Arab American University

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The short-term effect of Blood Flow Restriction walk training on insulin resistance and aerobic capacity on people with type2 diabetes mellitus – randomized feasibility trial

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This thesis was submitted in partial fulfillment of the requirements for the Master`s degree in

Physiotherapy

Oct / 2023

Thesis Approval

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Declaration

I declare that the contents of the thesis are the result of my own effort and this thesis as a whole, or part of it, has not previously been submitted for a degree or research at any other educational or research institution.

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Acknowledgement

This endeavor would not have been possible without Allah, I would thank GAD for letting me through all the difficulties.

I am deeply indebted to my supervisor Dr. Motaz Alawnah for his invaluable patience and feedback. I could not have completed this journey without my defense committee, who generously shared their knowledge and expertise.

I am also grateful to my classmates and cohort members, especially my office mates, for their editing help, late night feedback sessions and moral support. I would also like to thank the research assistants and study participants at the university who have influenced and inspired me.

I would be remiss not to mention my family, especially my parents and brothers. Their belief in me has kept my spirits up and motivation high throughout this process. I would also like to thank my colleagues for all the entertainment and emotional support.

Finally, I would like to thank my patients for giving me the time and confidence to assess and treat them.

I would also like to thank everyone who has supported me in this important and exciting phase of my professional life.

Abstract

Background: Exercise intervention combined with blood-flow restriction (BFR) is comprehended to induce significant health improvement with less effort and time than the traditional exercises, this method of training is increasingly used with both healthy and unhealthy individuals . Insulin resistance which called pre diabetes condition, is a pathogenic driver of many modern diseases such as T2DM which are in origin due to the sedentary lifestyle. It is well known now that 75 - 150 minutes per week of moderate to high intensity exercise therapy is a major and safe component of the management program for type 2 diabetes. Exercising with moderate to high intensity 2 - 4 times/week could be a big challenge for diabetes population, health and time wise. Performing a low intensity BFR exercises can produce the same result as moderate - high intensity exercises among both healthy and unhealthy individuals. BFRT have been investigated among several cases, and showed a safe, interested and positive results. But to our knowledge, it is still not clearly evident with type 2 diabetes.

Objectives: This study aims to investigate the acceptability and feasibility of BFR walk training intervention to adult with T2D. And to study the effects of walk training with BFR on aerobic capacity and insulin sensitivity on people with type 2 diabetes.

Design: This study is a randomized feasibility study for a larger randomized controlled trial

Methods: A total of 30 male participants, aged 40-65 years, took part in this trial. Participants were randomized to one of two groups; the first group received BFRT with aerobic exercise, and the second one received aerobic exercise alone. The intervention

programme consisted of 2 sessions per week for a period of 4 weeks. The outcomes measures were aerobic capacity by VO2Max, 6-minute walk test (6MWT), insulin resistance by HOMA score and physical function SF-36 scale. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 21, with statistical significance set at $P < 0.05$.

Results: Significant improvements between baseline and discharge scores were seen in both groups. However, there was a significant improvement in insulin resistance and aerobic capacity in favor of the BFRT group ($P>0.05$).

Conclusion: This study shows that AE with BFRT was more effective in the management of IR and AC than AE alone in individuals with T2D.

Keywords: blood flow restriction training, aerobic exercise, aerobic capacity, insulin resistance, type two diabetes.

Table of Contents

List of Tables

List of Figures

List of Appendices

List of Abbreviations

- BFRT: blood flow restriction training
- AC: aerobic capacity
- AE: aerobic exercise
- IR: insulin resistance
- CVD: cardiovascular disease
- LOP: limb occlusion pressure
- DM: diabetes mellitus
- T2D: type two diabetes
- T1D: type one diabetes
- HT: hyper tension
- AOP : arterial occlusion pressure
- IFG: impaired fasting glucose
- IGT: impaired glucose tolerance
- Hb A1C: glycated hemoglobin test
- BMI: body mass index
- 6MWT: 6 minute walk test
- GLUT4: glucose transporter type 4
- HGP: hepatic glucose production

- NHGO : net hepatic glucose output
- OGTT: oral glucose tolerance test
- WHO: world health organization
- ADA: American Diabetes Association

Chapter One

1.1 Introduction

1.2 Scope

1.3 Problem statement

1.4 Study Objectives

1.5 Research Questions

1.6 Study Hypothesis

1.1 Introduction

Diabetes mellitus (DM) all around the world, is a chronic condition impacting lives and well- being at personal, family and society levels(Saeedi et al., 2019). The global diabetes prevalence in 2019, 2021 was estimated to be 9.3% and 10.5% respectively, and suspected to rise to 12.2% by the year of 2045(Saeedi et al., 2019)(Sun et al., 2022). This rapidly growing condition poses a great financial load on the healthcare system as well as on individuals and the community especially in low and lower-middle income countries with health expenditures expected to hit $490 billion in 2030 globally due to DM (Afroz et al., 2018). So, effective management is an urgent need(Lovic et al., 2020).

WHO define diabetes mellitus as " a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which can leads over time to serious damage to several body systems like, heart, blood vessels, eyes, kidneys and nerves."(*Diabetes*, n.d.). According to American Diabetes Association (ADA), any adult above 45years old or at any age with one or more risk factors(overweight or obese) are at high risk to develop the disease and should perform the screening tests for diabetes(Association, 2013a).

This asymptomatic period of high-risk obese, overweight and adults above 45 years old is called pre diabetes stage and can be detected by elevated measures of a diagnostic and screening tests (presence of IFG (FPG levels from 100 to 125 mg/dL)and/or IGT (2-h PG levels during 75-g OGTT from 140 to 199 mg/dL)and/or A1C 5.7–6.4% (39–47 mmol/mol)and with certain levels of these test will considering as a diagnostic criteria for T2D(Association, 2013b). According to The American Diabetes Association (ADA) annually up to date recommendations, diagnosis of diabetes is based on A1C criteria ≥6.5%

(48 mmol/mol) or plasma glucose criteria using fasting plasma glucose (FPG) value ≥126 mg/dL (7.0 mmol/L) or the 2-h plasma glucose (2-h PG) value ≥200 mg/dL (11.1 mmol/L)during a 75-g oral glucose tolerance test (OGTT)(Committee, 2022).

In normal individual, after an overnight fasted state the insulin secretion is diminished while glucagon hormone is released from alpha-cells in the pancreas to act in the liver as a response of low level of plasma glucose(Vega et al., 2021). This hormone act as the first line of defense against hypoglycemia due to food deprivation or exercise and provides the basal lead to glucose production by the liver that let insulin adjustment to hepatic glucose production according to the body's needs(Ramnanan et al., 2011)(Lin & Accili, 2011). The glucose enter the blood circulation at a mean rate of 220 g day after the liver increase glucose production (HGP) to be utilized in the peripheral tissues by glycogenolysis of the glycogen regulatory hormone(Ramnanan et al., 2011)(Lin & Accili, 2011)(*International Textbook of Diabetes Mellitus, 2 Volume Set - كتب Google*, n.d.). During glycogenolysis the net hepatic glucose output (NHGO) will decline rabidly, the HGP will decrease due to increase of the glucose-6-phosphate (G6P) in hepatocytes after glycogen breakdown(Pedersen et al., 2020).

In addition to glycogenolysis , liver(with 80% production) and renal(20% production) gluconeogenesis is also continued with equal contributions from both pathways and the ratio of gluconeogenesis will increase if the fasting state continued(Ferrannini & DeFronzo, 2015). Also decreased in hepatic lipid production while adipose lipolysis increases(Samuel & Shulman, 2012).

On the other hand, in the fed state, food is digested in the gastrointestinal tract and glucose, fatty acids and amino acids are absorbed into the blood and transported through the circulatory system to the liver (Rui, 2014). The plasma glucose increased due to dietary carbohydrate and insulin action or secretion that stimulated from β-cells in the pancreas and act in the liver in a way of increased of glycogen synthesis and inhibited gluconeogenesis, while in skeletal muscles in a way of increased in glucose uptake and glycogen synthesis and in the adipose tissue in a way of increased in lipogenesis and decreased lipolysis(Samuel & Shulman, 2012). This action of insulin is for convert taken carbohydrates and proteins into efficient storage as a lipids in the storage sites of the body(Adeva-Andany et al., 2016).

So, Insulin, is the master glucose regulatory hormone, play an essential role by multiple mechanisms in regulating the hepatic glucose production (HGP)(Lin & Accili, 2011). Insulin bends to its hepatic receptor which result in intracellular signals that inhibit HGP and therefore glycogenolysis rapidly reduced(Titchenell et al., 2017). Insulin also act to HGP reduction indirectly by lipolysis inhibition, suppress glucagon secretion and changing neural input from the brain(Leavens & Birnbaum, 2011).

Glucose uptake is mediated by Tissue-specific glucose transporters (GLUTs), which are types of proteins existing in the plasma and microsomal membranes, acting in either insulin independent tissues which include placenta, intestine, kidney, liver and brain like GLUT1 and GLUT3 or in insulin dependent tissues include adipose tissue , skeletal and cardiac muscle like GLUT4(Ferrannini & DeFronzo, 2015). Which is considers as the predominant glucose transporter in these insulin sensitive tissues(Chadt & Al-Hasani,

2020). Especially in skeletal muscles that consider as a major storage of glucose with approximately 75% disposal of glucose(Minokoshi et al., 2003). And any defect in GLUT4 function in skeletal muscle will led markedly to insulin resistance(Minokoshi et al., 2003).

Normal glucose level is a crucial matter for the whole body to be healthy; So any decrease (hypoglycemia)or increase(hyperglycemia)of plasma glucose levels can lead to impaired brain function and increase the risk of diabetes respectively, this level is maintained by liver, skeletal muscle, adipose tissues and other organs in addition to insulin and glucagon that are hormones that play important role of glucose homeostasis (Sharabi et al., 2015). So, resistance of these insulin-sensitive tissue to insulin combined with islet β-cell dysfunction led to impairment in glucose homeostasis and hyperglycemia then the occurrence of type two diabetes(Kahn et al., 2014).

In type two diabetic individuals, all these processes are impaired, and both insulin and glucagon secretion are affected(Jiang & Zhang, 2003). A study in 2021 on obese people with insulin resistance and beta-cell dysfunction showed that in contrast to normal individuals, in fed state T2D insulin secretion is delayed while the glucagon secretion stay the same or even elevated, this impairment of glucagon/insulin ratio is related with insulin resistance and suggested to be more affected to insulin resistance than with plasma glucose levels (Chen et al., 2021). Compared with normal individuals, in fasting state the liver produce glucose in about 2.5 mg/kg/min instead of 2 mg/kg/min of basal hepatic glucose production, causing elevation in fasting plasma glucose (FPG), while in the fed state about 85% to 90% of insulin resistance are related to impairment in glucose uptake in muscle

tissue, this is also not far away and is affected by an increase of plasma free fatty acid level(Unger & Parkin, 2010).

Mainly, there are two main types of diabetes: type 1, or insulin-dependent diabetes, and juvenile-onset diabetes, which is caused by an absolute lack of insulin secretion and occurs in only 5-10% of all cases of diabetes (Association, 2013a). On the other hand, type 2 diabetes or 'noninsulin-dependent diabetes' or adult-onset diabetes, which is due to resistance to insulin action and impairment in glucose uptake led to metabolism deficits which are present in asymptomatic period before the clear diagnosis of diabetes(Association, 2013a). This form of diabetes accounts for 90%-95% of all forms of adults diabetes, these adults with relative insulin deficiency and peripheral insulin resistance do not have insulin treatment to survive(Association, 2013a). Beside insulin resistance, T2D are also characterized by present of beta cell dysfunction which is considered more severe than insulin resistance(Cerf, 2013).

The third type, Gestational diabetes mellitus (GDM)as a medical complication in pregnancy women, is another type of diabetes and suspected to developed to type two diabetes after pregnancy with percentage of 14% of pregnancies worldwide(Colberg et al., 2010)(Plows et al., 2018). These women are suspected in about sevenfold for developing T2DM in comparing with women without gestational diabetes mellitus(Zheng et al., 2018).

Insulin resistance which called pre diabetes, is a pathogenic driver of many modern diseases such as T2DM which are in origin due to the sedentary lifestyle (S. H. Lee et al., 2022). 90–95% of all diabetes people are T2D which is due to pancreatic beta cell

dysfunction and insulin resistance in target tissue(Yaribeygi et al., 2019). In obese people the function of B-cell increase as a compensatory of decrease in insulin action causing mild increase in concentrations of blood glucose at fasting and 2 h after glucose load that led overtime to B-cell dysfunction(Stumvoll et al., 2005). These normal obese people with relatively normal glucose tolerance will developing impaired glucose tolerance (IGT) due to insulin resistance worsening(Unger & Parkin, 2010). So, the fail of pancreatic B-cell to adapt to insulin action is a main component of pathogenesis of T2D or people with impaired glucose tolerance(Stumvoll et al., 2005). The studies showed that obese people had a 63% deficit in β-cell volume, and B-cell function will decreased up to 80% in people with IGT and a marked loss of its mass in T2D due to cell apoptosis(Unger & Parkin, 2010).

Insulin resistance defined as" the inability of a known quantity of exogenous or endogenous insulin to increase glucose uptake and utilization in an individual as much as it does in a normal population."(Lebovitz, 2001). By impairing the insulin action, glucose uptake by the muscle will reduced, the hepatic glucose production (HGP) will increased and the lipolysis will increased in the adipose tissue(Gastaldelli, 2022).

There are many studies advocate the concept that in people with type 2 diabetes, insulin action defection primarily locates in skeletal muscle(DeFronzo & Tripathy, 2009). So, muscle insulin resistance is one of the major causes of T2D development which may arise before twenty years of the clinical development of the disease(Yaribeygi et al., 2019). Thus, Muscles are essential key elements for glucose homeostasis(Lebovitz, 2001). And therefore, marked reduction of insulin resistance, improved VO2max and other important

related metabolic parameters were approved after a long program of aerobic exercise training with type 2 diabetes(Kadoglou et al., 2007)(N. G. Boulé et al., 2003)(Hawley & Lessard, 2008).

Genetic factors, advancing in age, physical inactivity, obesity and many other factors all are risk factors for developing Cardiovascular Disease and type 2 diabetes which can be present several years before clear diagnosis of diabetes(Nascimento et al., 2022). Obesity itself led to insulin resistance and so called pre- diabetes condition. The strongest risk factor for T2D is being obese and its relation to physical inactivity(Henning, 2018). Noteworthy, there is positive relationship between obese people, physical inactivity and to have diabetes(Kahn et al., 2014).

Active lifestyle and regular exercise showed marked improvement in cardiorespiratory fitness especially people with diabetes who are more likely to suffer from cardiovascular disease in about 2 to 4 times than healthy people, which is a strong predictor of mortality within this group(Kirwan et al., 2017)(Tipton, 2014). These exercise programs have been adopted by different international organizations(Pan et al., 2018). So, beside the medications, It is well known now that 75 - 150 minutes per week of moderate to high intensity exercise therapy is a major and safe component of the management program for type 2 diabetes(Zanuso et al., 2010). To decrease disease complications, decreasing insulin resistance, enhancing glycemic control and to improve their aerobic capacity(Sampath Kumar et al., 2019).

A Systematic Review with Meta-analysis by Jadhav RA et al in 2017 studied physical activity intervention in individuals with pre diabetes showed positive effects on maximum oxygen uptake (VO2max) and body composition(Jadhav et al., 2017). According to J. Kirwan in his review reported that regardless to the type of exercise, but with sufficient intensity, it plays a central role in prevention and management of T2D(Kirwan et al., 2017).

Besides that, The American College of Sports Medicine has stated that "Physical activity, including appropriate endurance and resistance training, is a major therapeutic modality for T2D". The American Diabetes Association Clinical Practice Recommendations declare that "the possible benefits of exercise in T2D are substantial". So, It is well known now that exercise therapy is a major part of management for people with type 2 diabetes(Zanuso et al., 2010).

However, exercising with moderate to high intensity 2 - 4 times/week could be a big challenge for diabetes population, health and time wise, and because they may have aerobic exercise capacity limitations and other disease related manifestations(Patterson et al., 2017)(Gulsin et al., 2020). So, many barriers facing patients with DM and health care providers in adherence to exercise program(Jenkins & Jenks, 2017). Including lack of time, functional limitations and exercise physical demand to reach an effective exercise intensity and duration (Lidegaard et al., 2016).

As a good and safe alternative method, blood flow restriction(BFR) training came to light(Nascimento et al., 2022). Applied by using partial vascular occlusion devise with low

intensity exercise mood(J. P. Loenneke et al., 2012). The past researches about this technique showed results similar to high intensity exercise without BFR in different healthy and non-healthy people on a wide range of outcomes(Centner et al., 2019)So, the diabetes patients do not have to work extensively to meet exercise goals. And applying this technique will help patients in the first line and medical services secondly in providing a safe, time consuming, affordable, and effective tool that can help in the management of T2D disease.

The type of exercise, resistance or aerobic or combination of them, to be effective, it must be with a moderate to high-intensity(Zanuso et al., 2010)(Garber et al., 2011). Traditionally, to improve muscle mass and strength, high intensity resistance training using loads of ~70-85% of a one-repetition max (1-RM) is most often indicated (Miller et al., 2021). And moderate (40–60% of Vo2max) to vigorous(>60% of Vo2max) aerobic training(Sigal et al., 2006b).

This may be unattainable or not suitable for all patients, Particularly for people with musculoskeletal (MSK) impairments who cannot tolerate high levels of resistance due to the stress on joints, soft tissues and surgical sites (Patterson et al., 2017)(Vopat et al., 2020). BFRT using low intensity exercise training [i.e. 20% of 1 repetition maximum (1RM) dynamic strength] has been shown to increase muscle size and strength comparable to conventional high intensity exercise training (i.e., 80 % 1-RM)(Lixandrão et al., 2015).

Blood Flow Restriction Therapy (BFRT), originally developed in Japan in the late 1970s, where it was known as KAATSU training, an innovative technique for developing muscle

strength, function, hypertrophy and body mass in the athletic and clinical settings (Vopat et al., 2020). By using inflatable cuffs to create vascular occlusion, alter local interstitial pressure and trap exercise-induced metabolites within the exercised limb (Baker et al., 2020).

A study recently reported that the addition of BFR to training contributes to neuromuscular adaptations, changes in deoxyhaemoglobin concentration (i.e. metabolic stress) and increases in muscle cross-sectional area when resistance training is performed at low intensity only(Biazon et al., 2019). Another study reports that Light resistance exercise combined with occlusion stimulates growth hormone secretion through regional accumulation of metabolites without significant tissue damage(Takarada et al., 2000). Favorable hemodynamic and hemostatic responses in patients with Coronary Artery Disease have been reported using safe the BFR(Kambič et al., 2021).

In addition, BFR combined with resistance exercise has been shown to stimulate muscle protein synthesis, creating a metabolic "overload" normally associated with the higher muscle activations observed during high-intensity resistance exercise, and may be partly related to the concomitant decrease in mRNA gene expression of MURF-1, atrogin and myostatin (Jeremy P. Loenneke et al., 2012). The physiological mechanisms behind these muscle adaptations include acute muscle cell swelling, increased fibre type recruitment, decreased myostatin, decreased atrogens and satellite cell proliferation, which can be induced by low-load BFRT and may provide an additional stimulus for muscle adaptation that conventional RT does not, and which is seen in both younger and older adults(Minniti et al., 2020).

And so, because BFR combined with low-intensity aerobic exercise can safely and significantly improve functional capacity, it may be an effective intervention for patients who are unable to perform traditional exercise training (Miller et al., 2021).

1.2 Scope

Whilst the exercise intervention with type two diabetes have been well approved, the BFRT impact on insulin resistance and aerobic capacity of older adults (40-60 years) is poorly understood**.** The aim of this study is to report on aerobic capacity and insulin sensitivity changes in the population group. In addition to the physical functional improvement.

The scope of the study is limited to the recruitment of 30 volunteers between the ages of 40 and 65 who have been contacted through their phone numbers and social networks. This recruitment period will last a maximum of 4 months and will end when either 30 volunteers have been recruited or 4 months have passed. Each volunteer in the study will be asked to complete a short questionnaire to assess any changes in their status.

1.3 Problem Statement

Active lifestyle and regular exercise showed marked improvement in cardiorespiratory fitness especially people with diabetes who are more likely to suffer from cardiovascular disease in about 2 to 4 times than healthy people, which is a strong predictor of mortality within this group(Kirwan et al., 2017)(Tipton, 2014). The past literature showed that 75 - 150 minutes per week of moderate to high intensity exercise therapy is a major and safe component of the management program for type 2 diabetes (Zanuso et al., 2010, Zanuso et

al., 2010). Exercising with moderate to high intensity 2 - 4 times/week could be a big challenge for diabetes population, health and time wise.(Patterson et al., 2017).

Performing a low intensity BFR exercises can produce the same result as moderate - high intensity exercises among both healthy and unhealthy individuals. BFRT have been investigated among several cases, and showed a safe, interested and positive results(Miller et al., 2021)(Centner et al., 2019)(Hughes et al., 2017). But to our knowledge, it is still not clearly evident with type 2 diabetes(Da Cunha Nascimento et al., 2019). Blood flow restriction training may critically solving these problems and be an excellent alternative choice to be applied in the clinical field with less effort and less time.

This novel study findings will further reveal how aerobic capacity and insulin sensitivity can be enhanced while applying BFR walk training for people with type2 diabetes. So the findings would be of major importance in improving performance in their daily life. BFR walk training would have a preventable and treatable role.

1.4 Study Objectives

The aim of this feasibility study was to explore trial design, staff and resident acceptance of the intervention and outcome measurements, and to provide data to estimate the parameters required to design a final RCT.

The primary objectives of the study were as follows:

1. To determine whether the eligibility criteria for the intervention were too open or too restrictive, by estimating feasible eligibility and recruitment rates.

2. To investigate the acceptability of a BFR walking training intervention for adults with T2D in terms of compliance and adherence to the intervention schedule.

3. To assess the acceptability and feasibility of the outcome measures as methods for measuring the effectiveness of the intervention in a definitive trial.

4. To collect and synthesise data from which the sample size of a definitive cluster RCT (CRCT) could be estimated.

The secondary objectives of the trial were as follows:

1. The trial aims to establish appropriate procedures for delivering the intervention and conducting assessments, as well as procedures to ensure recruitment and retention in the trial.

2. To measure key outcome domains including the effects of walk training with BFR on aerobic capacity, insulin sensitivity,6minute walk test and physical function on people with type 2 diabetes.

3. To determine any side effects could be elected in using BFR for people with type 2 diabetes.

1.5 Research Questions

1-Does BFRT impact on aerobic capacity, insulin sensitivity, 6minute walk test and physical function in individuals with T2D?

2- Does BFRT raise additional safety concerns specifically for people with T2D?

