Jurnal Ners
Jurnal Ners
Vol. 15, No. 2, Special Issue 2020
http://dx.doi.org/10.20473/jn.v15i2(si).20521

Systematic Review

Effect of Physical Exercise on Insulin Sensitivity and the Modifiable Cardiovascular Risk Factors of Patients with T2DM: A Systematic Review

Wahyu Sukma Samudera, Ferry Efendi, and Retno Indarwati

Faculty of Nursing, Universitas Airlangga, Surabaya, East Java, Indonesia

ABSTRACT

Introduction: Diabetes mellitus is one of the chronic diseases that have increased in prevalence in Indonesia and the world. Optimal glycemic control is important to prevent the complications of diabetes mellitus. Several recommendations that are used in diabetes treatment involve regular exercise training. This study was undertaken to verify effect of regular exercise training on insulin sensitivity and the modifiable cardiovascular risk factors, and to determine if there was any effect from the different regular exercises.

Methods: A database search using PRISMA examined articles from Scopus, ScienceDirect and ProQuest. The inclusion criteria were that the article used a randomized controlled trial within the last 10 years, that the respondents were people with type 2 diabetes mellitus and that only physical exercise was the intervention involved. In total, 1,303 articles were screened and 16 articles were included that fit the criteria of inclusion in this systematic review.

Results: Based on the review of the 15 articles, the findings show that regular exercise training has some benefits related to glycemic control. It can reduce insulin resistance, plasma insulin, fasting blood glucose, postpandrial blood glucose and hbA1c. It also can increase insulin sensitivity and the disposition index of insulin as well. Furthermore, regular exercise training has benefits concerning some of the cardiovascular risk factors. It can reduce the systolic and diastolic blood pressure, waist circumference, fat mass, visceral fat, total cholesterol, and improve the lipid profile and endothelial function by decreasing the carotid intima media thickness and left ventricle wall mass.

Conclusion: Regular exercise training has benefits for people with type 2 diabetes mellitus and it can allow them to achieve of optimal glycemic control by improving insulin resistance and decreasing the cardiovascular risk factors. Physical exercise such as combined exercises (aerobic and resistance exercise) or a single exercise such as aerobic exercise can be recommended to improve insulin sensitivity and the modifiable cardiovascular risk factors in patients with T2DM.

ARTICLE HISTORY

Received: Feb 27, 2020
Accepted: April 1, 2020

KEYWORDS

regular physical training; insulin resistance; cardiovascular risk factors; type 2 diabetes mellitus

CONTACT

Ferry Efendi
✉ ferry-e@fkp.unair.ac.id
Faculty of Nursing, Universitas Airlangga, Surabaya, East Java, Indonesia

Cite this as: Samudera,W. S., Efendi, F., & Indarwati, R. (2020). Effect of Physical Exercise on Insulin Sensitivity and the Modifiable Cardiovascular Risk Factors of Patients with T2DM: A Systematic Review. *Jurnal Ners, Special Issues*, 518-530. doi: http://dx.doi.org/10.20473/jn.v15i2(si).20521

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic disease. It is one of the most common metabolic diseases. The hyperglycemic condition in T2DM is related to 3 main defects. This defects include increased hepatic glucose, decreased insulin secretion and impaired insulin action (Teixeira-lemos, Nunes, Teixeira, & Reis, 2011). The total prevalence of diabetes mellitus has increased in the last few years. Based on the International Diabetes Federation data from 2017 about the prevalence of diabetes mellitus, it was

estimated around 425 million or 8.8% people aged 20-79 years old in the world have diabetes mellitus (International Diabetes Federation, 2017). There are many reasons for this, among which is the increase in a few of the risk factors that are related with T2DM. These risk factors include less activity, an increased life span and an increased prevalence of obesity as a key component (Shaw, Sicree, & Zimmet, 2010).

Glycemic control in people with T2DM is an indicator that is used as outcome to evaluate the effect of any treatment that has been done. This requires a combination role between the health provider and patient. Diabetes treatment needs to control for a few risk factors by maintaining a level of physical exercise necessary to remain active. Physical inactivity has contributed significantly to the increased prevalence of T2DM worldwide by increasing the level of insulin resistance (Cornell, 2015). Moreover, glycemic control in T2DM is determined by insulin sensitivity and pancreatic endocrine function. Improving insulin sensitivity is an important thing to achieve in relation to the goal of the optimum glycemic target (Karstoft et al., 2014). Previous studies have shown that during exercise there is decreased peripheral insulin resistance. This leads to an increase peripheral glucose uptake (AminiLari et al., 2017). Insulin resistance decreases the capability of insulin to stimulate absorption and to save glucose (AminiLari et al., 2017).

