of exercise in middle-aged Japanese women. Springerplus. 2013;2(1):83.
30. Heden TD, Liu Y, Kearney ML, Park Y, Dellsperger KC, Thomas TR, et al. Prior exercise and postprandial incretin responses in lean and obese individuals. Med Sci Sports Exerc. 2013;45(10):1897–905.
31. Hazell TJ, Islam H, Hallworth JR, Copeland JL. Total PYY and GLP-1 responses to submaximal continuous and supramaximal sprint interval cycling in men. Appetite. 2017;108:238–44.
32. Adam TCM, Westerterp-Plantenga MS. Activity-induced GLP-1 release in lean and obese subjects. Physiol Behav. 2004;83(3):459–66.
33. Weiss EP, Royer NK, Fisher JS, Holloszy JO, Fontana L. Postprandial plasma incretin hormones in exercise-trained versus untrained subjects. Med Sci Sports Exerc. 2014;46(6):1098–103.
34. Dekker MJ, Graham TE, Ooi TC, Robinson LE. Exercise prior to fat ingestion lowers fasting and postprandial VLDL and decreases adipose tissue IL-6 and GIP receptor mRNA in hypertriacylglycerolemic men. J Nutr Biochem. 2010;21(10):983–90.
35. Nyhoff LM, Heden TD, Leidy HJ, Winn NC, Park Y-M, Thyfault JP, et al. Prior exercise does not alter the incretin response to a subsequent meal in obese women. Peptides. 2015;71:94–9.
36. Douglas JA, King JA, Clayton DJ, Jackson AP, Sargeant JA, Thackray AE, et al. Acute effects of exercise on appetite, ad libitum energy intake and appetite-regulatory hormones in lean and overweight/obese men and women. Int J Obes. 2017;41(12):1737–44.
37. Kawano H, Mineta M, Asaka M, Miyashita M, Numao S, Gando Y, et al. Effects of different modes of exercise on appetite and appetite-regulating hormones. Appetite. 2013;66:26–33.
38. Motahari Rad M, Bijeh N, Attarzadeh Hosseini SR, Raouf SA. The effect of two concurrent exercise modalities on serum concentrations of FGF21, irisin, follistatin, and myostatin in men with type 2 diabetes mellitus. Arch Physiol Biochem. 2020:1–10.

AUTHOR QUERIES

AUTHOR PLEASE ANSWER ALL QUERIES.

Q1. Please check if the affiliation section is presented correctly. Also, please check if all the authors' telecommunications data are correctly captured or indicated.
Q2. The sentence "By March 29, 2020, Google Scholar, PubMed, Medline, Scopus database, Science Direct, and reference lists of articles had...." has been modified. Please check if the modification is correct and retained the intended meaning.
Q3. The sentence "Separately investigated, the level of GLP-1 in short-term training was...." has been modified. Please check if correct and retained the intended meaning.
Q4. Several modifications were made in the body. Please check if the modifications are correct and retained the intended meaning.
Q5. The sentence "In these studies, the following criteria were...." has been modified. Please check if the modification is correct and retained the intended meaning.
Q6. A citation for Table 1 was inserted. Please check if the insertion is correct; otherwise, please provide the correct insertion for Table 1.
Q7. Please check if Tables 1 and 2 are presented correctly.
Q8. Figure 5 contains overlapping text. Kindly confirm if figures are captured correctly.
Q9. References [4 & 33]; [19 & 23 & 24]; [30 & 34] based on original manuscript we received were identical. Hence, the latter was deleted and reference list and citations were adjusted. Please check if appropriate.