1.6 Research Hypotheses

1. There is a positive effect of aerobic exercise with BFRT on aerobic capacity in people with type two diabetes.

2. There is a positive effect of aerobic exercise with BFRT on insulin resistance in people with type two diabetes.

3. There is a positive effect of aerobic exercise with BFRT on 6minute walk test in people with type two diabetes.

4. There is a positive effect of aerobic exercise with BFRT on physical function in people with type two diabetes.

Chapter Two

2.1 Theoretical studies

2.2 Similar Studies

2.3 Summary

2.1 Theoretical Studies

2.1.1 Type Two Diabetes : Risk factors and pathophysiology

The risk factors for T2D is either modifiable(unhealthy diet, physical inactivity and obesity) or non-modifiable ones (genetic, family history and ethnicity)or combination of them(Zheng et al., 2018). These risk factors should be considered when screening for prediabetes or diabetes in asymptomatic adults with 3-year interval between testing(Association, 2021). Adult with more than 45 years, BMI ≥25 kg/m2, some medication and adult with HIV all are at higher risk for developing prediabetes and diabetes(Association, 2021). There is a criteria for testing diabetes and a criteria for prediabetes categories, also, American Diabetes Association (ADA) diabetes risk test is an additional assessment tool help in determine the appropriateness of testing for diabetes or prediabetes in asymptomatic adults(Association, 2021). A1C value of ≥6.0% is considered

as a high risk factor of developing diabetes in the following next year with 5-year risks ranging from 25 to 50% and 20 times higher risk comparing with A1C <5%(X. Zhang et al., 2010).

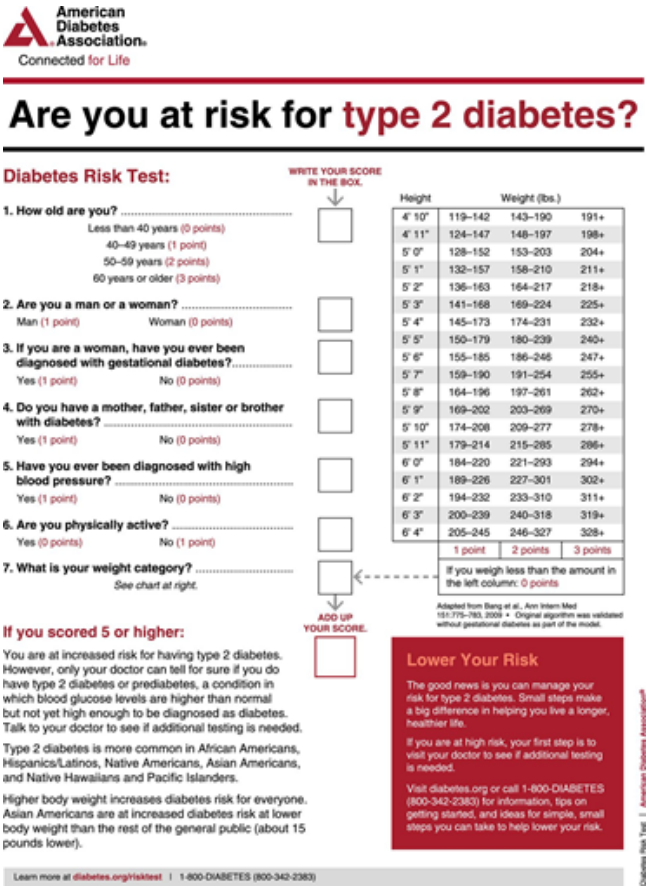


Figure 2.1: The ADA diabetes risk test

In type2 diabetes the hyperglycemia usually develops gradually and initially not severe enough to be noticed and diagnosed(Association, 2013a). This occur in the presence of sedentary lifestyle which expressed as an energy expenditure of less than 1.5 Metabolic Equivalent of Task (MET) and physical inactivity as main risk factors for T2D and other

associated chronic diseases(Sgrò et al., 2021). This can complicate the disease management and the incidence of the associated diseases will increase in the level of cardiovascular, body weight, blood parameters and others which all have been approved its improvement with physical activity(Cannata et al., 2020). So, physical exercise and physical activity is in the first line when treating T2D people non pharmacologically(Balducci et al., 2019)(Sgrò et al., 2021).

For instance, glycolysis is stimulated by aerobic exercise producing the ATP and lactate rapidly, this can lower the insulin resistance, improve cardiovascular capacity and immune system in T2D(Garber et al., 2011). In addition to the enhancement of blood pressure and and glycated haemoglobin (HbA1C)(Chimen et al., 2012), therefore lowering the mortality rate from such diseases(Sluik et al., 2012).

The other risk factor is not separated from the first one, the literature reported that with increase in sedentary activity by one hour, the risk of becoming overweight and grow of high abdominal fat will increase by 13%and 26% respectively(González et al., 2017). In a randomized clinical trial by Balducci et al in 2019 investigated the effect of practical and theoretical behavioral intervention on 267 participants with T2D aimed to decrease the sedentary time and replace it with light-intensity physical activity and progressed to moderate- to vigorous-intensity physical activity over 3-year period, reported as a secondary outcome measure that the cardiorespiratory fitness and muscle strength well increased(Balducci et al., 2019). Also, β-cell function well improved in prediabetes or T2D whom trained two weeks of a moderate intensity continuous training and decreased pancreatic fat content(Teich et al., 2019).

A good normal glucose level is maintained by interaction between insulin secretion from B cells and insulin absorption from insulin sensitive tissue(Cerf, 2013). Any disruption of this feedback loops caused by β-cell dysfunction or insulin resistance will led to T2D progression(Stumvoll et al., 2005). In this study, reviewing all risk factors or disease mechanisms are out of the scope. So, the study focused on the main drivers for T2D which is obesity and physical inactivity which resulting in insulin resistance.

After a nutrient uptake, pancreatic beta cells secreting insulin hormone while inhibiting liver glucose production and increase glucose absorption from adipose tissue and muscle(Czech, 2017). This blood glucose hemostasis is maintained by mechanism of insulin release and insulin action(Galicia-Garcia et al., 2020). When this mechanism failed to keep on control it undergo into three category of insulin resistance: I β-cell dysfunction, II insulin antagonists in the plasma which impaired insulin signaling due to counter-regulatory hormones or non-hormonal bodies, III target tissue impaired insulin response(Pearson et al., 2016).

The most affected target tissue is muscle insulin resistance(Petersen et al., 2007) and liver as the less affected one(Bock et al., 2007). Physical activity increasing effect on glucose uptake of active skeletal muscle is impaired in insulin resistance or type2 diabetes due to defect in insulin hormone and sensitive glucose transporter-4 (GLUT4) proteins translation to plasma membrane(*Regulation of Blood Glucose Homeostasis during Prolonged Exercise - PubMed*, n.d.). Even though, the exact mechanism of insulin resistance and the order the obese or T2D people get it still under research(Pearson et al., 2016).

2.1.2 Type 2 diabetes with cardiovascular diseases:

One of the most disease complications in young adults with type 2 diabetes is cardiovascular dysfunction(Schmidt, 2018). The co-existence of cardiovascular disease and diabetes higher the numbers of premature death among these population(Henning, 2018). In 2016, Yamazoe and coworkers in their study on 40–79 years old participants with follow-up of 4.9±1.3 years reported that coronary artery calcification (CAC) may be worsen in case of insulin resistance even in non-diabetic people(Yamazoe et al., 2016). With two- to fourfold tendency for developing myocardial infarction and coronary artery disease in diabetic patients(De Rosa et al., 2018). The CVDs are considered to be the cause of death in 70% of persons with diabetes at an age ≥65 years(De Rosa et al., 2018)(Grundy et al., 1999). Diabetes as an independent risk factor for macrovascular disease like stroke, an increase prevalence of such diseases are even in pre diabetes people with insulin resistance which is the stage before the clear diagnosis of T2D(Henning, 2018).

There were numerous studies investigating in this area of research. In Haffner and others cohort study, 8 years of follow up of 614 nondiabetic people at the time of baseline examination, 43 of them developed type II diabetes caused by obesity, hyperglycemia, and especially hyperinsulinemia which contribute to the risk of macrovascular disease(SM et al., 1990). In addition, a sixteen year follow-up study by Kannell and others showed that increased prevalence of morbidity and mortality from all cardiovascular problems in diabetes people even before or with newly clear diagnosis.(Garcia et al., 1974). On another epidemiological study by Andreas Festa and colleges in 2000, on a total of 1008 nondiabetic individuals confirmed the previous study regarding the independent relation

between insulin resistance and developing atherosclerosis and cardiovascular disease in non-diabetes people who suspected to developed T2D and the importance of treatment(Festa et al., 2000).

The risk for cardiovascular mortality increase especially in an inactive diabetes adult in about 2.81% comparing with inactive adults without diabetes(Henning, 2018). So increase physical activity with exercise will improve physical fitness when performing it following the recommended guideline but it is still not clear for reducing the incidence of CVD and must have more investigation(Henning, 2018). Numerous studies investigated that increased physical activity in pre diabetes stage(Grundy, 2012) or in newly acute type two diabetes (Kim et al., 2022)or even chronic one will prevent or reduce risk of CVD and improve physical function (Hu et al., 2022)(Tanasescu et al., 2003). In a randomized control trial by Kadoglou and colleges on 60 participants with type 2 DM, the intervention group received aerobic exercise training programme for 6-month and control group who maintained the habitual activities, the result showed improvement in VO2 Max, decreased systolic blood pressure, Insulin resistance in intervention group(Kadoglou et al., 2007). And finally in Sigal and others' systematic review, a consensus statement from the American Diabetes Association summarized all the previous conclusion in the same field of exercising diabetic people(Sigal et al., 2006a).

In 2022 by Masuku and others , a three systematic reviews were carried out in South Africa about the cost of treating T2D, HT, CVD found that drugs in the first place is a major cost driver for treating HT, T2DM and CVD hospitalization and the cost increase

when treating diabetes-related complications more than uncomplicated diabetes(Masuku et al., 2022).

2.2 Similar Studies

2.2.1 BFRT on aerobic capacity

When we look to the history of this technique, there is an increasing body of data that studied the effects of blood flow restriction therapy on various outcomes and for the most is their effect on aerobic capacity(Bennett & Slattery, 2019a). In Miller and others' systematic review in 2021 have been studied the systemic effects of BFRT from 35 articles on musculoskeletal, cardiovascular, endocrine, and psychosocial(Miller et al., 2021) in two studies involved in it carried out in 2015 and 2010 on 15 and17 healthy adults respectively showed that low intensity aerobic exercise with BFR treadmill walking increased blood pressure, heart rate and cardiac work so place the technique under questions(Sugawara et al., 2015)(Renzi et al., 2010). In contrast to another study in 2015 on 17 healthy adult received BFR without any hemodynamic changes documented(Yasuda et al., 2015).

Indeed, these were before the development of performing this technique in a more safe and structured way, variety in cuff pressure from high (e.g. 80% of arterial occlusion pressure (AOP))which affect the result negatively or without additional benefit(Mouser et al., 2019) from low (e.g. 40% of AOP))that affect the result positively without cardiac laud(Ozaki et al., 2013)(Renzi et al., 2010)(Renzi et al., 2010)or . And cuff size from narrow which exacerbate the blood pressure and cardiac output(Fujita et al., 2007)(Fry et al., 2010) to

wide which is more safe and comfortable(Gundermann et al., 2012)make the result seems to be conflicted.

The guideline from Patterson and colleagues in 2019 and 2013 Loenneke's recommendations facilitate the use of BFR to research committee and made the researches after that more unified in there protocols(Patterson et al., 2019a)(Jeremy P. Loenneke et al., 2013). In Oliveira and Mendonca in 2015, both studies investigated the effects of BFR on VO2 peak and muscle strength for short-term and showed significance positive result of healthy young men(de Oliveira et al., 2016)(Mendonca et al., 2015). A Systematic Review in February 2019 reviewed the short term BFR aerobic exercise effects on aerobic capacity from fourteen studies, the result divided to good enhancement of aerobic performance and fitness in young adult but in older adult showed only aerobic performance enhancement with aerobic fitness remain unchanged, though some methodological limitation in the studies involved(Bennett & Slattery, 2019c). This can be explained from another study which showed the same result, improvement in V̇O2max in aging adults is correlated with adaptation in muscle oxidative capacity and higher walking speed may improve aerobic capacity(Abe et al., 2010).

Despite all the rich data from the previous researches, and as the study mentioned above about the effects of BFR on vascular abnormalities, there were a lack of information about the effects of aerobic training with BFR on older diabetic people whom the high intensity exercises are not suitable for them(Hughes et al., 2017).

2.2.2 BFRT on physical function

When the literature reviewed the effects of BFRT on physical performance, the results vary according to which group category have been studied. In systematic review in 2021 analyzed the effects of BFR from 10 studies found a significant improvement in body performance among healthy athletes(Wortman et al., 2021). With a clinical sitting, the BFR showed a positive significance result as a MSK rehabilitation tool regarding muscle strength mainly with less emphasis on physical function improvement(Hughes et al., 2017). A randomized control trial was reported marked physical function improvement when using low-intensity blood flow restriction walk training with Sedentary elderly aged between 60 – 80 years(Matthew John Clarkson et al., 2017). While in a systematic review in 2019 comparing the effects of BFRT on aerobic fitness and performance in younger and older adult reported improvement in aerobic performance with no change in aerobic fitness in older adults(Bennett & Slattery, 2019c).

Despite that, systematic review in 2020 concluded that BFRT effects with adult older than 50 years still not clear due to variation in BFR protocols that have been used in the previous body of data but with clear BFRT effects using ideal methodology with young adults(Baker et al., 2020).

2.2.3 BFRT on insulin sensitivity

As the study mentioned in the first line and according to the American Diabetes Association(ADA) guidelines, exercise medicine is integral part in management of type two diabetes(Peng et al., 2023)(Colberg et al., 2010). At the top of lifestyle interventions is physical exercise in reducing the incidence of type two diabetes by 58% and in in

improving glucose homeostasis and insulin sensitivity(Magkos et al., 2020)(Group, 2002). In specific, aerobic exercise with obese and type two diabetes has a very interesting physiological effects, in particular on insulin resistance(De Sousa et al., 2022) and on β-cell functional in T2D(Lv et al., 2022).

2.3 Summary

Despite all these numerous studies and systematic reviews on the definitive positive relationship between aerobic capacity, insulin sensitivity and physical function with exercise therapy in different categories, there is a lack of information and a gap knowledge about the effect of exercise combined with BFR on the same outcomes in T2D.

Chapter Three

3.1 Study design

3.2 Study sitting

3.3 Participants

3.4 Recruitment and Sampling

3.5 Data collection

3.6 Intervention

3.7 Statistical analysis

3.8 Ethical considerations

3.1 Study design

This study is a randomized feasibility study for a larger randomized controlled trial to compare and track the acute effect of BFR walk training on insulin sensitivity and aerobic capacity among T2D. This feasibility study exploring how an full-scale RCT can be implemented, which is a critical component prior to intervention development(Gadke et al., 2021). Iterative, formative, and adaptive feasibility study focuses on conducting research to examine whether the study can be done and to assess the intervention process especially for this novel intervention(Orsmond & Cohn, 2015). This study was reported according to The Consolidated Standards of Reporting Trials (CONSORT) statement: extension to randomised pilot and feasibility trials(Eldridge et al., 2016). And PEDro scale (*English - PEDro*, n.d.).

3.2 Clinical sittings

All experimental procedures were carried out at in Medical Rehabilitation Complex of the Arab American University of Palestine(AAUP) which is fit place for performing the experiment. In addition to the participant's private physician for following up their conditions and help in eligibility, Participants who met initial eligibility criteria undergo in-person evaluation and comprehensive examination by a medic rehabilitation doctor(Dr. Yousef Alhamdan: medical staff in AAUP and the head of AAUP Medical Rehabilitation Complex) to insure that their conditions do not conflict with study protocol. Nurses and medical staff were existed for safety and laboratory technician for helping researchers in collecting data.

3.3 Participants

Adults male diagnosed with type2 diabetes aged between 40 and 60 years have been selected to participate in this study. The participants have been recruited from the local community using the social networking.

3.3.1 Eligibility

Medical records were reviewed for preliminary eligibility. Participants who met preliminary eligibility criteria underwent a face-to-face assessment by a medical specialist and were asked to provide informed consent prior to study entry.

3.3.2 Inclusion criteria

- Palestinian male

- 40-65 years old

- a course of type 2 diabetes of 2-10 years, under supervision and follow-up by a doctor.

- Able to understand and adhere to the experiment instruction, programs, and protocols.

3.3.3 Exclusion criteria

- Females, because of the differences in body hormones and metabolism.

- any younger or older patients exceed the target age, due to age related differences existing with DM.

- any patient with serious problems or comorbidities that may affect walking ability and increase BFRT risk possibilities.

- Ankle Brachial Pressure Index (ABI) <0.9.

ABI is a non-invasive diagnostic procedure to detect any vascular abnormalities by taking the ratio between lower extremity systolic blood pressure of posterior tibial artery (the ankle) and the upper extremity systolic blood pressure of brachial artery, which reflects the resistance in blood vessels, with normal value 0.9 to 1.4 (McClary & Massey, 2023). Lower and higher values of ABI may indicate Peripheral arterial disease (PAD) or cardiovascular disease (CVD)(Criqui et al., 2010).

3.3.4 Sample size

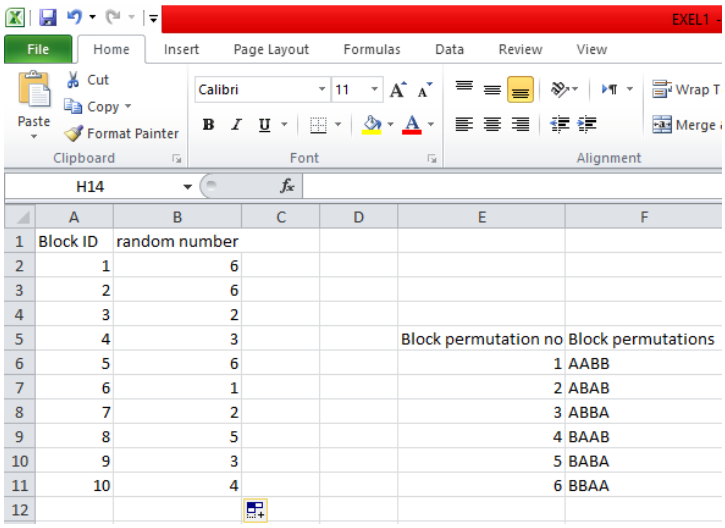
As this is a feasibility study, no formal power calculation is required. However, the study estimated the number of participants required to be approximately 10% of the number required for the RCT. The sample size calculation for the RCT suggests that 60 participants need to be recruited. Given the participant population, a high level of attrition can be

expected. The study therefore aimed to recruit 30 participants to the feasibility study to estimate recruitment and inform the design and sample size of the RCT, with a completion rate close to 10% with 95% CI, based on a worst case estimate of 50%.

3.4 Recruitment and Sampling

3.4.1 Procedure

Participants were recruited (May 2023–July 2023) and were randomly allocated to the intervention (aerobic exercise with BFR)(AE-BFR) or control group(aerobic exercise alone)(AE). Randomization sequence was created using Microsoft Excel 2010 with a 1:1 allocation using random block size of 4 by an independent researcher(Figure 3.1).



	A	B	C	D	E	F
1	Block ID	random number				
2	1	6				
3	2	6				
4	3	2				
5	4	3			Block permutation no	Block permutations
6	5	6			1	AABB
7	6	1			2	ABAB
8	7	2			3	ABBA
9	8	5			4	BAAB
10	9	3			5	BABA
11	10	4			6	BBAA
12						

Figure 3.1: randomization using Excel

The Allocation concealment was done by having a 10 opaque, same sized envelopes. Written and closed by the first independent researcher (who performed the prescreening examination) and given to the investigator. Each of them written in it one of the two groups(A or B). Then give each participant an envelope to know what intervention he will

received after completing familiarization session and baseline testing. The investigator and participants were aware of patients' group assignment.

Pretest out: At the first, each participant came to the university camp in Jenin, welcomed him to the rehabilitation center to perform familiarization session by explaining all the procedures, showing them the experiment room and equipment available for the exercise sessions, and familiarized them into the protocol via demonstration and verbal explanation. Basic demographic and clinical information have been collected from the participants using data collection sheet. Participants underwent a pre-screening session by doctor of rehabilitation who followed the inclusion criteria that include ABPI, HR, BP and others using assessment form(appendix1). Then provided written informed consent(appendix2). The study participants were physically active in their daily life.

Intervention: AE-BFR group have been received a 4weeks of training program using treadmill with 50% of LOP on the right lower extremity two days per week with 20 minute for each session taking into account the warm up and cooling down period, and with individualized preferable speed. The AE control group received the same procedures but without any BFR.

Post intervention: after each participant finished the 4week training program, they underwent post intervention tests for analyze the result regarding aerobic capacity and insulin sensitivity improvement. The post intervention tests have been taken one day after the program have been finished.

3.5 Data collection

3.5.1 Demographic and medical data: Basic demographic and clinical information have been collected from the participants using a sociodemographic questionnaire and medical data sheet(appendix3). Participants characteristics in this study included personal characteristics (age, gender, address, income level, lifestyle, nutrition habits, smoking habits). And clinical characteristics (disease onset, hypertension, BMI) have been conducted. The data of the participants have been recorded and kept on excel sheet.

3.5.2 Outcome measures

Primary outcomes: are as follow:

Feasibility of the Intervention: Feasibility was assessed in terms of eligibility rates, referring to the proportion of patients who met the inclusion criteria compared to the total number of patients with T2D attending the clinic. And recruitment rates by divide the total number of randomizations needed by the number of sites, and then multiply that by the length of the enrollment period in months. Also adherence to the group intervention, which is the proportion of participants in the intervention arm who received the intervention and the average number of sessions attended. And follow-up rates by treatment condition, which refers to the proportion of participants who completed the post-intervention assessment measure.

Secondary outcome measures: Clinical outcome measures were conducted to characterise the sample and estimate how the intervention could guide the sample size of the next efficacy trial. These clinical outcome measures were assessed at the pre-intervention assessment and at the 4-week post-intervention assessment.