Glycemia when uncontrolled leads to several complications such as cardiovascular disease (International Diabetes Federation, 2017). People with T2DM must be in control of their glycemic index. They need to reduce any cardiovascular risk factors that arise as soon as possible. Both things are an important part of preventing cardiovascular disease as a complication of T2DM. Previous studies have showed that moderate to high physical exercise has been related to a reduction in cardiovascular mortality (Stefano et al., 2010).

Regular physical exercise as a non-pharmacological treatment for people with type 2 diabetes mellitus has an important role in the prevention of diabetes complication (International Diabetes Federation, 2017). This is recommended as a part of diabetes treatment according to the International Diabetes Federation (International Diabetes Federation, 2017). There were few studies that showed the benefits of physical exercise in terms of improving the outcome of the people with T2DM (Comtec, 2012; Ng et al., 2010; Rodrigo et al., 2015). Physical exercise is generally beneficial for preventing cardiovascular disease but there is little known about the impact of physical exercise on the cardiovascular risk factors of people with T2DM. The purpose of this study was to verify the effect of regular physical exercise on insulin sensitivity and the modifiable cardiovascular risk factors of people with T2DM. Moreover, we intend to see if there are any different effects as a result of different regular physical exercises for people with T2DM.

MATERIALS AND METHODS

Design

This study used a systematic review of randomized controlled trials to find out the effect of regular physical training on insulin sensitivity and cardiovascular risk factors in people with type 2 diabetes mellitus. Electronic database searches were performed involving Scopus, Science Direct and ProQuest. The search strategy of this systematic review used the following keywords: regular physical training; insulin resistance; cardiovascular risk factors and type 2 diabetes mellitus. The type of articles examined were randomized controlled trials as a result of screening for articles published in the last 10 years. Non-randomized controlled trials were excluded from the review.

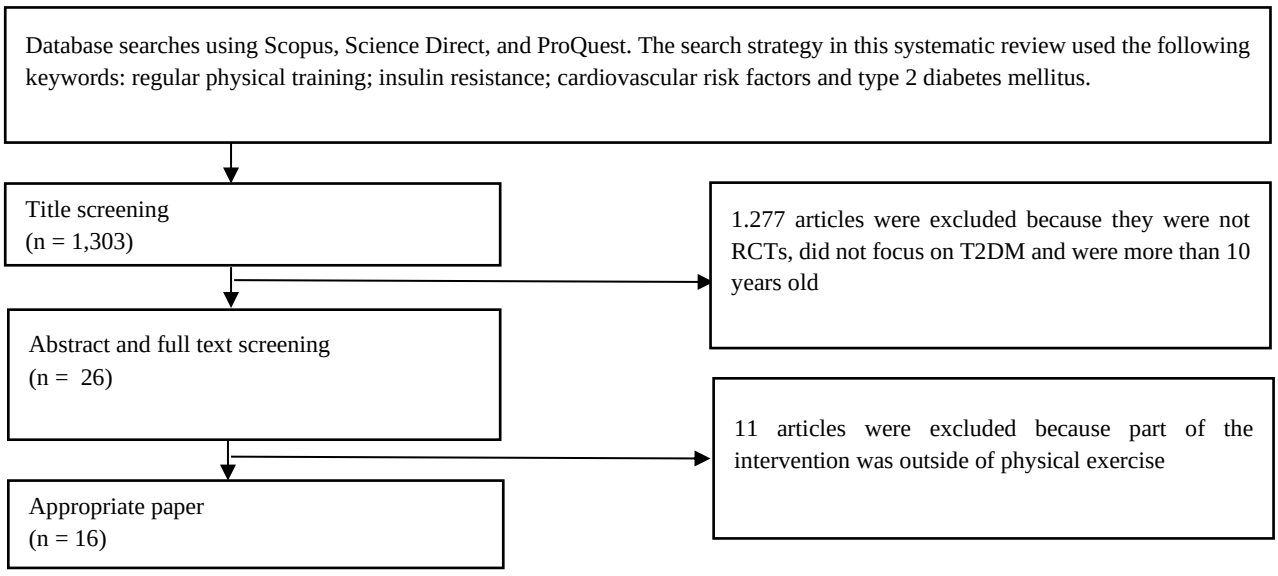

Figure 1 – Flowchart for the search and selection of the studies

Table 1. Characteristics of the studies

Category	n	%
Year of publication		
2010	3	18.75
2011	2	12.5
2012	3	18.75
2014	1	6.25
2015	3	18.75
2017	2	12.5
2019	2	12.5
Type of DM		
T2DM	16	100
Type of study		
RCT	16	100

Inclusion of articles criteria

The inclusion criteria of this systematic review was as follows: 1) patients/people with type 2 diabetes mellitus (T2DM), 2) aged between 18 and 65 years old, 3) only physical exercise or combined more than one type of physical exercise used as the intervention, 4) the reporting of insulin sensitivity as an outcome and 4) the reporting of cardiovascular risk factors as an outcome.

The exclusion criteria were: 1) a sample sizes less than 25, 2) any additional intervention or combined intervention outside of physical exercise, 3) patients with T2DM had complications and 4) women who were pregnant.

The information and the results of the selected articles was organized into a systematic table containing the following information: first author, research design, sample size, the type of physical exercise(s), the outcome of articles that were measured and the results of the studies (Figure 1).

RESULTS

A total of 1,303 articles were found and screened in this study. There were 1,277 articles excluded because they were not a randomized controlled trial, because they did not focus on type 2 diabetes mellitus and because they were more than 10 years old. A total of 26 articles were analyzed according to the abstract and full text. After this, 11 articles were excluded because they did not use physical exercise as an intervention or because there was an additional combined intervention outside of physical exercise. Finally, 16 articles were analyzed and included in this study.

Insulin sensitivity

The study by (Motahari-tabari, Shirvani, & Shirzad-e-ahoodashty, 2015) performed 8 weeks of aerobic exercise focused on insulin resistance in type 2 diabetes mellitus patients. The sample consisted of women aged between 30 and 65 years old divided into 2 groups: 1) the group sample with 8 weeks of aerobic exercise as the intervention and 2) the control group without an intervention. This study showed that 8 weeks of aerobic exercise decreased insulin resistance, fasting blood glucose, and insulin plasma.

The study by (Brinkmann et al., 2019) performed a comparison between exercise in an overnight fasted state and exercise without being n an overnight fasted state over 4 months. The sample was divided into 2 groups: 1) the group sample for exercise in an overnight fasted state and 2) the group ample for exercise without being in an overnight fasted state. The entire sample completed an 8 week combined endurance and strength training program. This study showed that both exercise groups benefited in terms of improved physical fitness, body composition and glycemic regulation (hbA1c values, insulin values, HOMA-IR Index).

The study by (AminiLari et al., 2017) performed a comparison between aerobic exercise and resistance exercise carried out over 12 weeks. The sample was divided into 4 groups: 1) the group sample for aerobic exercise, 2) the group sample for resistance exercise, 3) the group sample for combined aerobic and resistance exercise and 4) the group sample as a control. All of the participants in the exercise groups finished after 12 weeks according to the group division. This study showed that aerobic exercise, resistance exercise and a combination of both were effective at decreasing fasting blood glucose. Moreover, aerobic exercise and combined exercises (aerobic + resistance) were effective at decreasing insulin resistance. Furthermore, combined exercise (aerobic + resistance) was effective at increasing the omentin-1 level.

The study by (Karstoft et al., 2014) performed a comparison between interval walking training and continuous walking training and how it relates to glycemic control and insulin sensitivity. The sample was divided into 3 groups: 1) the group sample for interval walking training, 2) the group sample for continuous walking training and 3) the group sample for the control without an intervention. All of the participants finished the exercises after 4 months according to the group division. In this study, only interval walking training had an effect in terms of improving glycemic control and increasing the insulin disposition.

The study by (El-kader, 2011) performed a comparison between aerobic and resistance training and how it relates to insulin resistance, adipocytokines and inflammatory cytokines level.

The sample was divided into 2 groups: 1) the group sample for aerobic training and 2) the group sample for resistance training. All of the participants finished training after 3 months. This study showed that the aerobics group and resistance group had similar benefits in terms of reducing the insulin resistance, hbA1c, TNF-α and IL-6. The group for aerobic training had a greater impact on insulin resistance than the group for resistance training.

The study by (Luiza et al., 2011) performed a comparison between aerobics, resistance and a combination of both (aerobic + resistance) exercises on metabolic control, inflammatory markers, adipocytokines and muscle insulin signaling. The samples were divided into 4 groups: 1) the group sample for aerobics, 2) the group sample for resistance training, 3) the group sample for combined exercise (aerobic + resistance) and 4) the group sample as the control group. All of the participants finished the exercises after 12 weeks according to the group division. This study was showed that the 4 groups were effective at decreasing fasting blood glucose, postprandial blood glucose, blood pressure, lipid profile, and the high sensitivity of the C-reactive protein. Furthermore, the group for resistance exercise and the group for combined exercises showed an increase in the insulin receptor substrate (IRS)-1.