1- **Aerobic Capacity**: VO2 Max is the gold standard method of assessing maximal aerobic capacity and is the most important measurement during functional exercise testing(Weisman et al., 2012). higher VO2 scoring reflecting good cardiorespiratory fitness and lower risk of cardiovascular disease development(Waddoups et al., 2008). However, the gold standard'' for assessing VO2max by exercising to exhaustion is a complex process , difficult to apply and not safe especially for elderly with CVD or T2D, and because the estimated equations depending on age, gender or body composition are not accurate and not practical, so submaximal exercise testing is the best alternative options with good predictive validity and low risk(Waddoups et al., 2008). Ebbeling Single-Stage Treadmill Walking test is the most suitable modality for obese elderly without locomotion impairment and with adult with low to moderate fitness levels, safe, familiar more than cycling and because the speed and incline are easily defined(Sartor et al., 2013). Following Ebbeling protocol(Ebbeling et al., 1991), after calculating 50% and 70% of MHR according to the participant age, It is subdivided into two stages, the first warm up stage consist of 4min of walking in speed between m 3.4 to 4 mph with zero grade or between 50% and 70% of HR max, the second one with another 4 min with the same constant speed but with 5% grade gradually increased. The test is stopped when a steady-state heart rate of less than

five beats per minute is reached, otherwise the test is continued minute by minute until a steady state is reached. Then calculate VO2max by entering the average of the last two heart rates into the formula: Estimated VO2max (in ml - kg-1 - min-1) =15.1 + (21.8 x pace in mph) - (0.327 x SS HR in bpm) - (0.263 x pace x age in years) + (0.00504 x SS HR in bpm x age in years) + (5.98 x gender: female = 0, male = 1). The test sheet is present in Appendix 4.

2- **Insulin resistance :** HOMA-IR (Homeostatic Model Assessment of Insulin Resistance)is a valid index for estimating insulin resistance in people with hypertension and type II diabetes(Sarafidis et al., 2007). And it is a less invasive, inexpensive and time-consuming method of measuring insulin resistance (IR) relative to the glucose clamp test(Kang et al., 2005). The RI was evaluated using the computerized homeostasis model evaluation program (HOMA-IR)(*HOMA-IR (Homeostatic Model Assessment for Insulin Resistance)*, n.d.). This is based on fasting blood glucose and fasting insulin levels. The higher HOMA-IR, the greater resistance to insulin, levels greater than 1.9 indicate early insulin resistance and levels greater than 2.9 indicate significant insulin resistance(*HOMA-IR: A Test of Insulin Resistance + Ways to Decrease It - SelfDecode Labs*, n.d.).

3- **6 minute walk test (6MWT) :** is a simple, safe, self-administered and widely used test for the objective assessment of functional exercise capacity for pulmonary rehabilitation, medical intervention (pre- and post-treatment comparisons) and other conditions (Matthew John Clarkson et al., 2017) with a good test–retest reliability used to measure change over time as a response to rehabilitation effects in people

with chronic respiratory disease . following The American Thoracic Society procedural guidelines, Patient is asked to walk as far as possible in 6 min along a flat, straight corridor, recording the distance in meters with instructions and encouragement given during the test, performance complications of the 6MWT in clinical trials were unusual(Holland et al., 2014). High reliability and validity of this test in patients with type 2 diabetes mellitus(M. C. Lee, 2018)(Alfonso-Rosa et al., 2014)(Nolen-Doerr et al., 2018).

4- The short form 36 health survey questionnaire (SF36)(RAND-36):

The SF-36 is a new easy acceptable instrument for measuring health perception and health-related quality of life in a general population(Brazier et al., 1992) and for elderly patients(Singleton & Turner, 1993). Was designed to investigate health status as part of the Health Outcomes Study by Ware and Sherbourne(*The MOS 36-Item Short-Form Health Survey (SF-36). I. Conceptual Framework and Item Selection - PubMed*, n.d.). According to newly recent study, The SF-36 is suitable for patients with type II diabetes on the island of Réunion in both the Creole and the French versions(Soulaimana et al., 2023). The SF-36 also showed that it is a valid and reliable instrument for measuring QoL in Lebanese older people and could be used to monitor QoL in this population(Osta et al., 2019). And in other Arabic countries(Guermazi et al., 2012)(Sheikh et al., 2015).

The SF-36 measures eight scales: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH)(Lins & Carvalho, 2016). Sub-scale scores range from 0 to 100, 0 being the worst health condition and 100 indicating the best health condition(*The MOS 36-Item Short-Form Health Survey (SF-36). I. Conceptual Framework and Item Selection - PubMed*, n.d.). The percentile scores were transformed into percentiles and categorized as low (0-33), moderate (33.4-66.6), or high (66.7-100) based on their total scores(Alzboon & Vural, 2019). The questionnaire is present in appendix 5.

3.6 Intervention

3.6.1 pre intervention and familiarization session

In the first visit and after explaining all about the experiment to each participant and signing the consent form, each participant complete the SF-36 questionnaire by reading it from the researcher. To be familiarized, each participant trying to walk on treadmill in a slow speed for 10 minute even if it is not the first experience for him. After that, the researcher insures that the participant was at rest for minimum 10minute to begin the next pre experimental testing(Figure3.2).

Figure 2.2: familiarization for treadmill walking

Prior to the start of the tests, the tester records resting heart rate and blood pressure to obtain reference values by using blood pressure monitor. Pulse Oximeter was placed on participant's finger throwing all tests.

For 6 minute walk test, a 30meters flat straight corridor, free of obstacles, was divided by a red adhesive line each 3 meters, and a turnaround point marked with a cone in the start and at the end of it. With two chairs in between for more safety if any fatigue occur(figure3.3).

Figure 3.3: 6MWT familiarization

Instruct the participant to walk for 6 minute. Before starting the test, participants were told to cover as much ground as possible in 6 minutes, walking continuously if possible. And that the aim is to feel that no more ground could have been covered at the end of the test. The equipment required for the test was a countdown timer, a mechanical lap timer, cones to mark the turnaround and a chair that could be easily moved along the walking course. According to the American thoracic society 6minute guidelines recommendations, Phone, oxygen and was accessible for safety(Fell et al., 2021). A change of 45.8 meters is required to detect change beyond measurement error.

After that, the Ebbeling test was performed. By briefly explained the purpose of the test and how it is conducted to each participant. Then estimate the participant's age-predicted HRmax (280-(0.7x age)) in bpm then calculate 50% bpm and 70% bpm of his/her HRmax. For more safety, always use the safety key, 2 feet off each side of a treadmill and 6 feet behind it to avoid falling into a wall or getting stuck between the machine and a wall. large mattress was placed in the end of treadmill for any unsuspected falling or balance loss. Warm up for 4 minutes on a 0% incline at a walking pace that brings the HR to between 50% and 70% of HRmax. (The recommended walking speed is between 3.4 and 4 mph). If the HR is outside this range after the first minute, adjust the pace accordingly. After the warm-up, the participant will continue at the same speed for a further 4 minutes at 5% incline and then record the steady-state HR (SS HR) averaged over the last 30 seconds of the last two minutes at 5% incline. To reach steady state, the HR of the last two minutes should not differ by more than 5 bpm. If the HR differs by more than 5 bpm, extend the test by an additional minute and record the SS HR from the new last two minutes. Then entered

this SS HR into the equation to estimate VO2max (mL • kg-1 • min-1). Let the participant cool down while walking slowly and record 0% for 2-5 minutes. Monitor and record HR in bpm on a minute-by-minute basis.

The test was completed as suspected to all participants expect of one who had a shortness of breath, sweeting and severe fatigue so the test stopped after the first5 minute and the result recorded.

For determining the BFR device parameters, to assess LOP, BFR group were in standing position in which the same position was used for BFRW training(Sieljacks et al., 2018)(WEATHERHOLT et al., 2019)(Hughes et al., 2018) for determined the suitable cuff pressure which was for unilateral right thigh, 15cm above the apex of the patella using a tape measure. With a minimal threshold pressure of 50%, according to the recent previous literature which showed no differences in application of 40% or up to 80% of blood occlusion. BFR machine function with 11.5 cm width, nylon have been used to assess the arterial blood occlusion(AOP)(Matthew J. Clarkson et al., 2020).

This study used smart Cuff lower extremity limb occlusion pressure device (LOP) which is time-saving, reduce risks of soft-tissue and nerve injury and does not need to a skilled or trained personnel and specialized equipment like with Doppler ultrasound(Abbas et al., 2022).

LOP is defined as “the minimum pressure required, at a specific time in a specific type of tourniquet cuff applied to a specific patient’s limb at a specific location, to decrease the flow of arterial blood into the limb distal to the cuff”(Masri et al., 2016). The study used a

wide cuff size on one lower extremity; The wider the cuff the less the LOP which is more comfortable and safe for the participant(*Occlusion of Arterial Flow in the Extremities at Subsystolic Pressures through the Use of Wide Tourniquet Cuffs - PubMed*, n.d.)(McEwen et al., 2002). And more pressure to deep tissues than the narrowed cuffs therefore provide lower inflation pressures when restricting arterial blood flow(Hunt et al., 2016). Also, wide cuff showed limited impact of limb circumference on the cuff pressure required for partial blood flow restriction in contrast to narrow one(Hunt et al., 2016). With average pressure of 33-42% less than typical pressures(Younger et al., 2004). The attended cuff pressures used for training program for BFRW were 50% LOP. Wider cuff do not depend on thigh circumference(Patterson et al., 2019b). after that, each participant walk for few minute with BFR device to be familiarized with it.

For blood sample collection, fasting blood samples was obtained from the participants in the morning (8:30–9:30) by collecting 10 ml of venous blood. Patients were instructed to stop exercising for at least 24 hours before collecting blood and had to stop eating or drinking 8 h before taking samples. Samples were collected in vacuum tubing using sodium ethylenediamic acid (EDTA) for plasma separation. The blood sample had taken by a laboratory technician. The procedure done in the same research site at the familiarization session as a pretest and after 24 hours from the last training one as a posttest procedure. The blood sample which were taken in the rehabilitation center have been kept in specialized icebox for translation to laboratory lab. Including laboratory section with its staff who helped in data analysis.

3.6.2 intervention procedures

The time required to complete the walking programme was the same for the BFR group and the control group. After a baseline testing session, the therapist explained the procedures for the participants (BFR or control), Each session averaged about 20 min, twice weekly for 4weeks period.

Each session in control and intervention group subdivided into warm up, main exercise and cool down. The chosen speed and duration reflect common speeds and durations used in other BFR walking research. The treadmill speed is similar to the participant's preferable usual walking speed for both groups with an average of <50% VO2 max or HRR and with set pressure of Continuous 50% AOP for BFR group(Abe et al., 2010)(Patterson et al., 2019a).

With 20minute session, the main exercise subdivided by 2 minute of break to prevent patients fatigue. Participants tended to train on the same days each week and at the same time of day. Any discomfort during session reported by the participant should be considered to stop the treatment.

3.6.3 post intervention

All the pre testing procedures were repeated as the same at the end of the intervention period, posttest measurements were performed after 24hours of the last training session.

3.6.4 safety procedures and possible risks

To avoid adverse outcomes and ensure that BFRT is used appropriately, it is strongly recommended that a review of the patient's medical history and signs and symptoms that

may indicate an underlying pathology is undertaken using a risk assessment tool (Nascimento et al., 2022). Participant's blood pressure and glucose have been checked before and after each session using a good and clean working condition cuff.

3.7 Statistical analysis

Descriptive and Inferential statistics

The benchmark objectives for feasibility outcomes were set to guarantee that 85% of participants randomized were retained, 80% of intervention adherence was observed, and 85% of outcome assessments were completed. The recruitment rate will be calculated as the total randomizations needed / number of sites) / months of enrollment period(Walters et al., 2017).

Quantitative data will first be analyzed using descriptive analysis using means and standard deviations, and numbers and percentages (%) will be used to present categorical variables. Data analysis will be conducted using SPSS Statistics 23 software (IBM Corp, 2017).

In addition, two-tailed t-tests for continuous variables and chi-squared tests for categorical variables were used to determine demographic and biometric differences between the incentive groups over time (baseline to follow-up). Analysis of variance was used to test for changes in biometric data from baseline to follow-up. Significant demographic covariates were controlled for (P>.25).

3.8 Ethical consideration

Ethical and research governance approvals were obtained in accordance with the requirements necessary to conduct this study. Ethical approval was sought from the

Palestinian Ministry of Health after obtaining ethical approval from the Institutional Review Board of the Arab American University of Palestine. Written informed consent was obtained from participants for the relevant records used in the study. The purpose and requirements of this study were explained to each participant, and participants were aware that they have the right to withdraw from the study at any time without explanation. All documentation and data were anonymised and secure as this study was take place in Palestine.

Chapter Four

4.1 Result presentation and analysis

4.2 Study Limitation

4.3 Results Discussion

4.1 Results presentation and analysis

Over the planned recruitment period (4 months), 32 form 36 male diabetes patients consented to participate in the study, assessed for eligibility, performed the baseline tests, and were randomly allocated to 1 of the 2 groups (Figure4.1). Two participants did not complete the intended treatment and lost during the study period due to invasion and holidays. The rest of 30 participants who were retained completed all aspects of the assessments. Patient enrolment started in May 2023 and was completed in July 2023. The study end when the 4 weeks intervention were completed for each participant in both group.

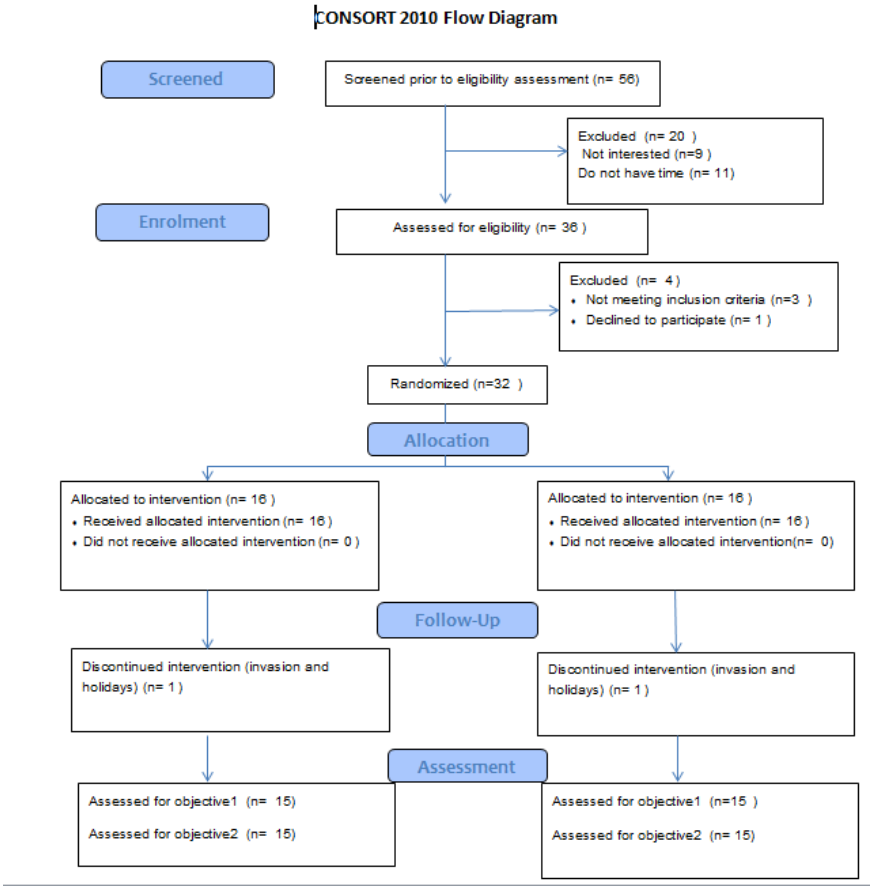


Figure 4.1: Flow diagram of a randomized pilot trial

4.1.1 Descriptive Statistics of variables

The participants' personal characteristics were assessed at baseline with no statically difference between the experimental and control groups. (Table 4.1) presents the details of the baseline characteristics.

Table 4.1: Baseline characteristics of participants

	Group					
	Intervention			Control		
	Mean	Standard Deviation	Count	Mean	Standard Deviation	Count
Age (y)	52	6		53	5	
Onset (y)	5	3		5	2	
Smoking yes			8			9

no	7	6

Y: years

Age of participants

The mean age of all participants in the study was 52.37 years, with a standard deviation of 5.810. The mean age of the participants in the BFRT group was 52.0 years/SD was 6, while the mean age of the control group was 53.0 years/SD was 5 (Figure 4.2). There were no significant differences between the two groups according to age P value = .878 >.05.

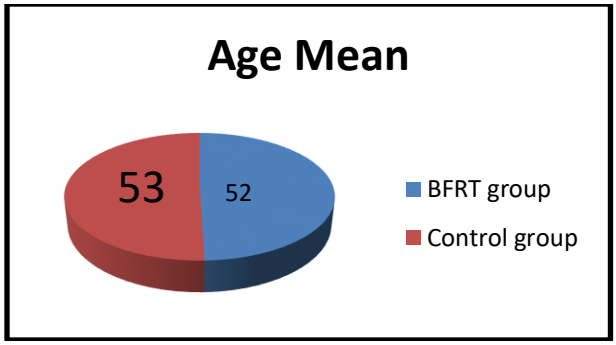


Figure 4.2: Mean Age of the Participants

Onset of disease

The mean age of onset for all participants in the study was 5.02 years with a standard deviation of 2.472. The mean age of onset for the participants in the BFRT group was 5.23 years/SD was 2.731, while the mean age of onset for the control group was 4.80 years/SD was 2.25 (Figure 4.3). No significant differences were found between the two groups according to the time of onset P value = .639 >.05.

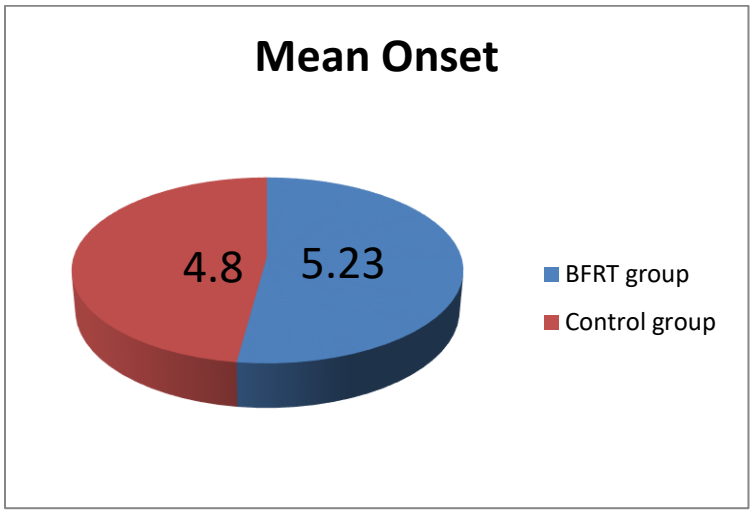


Figure 4.3: Mean Onset of the Participants

History of Smoking

In the BFRT group, 8 (53.3%) of the participants were smokers and 7 (46.6%) were non-smokers, while in the control group the distribution was 9 (60%) smokers and 6 (40%) non-smokers (Figure 4-4).

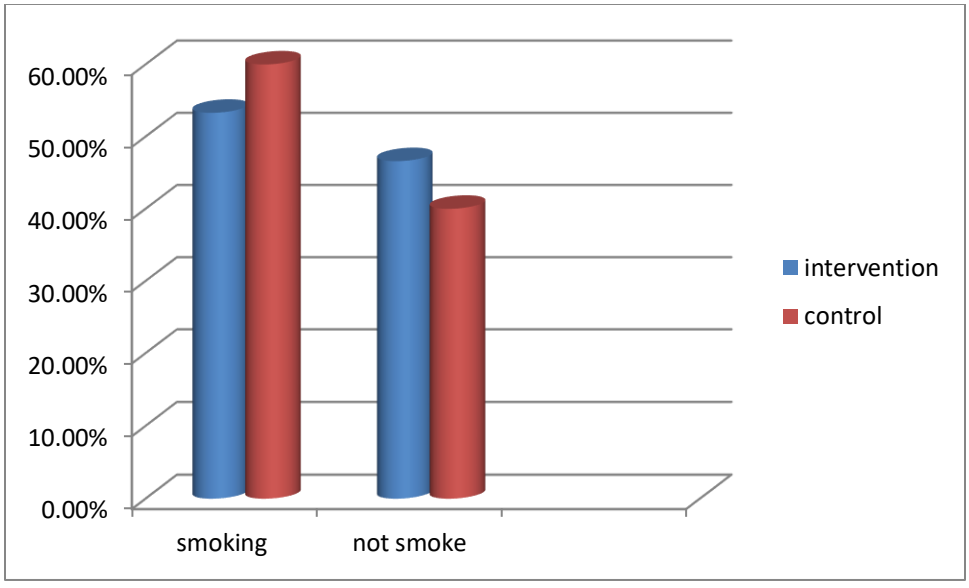


Figure 4.4: History of smoking

Other variables :

BMI, Waist and thigh circumference and Sugar accumulation are the other variables the study was looked for pre and post intervention in relation to the study population. Table 4.2 summarize these variables and any differences occurred post intervention.

Table 4.2: Descriptive characteristic of other variables

	Group															
	Intervention								Control							
	BMI		Waist(cm)		Thigh(cm)		Sugar		BMI		Waist(cm)		Thigh(cm)		Sugar	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Overweight	4	4	93.37	93.23	55.23	51.50	8.28	7.20	3	4	93.53	93.20	55.47	55.20	8.53	8.35
Obese1	9	9							9	9						
Obese2	2	2							3	2						
Z (P value)	1.000				.001				.157				.208			
T(P value)			.469				.000				.296				.001	

Cm: centimeters

BMI of participants

The healthy BMI range is between 18.5 kg/m2 and 25 kg/m2(figure 4-5)(*BMI Calculator*, n.d.).

Classification	BMI range - kg/m^2
Severe Thinness	< 16
Moderate Thinness	16 - 17
Mild Thinness	17 - 18.5
Normal	18.5 - 25
Overweight	25 - 30
Obese Class I	30 - 35
Obese Class II	35 - 40
Obese Class III	> 40

Figure 4.5: BMI classification

At baseline, Body Mass Index (BMI) Categorization of the Participants, in BFRT group, the distribution was: 4(26.6%) were over- weight, and 9(60%) were obese class1 and 2(13.3%) were obese class2. While in the Control group, 3(20%) were overweight, 9(60%) were obese class1 and 3(20%) were obese class2.(Figure 4.6). No significant differences were recorded at baseline according to BMI between the two groups P value = .624 >.05.

At the end of study, BMI for BFRT group the distribution remain the same: 4(26.6%) were over- weight, and 9(60%) were obese class1 and 2(13.3%) were obese class2. While in the Control group was 4(26.6%) were overweight, 9(60%) were obese class1 and 2(13.3%) were obese class2. No significant differences were recorded at the end of study according to BMI between the two groups P value = 1.000 >.05.