The study by (Stefano et al., 2010) performed an examination of intensive exercise (aerobic + resistance) and its impact on the modifiable cardiovascular risk factors. The sample was divided into 2 groups: 1) the group sample for intensive exercise and 2) the group sample as a control. All of the participants in the exercise group carried out the program for 12 months. This study showed that intensive exercise (aerobic + resistance) benefited the patient by decreasing insulin resistance and hbA1c.

Modifiable cardiovascular risk factors

The study by (Stefano et al., 2010) performed an examination of the impact of intensive exercise (aerobic + resistance) on the modifiable cardiovascular risk factors. The sample was divided into 2 groups: 1) the group sample for intensive exercise and 2) the group sample as a control. All of the participants in the exercise group carried out the exercise for 12 months. In this study, intensive exercise (aerobic + resistance) improved physical fitness, blood pressure, LDL, cholesterol and body mass index.

The study by (Comtec, 2012) performed a comparison between interval walking training and continuous walking training and how it impacts on glycemic control, body composition and physical fitness. The sample was divided into 3 groups: 1) the group sample for interval walking training, 2) the group sample for continuous walking and 3) the group sample as a control. All of the participants in the 2 intervention groups carried out the stated exercise for 4 months. In this study, the group for interval walking training showed a decrease in body mass index, body mass fat, visceral fat and blood glucose level.

The study by (Bacchi et al., 2012) performed a comparison between aerobic exercise and resistance exercise and how it impacts metabolic effect, the V02 peak and fat. The sample was divided into 2 groups: 1) the group sample for aerobics and 2) the group sample for resistance exercise. All of the participants had finished each exercise according to the group division after 4 months. This study showed that the group for aerobic exercise and the group for resistance exercise both showed a decrease in total fat, visceral fat, subcutaneous fat, hbA1c and an increased consumption rate 02 (V02 peak). The group sample for resistance exercise showed greater benefits than aerobic exercise.

The study by (Magalhães et al., 2019) performed a comparison between (continuous + resistance training) and (interval + resistance training) and how it impacts on vascular health. The samples were divided into 3 groups: 1) group sample for combined exercise (continuous + resistance training) and 2) group sample for combined exercise (interval + resistance training). All of the participants finished according to the group division after 12 months. In this study, (continuous + resistance training) and (interval + resistance training) both decreased the carotid intime media thickness.

The study by (Cassidy et al., 2015) performed a high intensity intermittent exercise in order to determine its effect on cardiac structure, function and liver fat. The sample was divided into 2 groups: 1) the group sample for high intensity intermittent exercise and 2) the group sample for the control. All of the participants finished according to the group division after 12 weeks. This study showed that high intensity intermittent exercise improved the cardiac structure (mass left ventricle wall), systolic function, early refill rate diastolic and decreased the fat in the liver and hbA1c.

The study by (Rahbar, Naimi, Rezasoltani, & Rahimi, 2017) performed for 8 weeks examined aerobic exercise and its relation to vascular structure. The sample was divided into 2 groups: 1) group sample of 8 weeks of aerobic exercise and 2) the group sample as a control. The participants finished according to the group division after 8 weeks. In this study, it showed that aerobic exercise indicated a decrease in carotid intima media thickness, a decrease in the intima-media/lumen thickness of the carotid bulb in addition to a decrease in the thickness of the common carotid, internal carotid and bulb wall.

The study by (Ng et al., 2010) performed a comparison between progressive resistance training and aerobic training on metabolic profile and fitness. The sample was divided into 2 groups: 1) the group sample doing progressive resistance training and 2) the group sample doing aerobic training. All of the participants finished each set of exercises according to the group division after 8 weeks. In this study, both

exercises showed an improvement in hbA1c and peak oxygen consumption. The group for aerobic exercise showed a greater improvement in peak oxygen consumption. Moreover, only in the group for progressive resistance exercise was there a decrease in waist circumference.

The study by (Randomized & Trial, 2012) examined moderate walking exercise related to the soluble receptors of advanced glycation products and cardiometabolic risk factors. The samples were divided into 2 groups: 1) group sample for moderate walking exercise and 2) group sample as a control. All of the participants in the group for moderate aerobic exercise finished exercising after 12 weeks. In this study, the results showed that moderate walking exercises decrease body weight, waist circumference, hbA1c, apolyprotein B, body fat, visceral fat, free fatty acid level and high sensitivity c-reactive protein. Moreover, moderate walking exercise increased the number of soluble receptors of advanced glycation product.

The study by (Rodrigo et al., 2015) performed a comparison between aquatic aerobic training and dry land aerobic training by examining glucose control, cholesterol, blood pressure and c-reactive protein. The samples were divided into 2 groups: 1) the group sample for aquatic aerobic training and 2) the group sample for dry land aerobic training. All of the participants had finished each exercise according to the group division after 12 weeks. In this study, it was shown that both exercises showed a decrease in hbA1c, total cholesterol, high density lipoprotein (HDL), plasma renin activity, the concentration of angiotensin II, c-reactive protein and systolic blood pressure.