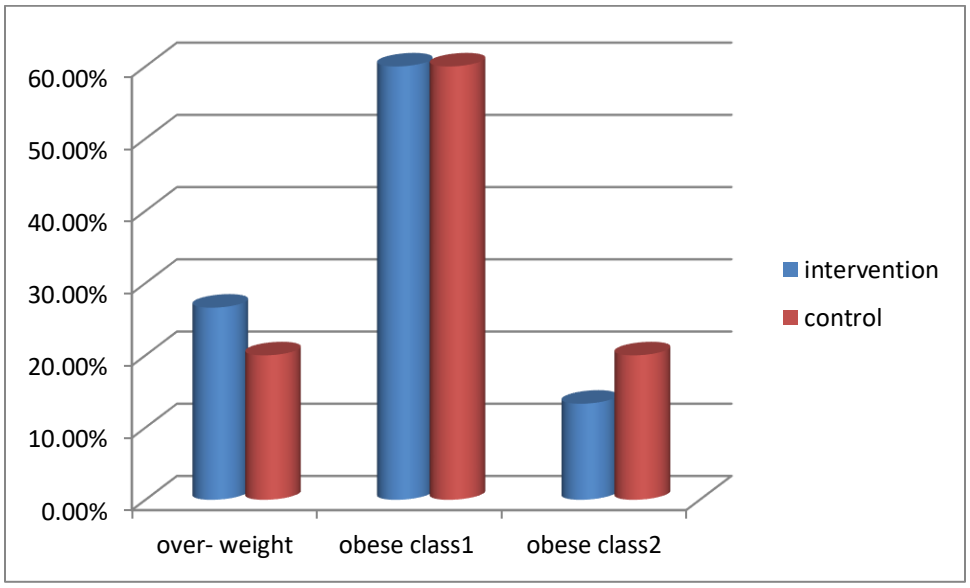


Figure 4.6: Pre BMI categories of the Participants

Cumulative sugar:

At baseline, the mean of cumulative sugar level of the Participants in BFRT group was 8.2. While in the Control group was 7.20.(Figure 4.7). No significant differences were recorded at baseline according to cumulative sugar level between the two groups P value = .715 >.05.

At the end of study, the mean of cumulative sugar level for BFRT group lowered to 7.20. While in the Control group lowered to 8.35. A significant differences were recorded at the end of the study according to cumulative sugar for both groups with larger effect size for the intervention one, P value = .001 <.05.

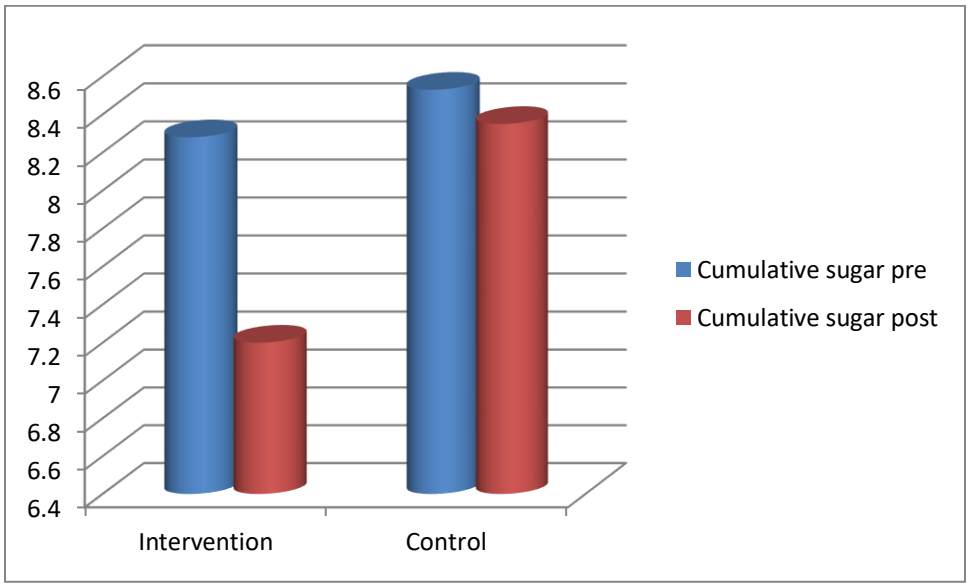


Figure 4.7: cumulative sugar level of the Participants

4.1.2 primary outcomes: Feasibility of conducting a definitive RCT

Out of the 36 eligible participant who have diabetes, 32 (88%) agreed to participate in the study. The recruitment rate was, therefore, 3.75 patients per month. 20 participants (66%) were informed of the study from local region and 10 participants (33%) were recruited through social networking. The retention rate exceeded the 85% benchmark, with 30 of the 32 participants (94%) completing the trial. The individual who dropped out was a result of time commitment to the study.

4.1.3 Secondary outcomes: Inferential statistical analysis of the tested variables

Normality distribution of parametric data

Prior to data analysis, a test of normality was performed for all study variables between study groups (BFRT and control). The Shapiro-Wilk test was used for this purpose. The results of this test are shown in the following table (Table 4.3):

Table 4.3: the normality test for study variables

	Shapiro-Wilk		
Study variables	Statistic	df	Sig.
VO2_max_Pre	.926	30	.039
sixMWT_Pre	.910	30	.015
IR_Pre	.840	30	.000

The results of the tests of normality in the table above show that the study variables of the two groups (BFRT, Control) are not normally distributed, as the P-values of the Shapiro test are less than 0.05. (figure4.8)

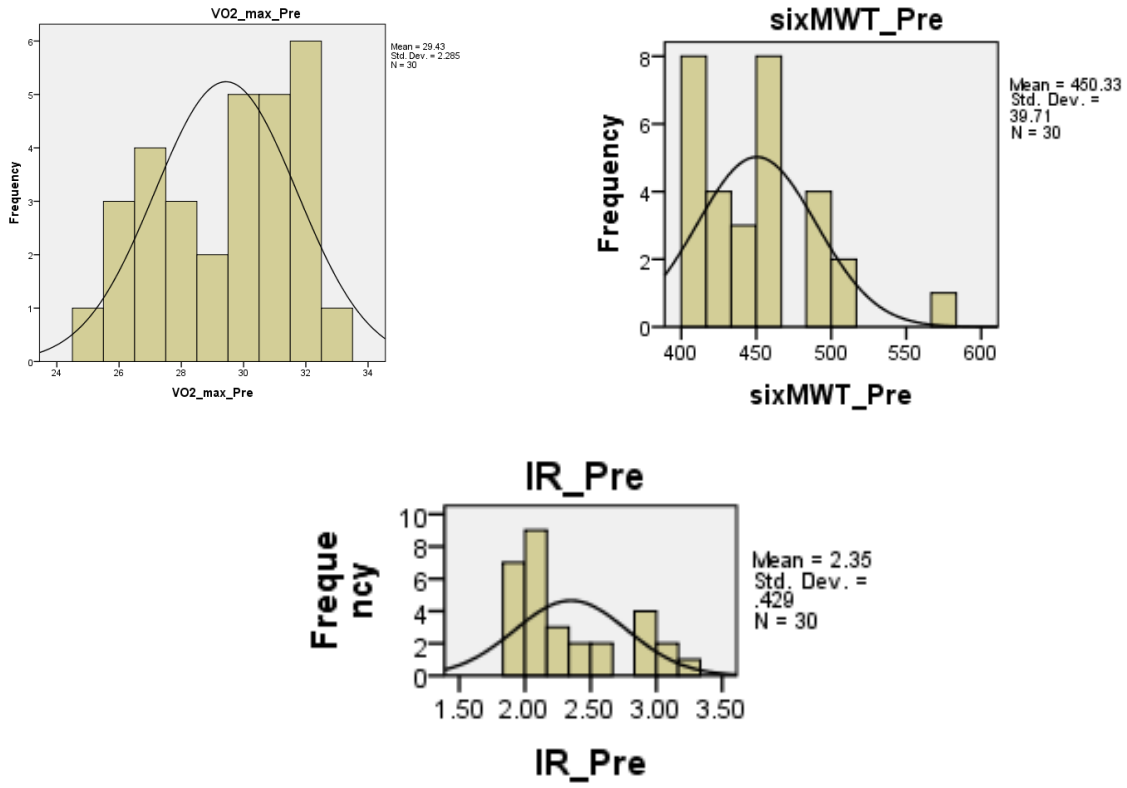


Figure 4.8: Histogram with normal distribution for VO2Max, 6MWT and IR

First test: VO2 Max

Test variables between groups at baseline, pre and post within group and post test for both groups.

The results in Table 4.4 shows no significant difference in of VO2 max pre-test among intervention group and control group, P value was .935 >.05.

Table 4.4: Testing VO2 Max Mean pre-test between both groups

Mann-Whitney U test	VO2Max pre Mean at baseline ± SD	Median	Interquartile Range	Sig
intervention	29.47 ± 2.35	30.00	5	.935
Control	33.93 ± 1.98	30.00	4	

The results in table 4.5 shows a significant difference in the VO2 max pre and post test of VO2 max among the intervention group, P value was .000 > .05; also it shows significant difference in the VO2 max pre and post test among the control group, P value was .000 > .05. VO2 max was significantly increased in both groups.

Table 4.5: Testing VO2 Max Mean pre and post-test for both groups

test	VO2Max pre Mean at baseline ± SD	VO2Max pre Mean at the end ±SD	Mean Difference	T test	df	Sig	**Z**
intervention	29.47 ± 2.35	33.93 ± 1.98	-4.467-	-33.500-	14	.000	**.000**
Control	29.40 ± 2.29	30.53 ± 2.26	-1.133-	-5.906-	14	.000	**.001**

Table 4.6 Shows the mean and SD at post-test of VO2Max in the intervention and control groups. The results shows that there was a significant difference between the intervention

and control groups in aerobic capacity (VO2Max) at post-test (P = .000 <0.05) in favor of intervention group.

Note : Cohen's d = (30.53 - 33.93)/2.124618 = 1.600288.

The average VO2 Max of participants who were in intervention group is 1.600288 standard deviations greater than the participants who were in control group.

Table 4.6: Testing VO2Max Mean Post the intervention between both groups

Test	Mean post intervention ±SD	Mean post Control±SD	Mean Difference	T test	df	Sig.(2 tailed)
VO2Max	33.93 ± 1.981	30.53±2.264	3.400	4.378	28	.000

In VO2Max, the intervention group VO2Max Mean improves from 29.47 at pre-test to 33.93 at post-test, while control group improves from 29.40 to 30.53, as showed in Figure 4-9.

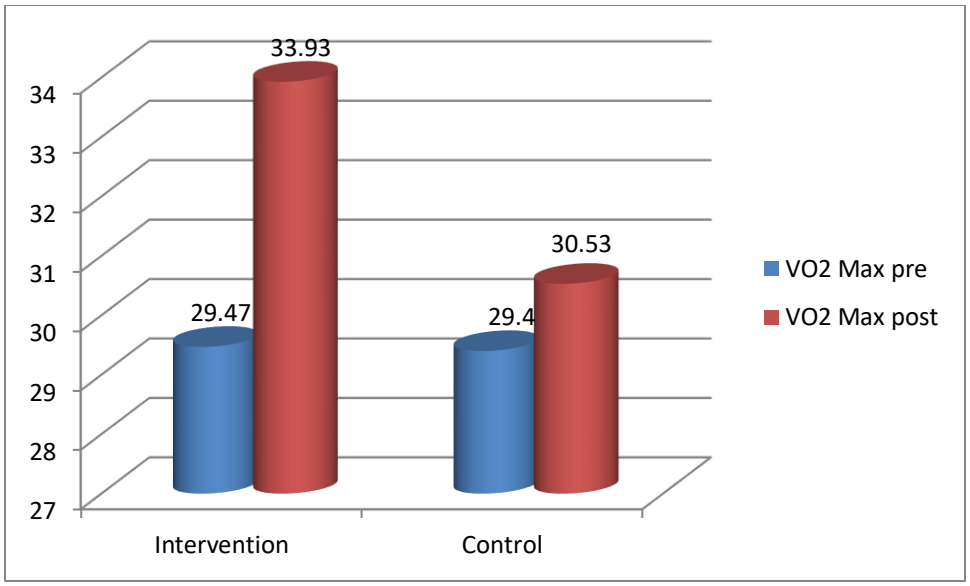


Figure 4-9: VO2Max means' differences in both groups pre-test and post-test

Second Test: 6minute walk test

The results in Table 4.7 shows no significant difference in of 6MWT pre-test among intervention group and control group, P value was .838 >.05.

Table 4.7: Testing 6MWT Mean pre-test between both groups

Mann-Whitney U test	6MWT pre Mean at baseline ± SD	Median	Interquartile Range	Sig
intervention	446.73 ± 33.87	451.00	49	.838
Control	453.93 ± 45.72	449.00	76	

The results in Table 4.8 show a significant difference in 6MWT before and after the test among the intervention group, P value was .000 < .05; also it shows a significant difference in 6MWT before and after the test among the control group, P value was .000 < .05. The 6MWT was significantly increased in both groups.

Table 4.8: Testing 6MWT Mean pre and post-test of both groups

Test	6MWT Mean at baseline ± SD	6MWT Mean at the end ±SD	Difference	df	t-test	Sig.	**Z**
6MWT in intervention	446.73 ± 33.87	569.87 ± 49.27	-123.133-	14	-11.011-	.000	**.001**
6MWT in Control	453.93 ± 45.72	463.07 ± 34.85	-1.133-	14	-5.906-	.000	**.010**

Table 4.9 Shows the mean and SD at post-test of 6MWT in the intervention and control group. The results shows that there was a significant difference between the intervention and control group in 6MWT at post-test (P = .000 <0.05) in favor of BFRT group.

Table 4.9: 6MWT Post the intervention between both groups

Test	Mean post BFRT ±SD	Mean post Control±SD	Mean Difference	T test	df	Sig.(2 tailed)
6MWT	569.87 ±49.27	463.07±34.85	106.800	6.854	28	.000

Note : Cohen's d = (463.07 - 569.87)/42.676388 = 2.502555.

The average 6MWT of participants who were in intervention group is 2.502555standard deviations greater than the participants who were in control group.

In 6MWT, the intervention group 6MWT Mean improves from 446.73 at pre-test to 569.87 at post-test, while control group improves from 453.93 to 463.07, as showed in Figure 4-10.

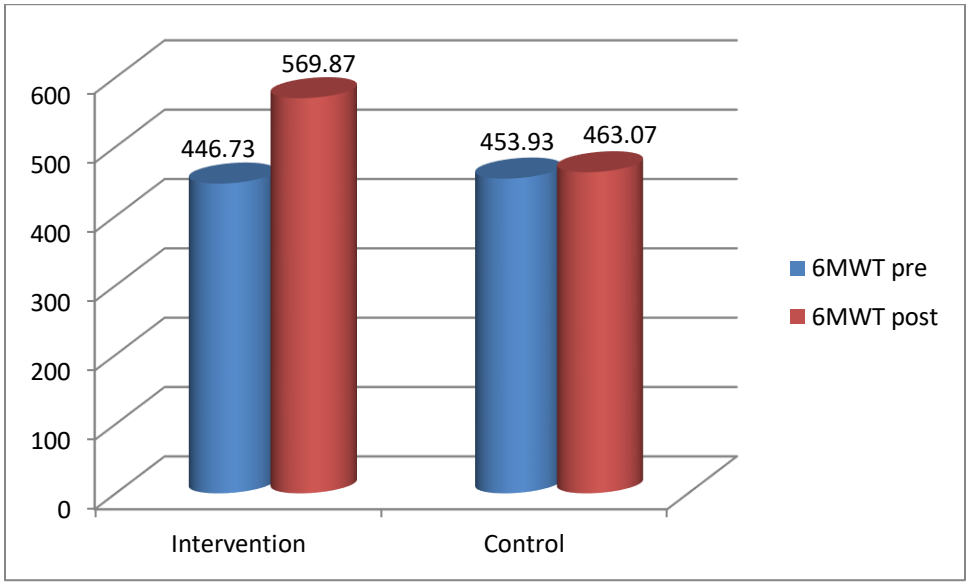


Figure 4-10: 6MWT means' differences in both groups pre-test and post-test

Third: Insulin sensitivity

The results in Table 4.10 shows no significant difference in of IR pre-test among intervention group and control group, P value was .967 >.05.

Table 4.10: Testing IR Mean pre-test between both groups

Mann-Whitney U test	IR pre Mean at baseline ± SD	Median	Interquartile Range	Sig
intervention	2.38± .45	2.11	.99	.967
Control	2.31± .40	2.11	.56	

The results in Table 4.11 shows a significant difference in IR pre and post-test among intervention group, P value was.000 < .05; while in the control group it shows no significant difference in pre and post-test of IR, P value was.263 > .05.

Table 4.1: Testing IR Mean pre and post-test of both groups

Test	IR Mean at baseline ± SD	IR Mean at the end ±SD	Difference	df	T test	Sig.	**Z**
IR in intervention	2.38 ± .45	1.91 ± .47	.47267	14	15.320	.000	**.001**
IR in Control	2.31± .40	2.39 ± .48	-.08402-	14	-1.167-	.263	**.955**

Table 4.12 Shows the mean and SD at post-test of IR in the intervention and Control. The results shows that there was a significant difference between the intervention and Control groups in insulin sensitivity (IR) at post-test (P = .011 <0.05) in favor of BFRT group.(figure 4-11).

Table 4.2: IR Post the intervention between both groups

MANN-WHITNEY U-TEST	Mean post ±SD	Median	Interquartile Range	Sig.
IR in BFRT	2.15±.52	2.0350	.69	.001
IR in Control	2.39±.48	2.1900	.82	

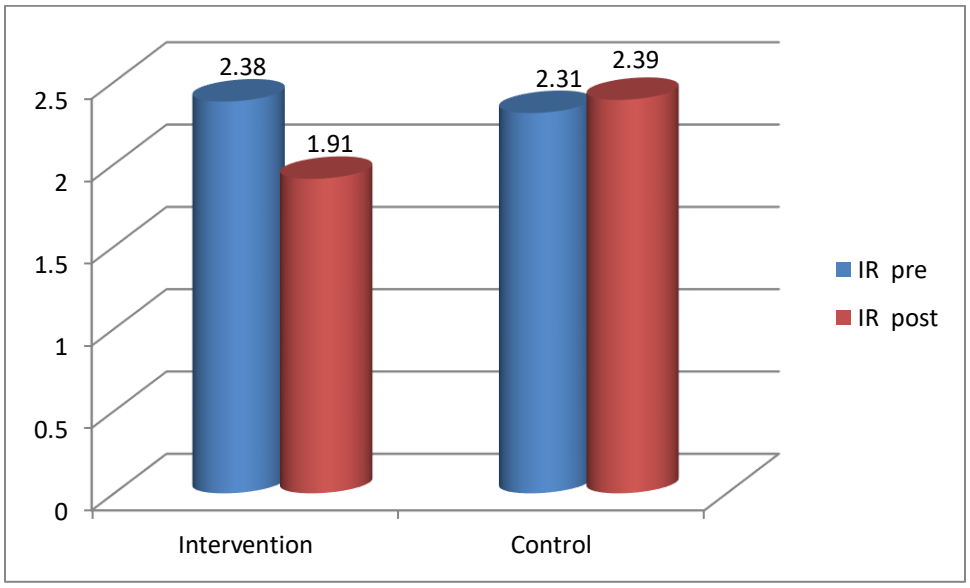


Figure 4-11: IR means' differences in both groups pre-test and post-test

Fourth: Physical function(SF-36 physical)

Testing variables in between groups at baseline and post-test for both groups

Table 4.13 exhibits Physical function in both groups pre-test and post-test, it shown all the sample from both groups are considered as a moderate level of physical function at baseline analysis. While Physical function increased from "moderate" to." high" status in BFRT group, the "moderate" level remain the same in Control group.

Table 4.3: of the Physical function of both groups (pre and post-test

		Frequency percent Pre-test	**And Frequency And percent Post-test**
Patient Group		**N (%)**	**N(%)**
Intervention	low	0 (0)	0(0)
	moderate	**15(100%)**	0(00)
	high	0(0)	**15(100%)**
Control	low	0(0)	0(0)
	moderate	**15(100%)**	**15(100%)**
	high	0(0)	0(0)

Correlations between Study variables:

Table 4.14 shows that (age, onset, smoking status, sugar accumulation) were not significantly correlated with any of the dependent variables (VO2max, IR, 6MWT) as they did not show a statistically significant correlation ($p>0.05$). Statistical significance for α was set at ($P<0.05$).

Table 4.4: Correlations between Study variables

variables with outcomes.		Spearman-correlations	Sig
age	VO2Max	.093	.624
	IR	.206	.275
	6MWT	.091	.631
onset	VO2Max	.121	.522
	IR	.137	.472
	6MWT	.008	.967
smoking state	VO2Max	-.232-	.218
	IR	.055	.775
	6MWT	-.043-	.822
sugar accumulation	VO2Max	-.121-	.524
	IR	.073	.700
	6MWT	.011	.952

Potential harm

The BFRT intervention was proposed to participants in the experimental group to increase their level of AC, reduce IR and improve physical fitness and quality of life. However, due to the small sample size of the present feasibility study, any conclusion about the potential efficacy of the BFRT intervention in relation to these variables would be highly speculative.

The risks involved for study participation were minimal; however, safety was highly monitored and one participant in the control arm experienced an exhaustion that was controlled immediately. A good positive feedback from all participants regarding pressure

comfort during technique with no adverse events were observed with the experimental intervention.

4.2 Results Discussion

limitations

While conducting this feasibility study, many limitations were facing the whole process, decision making according to the evidence based literature was the first challenge. Blood flow training protocol were vary among the past studies in case of applications of technique procedures. Beside the variety of technique parameters, the type of exercise was vary. BFR with aerobic exercise (BFR-AE) is less standardized comparing with resistance exercise (BFR-RE) in term of cuff widths, pressure and intensities during exercise(Patterson et al., 2019b). A guidelines by Patterson et al in 2019 has been presented a recommend model of exercise prescription of BFR-AE, BFR-RE and passively without exercise for enhanced muscle stren`1`gth and hypertrophy(Patterson et al., 2019b).

In healthy and young population the literature were more organized. Many systematic reviews recently tried to summarize the benefits of BFR training despite of its application variety. Part of the reviews have been focused on the target population such as on athletes(Castilla-López et al., 2022)(Smith et al., 2022)(Wortman et al., 2021) In younger and older adults(Bennett & Slattery, 2019b) and in healthy older Adults(Centner et al., 2019)(Labata-Lezaun et al., 2022)(T. Zhang et al., 2022). While in rehabilitation sitting the literature were less comprehensive expect of specific condition such as in knee osteoarthritis(Grantham et al., 2021)(Álvarez et al., 2021)(Minniti et al., 2020), After

Anterior Cruciate Ligament(Kruse et al., 2012), in cardiovascular diseases(Angelopoulos et al., 2023)(Cuyul-Vásquez et al., 2020). One study by Saatmann et al in 2021 has been reviewing the possibility of using blood flow restriction exercise in type 2 diabetes(Saatmann et al., 2021).

The second challenge was about data collection; despite the large number of T2D in the society, the study hardly collect this number of participants. Also, because the study was conducted by mainly one investigator, the study was loss of blinding(subject were aware which group they were in, therapist and assessor was the same person).

The last one was about the longtime of treatment course (4 weeks) and the loss of follow up due to the Israel occupation and continuation difficulties. These limitations can be overcome in a future definitive RCT.

Generalizability of findings

although, In practice and clinical research, safety issues are of utmost importance, and it is common to use rigorous exclusion criteria to enhance the perceived safety of trials, the generalizability of trial results is hindered and answers to crucial clinical questions are delayed. A large RCT is needed to defiantly determine the safety and effectiveness of BFR Aerobic training among patients with T2D.

Interpretation

This Feasibility RCT is the first to assess the efficacy of aerobic exercise with BFRT to aerobic exercise alone in the management of patients with diabetes mellitus. Overall, both

exercise effectively increased aerobic capacity, decreased IR scores, and increased physical function after 4 weeks of the intervention. To the best of the study team's knowledge, one review study the possibility effect of BFR exercise for maintaining physical performance and health in T2D(Saatmann et al., 2021).

The primary objective of the study was to determine the feasibility of carrying out BFR aerobic training for DT2. This pilot study consisted of 30 diabetic participant, n=15 per study arm. The sample size calculation for a pilot RCT has been determined to be adequate, with 15 participants per study arm(Julious & Owen, 2006).

The mean age of the BFRT group was 52, while the mean age of the control group was 53, which was expected as the inclusion criteria ranged from 40 to 65. Regarding onset, the mean onset in the BFRT group was 5.23 years compared to 4.80 years in the control group.

In term of aerobic capacity, Even thought, the control group perceived a low intensity aerobic exercise the same as intervention one, taking into consideration the study population's abilities, a significance enhance of VO2Max was observed in both groups pre and post intervention, but with larger effect size in intervention one and a significance difference form control group post intervention. This may be related to that aerobic exercise alone can improve physical fitness (VO2peak, maximum heart rate) in type two diabetes(Yang et al., 2014)and in elderly(Ozaki et al., 2011). Boulé et al in their meat analysis of randomized control trial reported >10% improvement in VO2max values after a low intensity aerobic exercise program(Normand G. Boulé et al., 2001). Adding BFR to the intervention led to greater change in VO2Max which was confirmed in other similar

populations in other past literature(Hughes et al., 2017)(Tanaka & Takarada, 2018)(Cuyul-Vásquez et al., 2020). Conversely, Abe et al in 2010 reported that the estimated VO2peak was not significantly improved in the elderly participants after 6 weeks of slow (67 m/min) BFR walk training(Abe et al., 2010). That was because the average exercise intensity (about 45% of HRR) was less than the necessary to evoke changes which is must to be 50% of VO2max. while in this study the average speed and intensity of exercise sessions were in the required average. The improvement of aerobic capacity using BFRT in individuals with T2D could be related to the metabolic control improvement by improving muscle metabolism, lowering insulin and HbA1c levels, or increasing GLUT4 translocation.

Combined to the first outcome, aerobic exercise may be associated with better physical function and greater BMI reduction(Łuniewski et al., 2023). In this feasibility study, the BMI in both study group recorded no significance differences between and within group statistic. The reason for this could be directly related the relatively short treatment period and loss of dietary control. According to the Łuniewski et al review of Guidelines reported that there is no single method can provide the desired outcome; instead it is attainable by a combination of diet therapy, lifestyle change, and physical activity and other diverse methods(Łuniewski et al., 2023).

Regarding to participants physical function, the intervention group increased from moderate to high level while in control group remain the same. That's confirm the past studies regarding the BFR with AE in enhancing endurance performance and aerobic metabolism beside its effects on muscle mass and strength(Saatmann et al., 2021). In contrast the control group had no significance improvement, this result could be possibly

related to that they did not reach the required recommended level of physical exercise per week to make any changes in their physical function.

Regarding to 6 minute walk test, as a valid core test used in vast studies with different populations(Nolen-Doerr et al., 2018)(Bohannon & Crouch, 2017). This feasibility study used it as a functional exercise capacity test with T2D. These findings are consistent with past studies on the same population used the test after an exercise interventions(Janssen & Connelly, 2021) and revealed an improvements in 6MWT scores the same as our results. Although both groups improved their distance walked after the four-week programme, the intervention group showed a greater improvement in distance walked on the 6MWT after four weeks of training compared to the control group. Performance on the 6MWT is a good indicator of cardiopulmonary function in the body and has a strong correlation with treadmill-based tests of aerobic capacity(Matthew John Clarkson et al., 2017). So, improvements in aerobic capacity most likely contributed to BFRW's longer 6MWT distance.

One of the core findings in this study is Insulin resistance. The IR was a novel inclusion to the present study as a measure of insulin resistance more commonly associated with T2D. Our study using HOMA scale because of its simplicity, a remarkable improvement of HOMA-IR index in intervention group pre and post 4 weeks of training whereas was recorded, while no significance differences in control one. This result cannot be separated from other outcomes results. Regular exercise program to the people with T2DM has positive effects on the level of glycemic control and disease complications, whereas the reduction in cumulative sugar will lead to decrease in insulin resistance(Yavari et al.,

2014)(Zanuso et al., 2010). Because the muscle tissue have the highest level of insulin sensitivity, regular physical activity aids the body cells boost glucose and thus lower glucose levels in the blood, also aids with weight loss and controlling blood cholesterol and pressure(Asif, 2014).

A majority of researchers believe that enhanced GLUT4 translocation to the surface membrane is the primary cause of increased insulin action, which is only observed in the working muscles(Maarbjerg et al., 2011). Some literature have been studied the effects of one bout of endurance exercise on muscle insulin sensitivity in people with IR and showed a positive results by increased insulin-stimulated glucose transport/phosphorylation(Van Dijk et al., 2012). Others studied that long term effects of endurance exercise three times a week significantly improved whole-body insulin sensitivity and normalized muscle glucose transport/phosphorylation within 6 weeks in first-degree relatives of patients with type 2 diabetes(Perseghin et al., 1996)(Najafipour et al., 2017).

Even though, careful attention must be given to this result considering the variety of exercise type, intensity and duration in relation to the past literature. This study reports only the acute effects of AE with BFR on IR in people with T2D.

Chapter Five

5.1 Conclusions

5.2 Recommendations

5.1 Conclusions

After conducting this feasibility study, the researcher concluded the following:

- AE with BFRT is efficient in reducing insulin resistance according to HOMA score.
- AE with BFRT is efficient in increasing physical function according to SF-36 scale.
- Both AE with BFRT and AE alone are effective in improving VO2Max scores. However, the BFRT group recorded a higher score on the VO2Max.

- Both AE with BFRT and AE alone are effective in improving 6MWT scores. However, the BFRT group recorded a higher score on the 6MWT.

5.2 Recommendations

The researcher's recommendations, based on the results of this study, are as follows

<u>Recommendations for physiotherapists:</u>

- Consider the implementation of AE with BFRT in the management of T2D.

Promote the use of standardised outcome measures in national hospital physiotherapy departments to allow comparison between the results of this study and potential future studies.

Recommendations for Researchers, Conduction of further studies to investigate:

- The long term effect of using AE with BFRT on IR and AC.
- The effect of BFRT with other types of exercise such as resistance exercise on the same population.
- The effect of the suggested protocol on wider ages and larger sample size.
- The effects of this intervention on patients who were excluded from this study, such as those with co-morbidities.
- The effect of this intervention but on other clinical populations, such as type one diabetes.

References

Abbas, M. J., Dancy, M. E., Marigi, E. M., Khalil, L. S., Jildeh, T. R., Buckley, P. J., Gillett, J., Burgos, W., & Okoroha, K. R. (2022). An Automated Technique for the Measurement of Limb Occlusion Pressure During Blood Flow Restriction Therapy Is Equivalent to Previous Gold Standard. *Arthroscopy, Sports Medicine, and Rehabilitation*, *4*(3), e1127. https://doi.org/10.1016/J.ASMR.2022.04.002

Abe, T., Sakamaki, M., Fujita, S., Ozaki, H., Sugaya, M., Sato, Y., & Nakajima, T. (2010). Effects of low-intensity walk training with restricted leg blood flow on muscle strength and aerobic capacity in older adults. *Journal of Geriatric Physical Therapy*, *33*(1), 34–40. https://doi.org/10.1097/JPT.0B013E3181D07A73

Adeva-Andany, M. M., Pérez-Felpete, N., Fernández-Fernández, C., Donapetry-García, C., & Pazos-García, C. (2016). Liver glucose metabolism in humans. *Bioscience Reports*, *36*(6), 416. https://doi.org/10.1042/BSR20160385

Afroz, A., Alramadan, M. J., Hossain, M. N., Romero, L., Alam, K., Magliano, D. J., & Billah, B. (2018). Cost-of-illness of type 2 diabetes mellitus in low and lower-middle income countries: a systematic review. *BMC Health Services Research*, *18*(1). https://doi.org/10.1186/S12913-018-3772-8

Alfonso-Rosa, R. M., Del Pozo-Cruz, B., Del Pozo-Cruz, J., Sañudo, B., & Rogers, M. E. (2014). Test–Retest Reliability and Minimal Detectable Change Scores for Fitness Assessment in Older Adults with Type 2 Diabetes. *Rehabilitation Nursing*, *39*(5), 260–268. https://doi.org/10.1002/RNJ.111

Álvarez, C. B., Santamaría, P. I. K., Fernández-Matías, R., Pecos-Martín, D., Achalandabaso-Ochoa, A., Fernández-Carnero, S., Martínez-Amat, A., & Gallego-Izquierdo, T. (2021). Comparison of Blood Flow Restriction Training versus Non-Occlusive Training in Patients with Anterior Cruciate Ligament Reconstruction or Knee Osteoarthritis: A Systematic Review. *Journal of Clinical Medicine*, *10*(1), 1–23. https://doi.org/10.3390/JCM10010068

Alzboon, G., & Vural, G. (2019). Factors Influencing the Quality of Life of Healthy Pregnant Women in North Jordan. *Medicina*, *55*(6). https://doi.org/10.3390/MEDICINA55060278

Angelopoulos, P., Tsekoura, M., Mylonas, K., Tsigkas, G., Billis, E., Tsepis, E., & Fousekis, K. (2023). The effectiveness of blood flow restriction training in cardiovascular disease patients: A scoping review. *Journal of Frailty, Sarcopenia and Falls*, *8*(2), 107–117. https://doi.org/10.22540/JFSF-08-107

Asif, M. (2014). The prevention and control the type-2 diabetes by changing lifestyle and dietary pattern. *Journal of Education and Health Promotion*, *3*(1), 1. https://doi.org/10.4103/2277-9531.127541

Association, A. D. (2013a). Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care*, *36*(Suppl 1), S67. https://doi.org/10.2337/DC13-S067

Association, A. D. (2013b). Standards of Medical Care in Diabetes—2013. *Diabetes Care*, *36*(Suppl 1), S11. https://doi.org/10.2337/DC13-S011

Association, A. D. (2021). 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2021. *Diabetes Care*, *44*(Supplement_1), S15–S33. https://doi.org/10.2337/DC21-S002

Baker, B. S., Stannard, M. S., Duren, D. L., Cook, J. L., & Stannard, J. P. (2020). Does Blood Flow Restriction Therapy in Patients Older Than Age 50 Result in Muscle Hypertrophy, Increased Strength, or Greater Physical Function? A Systematic Review.

Clinical Orthopaedics and Related Research, *478*(3), 593. https://doi.org/10.1097/CORR.0000000000001090

Balducci, S., D'Errico, V., Haxhi, J., Sacchetti, M., Orlando, G., Cardelli, P., Vitale, M., Bollanti, L., Conti, F., Zanuso, S., Lucisano, G., Nicolucci, A., & Pugliese, G. (2019). Effect of a Behavioral Intervention Strategy on Sustained Change in Physical Activity and Sedentary Behavior in Patients With Type 2 Diabetes: The IDES_2 Randomized Clinical Trial. *JAMA*, *321*(9), 880–890. https://doi.org/10.1001/JAMA.2019.0922

Bennett, H., & Slattery, F. (2019a). Effects of blood flow restriction training on aerobic capacity and performance: A systematic review. *Journal of Strength and Conditioning Research*, *33*(2), 572–583. https://doi.org/10.1519/JSC.0000000000002963

Bennett, H., & Slattery, F. (2019b). Effects of blood flow restriction training on aerobic capacity and performance: A systematic review. *Journal of Strength and Conditioning Research*, *33*(2), 572–583. https://doi.org/10.1519/JSC.0000000000002963

Bennett, H., & Slattery, F. (2019c). Effects of Blood Flow Restriction Training on Aerobic Capacity and Performance: A Systematic Review. *Journal of Strength and Conditioning Research*, *33*(2), 572–583. https://doi.org/10.1519/JSC.0000000000002963

Biazon, T. M. P. C., Ugrinowitsch, C., Soligon, S. D., Oliveira, R. M., Bergamasco, J. G., Borghi-Silva, A., & Libardi, C. A. (2019). The Association Between Muscle Deoxygenation and Muscle Hypertrophy to Blood Flow Restricted Training Performed at High and Low Loads. *Frontiers in Physiology*, *10*(APR). https://doi.org/10.3389/FPHYS.2019.00446

BMI Calculator. (n.d.). Retrieved August 17, 2023, from https://www.calculator.net/bmi-calculator.html

Bock, G., Chittilapilly, E., Basu, R., Toffolo, G., Cobelli, C., Chandramouli, V., Landau, B. R., & Rizza, R. A. (2007). Contribution of hepatic and extrahepatic insulin resistance

to the pathogenesis of impaired fasting glucose: role of increased rates of gluconeogenesis. *Diabetes*, *56*(6), 1703–1711. https://doi.org/10.2337/DB06-1776

Bohannon, R. W., & Crouch, R. (2017). Minimal clinically important difference for change in 6-minute walk test distance of adults with pathology: a systematic review. *Journal of Evaluation in Clinical Practice*, *23*(2), 377–381. https://doi.org/10.1111/JEP.12629

Boulé, N. G., Kenny, G. P., Haddad, E., Wells, G. A., & Sigal, R. J. (2003). Meta-analysis of the effect of structured exercise training on cardiorespiratory fitness in Type 2 diabetes mellitus. *Diabetologia*, *46*(8), 1071–1081. https://doi.org/10.1007/S00125-003-1160-2

Boulé, Normand G., Haddad, E., Kenny, G. P., Wells, G. A., & Sigal, R. J. (2001). Effects of Exercise on Glycemic Control and Body Mass in Type 2 Diabetes Mellitus: A Meta-analysis of Controlled Clinical Trials. *JAMA*, *286*(10), 1218–1227. https://doi.org/10.1001/JAMA.286.10.1218

Brazier, J. E., Harper, R., Jones, N. M. B., O'Cathain, A., Thomas, K. J., Usherwood, T., & Westlake, L. (1992). Validating the SF-36 health survey questionnaire: new outcome measure for primary care. *BMJ : British Medical Journal*, *305*(6846), 160. https://doi.org/10.1136/BMJ.305.6846.160

Cannata, F., Vadalà, G., Russo, F., Papalia, R., Napoli, N., & Pozzilli, P. (2020). Beneficial Effects of Physical Activity in Diabetic Patients. *Journal of Functional Morphology and Kinesiology 2020, Vol. 5, Page 70*, *5*(3), 70. https://doi.org/10.3390/JFMK5030070

Castilla-López, C., Molina-Mula, J., & Romero-Franco, N. (2022). Blood flow restriction during training for improving the aerobic capacity and sport performance of trained athletes: A systematic review and meta-analysis. *Journal of Exercise Science and Fitness*, *20*(2), 190–197. https://doi.org/10.1016/J.JESF.2022.03.004

Centner, C., Wiegel, P., Gollhofer, A., & König, D. (2019). Effects of Blood Flow

Restriction Training on Muscular Strength and Hypertrophy in Older Individuals: A Systematic Review and Meta-Analysis. *Sports Medicine (Auckland, N.Z.)*, *49*(1), 95–108. https://doi.org/10.1007/S40279-018-0994-1

Cerf, M. E. (2013). Beta Cell Dysfunction and Insulin Resistance. *Frontiers in Endocrinology*, *4*(MAR). https://doi.org/10.3389/FENDO.2013.00037

Chadt, A., & Al-Hasani, H. (2020). Glucose transporters in adipose tissue, liver, and skeletal muscle in metabolic health and disease. *Pflugers Archiv*, *472*(9), 1273. https://doi.org/10.1007/S00424-020-02417-X

Chen, X., Maldonado, E., Defronzo, R. A., & Tripathy, D. (2021). Impaired Suppression of Glucagon in Obese Subjects Parallels Decline in Insulin Sensitivity and Beta-Cell Function. *The Journal of Clinical Endocrinology and Metabolism*, *106*(5), 1398. https://doi.org/10.1210/CLINEM/DGAB019

Chimen, M., Kennedy, A., Nirantharakumar, K., Pang, T. T., Andrews, R., & Narendran, P. (2012). What are the health benefits of physical activity in type 1 diabetes mellitus? A literature review. *Diabetologia*, *55*(3), 542–551. https://doi.org/10.1007/S00125-011-2403-2/TABLES/2

Clarkson, Matthew J., May, A. K., & Warmington, S. A. (2020). Is there rationale for the cuff pressures prescribed for blood flow restriction exercise? A systematic review. *Scandinavian Journal of Medicine & Science in Sports*, *30*(8), 1318–1336. https://doi.org/10.1111/SMS.13676

Clarkson, Matthew John, Conway, L., & Warmington, S. A. (2017). Blood flow restriction walking and physical function in older adults: A randomized control trial. *Journal of Science and Medicine in Sport*, *20*(12), 1041–1046. https://doi.org/10.1016/J.JSAMS.2017.04.012

Colberg, S. R., Sigal, R. J., Fernhall, B., Regensteiner, J. G., Blissmer, B. J., Rubin, R. R., Chasan-Taber, L., Albright, A. L., & Braun, B. (2010). Exercise and Type 2 Diabetes:

The American College of Sports Medicine and the American Diabetes Association: joint position statement. *Diabetes Care*, *33*(12), e147. https://doi.org/10.2337/DC10-9990

Committee, A. D. A. P. P. (2022). 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2022. *Diabetes Care*, *45*(Supplement_1), S17–S38. https://doi.org/10.2337/DC22-S002

Criqui, M. H., McClelland, R. L., McDermott, M. M., Allison, M. A., Blumenthal, R. S., Aboyans, V., Ix, J. H., Burke, G. L., Liu, K., & Shea, S. (2010). The Ankle-Brachial Index and Incident Cardiovascular Events in the Multi-Ethnic Study of Atherosclerosis (MESA). *Journal of the American College of Cardiology*, *56*(18), 1506. https://doi.org/10.1016/J.JACC.2010.04.060

Cuyul-Vásquez, I., Leiva-Sepúlveda, A., Catalán-Medalla, O., & Berríos-Contreras, L. (2020). [Blood flow restriction training for people with cardiovascular disease: An exploratory review]. *Rehabilitacion*, *54*(2), 116–127. https://doi.org/10.1016/J.RH.2020.01.005

Czech, M. P. (2017). Insulin action and resistance in obesity and type 2 diabetes. *Nature Medicine*, *23*(7), 804. https://doi.org/10.1038/NM.4350

de Oliveira, M. F. M., Caputo, F., Corvino, R. B., & Denadai, B. S. (2016). Short-term low-intensity blood flow restricted interval training improves both aerobic fitness and muscle strength. *Scandinavian Journal of Medicine & Science in Sports*, *26*(9), 1017–1025. https://doi.org/10.1111/SMS.12540

De Rosa, S., Arcidiacono, B., Chiefari, E., Brunetti, A., Indolfi, C., & Foti, D. P. (2018). Type 2 Diabetes Mellitus and Cardiovascular Disease: Genetic and Epigenetic Links. *Frontiers in Endocrinology*, *9*(JAN), 1. https://doi.org/10.3389/FENDO.2018.00002

De Sousa, R. A. L., De Magalhaes, C. O. D., Dias, I. R., De Oliveira, L. R. S., Improta-Caria, A. C., & Cassilhas, R. C. (2022). Cross talk mechanisms of aerobic exercise

training on obesity, type 2 diabetes, and Alzheimer's disease: the role of insulin resistance. *Revista Da Associação Médica Brasileira*, *68*(7), 963. https://doi.org/10.1590/1806-9282.20211210

DeFronzo, R. A., & Tripathy, D. (2009). Skeletal Muscle Insulin Resistance Is the Primary Defect in Type 2 Diabetes. *Diabetes Care*, *32*(Suppl 2), S157. https://doi.org/10.2337/DC09-S302

Diabetes. (n.d.). Retrieved January 16, 2023, from https://www.who.int/health-topics/diabetes#tab=tab_1

Ebbeling, C. B., Ward, A., Puleo, E. M., Widrick, J., & Rippe, J. M. (1991). Development of a single-stage submaximal treadmill walking test. *Medicine and Science in Sports and Exercise*, *23*(8), 966–973. https://doi.org/10.1249/00005768-199108000-00014

Eldridge, S. M., Chan, C. L., Campbell, M. J., Bond, C. M., Hopewell, S., Thabane, L., Lancaster, G. A., Altman, D., Bretz, F., Campbell, M., Cobo, E., Craig, P., Davidson, P., Groves, T., Gumedze, F., Hewison, J., Hirst, A., Hoddinott, P., Lamb, S. E., … Tugwell, P. (2016). CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *BMJ (Clinical Research Ed.)*, *355*. https://doi.org/10.1136/BMJ.I5239

English - PEDro. (n.d.). Retrieved June 16, 2023, from https://pedro.org.au/

Fell, B. L., Hanekom, S., & Heine, M. (2021). Six-minute walk test protocol variations in low-resource settings – A scoping review. *The South African Journal of Physiotherapy*, *77*(1). https://doi.org/10.4102/SAJP.V77I1.1549

Ferrannini, E., & DeFronzo, R. A. (2015). Insulin actions in vivo: glucose metabolism. *International Textbook of Diabetes Mellitus*, 211–233. https://doi.org/10.1002/9781118387658.CH14

Festa, A., D'Agostino, R., Howard, G., Mykkänen, L., Tracy, R. P., & Haffner, S. M. (2000). Chronic Subclinical Inflammation as Part of the Insulin Resistance Syndrome.

Circulation, *102*(1), 42–47. https://doi.org/10.1161/01.CIR.102.1.42

Fry, C. S., Glynn, E. L., Drummond, M. J., Timmerman, K. L., Fujita, S., Abe, T., Dhanani, S., Volpi, E., & Rasmussen, B. B. (2010). Blood flow restriction exercise stimulates mTORC1 signaling and muscle protein synthesis in older men. *Journal of Applied Physiology*, *108*(5), 1199. https://doi.org/10.1152/JAPPLPHYSIOL.01266.2009

Fujita, S., Abe, T., Drummond, M. J., Cadenas, J. G., Dreyer, H. C., Sato, Y., Volpi, E., & Rasmussen, B. B. (2007). Blood flow restriction during low-intensity resistance exercise increases S6K1 phosphorylation and muscle protein synthesis. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, *103*(3), 903–910. https://doi.org/10.1152/JAPPLPHYSIOL.00195.2007

Gadke, D. L., Kratochwill, T. R., & Gettinger, M. (2021). Incorporating feasibility protocols in intervention research. *Journal of School Psychology*, *84*, 1–18. https://doi.org/10.1016/J.JSP.2020.11.004

Galicia-Garcia, U., Benito-Vicente, A., Jebari, S., Larrea-Sebal, A., Siddiqi, H., Uribe, K. B., Ostolaza, H., & Martín, C. (2020). Pathophysiology of Type 2 Diabetes Mellitus. *International Journal of Molecular Sciences*, *21*(17), 1–34. https://doi.org/10.3390/IJMS21176275

Garber, C. E., Blissmer, B., Deschenes, M. R., Franklin, B. A., Lamonte, M. J., Lee, I. M., Nieman, D. C., & Swain, D. P. (2011). Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: Guidance for prescribing exercise. *Medicine and Science in Sports and Exercise*, *43*(7), 1334–1359. https://doi.org/10.1249/MSS.0B013E318213FEFB

Garcia, M. J., McNamara, P. M., Gordon, T., & Kannell, W. B. (1974). Morbidity and Mortality in Diabetics In the Framingham Population: Sixteen Year Follow-up Study.