The study by (Okada et al., n.d.) performed combined exercises (aerobic and resistance) and focused on endothelial function and the incidence of cardiovascular disease. The samples were divided into 2 groups: 1) combined exercise and 2) a control without an intervention. All of the participants in the group sample for combined exercise did so for 3 months. In this study, the results showed that combined exercise has shown to improve endothelial function by increasing the flow-mediated endothelium dependent vasodilation. All of the participants were followed for 24 months after randomization. In the control group, there were 3 patients who had developed a cerebral infarction and 1 developed angina pectoris.

DISCUSSION

The most common exercise used as an intervention in this systematic review was aerobic exercise with differences in terms of frequency, duration and intensity. There were 11 articles that used aerobics as the main intervention in at least in 1 group while 3 articles used aerobics as a combined exercise.

Motahari et al's (Motahari-tabari et al., 2015) study demonstrated that 8 weeks of aerobic exercise lasting for 50 minutes 3 times a week was able to decrease insulin resistance, fasting blood glucose and plasma insulin in patients with T2DM. In another randomized controlled trial (Luiza et al., 2011), 12 weeks of aerobic exercise lasting for 60 minutes 3 times a week was able to decrease the fasting blood glucose. Furthermore, combined exercise (aerobic and resistance) benefited insulin sensitivity by increasing the insulin receptor substrate (IR) -1. Another study that was a randomized controlled trial (El-kader, 2011) referred to 12 weeks of aerobic exercise lasting for 40 minutes for 3 times a week. It was able to decrease the insulin resistance and hbA1c. Another study that was a randomized control trial (Karstoft et al., 2014) showed that 4 months of interval walking training lasting 60 minutes 5 times a week was able to improve insulin sensitivity and glycemic control. The results in this systematic review are similar to those of the previous studies (Way, Hackett, Baker, & Johnson, 2016) which show that regular exercise can be used as a non-pharmacological treatment for improving the insulin sensitivity of patients with T2DM. Based on the explanation above, it shows that most of the results of the studies showed that aerobic exercise can be used as a physical exercise to improve the insulin sensitivity of patients with T2DM. Only 1 article used interval walking training as a physical intervention for improving insulin sensitivity.

Balducci et al's (Stefano et al., 2010) study demonstrated that 12 months of combined exercise (aerobic and resistance) for 150 minutes a week across 2 supervised sessions was able to improve the physical fitness, blood pressure, low density lipoprotein (LDL), waist circumference, cholesterol and body mass index (BMI) of the patients with T2DM. Another study that consisted of a randomized controlled trial (Randomized & Trial, 2012) of 12 weeks of moderate aerobic exercise lasting for 60 minutes for 5 times a week was able to decrease body weight, waist circumference, hbA1c, apolyprotein B, body fat, visceral fat, the free fatty acid level and high sensitivity c-reactive protein. Another study that was a randomized controlled trial (Rodrigo et al., 2015) showed that 12 weeks of aquatic aerobic and dry land aerobic exercise lasting for 45 minutes for each exercises 3 times a week was able to decrease hbA1c, total cholesterol, high density lipoprotein (HDL), plasma renin activity, the concentration of angiotensin II, c-reactive protein and systolic blood pressure. Another study (Magalhães et al., 2019) examined the results of 1 year of different combined exercise (continuous + resistance training and interval + resistance training) with a duration according to the results of the calculated weekly target of 10 kcal. This considered the peak individual oxygen uptake 3 times a week. This study showed that in the groups for the combined exercises (continuous + resistance training and interval + resistance training), each one decreased the carotid intime media thickness. Another study (Cassidy et al., 2015) involved 12 weeks of high intensity intermittent exercise consisting of 36 circular ergometry sessions

for 3 sessions a week. This study showed that high intensity intermittent exercise resulted n an improvement in the cardiac structure (mass left ventricle wall), systolic function, increased the early refill rate diastolic, decreased the fatty liver and hbA1c. Another study (Rahbar et al., 2017) focused on 8 weeks of aerobic exercise on a treadmill lasting for 30 minutes per session over 3 sessions a week. The study found that it is able to decrease carotid intima media thickness, the intima-media/lumen thickness of the carotid bulb in addition to the thickness of the common carotid, internal carotid and bulb wall. The article results in the systematic review were similar to those in the previous studies (Jansen, Hoorweg, Hoeks, & Den, n.d.). This showed that physical exercise can be used as a non-pharmacological treatment for improving the modifiable cardiovascular risk factors, specifically blood pressure and cholesterol level. Based on the explanation above, several types of physical exercise such as aerobic, resistance and high intensity intermittent exercise can be used to improve the modifiable cardiovascular risk factors. Physical exercise can be used in the form of a single exercise or combined exercise to assist in the prevention of cardiovascular risk in patients with T2DM.

CONCLUSION

The systematic review conducted by the researchers examined 15 articles that were selected based on the inclusion criteria in this study. The findings showed that physical exercise in a single exercise or combined format can be used as a non-pharmacological treatment for improving the insulin sensitivity of patients with T2DM. The most common exercise in this systematic review was aerobic exercise. Furthermore, physical exercise such as aerobic exercise or combined exercise (aerobic and resistance) can be recommended for use in physical exercise programs. Based on the review, there are benefits in the form of improving insulin sensitivity and the modifiable cardiovascular risk factors among the patients with T2DM. It can be in the form of a non-pharmacological intervention for preventing cardiovascular disease as a possible complication of T2DM. Further studies need to be carried out regarding the influence of aerobic physical exercise concerning insulin sensitivity and the cardiovascular risk factors of patient with T2DM.

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APPENDIX

Table 2. Summary of the intervention programs and results

Type of exercises	Frequency	Duration	Result
Aerobic (Motahari-tabari et al., 2015)	3 times/week for 50 mins	8 weeks	Aerobic exercise has been shown to be effective at decreasing plasma glucose (p = 0.05) and insulin resistance (p = 0.02).
Combined of endurance and strength exercises (Brinkmann et al., 2019)	3 times a week on non-consecutive days between 7am and 10am	8 weeks	Combined exercise program in the group in a fasted state (12 hours fasted before exercise) and the group in a fed state (eat breakfast at 1-2 hours before exercise) have been effective at improving physical exhaustion (p<0.001), hbA1c (p=0.001), insulin resistance (p=0.029), fat free mass (p=0.015) and serum triglycerides (p=0.024).
Aerobic, resistance and combined of both exercises (AminiLari et al., 2017)	3 times a week for each exercise	12 weeks for each exercise	Both exercises are effective at decreasing the fasting blood glucose. Insulin resistance showed a decrease in the group for aerobics (p=0.004) and in the group for combined exercise (p=0.005). Furthermore, the group for combined exercise (aerobic + resistance) was effective at increasing the omentin-1 level (p=0.001).
Interval walking training (IWT), contionus walking training (CWT) (Karstoft et al., 2014)	5 times a week for 60 minutes for each exercise	4 months	Interval walking training (IWT) has been effective at improving glycemic control, insulin sensitivity index (p<0.001), peripheral glucose disposal (p<0.005), disposition index (p<0.001) and insulin signaling in skeletal muscle (p<0.05).
Aerobic exercise, resistance exercise (El-kader, 2011)	3 times a week for 40 minutes for each exercise	3 months	Both exercises were effective at decreasing insulin resistance (p=0.005 in aerobic) (p=0.037 in resistance), hbA1c (p=0.008 in aerobic) (p=0.045 in resistance), TNF-α (p= 0.009 in aerobic) (p=0.016 in resistance) and IL-6 (p=0.007 in aerobic) (p=0.023 in resistance). There was a significant difference between aerobic and resistance exercise. Aerobic exercise is more appropriate for modulating insulin resistance and inflammatory cytokine levels than resistance exercise.
Aerobic, resistance and combined exercises (aerobic + resistance) (Luiza et al., 2011)	3 times a week for 60 minutes for each exercise	12 weeks	Both exercises were effective at decreasing the fasting blood glucose (p<0.05 in all group exercises), postpandrial blood glucose (p<0.05 in all group exercises), blood pressure (p<0.05 in all group exercises) and lipid profile (p<0.05 in all group exercises). The groups for resistance exercise and combined exercise (aerobic + resistance) were effective at increasing the insulin receptor substrate (IRS)-1.
Intensive exercise (aerobic + resistance) (Stefano et al., 2010)	2 times a week for 75 minutes	12 months	Intensive exercise (aerobic + resistance) was effective at improving insulin resistance (p<0.001), physical fitness (p<0.001), hbA1c (p<0.001), blood pressure (p<0.001), LDL (p<0.001), waist circumference (p<0.001), cholesterol (p<0.001) and body mass index (p<0.001).
Interval walking training, continuous walking training (Comtec, 2012)	5 times a week for 60 minutes	4 months	Interval walking continuous was effective at decreasing fat body mass (p<0.001), visceral fat (p<0.001), blood glucose level (p<0.001) and increasing the V02 max (p<0.001).
Aerobic exercise, resistance exercise (Reid et al., 2010)	3 times a week for 60 minutes for each exercise	4 months	Both exercises were effective at decreasing hbA1c (p<0.0001), total fat (p<0.0001), visceral fat (p<0.0001) and subcutaneous fat (p=0.001). It also increased the V02 peak ($0.001 \leq p < 0.01$ in group aerobic) ($p \leq 0.001$ in group resistance). The group of resistance exercise was more effective at increasing the V02 peak than the aerobics group.
Combined exercises (moderate continuous training + resistance training), combined	3 times a week	1 year	Both groups of combined exercise were effective at decreasing the carotid intima media thickness (p< 0.01)