Diabetes, *23*(2), 105–111. https://doi.org/10.2337/DIAB.23.2.105

Gastaldelli, A. (2022). Measuring and estimating insulin resistance in clinical and research settings. *Obesity (Silver Spring, Md.)*, *30*(8), 1549. https://doi.org/10.1002/OBY.23503

González, K., Fuentes, J., & Márquez, J. L. (2017). Physical Inactivity, Sedentary Behavior and Chronic Diseases. *Korean Journal of Family Medicine*, *38*(3), 111–115. https://doi.org/10.4082/KJFM.2017.38.3.111

Grantham, B., Korakakis, V., & O'Sullivan, K. (2021). Does blood flow restriction training enhance clinical outcomes in knee osteoarthritis: A systematic review and meta-analysis. *Physical Therapy in Sport : Official Journal of the Association of Chartered Physiotherapists in Sports Medicine*, *49*, 37–49. https://doi.org/10.1016/J.PTSP.2021.01.014

Group, D. P. P. R. (2002). REDUCTION IN THE INCIDENCE OF TYPE 2 DIABETES WITH LIFESTYLE INTERVENTION OR METFORMIN. *The New England Journal of Medicine*, *346*(6), 393. https://doi.org/10.1056/NEJMOA012512

Grundy, S. M. (2012). Pre-diabetes, metabolic syndrome, and cardiovascular risk. *Journal of the American College of Cardiology*, *59*(7), 635–643. https://doi.org/10.1016/J.JACC.2011.08.080

Grundy, S. M., Benjamin, I. J., Burke, G. L., Chait, A., Eckel, R. H., Howard, B. V., Mitch, W., Smith, S. C., & Sowers, J. R. (1999). Diabetes and Cardiovascular Disease. *Circulation*, *100*(10), 1134–1146. https://doi.org/10.1161/01.CIR.100.10.1134

Guermazi, M., Allouch, C., Yahia, M., Huissa, T. B. A., Ghorbel, S., Damak, J., Mrad, M. F., & Elleuch, M. H. (2012). Translation in Arabic, adaptation and validation of the SF-36 Health Survey for use in Tunisia. *Annals of Physical and Rehabilitation Medicine*, *55*(6), 388–403. https://doi.org/10.1016/J.REHAB.2012.05.003

Gulsin, G. S., Henson, J., Brady, E. M., Sargeant, J. A., Wilmot, E. G., Athithan, L., Htike,

Z. Z., Marsh, A. M., Biglands, J. D., Kellman, P., Khunti, K., Webb, D., Davies, M. J., Yates, T., & McCann, G. P. (2020). Cardiovascular Determinants of Aerobic Exercise Capacity in Adults With Type 2 Diabetes. *Diabetes Care*, *43*(9), 2248. https://doi.org/10.2337/DC20-0706

Gundermann, D. M., Fry, C. S., Dickinson, J. M., Walker, D. K., Timmerman, K. L., Drummond, M. J., Volpi, E., & Rasmussen, B. B. (2012). Reactive hyperemia is not responsible for stimulating muscle protein synthesis following blood flow restriction exercise. *Journal of Applied Physiology*, *112*(9), 1520. https://doi.org/10.1152/JAPPLPHYSIOL.01267.2011

Hawley, J. A., & Lessard, S. J. (2008). Exercise training-induced improvements in insulin action. *Acta Physiologica (Oxford, England)*, *192*(1), 127–135. https://doi.org/10.1111/J.1748-1716.2007.01783.X

Henning, R. J. (2018). Type-2 diabetes mellitus and cardiovascular disease. *Https://Doi.Org/10.2217/Fca-2018-0045*, *14*(6), 491–509. https://doi.org/10.2217/FCA-2018-0045

Holland, A. E., Spruit, M. A., Troosters, T., Puhan, M. A., Pepin, V., Saey, D., McCormack, M. C., Carlin, B. W., Sciurba, F. C., Pitta, F., Wanger, J., MacIntyre, N., Kaminsky, D. A., Culver, B. H., Revill, S. M., Hernandes, N. A., Andrianopoulos, V., Camillo, C. A., Mitchell, K. E., … Singh, S. J. (2014). An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. *European Respiratory Journal*, *44*(6), 1428–1446. https://doi.org/10.1183/09031936.00150314

HOMA-IR: A Test of Insulin Resistance + Ways to Decrease It - SelfDecode Labs. (n.d.). Retrieved July 15, 2023, from https://labs.selfdecode.com/blog/homa-ir/

HOMA-IR (Homeostatic Model Assessment for Insulin Resistance). (n.d.). Retrieved July 15, 2023, from https://www.mdcalc.com/calc/3120/homa-ir-homeostatic-model-assessment-insulin-

resistance?fbclid=IwAR0wdxcd565YqFWm0yjdyUthlxxPBY1Lv0TkMA7Rt9SPAbmQJPnQMCR4fpA

Hu, X., Mok, Y., Ding, N., Sullivan, K. J., Lutsey, P. L., Schrack, J. A., Palta, P., & Matsushita, K. (2022). Physical Function and Subsequent Risk of Cardiovascular Events in Older Adults: The Atherosclerosis Risk in Communities Study. *Journal of the American Heart Association*, *11*(17). https://doi.org/10.1161/JAHA.121.025780

Hughes, L., Jeffries, O., Waldron, M., Rosenblatt, B., Gissane, C., Paton, B., & Patterson, S. D. (2018). Influence and reliability of lower-limb arterial occlusion pressure at different body positions. *PeerJ*, *2018*(5). https://doi.org/10.7717/PEERJ.4697/SUPP-1

Hughes, L., Paton, B., Rosenblatt, B., Gissane, C., & Patterson, S. D. (2017). Blood flow restriction training in clinical musculoskeletal rehabilitation: a systematic review and meta-analysis. *British Journal of Sports Medicine*, *51*(13), 1003–1011. https://doi.org/10.1136/BJSPORTS-2016-097071

Hunt, J. E. A., Stodart, C., & Ferguson, R. A. (2016). The influence of participant characteristics on the relationship between cuff pressure and level of blood flow restriction. *European Journal of Applied Physiology*, *116*(7), 1421. https://doi.org/10.1007/S00421-016-3399-6

International Textbook of Diabetes Mellitus, 2 Volume Set - كتب Google. (n.d.). Retrieved August 9, 2023, from https://books.google.ps/books?id=h5WDBgAAQBAJ&pg=PA218&lpg=PA218&dq=The+glucose+enter+the+blood+circulation+at+a+mean+rate+of+220+g+day−1&source=bl&ots=r4ZLHJMoa_&sig=ACfU3U0JKpZ_zo7j3x8jLBjaXB8SA-rGlQ&hl=ar&sa=X&ved=2ahUKEwiE64uXis-AAxVEgv0HHWyYAucQ6AF6BAgwEAM#v=onepage&q=The glucose enter the blood circulation at a mean rate of 220 g day−1&f=false

Jadhav, R. A., Hazari, A., Monterio, A., Kumar, S., & Maiya, A. G. (2017). Effect of Physical Activity Intervention in Prediabetes: A Systematic Review With Meta-analysis. *Journal of Physical Activity and Health*, *14*(9), 745–755. https://doi.org/10.1123/JPAH.2016-0632

Janssen, S. M., & Connelly, D. M. (2021). The effects of exercise interventions on physical function tests and glycemic control in adults with type 2 diabetes: A systematic review. *Journal of Bodywork and Movement Therapies*, *28*, 283–293. https://doi.org/10.1016/J.JBMT.2021.07.022

Jenkins, D. W., & Jenks, A. (2017). Exercise and Diabetes: A Narrative Review. *The Journal of Foot and Ankle Surgery : Official Publication of the American College of Foot and Ankle Surgeons*, *56*(5), 968–974. https://doi.org/10.1053/J.JFAS.2017.06.019

Jiang, G., & Zhang, B. B. (2003). Glucagon and regulation of glucose metabolism. *American Journal of Physiology. Endocrinology and Metabolism*, *284*(4). https://doi.org/10.1152/AJPENDO.00492.2002

Julious, S. A., & Owen, R. J. (2006). Sample size calculations for clinical studies allowing for uncertainty about the variance. *Pharmaceutical Statistics*, *5*(1), 29–37. https://doi.org/10.1002/PST.197

Kadoglou, N. P. E., Iliadis, F., Angelopoulou, N., Perrea, D., Ampatzidis, G., Liapis, C. D., & Alevizos, M. (2007). The anti-inflammatory effects of exercise training in patients with type 2 diabetes mellitus. *European Journal of Cardiovascular Prevention and Rehabilitation : Official Journal of the European Society of Cardiology, Working Groups on Epidemiology & Prevention and Cardiac Rehabilitation and Exercise Physiology*, *14*(6), 837–843. https://doi.org/10.1097/HJR.0B013E3282EFAF50

Kahn, S. E., Cooper, M. E., & Del Prato, S. (2014). PATHOPHYSIOLOGY AND TREATMENT OF TYPE 2 DIABETES: PERSPECTIVES ON THE PAST, PRESENT AND FUTURE. *Lancet*, *383*(9922), 1068. https://doi.org/10.1016/S0140-

6736(13)62154-6

Kambič, T., Novaković, M., Tomažin, K., Strojnik, V., Božič-Mijovski, M., & Jug, B. (2021). Hemodynamic and Hemostatic Response to Blood Flow Restriction Resistance Exercise in Coronary Artery Disease: A Pilot Randomized Controlled Trial. *The Journal of Cardiovascular Nursing*, *36*(5), 507–516. https://doi.org/10.1097/JCN.0000000000000699

Kang, E. S., Yun, Y. S., Park, S. W., Kim, H. J., Ahn, C. W., Song, Y. D., Cha, B. S., Lim, S. K., Kim, K. R., & Lee, H. C. (2005). Limitation of the validity of the homeostasis model assessment as an index of insulin resistance in Korea. *Metabolism: Clinical and Experimental*, *54*(2), 206–211. https://doi.org/10.1016/j.metabol.2004.08.014

Kim, D., Seo, J., Ha, K. H., & Kim, D. J. (2022). Maintaining Physical Activity Is Associated with Reduced Major Adverse Cardiovascular Events in People Newly Diagnosed with Diabetes. *Journal of Obesity & Metabolic Syndrome*, *31*(2), 187. https://doi.org/10.7570/JOMES22007

Kirwan, J. P., Sacks, J., & Nieuwoudt, S. (2017). The essential role of exercise in the management of type 2 diabetes. *Cleveland Clinic Journal of Medicine*, *84*(7 Suppl 1), S15. https://doi.org/10.3949/CCJM.84.S1.03

Kruse, L. M., Gray, B., & Wright, R. W. (2012). Rehabilitation after anterior cruciate ligament reconstruction: A systematic review. *Journal of Bone and Joint Surgery - Series A*, *94*(19), 1737–1748. https://doi.org/10.2106/JBJS.K.01246

Labata-Lezaun, N., Llurda-Almuzara, L., González-Rueda, V., López-de-Celis, C., Cedeño-Bermúdez, S., Bañuelos-Pago, J., & Perez-Bellmunt, A. (2022). Effectiveness of Blood Flow Restriction Training on Muscle Strength and Physical Performance in Older Adults: A Systematic Review and Meta-analysis. *Archives of Physical Medicine and Rehabilitation*, *103*(9), 1848–1857. https://doi.org/10.1016/J.APMR.2021.12.015

Leavens, K. F., & Birnbaum, M. J. (2011). Insulin signaling to hepatic lipid metabolism in

health and disease. *Http://Dx.Doi.Org/10.3109/10409238.2011.562481*, *46*(3), 200–215. https://doi.org/10.3109/10409238.2011.562481

Lebovitz, H. E. (2001). Insulin resistance: definition and consequences. *Experimental and Clinical Endocrinology & Diabetes : Official Journal, German Society of Endocrinology [and] German Diabetes Association*, *109 Suppl 2*(SUPPL. 2). https://doi.org/10.1055/S-2001-18576

Lee, M. C. (2018). Validity of the 6-minute walk test and step test for evaluation of cardio respiratory fitness in patients with type 2 diabetes mellitus. *Journal of Exercise Nutrition & Biochemistry*, *22*(1), 49. https://doi.org/10.20463/JENB.2018.0008

Lee, S. H., Park, S. Y., & Choi, C. S. (2022). Insulin Resistance: From Mechanisms to Therapeutic Strategies. *Diabetes & Metabolism Journal*, *46*(1), 15. https://doi.org/10.4093/DMJ.2021.0280

Lidegaard, L. P., Schwennesen, N., Willaing, I., & Færch, K. (2016). Barriers to and motivators for physical activity among people with Type 2 diabetes: patients' perspectives. *Diabetic Medicine*, *33*(12), 1677–1685. https://doi.org/10.1111/DME.13167

Lin, H. V., & Accili, D. (2011). Hormonal Regulation Of Hepatic Glucose Production In Health And Disease. *Cell Metabolism*, *14*(1), 9. https://doi.org/10.1016/J.CMET.2011.06.003

Lins, L., & Carvalho, F. M. (2016). SF-36 total score as a single measure of health-related quality of life: Scoping review. *SAGE Open Medicine*, *4*, 205031211667172. https://doi.org/10.1177/2050312116671725

Loenneke, J. P., Fahs, C. A., Rossow, L. M., Abe, T., & Bemben, M. G. (2012). The anabolic benefits of venous blood flow restriction training may be induced by muscle cell swelling. *Medical Hypotheses*, *78*(1), 151–154. https://doi.org/10.1016/J.MEHY.2011.10.014

Loenneke, Jeremy P., Abe, T., Wilson, J. M., Ugrinowitsch, C., & Bemben, M. G. (2012). Blood Flow Restriction: How Does It Work? *Frontiers in Physiology*, *3*. https://doi.org/10.3389/FPHYS.2012.00392

Loenneke, Jeremy P., Fahs, C. A., Rossow, L. M., Thiebaud, R. S., Mattocks, K. T., Abe, T., & Bemben, M. G. (2013). Blood flow restriction pressure recommendations: a tale of two cuffs. *Frontiers in Physiology*, *4*. https://doi.org/10.3389/FPHYS.2013.00249

Lovic, D., Piperidou, A., Zografou, I., Grassos, H., Pittaras, A., & Manolis, A. (2020). The Growing Epidemic of Diabetes Mellitus. *Current Vascular Pharmacology*, *18*(2), 104–109. https://doi.org/10.2174/1570161117666190405165911

Łuniewski, M., Matyjaszek-Matuszek, B., & Lenart-Lipińska, M. (2023). Diagnosis and Non-Invasive Treatment of Obesity in Adults with Type 2 Diabetes Mellitus: A Review of Guidelines. *Journal of Clinical Medicine*, *12*(13), 4431. https://doi.org/10.3390/JCM12134431

Lv, C., Sun, Y., Zhang, Z. Y., Aboelela, Z., Qiu, X., & Meng, Z.-X. (2022). β-cell dynamics in type 2 diabetes and in dietary and exercise interventions. *Journal of Molecular Cell Biology*, *14*(7). https://doi.org/10.1093/JMCB/MJAC046

Maarbjerg, S. J., Sylow, L., & Richter, E. A. (2011). Current understanding of increased insulin sensitivity after exercise – emerging candidates. *Acta Physiologica*, *202*(3), 323–335. https://doi.org/10.1111/J.1748-1716.2011.02267.X

Magkos, F., Hjorth, M. F., & Astrup, A. (2020). Diet and exercise in the prevention and treatment of type 2 diabetes mellitus. *Nature Reviews. Endocrinology*, *16*(10), 545–555. https://doi.org/10.1038/S41574-020-0381-5

Masri, B. A., Day, B., Younger, A. S. E., & Jeyasurya, J. (2016). Technique for Measuring Limb Occlusion Pressure that Facilitates Personalized Tourniquet Systems: A Randomized Trial. *Journal of Medical and Biological Engineering*, *36*(5), 644. https://doi.org/10.1007/S40846-016-0173-5

Masuku, S. D., Lekodeba, N., & Meyer-Rath, G. (2022). The costs of interventions for type 2 diabetes mellitus, hypertension and cardiovascular disease in South Africa – a systematic literature review. *BMC Public Health*, *22*(1). https://doi.org/10.1186/S12889-022-14730-4

McClary, K. N., & Massey, P. (2023). Ankle Brachial Index. *Assessment of Preclinical Organ Damage in Hypertension*, 75–79. https://doi.org/10.1007/978-3-319-15603-3_7

McEwen, J. A., Kelly, D. L., Jardanowski, T., & Inkpen, K. (2002). Tourniquet safety in lower leg applications. *Orthopedic Nursing*, *21*(5), 55–62. https://doi.org/10.1097/00006416-200209000-00009

Mendonca, G. V., Vaz, J. R., Pezarat-Correia, P., & Fernhall, B. (2015). Effects of Walking with Blood Flow Restriction on Excess Post-exercise Oxygen Consumption. *International Journal of Sports Medicine*, *36*(3). https://doi.org/10.1055/S-0034-1395508

Miller, B. C., Tirko, A. W., Shipe, J. M., Sumeriski, O. R., & Moran, K. (2021). The Systemic Effects of Blood Flow Restriction Training: A Systematic Review. *International Journal of Sports Physical Therapy*, *16*(4), 978. https://doi.org/10.26603/001C.25791

Minniti, M. C., Statkevich, A. P., Kelly, R. L., Rigsby, V. P., Exline, M. M., Rhon, D. I., & Clewley, D. (2020). The Safety of Blood Flow Restriction Training as a Therapeutic Intervention for Patients With Musculoskeletal Disorders: A Systematic Review. *American Journal of Sports Medicine*, *48*(7), 1773–1785. https://doi.org/10.1177/0363546519882652

Minokoshi, Y., Kahn, C. R., & Kahn, B. B. (2003). Tissue-specific Ablation of the GLUT4 Glucose Transporter or the Insulin Receptor Challenges Assumptions about Insulin Action and Glucose Homeostasis. *Journal of Biological Chemistry*, *278*(36), 33609–33612. https://doi.org/10.1074/jbc.R300019200

Mouser, J. G., Mattocks, K. T., Dankel, S. J., Buckner, S. L., Jessee, M. B., Bell, Z. W., Abe, T., & Loenneke, J. P. (2019). Very-low-load resistance exercise in the upper body with and without blood flow restriction: cardiovascular outcomes. *Applied Physiology, Nutrition, and Metabolism = Physiologie Appliquee, Nutrition et Metabolisme*, *44*(3), 288–292. https://doi.org/10.1139/APNM-2018-0325

Najafipour, F., Mobasseri, M., Yavari, A., Nadrian, H., Aliasgarzadeh, A., Abbasi, N. M., Niafar, M., Gharamaleki, J. H., & Sadra, V. (2017). Effect of regular exercise training on changes in HbA1c, BMI and VO2max among patients with type 2 diabetes mellitus: an 8-year trial. *BMJ Open Diabetes Research and Care*, *5*(1), e000414. https://doi.org/10.1136/BMJDRC-2017-000414

Nascimento, D. da C., Rolnick, N., Neto, I. V. de S., Severin, R., & Beal, F. L. R. (2022). A Useful Blood Flow Restriction Training Risk Stratification for Exercise and Rehabilitation. *Frontiers in Physiology*, *13*. https://doi.org/10.3389/FPHYS.2022.808622

Nolen-Doerr, E., Crick, K., Saha, C., de Groot, M., Pillay, Y., Shubrook, J. H., Donley, D., & Hornsby, W. G. (2018). Six-Minute Walk Test as a Predictive Measure of Exercise Capacity in Adults With Type 2 Diabetes. *Cardiopulmonary Physical Therapy Journal*, *29*(3), 124–129. https://doi.org/10.1097/CPT.0000000000000080

Occlusion of arterial flow in the extremities at subsystolic pressures through the use of wide tourniquet cuffs - PubMed. (n.d.). Retrieved February 4, 2023, from https://pubmed.ncbi.nlm.nih.gov/8425355/

Orsmond, G. I., & Cohn, E. S. (2015). The Distinctive Features of a Feasibility Study: Objectives and Guiding Questions. *OTJR : Occupation, Participation and Health*, *35*(3), 169–177. https://doi.org/10.1177/1539449215578649

Osta, N. El, Kanso, F., Saad, R., Khabbaz, L. R., Fakhouri, J., & Osta, L. El. (2019). Validation of the Arabic version of the SF-36, generic questionnaire of quality of life related to health among the elderly in Lebanon. *Eastern Mediterranean Health*

Journal = La Revue de Sante de La Mediterranee Orientale = Al-Majallah Al-Sihhiyah Li-Sharq Al-Mutawassit, *25*(10), 706–714. https://doi.org/10.26719/EMHJ.19.041

Ozaki, H., Sakamaki, M., Yasuda, T., Fujita, S., Ogasawara, R., Sugaya, M., Nakajima, T., & Abe, T. (2011). Increases in Thigh Muscle Volume and Strength by Walk Training with Leg Blood Flow Reduction in Older Participants. *The Journals of Gerontology: Series A*, *66A*(3), 257–263. https://doi.org/10.1093/GERONA/GLQ182

Ozaki, H., Yasuda, T., Ogasawara, R., Sakamaki-Sunaga, M., Naito, H., & Abe, T. (2013). Effects of high-intensity and blood flow-restricted low-intensity resistance training on carotid arterial compliance: role of blood pressure during training sessions. *European Journal of Applied Physiology*, *113*(1), 167–174. https://doi.org/10.1007/S00421-012-2422-9

Pan, B., Ge, L., Xun, Y. qin, Chen, Y. jing, Gao, C. yun, Han, X., Zuo, L. qian, Shan, H. qian, Yang, K. hu, Ding, G. wu, & Tian, J. hui. (2018). Exercise training modalities in patients with type 2 diabetes mellitus: a systematic review and network meta-analysis. *The International Journal of Behavioral Nutrition and Physical Activity*, *15*(1). https://doi.org/10.1186/S12966-018-0703-3

Patterson, S. D., Hughes, L., Head, P., Warmington, S., & Brandner, C. (2017). Blood flow restriction training: A novel approach to augment clinical rehabilitation: How to do it. *British Journal of Sports Medicine*, *51*(23), 1648–1649. https://doi.org/10.1136/BJSPORTS-2017-097738

Patterson, S. D., Hughes, L., Warmington, S., Burr, J., Scott, B. R., Owens, J., Abe, T., Nielsen, J. L., Libardi, C. A., Laurentino, G., Neto, G. R., Brandner, C., Martin-Hernandez, J., & Loenneke, J. (2019a). Blood Flow Restriction Exercise: Considerations of Methodology, Application, and Safety. *Frontiers in Physiology*, *10*(MAY), 533. https://doi.org/10.3389/FPHYS.2019.00533

Patterson, S. D., Hughes, L., Warmington, S., Burr, J., Scott, B. R., Owens, J., Abe, T., Nielsen, J. L., Libardi, C. A., Laurentino, G., Neto, G. R., Brandner, C., Martin-Hernandez, J., & Loenneke, J. (2019b). Blood Flow Restriction Exercise: Considerations of Methodology, Application, and Safety. *Frontiers in Physiology*, *10*(MAY), 533. https://doi.org/10.3389/FPHYS.2019.00533

Pearson, T., Wattis, J. A. D., King, J. R., MacDonald, I. A., & Mazzatti, D. J. (2016). The Effects of Insulin Resistance on Individual Tissues: An Application of a Mathematical Model of Metabolism in Humans. *Bulletin of Mathematical Biology*, *78*(6), 1189. https://doi.org/10.1007/S11538-016-0181-1

Pedersen, C., Kraft, G., Edgerton, D. S., Scott, M., Farmer, B., Smith, M., Laneve, D. C., Williams, P. E., Moore, L. M., & Cherrington, A. D. (2020). The kinetics of glucagon action on the liver during insulin-induced hypoglycemia. *American Journal of Physiology - Endocrinology and Metabolism*, *318*(5), E779. https://doi.org/10.1152/AJPENDO.00466.2019

Peng, Y., Ou, Y., Wang, K., Wang, Z., & Zheng, X. (2023). The effect of low volume high-intensity interval training on metabolic and cardiorespiratory outcomes in patients with type 2 diabetes mellitus: A systematic review and meta-analysis. *Frontiers in Endocrinology*, *13*. https://doi.org/10.3389/FENDO.2022.1098325

Perseghin, G., Price, T. B., Petersen, K. F., Roden, M., Cline, G. W., Gerow, K., Rothman, D. L., & Shulman, G. I. (1996). Increased Glucose Transport–Phosphorylation and Muscle Glycogen Synthesis after Exercise Training in Insulin-Resistant Subjects. *Https://Doi.Org/10.1056/NEJM199610313351804*, *335*(18), 1357–1362. https://doi.org/10.1056/NEJM199610313351804

Petersen, K. F., Dufour, S., Savage, D. B., Bilz, S., Solomon, G., Yonemitsu, S., Cline, G. W., Befroy, D., Zemany, L., Kahn, B. B., Papademetris, X., Rothman, D. L., & Shulman, G. I. (2007). INAUGURAL ARTICLE by a Recently Elected Academy Member:The role of skeletal muscle insulin resistance in the pathogenesis of the

metabolic syndrome. *Proceedings of the National Academy of Sciences of the United States of America*, *104*(31), 12587. https://doi.org/10.1073/PNAS.0705408104

Plows, J. F., Stanley, J. L., Baker, P. N., Reynolds, C. M., & Vickers, M. H. (2018). The Pathophysiology of Gestational Diabetes Mellitus. *International Journal of Molecular Sciences*, *19*(11). https://doi.org/10.3390/IJMS19113342

Ramnanan, C. J., Edgerton, D. S., Kraft, G., & Cherrington, A. D. (2011). Physiologic action of glucagon on liver glucose metabolism. *Diabetes, Obesity & Metabolism*, *13*(Suppl 1), 118. https://doi.org/10.1111/J.1463-1326.2011.01454.X

Regulation of blood glucose homeostasis during prolonged exercise - PubMed. (n.d.). Retrieved May 2, 2023, from https://pubmed.ncbi.nlm.nih.gov/17646701/

Renzi, C. P., Tanaka, H., & Sugawara, J. (2010). Effects of Leg Blood Flow Restriction during Walking on Cardiovascular Function. *Medicine and Science in Sports and Exercise*, *42*(4), 726. https://doi.org/10.1249/MSS.0B013E3181BDB454

Rui, L. (2014). Energy Metabolism in the Liver. *Comprehensive Physiology*, *4*(1), 177. https://doi.org/10.1002/CPHY.C130024

Saatmann, N., Zaharia, O. P., Loenneke, J. P., Roden, M., & Pesta, D. H. (2021). Effects of Blood Flow Restriction Exercise and Possible Applications in Type 2 Diabetes. *Trends in Endocrinology and Metabolism: TEM*, *32*(2), 106–117. https://doi.org/10.1016/J.TEM.2020.11.010

Saeedi, P., Petersohn, I., Salpea, P., Malanda, B., Karuranga, S., Unwin, N., Colagiuri, S., Guariguata, L., Motala, A. A., Ogurtsova, K., Shaw, J. E., Bright, D., & Williams, R. (2019). Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Research and Clinical Practice*, *157*, 107843. https://doi.org/10.1016/j.diabres.2019.107843

Sampath Kumar, A., Maiya, A. G., Shastry, B. A., Vaishali, K., Ravishankar, N., Hazari,

A., Gundmi, S., & Jadhav, R. (2019). Exercise and insulin resistance in type 2 diabetes mellitus: A systematic review and meta-analysis. *Annals of Physical and Rehabilitation Medicine*, *62*(2), 98–103. https://doi.org/10.1016/J.REHAB.2018.11.001

Samuel, V. T., & Shulman, G. I. (2012). Integrating Mechanisms for Insulin Resistance: Common Threads and Missing Links. *Cell*, *148*(5), 852. https://doi.org/10.1016/J.CELL.2012.02.017

Sarafidis, P. A., Lasaridis, A. N., Nilsson, P. M., Pikilidou, M. I., Stafilas, P. C., Kanaki, A., Kazakos, K., Yovos, J., & Bakris, G. L. (2007). Validity and reproducibility of HOMA-IR, 1/HOMA-IR, QUICKI and McAuley's indices in patients with hypertension and type II diabetes. *Journal of Human Hypertension*, *21*(9), 709–716. https://doi.org/10.1038/SJ.JHH.1002201

Sartor, F., Vernillo, G., De Morree, H. M., Bonomi, A. G., La Torre, A., Kubis, H. P., & Veicsteinas, A. (2013). Estimation of maximal oxygen uptake via submaximal exercise testing in sports, clinical, and home settings. *Sports Medicine (Auckland, N.Z.)*, *43*(9), 865–873. https://doi.org/10.1007/S40279-013-0068-3

Schmidt, A. M. (2018). Highlighting Diabetes – the Epidemic Continues. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *38*(1), e1. https://doi.org/10.1161/ATVBAHA.117.310221

Sgrò, P., Emerenziani, G. Pietro, Antinozzi, C., Sacchetti, M., & Di Luigi, L. (2021). Exercise as a drug for glucose management and prevention in type 2 diabetes mellitus. *Current Opinion in Pharmacology*, *59*, 95–102. https://doi.org/10.1016/J.COPH.2021.05.006

Sharabi, K., Tavares, C. D. J., Rines, A. K., & Puigserver, P. (2015). Molecular Pathophysiology of Hepatic Glucose Production. *Molecular Aspects of Medicine*, *46*,

21. https://doi.org/10.1016/J.MAM.2015.09.003

Sheikh, K. A., Yagoub, U., Elsatouhy, M., Al Sanosi, R., & Mohamud, S. A. (2015). Reliability and Validity of the Arabic Version of the SF-36 Health Survey Questionnaire in Population of Khat Chewers—Jazan Region-Kingdom of Saudi Arabia. *Applied Research in Quality of Life*, *10*(1), 1–13. https://doi.org/10.1007/S11482-013-9291-1

Sieljacks, P., Knudsen, L., Wernbom, M., & Vissing, K. (2018). Body position influences arterial occlusion pressure: implications for the standardization of pressure during blood flow restricted exercise. *European Journal of Applied Physiology*, *118*(2), 303–312. https://doi.org/10.1007/S00421-017-3770-2

Sigal, R. J., Kenny, G. P., Wasserman, D. H., Castaneda-Sceppa, C., & White, R. D. (2006a). Physical activity/exercise and type 2 diabetes: a consensus statement from the American Diabetes Association. *Diabetes Care*, *29*(6), 1433–1438. https://doi.org/10.2337/DC06-9910

Sigal, R. J., Kenny, G. P., Wasserman, D. H., Castaneda-Sceppa, C., & White, R. D. (2006b). Physical Activity/Exercise and Type 2 DiabetesA consensus statement from the American Diabetes Association. *Diabetes Care*, *29*(6), 1433–1438. https://doi.org/10.2337/DC06-9910

Singleton, N., & Turner, A. (1993). Measuring patients' views of their health. SF 36 is suitable for elderly patients. *BMJ (Clinical Research Ed.)*, *307*(6896), 126–127. https://doi.org/10.1136/BMJ.307.6896.126-B

Sluik, D., Buijsse, B., Muckelbauer, R., Kaaks, R., Teucher, B., Johnsen, N. F., Tjønneland, A., Overvad, K., Østergaard, J. N., Amiano, P., Ardanaz, E., Bendinelli, B., Pala, V., Tumino, R., Ricceri, F., Mattiello, A., Spijkerman, A. M. W., Monninkhof, E. M., May, A. M., … Nöthlings, U. (2012). Physical Activity and Mortality in Individuals With Diabetes Mellitus: A Prospective Study and Meta-analysis. *Archives of Internal Medicine*, *172*(17), 1285–1295.

https://doi.org/10.1001/ARCHINTERNMED.2012.3130

SM, H., MP, S., HP, H., BD, M., & JK, P. (1990). Cardiovascular risk factors in confirmed prediabetic individuals. Does the clock for coronary heart disease start ticking before the onset of clinical diabetes? *JAMA*, *263*(21), 2893–2898. https://doi.org/10.1001/JAMA.263.21.2893

Smith, N. D. W., Scott, B. R., Girard, O., & Peiffer, J. J. (2022). Aerobic Training With Blood Flow Restriction for Endurance Athletes: Potential Benefits and Considerations of Implementation. *Journal of Strength and Conditioning Research*, *36*(12), 3541–3550. https://doi.org/10.1519/JSC.0000000000004079

Soulaimana, I., Bruneau, L., Tisseaux, A., Safieddine, M., Debussche, X., Lafarge, S., Falissard, B., Ferdynus, C., & Huiart, L. (2023). Psychometric properties of a Creole version of Medical Outcome Study – Short Form 36 among type II diabetes patients on Reunion Island. *Frontiers in Public Health*, *11*. https://doi.org/10.3389/FPUBH.2023.1186153

Stumvoll, M., Goldstein, B. J., & Van Haeften, T. W. (2005). Type 2 diabetes: principles of pathogenesis and therapy. *Lancet (London, England)*, *365*(9467), 1333–1346. https://doi.org/10.1016/S0140-6736(05)61032-X

Sugawara, J., Tomoto, T., & Tanaka, H. (2015). Impact of leg blood flow restriction during walking on central arterial hemodynamics. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology*, *309*(7), R732–R739. https://doi.org/10.1152/AJPREGU.00095.2015

Sun, H., Saeedi, P., Karuranga, S., Pinkepank, M., Ogurtsova, K., Duncan, B. B., Stein, C., Basit, A., Chan, J. C. N., Mbanya, J. C., Pavkov, M. E., Ramachandaran, A., Wild, S. H., James, S., Herman, W. H., Zhang, P., Bommer, C., Kuo, S., Boyko, E. J., & Magliano, D. J. (2022). IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Research and Clinical Practice*, *183*. https://doi.org/10.1016/J.DIABRES.2021.109119

Takarada, Y., Nakamura, Y., Aruga, S., Onda, T., Miyazaki, S., & Ishii, N. (2000). Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. *Journal of Applied Physiology (Bethesda, Md. : 1985)*, *88*(1), 61–65. https://doi.org/10.1152/JAPPL.2000.88.1.61

Tanaka, Y., & Takarada, Y. (2018). The impact of aerobic exercise training with vascular occlusion in patients with chronic heart failure. *ESC Heart Failure*, *5*(4), 586. https://doi.org/10.1002/EHF2.12285

Tanasescu, M., Leitzmann, M. F., Rimm, E. B., & Hu, F. B. (2003). Physical activity in relation to cardiovascular disease and total mortality among men with type 2 diabetes. *Circulation*, *107*(19), 2435–2439. https://doi.org/10.1161/01.CIR.0000066906.11109.1F

Teich, T., Zaharieva, D. P., & Riddell, M. C. (2019). Advances in Exercise, Physical Activity, and Diabetes Mellitus. *Https://Home.Liebertpub.Com/Dia*, *21*(S1), S112–S122. https://doi.org/10.1089/DIA.2019.2509

The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection - PubMed. (n.d.). Retrieved July 23, 2023, from https://pubmed.ncbi.nlm.nih.gov/1593914/

Tipton, C. M. (2014). The history of "Exercise Is Medicine" in ancient civilizations. *Advances in Physiology Education*, *38*(2), 109. https://doi.org/10.1152/ADVAN.00136.2013

Titchenell, P. M., Lazar, M. A., & Birnbaum, M. J. (2017). Unraveling the Regulation of Hepatic Metabolism by Insulin. *Trends in Endocrinology and Metabolism: TEM*, *28*(7), 497. https://doi.org/10.1016/J.TEM.2017.03.003

Unger, J., & Parkin, C. G. (2010). Type 2 diabetes: an expanded view of pathophysiology and therapy. *Postgraduate Medicine*, *122*(3), 145–157. https://doi.org/10.3810/PGM.2010.05.2152

Van Dijk, J. W., Manders, R. J. F., Tummers, K., Bonomi, A. G., Stehouwer, C. D. A., Hartgens, F., & Van Loon, L. J. C. (2012). Both resistance- and endurance-type exercise reduce the prevalence of hyperglycaemia in individuals with impaired glucose tolerance and in insulin-treated and non-insulin-treated type 2 diabetic patients. *Diabetologia*, *55*(5), 1273. https://doi.org/10.1007/S00125-011-2380-5

Vega, R. B., Whytock, K. L., Gassenhuber, J., Goebel, B., Tillner, J., Agueusop, I., Truax, A. D., Yu, G., Carnero, E., Kapoor, N., Gardell, S., Sparks, L. M., & Smith, S. R. (2021). A Metabolomic Signature of Glucagon Action in Healthy Individuals With Overweight/Obesity. *Journal of the Endocrine Society*, *5*(9). https://doi.org/10.1210/JENDSO/BVAB118

Vopat, B. G., Vopat, L. M., Bechtold, M. M., & Hodge, K. A. (2020). Blood Flow Restriction Therapy: Where We Are and Where We Are Going. *The Journal of the American Academy of Orthopaedic Surgeons*, *28*(12), e493–e500. https://doi.org/10.5435/JAAOS-D-19-00347

Waddoups, L., Wagner, D., Fallon, J., & Heath, E. (2008). Validation of a single-stage submaximal treadmill walking test. *Journal of Sports Sciences*, *26*(5), 491–497. https://doi.org/10.1080/02640410701591425

Walters, S. J., Dos Anjos Henriques-Cadby, I. B., Bortolami, O., Flight, L., Hind, D., Jacques, R. M., Knox, C., Nadin, B., Rothwell, J., Surtees, M., & Julious, S. A. (2017). Recruitment and retention of participants in randomised controlled trials: a review of trials funded and published by the United Kingdom Health Technology Assessment Programme. *BMJ Open*, *7*(3), e015276. https://doi.org/10.1136/BMJOPEN-2016-015276

WEATHERHOLT, A. M., VANWYE, W. R., LOHMANN, J., & OWENS, J. G. (2019). The Effect of Cuff Width for Determining Limb Occlusion Pressure: A Comparison of Blood Flow Restriction Devices. *International Journal of Exercise Science*, *12*(3), 136. /pmc/articles/PMC6355123/

Weisman, I. M., Marciniuk, D., Martinez, F. J., Testing Measurements Frank Sciurba, E., Sue, D., Myers Bruce Johnson, J., Whipp, B., Zeballos, J., Beck, K., Mahler, D., Cotes, J., Sietsema, K., Dyspnea, U., Killian, K., & Casaburi, R. (2012). ATS/ACCP Statement on Cardiopulmonary Exercise Testing. *Https://Doi.Org/10.1164/Rccm.167.2.211*, *167*(2), 211–277. https://doi.org/10.1164/RCCM.167.2.211

Wortman, R. J., Brown, S. M., Savage-Elliott, I., Finley, Z. J., & Mulcahey, M. K. (2021). Blood Flow Restriction Training for Athletes: A Systematic Review. *The American Journal of Sports Medicine*, *49*(7), 1938–1944. https://doi.org/10.1177/0363546520964454

Yamazoe, M., Hisamatsu, T., Miura, K., Kadowaki, S., Zaid, M., Kadota, A., Torii, S., Miyazawa, I., Fujiyoshi, A., Arima, H., Sekikawa, A., Maegawa, H., Horie, M., & Ueshima, H. (2016). Relationship of Insulin Resistance to Prevalence and Progression of Coronary Artery Calcification beyond Metabolic Syndrome Components. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *36*(8), 1703–1708. https://doi.org/10.1161/ATVBAHA.116.307612

Yang, Z., Scott, C. A., Mao, C., Tang, J., & Farmer, A. J. (2014). Resistance exercise versus aerobic exercise for type 2 diabetes: a systematic review and meta-analysis. *Sports Medicine (Auckland, N.Z.)*, *44*(4), 487–499. https://doi.org/10.1007/S40279-013-0128-8

Yaribeygi, H., Farrokhi, F. R., Butler, A. E., & Sahebkar, A. (2019). Insulin resistance: Review of the underlying molecular mechanisms. *Journal of Cellular Physiology*, *234*(6), 8152–8161. https://doi.org/10.1002/JCP.27603

Yasuda, T., Fukumura, K., Uchida, Y., Koshi, H., Iida, H., Masamune, K., Yamasoba, T., Sato, Y., & Nakajima, T. (2015). Effects of Low-Load, Elastic Band Resistance Training Combined With Blood Flow Restriction on Muscle Size and Arterial Stiffness in Older Adults. *The Journals of Gerontology: Series A*, *70*(8), 950–958.

https://doi.org/10.1093/GERONA/GLU084

Yavari, A., Najafipoor, F., Aliasgarzadeh, A., Niafar, M., & Mobasseri, M. (2014). Original paper
EFFECT OF AEROBIC EXERCISE, RESISTANCE TRAINING OR COMBINED TRAINING ON GLYCAEMIC CONTROL AND CARDIO-VASCULAR RISK FACTORS IN PATIENTS WITH TYPE 2 DIABETES. *Biology of Sport*, *29*(2), 135–143. https://doi.org/10.5604/20831862.990466

Younger, A. S. E., McEwen, J. A., & Inkpen, K. (2004). Wide contoured thigh cuffs and automated limb occlusion measurement allow lower tourniquet pressures. *Clinical Orthopaedics and Related Research*, *428*(428), 286–293. https://doi.org/10.1097/01.BLO.0000142625.82654.B3

Zanuso, S., Jimenez, A., Pugliese, G., Corigliano, G., & Balducci, S. (2010). Exercise for the management of type 2 diabetes: A review of the evidence. *Acta Diabetologica*, *47*(1), 15–22. https://doi.org/10.1007/S00592-009-0126-3/TABLES/2

Zhang, T., Wang, X., & Wang, J. (2022). Effect of blood flow restriction combined with low-intensity training on the lower limbs muscle strength and function in older adults: A meta-analysis. *Experimental Gerontology*, *164*. https://doi.org/10.1016/J.EXGER.2022.111827

Zhang, X., Gregg, E. W., Williamson, D. F., Barker, L. E., Thomas, W., Bullard, K. M. K., Imperatore, G., Williams, D. E., & Albright, A. L. (2010). A1C Level and Future Risk of Diabetes: A Systematic Review. *Diabetes Care*, *33*(7), 1665–1673. https://doi.org/10.2337/DC09-1939

Zheng, Y., Ley, S. H., & Hu, F. B. (2018). Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nature Reviews. Endocrinology*, *14*(2), 88–98. https://doi.org/10.1038/NRENDO.2017.151

Appendices

Appendix 1

Assessment form

Appendix A: Outpatient admission from

AAUP- MEDICAL REHABILITATION COMPLEX

OUTPATIENT ADMISSION FORM

PART I:

PATIENT DETAILS

PATIENT COUD:

e date:_____/___/_____	Time:	OCCUPATION:
	Age:	Address
M or F	Mobile:	Marital Status: ☐ Single ☐ Married

Have you been admitted to us previously?