Type of exercises	Frequency	Duration	Result
exercises (high intensity + resistance training) (Magalhães et al., 2019)			
High intensity intermittent training (Cassidy et al., 2015)	3 times a week	12 weeks	High intensity intermittent training was effective at improving the left ventricle wall mass (p=0.03), systolic function (p<0.05) and early diastolic filling rate (p=0.02).
Aerobic exercise (Ng et al., 2010)	3 times a week for 30 minutes	8 weeks	Aerobic exercise was effective at improving the carotid intima media thickness, the intima-media/lumen in the carotid bulb, the common carotid and internal carotid and decreasing the bulb wall (p<0.05).
Aerobic exercise, progressive resistance exercise (El-kader, 2011)	18 sessions for 50 minutes	8 weeks	Both exercises were effective at decreasing hbA1c and increasing the V02 peak. In the group for progressive resistance training, there was decreased waist circumference.
Moderate walking (Randomized & Trial, 2012)	5 times for 60 minutes	12 weeks	Moderate walking was effective at decreasing body weight (p<0.001), waist circumference (p<0.001), apolipoprotein b (p<0.032), hbA1c (p=0.003), free fatty acid (p<0.001), systolic blood pressure (p=0.006) and diastolic blood pressure (p<0.001) while increasing the soluble receptor for advanced glycation end-products (p=0.003).
Aquatic aerobic training, dry land aerobic training (Okada et al., n.d.)	3 times a week for 45 minutes	12 weeks	Both exercises decreased hbA1c, low density lypoprotein, plasma renin activity, the concentration of angiotensin II and systolic blood pressure (p<0.05).
Combined exercises (aerobic + resistance) (Okada et al., n.d.)	3-5 times a week for 75 minutes	3 months	Combined exercises (aerobic + resistance) improved endothelium dysfunction by increasing the flow-mediated endothelium dependent vasodilation (p<0.005).

Table 3. Summary of the selected studies

Author	Design	Sample	Variable	Results
(Balducci, Stefano, et al, 2010)	RCT	606 respondents with T2DM	Intensive exercise intervention strategy; Modifiable cardiovascular risk factors; insulin resistance	The results of the study showed that intensive exercise with supervision for 12 months was effective at improving physical fitness, hbA1c, systolic and diastolic blood pressure, low density lipoprotein (LDL), waist circumference, cholesterol, body mass index and insulin resistance in patients with T2DM.
(Motahari-Tabari, Narges, et al, 2015)	RCT	54 respondents with T2DM	Aerobic exercise; insulin resistance	The results of the study showed that aerobic exercise for 8 weeks was effective at decreasing the fasting blood glucose, plasma in the insulin and insulin resistance in patients with T2DM.
(Karstoft, Kristian, et al, 2012)	RCT	32 respondents with T2DM	Continuous walking training (CWT); interval walking training (IWT); glycemic control; body composition; physical fitness	The results of the study showed that only the IWT group that carried on for 4 months was effective at increasing the VO2 max and decreasing the body mass, fat

Author	Design	Sample	Variable	Results
				mass, visceral fat and blood glucose level of the patients with T2DM.
(Choi, Mook, Kyung, et al, 2012)	RCT	75 respondents with T2DM	Exercise; soluble receptor of advanced glycation product level; cardiometabolic risk factors	The results of the study showed that moderate walking exercise for 12 weeks was effective at decreasing body mass, waist circumference, hbA1c, apolypoprotein B, body fat, visceral fat, free fatty level and the high sensitivity c-reactive protein level. Furthermore, it can increase the soluble receptor of advanced glycation products.
(Bacchi, Elisabetta, et al, 2012)	RCT	40 respondents with T2DM	Aerobic training; resistance training; metabolic effects	The results of the study showed that regarding aerobic exercise and resistance exercise, each one showed an effective decrease in insulin resistance, hbA1c, total fat, visceral fat and subcutaneous fat. Furthermore, both exercises can increase the peak consumption 02 but in the group for resistance exercise, they benefited greater than the group for aerobic exercise in terms of improving the peak consumption of O2.
(Jorge, Maria, et al, 2011)	RCT	48 respondents with T2DM	Aerobic exercise; resistance exercise; combined exercise (aerobic and resistance); metabolic control; Inflammatory markers; adipocytokines; muscle insulin signaling	The results of the study showed that the entirety of the group exercises (aerobic, resistance, and combined of aerobic and resistance) were carried for 12 weeks. All of the exercises resulted in effective decreases in blood pressure, blood glucose level, lipid profile and high sensitivity c-reactive protein in the patients with T2DM.
(Rodrigo, et al, 2015)	RCT	35 respondents with T2DM	Aquatic aerobic training; dry land aerobic training; glucose control; cholesterol; blood pressure; c-reactive protein	The results of the study showed that both exercises (aquatic aerobic and dry land aerobic training) for 12 weeks showed a decrease in hbA1c, total cholesterol, high density lipoprotein