☐ Yes No ☐

If yes, when:_____

Referring Dr.: _____

Family Dr.:_____

PERSON TO CONTACT / NEXT OF KIN

	Mobile:	Address
nship to patient		

ACCOUNT DETAILS

HEALTH care insurance exists? Yes ☐ No ☐

Fund Name:_____
Member No:_____
Insurance Company:_____
Address:_____

☐ UNINSURED (Payment methods):_____

MEDICAL HISTORY & SUBJECTIVE PATIENT INFORMATION – MEDICAL ASSESSMENT FORM

PART 2:

1. Do you have any **Allergies** or Sensitivities to any drugs, materials or foods?

☐ Yes No ☐

Please list:_____

2. Do you have any **heart problems**? Yes ☐ No ☐

- ☐ Heart attack
- ☐ Vascular heart disease
- ☐ Bypass surgery
- ☐ Stent
- ☐ Palpitations
- ☐ Heart valve replacement
- ☐ Pacemaker – date last checked: _____

Heart specialist name: _____

Phone:_____

3. Have you had, or have you/family member any of the following **conditions/diseases**?

- ☐ Blood clots
- ☐ Hypertension
- ☐ Asthma/ Lung disease
- ☐ Diabetes mellitus: Type 1 or Type 2
- ☐ Cancer
- ☐ Stroke
- ☐ Epilepsy
- ☐ Neck or jaw trouble
- ☐ Ankle swelling
- ☐ Arthritis
- ☐ Bladder / kidney disease
- ☐ Bowel problems

☐ Hepatitis

☐ HIV/AIDS

☐ Depression / Anxiety/ Sleep problems

☐ Current infection/Fever

Comment:_____
_____
_____
_____
_____
_____
_____

1. Do you currently **smoke**? ☐ Yes ☐ No

Number of cigarette per day: _____

If you have smoked in the past, year ceased: _____

2. Are you **pregnant** (women)?

☐ Yes ☐ No

3. Have you had **surgery** before? ☐ Yes ☐ No

If yes, please list:

_____
_____
_____

4. Are you currently taking any regular **medications**?

☐ Yes ☐ No

If yes, please list:

_____

1. Do you currently need assistance to:

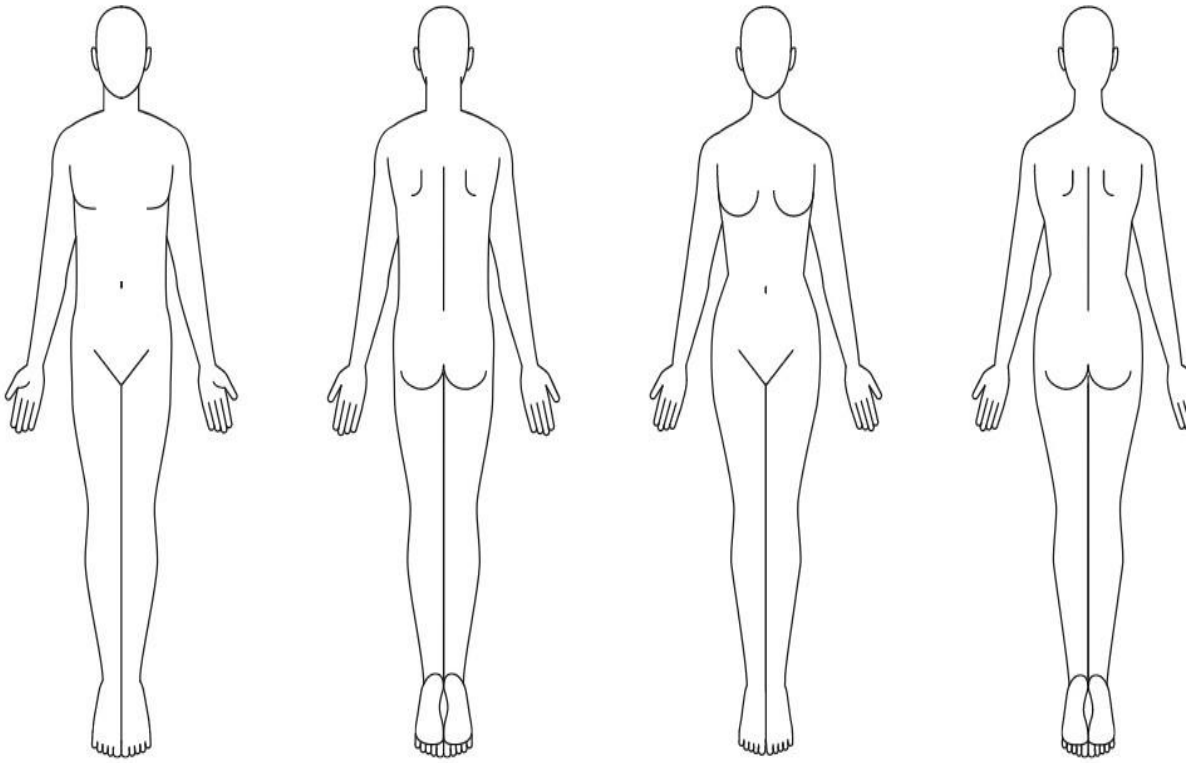
Shower / Bathe	☐	Yes	☐	No
Dress	☐	Yes	☐	No
Walk	☐	Yes	☐	No

Aids **required:**

_____
_____

Chief Complaints/Symptoms

_____
_____
_____
_____
_____
_____
_____
_____



<u>History of Present illness</u>

_____
_____
_____
_____
_____
_____
_____

Past History

Previous Medical treatments/ surgeries/diseases/traumas:

_____
_____
_____

Social History

- Psychological Status:
  _____
- Living environment:
  _____
- Life style _____
- Community participation:
  _____
- Personal Limitations:
  _____
- Environmental Restrictions :
  _____
- **Economic Status:**
  _____

OBJECTIVE MEDICAL EVALUATION FORM

Height:_____Cm Weight:_____Kg
BMI:_____
Vital Signs: Position:___Seated/_____
BP:_____/_____mmHg HR:_____/min.
RR:_____ /min. Temperature:_____°C
O2-Saturation:_____%
Physical Findings (exam):
_____
General Appearance:
_____
Skin:
_____
Cardiovascular
_____
Pulse: Regular; Irregular; Absent
_____
Heart Sounds:
_____
Normal/Abnormal (Extra Sounds; Systolic- /or Diastolic Murmurs) _____

Carotidarteries: _____

Circulation: _____

Abnormal findings:
_____

Pulmonary
Breath Sounds : Clear vesicular ; Bronchial, Wheezing; Crackles; Diminished; Absent
_____
Abnormal findings:
_____
_____
Abdomen
_____
_____

Abnormal findings:

Musculoskeletal

Back/Spine:

Pelvis:

Extremities

Neurological

Mental Status:

Speech & Hearing Status:

Abnormal findings:

Physical & Mental Limitations:

Anticipated Problems:

Primary Diagnosis

Secondary Diagnosis(es)

_____

MD Admission orders required

☐ ECG: ☐ Yes ☐ No
☐ Laboratory: ☐ Yes ☐ No
☐ X- Ray: ☐ Yes ☐ No
☐ Others:

_____

PART 3 : TREATMENT ORDER

Evaluate & Treatment, Recommended:

PT Department

☐ - ADLs activity/Gait & Balance training
☐ - Cold therapy
☐ - Heat therapy (IRR, Laser, US, SW/MW)
☐ - HT
☐ - Massage
☐ - Traction
☐ - ET
☐ - Aids-equipment clarification
☐ - Pulmonary PT
☐ - Incontinence/Pelvic Floor M. Training
☐ - Lymphedema Management

☐ - Amputee Rehab; Home Exercise Program, ROM& Strengthening Exercise, Prenatal Back Care, Vestibular Rehab, Pediatric Rehab, Posture & Ergonomics, TMJ Therapy, Reduction/ Mob. Of scars _

☐ - Others _____

Frequency: 1 2 3 4 5 x /Week

Duration: _____Weeks

OT Department

☐ - Sensory-/ Proprioception therapy

☐ - Fine/Gross/Visual Motor Coordination

☐ - Neuromotor Re-Education

☐ - Ergonomic therapy

☐ - Cognitive therapy

☐ - Hand Rehab

☐ - Aids- equipment clarification

☐ - Others: _____

☐ - UE /LE Splinting, Home Exercise Program, Pediatric Rehab

☐ - ADLs activity/ Gait & Balance training

Frequency: 1 2 3 4 5 x /Week

Duration: _____Weeks

Speech and - Hear Difficulties Department

☐ - Speech evaluation- and therapy

☐ - Hear evaluation- and therapy

☐ - Dysphagia/Oral Motor evaluation- and therapy

☐ - Aids-Device clarification

☐ - Others: _____

☐ - Home Exercise Program,

_____

Frequency: 1 2 3 4 5 x /Week

Duration: _____Weeks

Adaptive Equipment Department

☐ - Postoperativ dressing residual limb

☐ - Below knee prosthesis

☐ - Above knee prosthesis

☐ - UL Prostheses

☐ - LL Orthoses

☐ - UL Orthoses

☐ - Spinal Orthoses

☐ - Shoes and Orthoses for Foot

☐ - Others:_____

Frequency: 1 2 3 4 5 x /Week

Duration: _____Weeks

Socialpsychology

Frequency: 1 2 3 4 5 x /Week

Duration: _____Weeks

Short term- Goals:

_____
_____
_____
_____
_____
_____

Mid term- Goals:

_____
_____
_____
_____
_____
_____

Long term-Goals:

_____
_____
_____
_____
_____
_____

Physician name / Signature:.....

Dr. Yousif Al_Hamdan

Appendix B: written informed consent

موافقة مسبقة

AAUP-IRB Code No.: …….

AAUP-IRB Date: ……..

أنا .....

(اسم المشارك / اختياري) أوافق بموجبه على المشاركة في البحث السريري (دراسة سريرية)المحددة أدناه:

التأثير قصير المدى للمشي بوجود تقنية تقييد تدفق الدم على السعة الهوائية للرئتين وعلى مقاومة الانسلونين لدى مرضى السكري النوع الثاني.

تم شرح طبيعة الدراسة وهدفها وتفسيرها عن طريق الباحث الأساسي نسيبة احمد محمود تركمان.

لقد تم إخباري عن طبيعة البحث من حيث المنهجية والآثار السلبية المحتملة والمضاعفات (حسب ورقة معلومات المشارك).

بعد معرفة وفهم جميع المزايا والعيوب المحتملة لهذا البحث ، أوافق طواعية بمحض إرادتي على المشاركة في البحث السريري المحدد أعلاه.

أفهم أنه يمكنني الانسحاب من هذا البحث في أي وقت دون إبداء أي سبب على الإطلاق.

التاريخ: ..... إمضاء المشارك: .....

في حضور:

اسم: .....

تعيين: . ..... إمضاء: .....

(شاهد على توقيع المشارك)

أؤكد أنني أوضحت للمريض طبيعة وهدف البحث المذكور أعلاه.

تاريخ: ..... إمضاء: .....

(الباحث)

Appendix C: medical data sheet

PATIENT INFORMATION FORM

Please take a few moments to read and complete the following:

SECTION 1 - Patient personal Information			
Name:			Date of birth:
Age:		Gender:	
Address:		Phone number:	
Marital state: (please circle):	Married	single	Divorced
Education level (please circle):	Basic	intermediate	High
Occupation:			
SECTION 2- Patient Medical information:			
Smoking status (please circle):	Non smoker	Smoker	Ex-smoker
Height :		Weight	
Medications:			
Other related diseases(comorbidities) :			
Onset of diabetes:			
Level of physical activity (please circle):	low	Moderate	High
Family history of diabetes (please circle):	present	Absent	
Section 3: outcome measures :			

	Pre experiment	Post experiment	
1-Insulin sensitivity			
2-VO2 Max			
3- 6 MWT			
4- 36FMS			

Appendix D: Ebbeling Single-Stage Treadmill Walking test

Data Sheet – Submaximal Treadmilll Test

Data (1/2 point)
Tester Name: _____
Subject Name: _____
Sex: M / F (circle one) Age: _____ y Height: _____ m _____ (in)
Weight: _____ kg _____ (lb)
Age-Predicted HRmax: _____ bpm
50% to 70% age-predicted HR max: _____ - _____ bpm
Resting HR: _____ bpm

	Time (min)	Speed (mph)	Grade (%)	HR palpation (beats · min^{-1})	HR monitor (beats · min^{-1})	BP (mmHg)	RPE
Warm-up	2		0				
	4		0				
Stage 1	6		5				
	8		5				
Cool-down	10		0				
	12		0				

Appendix E: The short form 36 health survey questionnaire

استبيان صحي

الجنس☐ ذكر

☐ انثى

العمر_____سنة

المؤهل العلمي: ☐ ابتدائي

☐ اعدادي

☐ ثانوي

☐ بكالوريوس

☐ ماجستير

☐ دكتوراه

من فضلك، أجب على كل الأسئلة الموجودة في هذا الاستبيان. في حالة عدم وضوح أي سؤال، أرجو اختيار أقرب اجابة لمفهومك للسؤال.

١- بصورة عامة، كيف ترى حالتك الصحية؟

(اختر اجابة واحدة وضع علامة ✓ أمام الاجابة المناسبة)

☐ ممتازة

☐ جيدجدا

☐ جيدة

☐ لا بأس بها

☐ سيئة

٢- **مقارنة بعام مضى**، كيف تقيم حالتك الصحية **الآن** بصورة عامة؟

(اختر اجابة واحدة وضع علامة ✓ أمام الاجابة المناسبة)

☐ أفضل بكثير مما كانت عليه قبل عام

☐ أفضل نوعا ما من العام الماضي

☐ تقريبا على ما هي عليه

☐ أسوأ نوعا ما من العام الماضي

☐ أسوأ بكثير مما كانت عليه قبل عام

٣- تتعلق البنود التالية بانشطة يمكن ان تقوم بها خلال يومك العادي. **في الوقت الحالي**، الى اي مدى **تقيدك حالتك الصحية**:	(اختر اجابة واحدة وضع علامة ✓ تحت الاجابة المناسبة)		
	نعم تقيدني كثيرا	نعم تقيدني قليلا	لا تقيدني اطلاقا
أ) من ممارسة **الأنشطة الشاقة** مثل: الجري، حمل الاشياء الثقيلة او مزاولة الأنشطة الرياضية المجهدة جدا؟	☐	☐	☐
ب) من ممارسة **الأنشطة متوسطة الجهد**، كتحريك الطاولة او التنظيف باستخدام المكنسة الكهربائية او تنظيف حديقة المنزل والعناية بها ؟	☐	☐	☐
ج) من حمل المشتريات من البقالة او السوق المركزي (السوبرماركت)؟	☐	☐	☐
د) من صعود الدرج **لعدة ادوار**؟	☐	☐	☐
هـ) من صعود الدرج **لدور واحد فقط**؟	☐	☐	☐
و) من الانحناء او الركوع او السجود ؟	☐	☐	☐
ز) من المشي لأكثر من **كيلومتر ونصف**؟	☐	☐	☐
ح) من المشي لمسافة **نصف كيلومتر**؟	☐	☐	☐
ط) من المشي لمسافة **مئة متر**؟	☐	☐	☐
ي) من الاستحمام او ارتداء الملابس بنفسك؟	☐	☐	☐

- 3 -

الصحة الجسمية

٤- تتعلق البنود التالية (أ ، ب ، ج ، د) بالمشاكل التي يمكن ان تواجهـــك خلال تأديتك لعملك او للأنشطة اليومية المعتادة نتيجة لحالتك الصحية الجسمية. **خلال الأسابيع الأربعة الماضية**، هل تسببت **حالتك الصحية الجسمية في**: (اختر اجابة واحدة وضع علامة ✓ تحت الاجابة المناسبة)	نعم	لا
أ) **التقليل من الوقت** الذي تقضيه في العمل او اي انشطة اخرى؟	☐	☐
ب) **التقليل** مما تود **انجازه** من العمل أو أي أنشطة أخرى؟	☐	☐
ج) **تقييدك في أداء نوع** معين من الأعمال أو أي أنشطة أخرى؟	☐	☐
د) **أن تجد صعوبة في** تأدية العمل أو أي أنشطة أخرى؟ (على سبيل المثال، احتجت الى جهد اضافي لتأديتها)	☐	☐

الصحة النفسية

٥- تتعلق البنود التالية (أ ، ب ، ج) بالمشاكل التي يمكن ان تواجهك خلال تأديتك لعملك او الانشطة اليومية المعتادة كنتيجة لحالتك الصحية النفسية. (مثلا الشعور بالاكتئاب او القلق) **خلال الاسابيع الأربعة الماضية**، هل تسببت **حالتك الصحية النفسية في**: (اختر اجابة واحدة وضع علامة ✓ تحت الاجابة المناسبة)	نعم	لا
أ) **التقليل من الوقت** الذي تقضيه في العمل او اي انشطة اخرى؟	☐	☐
ب) **التقليل** مما تود **انجازه** من العمل أو أي أنشطة أخرى؟	☐	☐
ج) **عدم انجاز** العمل او اي انشطة اخرى **بالحرص المعتاد**؟	☐	☐

- 4 -

الصحة الجسمية او النفسية

٦- **خلال الاسابيع الاربعة الماضية**، الى اي مدى تعارضت **صحتك الجسمية او النفسية** مع تأديتك لنشاطاتك الاجتماعية المعتادة مع عائلتك او اصدقائك او جيرانك او اي من المناسبات الاجتماعية الأخرى؟

(اختر اجابة واحدة وضع علامة ✓ أمام الاجابة المناسبة)

- ☐ لم يكن هناك أي تعارض اطلاقا
- ☐ كان هناك تعارض قليل
- ☐ كان هناك تعارض متوسط
- ☐ كان هناك تعارض كبير
- ☐ كان هناك تعارض كبير جدا

شدة الألم

٧- ما شدة **الألم الجسمي** الذي عانيت منه خلال **الاسابيع الاربعة الماضية**؟

(اختر اجابة واحدة وضع علامة ✓ أمام الاجابة المناسبة)

- ☐ لم يكن هناك أي ألم
- ☐ كان هناك ألم خفيف جدا
- ☐ كان هناك ألم خفيف
- ☐ كان هناك ألم متوسط
- ☐ كان هناك ألم شديد
- ☐ كان هناك ألم شديد جدا

٨- **خلال الاسابيع الاربعة الماضية**، الى اي مدى ادى **الالم الجسمي** الى التعارض مع تاديتك لأعمالك المعتادة (سواء داخل المنزل او خارجه)؟

(اختر اجابة واحدة وضع علامة ✓ أمام الاجابة المناسبة)

- ☐ لم يكن هناك أي تعارض
- ☐ كان هناك تعارض قليل جدا
- ☐ كان هناك تعارض متوسط
- ☐ كان هناك تعارض كبير
- ☐ كان هناك تعارض كبير جدا

- 6 -

٩- الأسئلة التالية تتعلق بكيفية شعورك وطبيعة سير الأمور معك **خلال الأسابيع الأربعة الماضية**. الرجاء اعطاء اجابة واحدة لكل سؤال بحيث تكون هذه الاجابة هي الأقرب الى الحالة التي كنت تشعر بها.

خلال الأسابيع الأربعة الماضية، كم من الوقت:

(اختر اجابة واحدة وضع علامة ✓ تحت الاجابة المناسبة)

	في كل الأوقات	في معظم الأوقات	في كثير من الأوقات	في بعض الأوقات	في قليل من الأوقات	لم اشعر في أي وقت من الأوقات
أ) شعرت بأنك مليء بالحيوية والنشاط؟	☐	☐	☐	☐	☐	☐
ب) كنت شخصا عصبيا جدا؟	☐	☐	☐	☐	☐	☐
ج) شعرت بأنك في حالة اكتئاب الى درجة لم يمكن معها ادخال السرور اليك؟	☐	☐	☐	☐	☐	☐
د) شعرت بالهدوء والطمأنينة؟	☐	☐	☐	☐	☐	☐
هـ) كانت لديك طاقة كبيرة؟	☐	☐	☐	☐	☐	☐
و) شعرت بالاحباط واليأس؟	☐	☐	☐	☐	☐	☐
ز) شعرت بأنك منهك (استُنْفِذت قُواك)؟	☐	☐	☐	☐	☐	☐
ح) شعرت بأنك شخص سعيد؟	☐	☐	☐	☐	☐	☐
ط) شعرت بأنك تعبان؟	☐	☐	☐	☐	☐	☐

١٠- **خلال الاسابيع الأربعة الماضية**، ما مقدار الوقت الذي تعارضت فيه **صحتك الجسمية او مشاكلك النفسية** مع نشاطاتك الاجتماعية (مثل زيارة الأصدقاء والأقارب وغير ذلك) ؟

(اختر اجابة واحدة وضع علامة ✓ أمام الاجابة المناسبة)

- ☐ كان التعارض في كل الأوقات
- ☐ كان التعارض في معظم الأوقات
- ☐ كان التعارض في بعض الأوقات
- ☐ كان التعارض في قليل من الأوقات
- ☐ لم يكن هنالك تعارض في أي وقت من الأوقات

١١- **ما مدى صحة او خطأ كل من** العبارات التالية (أ ، ب ، ج ، د) بالنسبة الى حالتك الصحية؟

(اختر اجابة واحدة وضع علامة ✓ تحت الاجابة المناسبة)

	صحيحة بلا شك	صحيحة غالبا	لا اعلم	خطأ غالبا	خطأ بلا شك
أ) يبدو أنني أصاب بالمرض أسهل من الآخرين.	☐	☐	☐	☐	☐
ب) حالتي الصحية مساوية لأي شخص أعرفه.	☐	☐	☐	☐	☐
ج) أتوقع أن تسوء حالتي الصحية.	☐	☐	☐	☐	☐
د) حالتي الصحية ممتازة.	☐	☐	☐	☐	☐

****** شكرا لتعاونكم ******

الملخص

خلفية: استخدام تقنية حصر تدفق الدم مع التمارين الرياضية اثبتت دلالتها فيه تحسين الصحة بجهد ووقت اقل من مجرد التمارين التقليدية، هذه التقنية من التمارين تستخدم بشكل متزايد مع الناس الاصحاء وغير الاصحاء بدنيا. مقاومة الانسولين والتي تسمى مرحلة ما قبل السكري، تعتبر المحفز المرضي للعديد من الامراض الحديثة مثل السكري من النوع الثاني والذي هو بالأساس نتيجة نمط الحياة غير النشيط .اصبح معروفا ان 75 الى 150 دقيقة من التمارين المتوسطة الى كبيرة الشدة اسبوعيا يعتبر جزء اساسي وامن في التعامل مع السكري من النوع الثاني. التمرن بهذه الشدة المتوسطة او الكبيرة 2 الى4 مرات اسبوعيا يعتبر تحدي كبير لمن يعانون من السكري النوع الثاني. بينما التمرن بشدة منخفضة مع تقنية حصر تدفق الدم لها نفس التأثير والنتائج التي تحدثها التمارين ذات الشدة الكبيرة. تم دراسة اثر هذه التقنية على العديد من الحالات وقد اثبتت امانها ونتائجها الايجابية الواعدة. لكن الى الان والى حد علمنا لم يتم دراستها على فئة السكري من النوع الثاني

الاهداف: تهدف هذه الدراسة الى فحص قبول وامكانية استخدام تقنية حصر تدفق الدم على الكبار ممن يعانون من السكري النوع الثاني. ولدراسة اثر ذلك على السعة الهوائية للرئتين وعلى مقاومة الانسولين لديهم.

تصميم الدراسة: هذه الدراسة تعتبر دراسة جدوى تجريبية لدراسة تجريبية أكبر.

الادوات: مجموع 30 شخص ممن يعانون من السكري النوع الثاني اعمارهم تتراوح بين 40الى 65 شاركوا في الدراسة. تم توزيعهم بشكل عشوائي الى مجموعتين: الاول حيث تلقى التمارين الهوائية باستخدام تقنية حصر تدفق الدم، والاخر تلقى التمارين الهوائية لوحدها. البرنامج العلاجي يتضمن من جلستين اسبوعيا لمدة اربع اسابيع. قياس النتائج تضمن قياس السعة الهوائية، فحص المشي لستة نسخة SPSS 21 دقائق، مقاومة الانسولين و الوظائف الفيزيائية. تحليل النتائج تم باستخدام برنامج

النتائج: كلا المجموعتين اظهرت تحسن ذا دلالة احصائية بين القياس الاولي والبعدي. حيث ان التحسن الملحوظ في السعة الهوائية ومقاومة الانسولين كان لصالح مجموعة التمارين الهوائية باستخدام تقنية حصر تدفق الدم.

الاستنتاج: هذه الدراسة اثبتت ان التمارين الهوائية باستخدام تقنية حصر تدفق الدم لها تأثير افضل في التعامل مع مرضى السكري النوع الثاني بالنسبة للسعة الهوائية و مقاومة الانسولين.