Author	Design	Sample	Variable	Results
				(HDL), plasma renin activity, concentration of angiotensin II, c-reactive protein and systolic blood pressure.
(Brinkmann, Christian, et al, 2019)	RCT	30 respondents with T2DM	Exercise in a fasted state, exercise in a fed state; health of T2DM patients	The results of the study showed that both exercise groups (exercise in a fasted state and exercise in a fed state) for 8 weeks benefited in terms of improved physical fitness, better body composition and improved glycemic regulation (hbA1c values, insulin values, HOMA-IR Index).
Magalhaes, Joao, et al, 2019)	RCT	80 respondents with T2DM	Combined training at different intensities; vascular health	The results of the study showed that in the group of combined exercises (continuous + resistance training) and the group of combined exercises (interval + resistance training) for 12 months, each one showed decreased carotid intime media thickness
(Aminilari, Zeinab, et al, 2017)	RCT	60 respondents with T2DM	Aerobic exercise; resistance exercise; combined exercises; omentin-1 levels; insulin resistance	The results of the study showed that aerobic exercise, resistance exercise and a combination of both carried out for 12 weeks was effective at decreasing the fasting blood glucose. Moreover, aerobic exercise and combined exercise (aerobic + resistance) were effective at decreasing insulin resistance. Furthermore, combined exercise (aerobic + resistance) was effective at increasing the omentin-1 level.
(Cassidy, Sophie, et al, 2015)	RCT	28 respondents with T2DM	High intensity-intermittent training; cardiac structure and function; liver fat	The results of the study showed that high intensity intermittent exercise for 12 weeks was shown to improve cardiac structure (mass left ventricle wall), systolic function, increase the early refill rate diastolic and decreased liver fat and hbA1c

Author	Design	Sample	Variable	Results
(Karstoft, Kristian, et al, 2014)	RCT	32 respondents with T2DM	Interval walking training (IWT); continuous walking training; glycemic control	The results of the study showed that only interval walking training for 4 months had an effect in terms of improving glycemic control and increasing insulin disposition.
(Rahbar, Soulmaz, et al, 2017)	RCT	28 respondents with T2DM	Aerobic physical exercise; vascular structure	The results of the study showed that aerobic exercise for 8 weeks resulted in a decrease in the carotid intima media thickness, a decrease in the intima-media/lumen in the carotid bulb and common carotid and a decrease in the internal carotid and bulb wall.
(Shehab, et al, 2011)	RCT	40 respondents with T2DM	Aerobic exercise training, resistance exercise training; insulin resistance; adipocytikens; inflammatory cytokine levels	The results of the study showed that the group of aerobics and the group of resistance training for 3 months had similarly benefited from reduced insulin resistance, hbA1c, TNF-α and IL-6. In the group of aerobic training, there was a greater impact on insulin resistance than in the group of resistance training.
(Cindy, et al, 2010)	RCT	60 respondents with T2DM	Aerobic exercise; progressive resistance exercise; metabolic profile	The results of the study showed that both exercises for 8 weeks improved hbA1c and peak oxygen consumption. In the group that did aerobic exercise, there was a greater improvement in the peak oxygen consumption than in the group of progressive resistance exercise. Moreover, only in the group of progressive resistance exercise was there a decrease in waist circumference.
(Okaada, et al, 2010)	RCT	38 respondents with T2DM	Exercise intervention; endothelial function; incident of cardiovascular disease	In this study, the results show that combined exercises result in improved endothelial function by increasing the flow-

Author	Design	Sample	Variable	Results
				mediated endothelium dependent vasodilation. All of the participants were followed for 24 months after randomization. In the control group, 3 patients developed a cerebral infarction and 1 other developed angina pectoris.

T2DM: Type 2 Diabetes Mellitus; LDL: Low density lipoprotein; RCT: Randomized controlled trial.