**ADDIS ABABA UNIVERSITY**
**COLLEGE OF EDUCATION AND LANGUAGE STUDIES**
**DEPARTMENT OF SPORT SCIENCE AND PHYSICAL EDUCATION**

# Cardiovascular Function and Biochemical Biomarkers Response to Concurrent Training: Effect of Exercise Sequence on Type 2 Diabetic Patients

**By**
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A Dissertation Submitted to the Department of Sport Science and Physical Education in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy (PhD) in Exercise Physiology

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## DECLARATION OF ORIGINAL LITERARY WORK

This is to certify that the dissertation entitled "Cardiovascular Function and Biochemical Biomarkers Response to Concurrent Training: Effect of Exercise Sequence on Type 2 Diabetic Patients", submitted to the Department of Sport Science and Physical Education, Addis Ababa University, in partial fulfillment of the requirements for the degree of Doctor of Philosophy (PhD) in Exercise Physiology, is a record of original work carried out by me and has never been submitted to this or any other institution to get any other degree or certificates. All sources of assistance and support received during the conduct of this research have been appropriately acknowledged.

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## Approval of Dissertation for Defense

I hereby certify that I have supervised, read, and evaluated this dissertation titled "Cardiovascular Function and Biochemical Biomarkers Response to Concurrent Training: Effect of Exercise Sequence on Type 2 Diabetic Patients: A Randomized Controlled Trial" by Friew Amare, prepared under my guidance. This dissertation submitted to the Department of Sport Science and Physical Education, Addis Ababa University, in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Sport Science (Exercise Physiology), is a record of original work and I recommend that it be submitted for oral defense.

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## Approval of the dissertation for the defense result

As members of the board of examiners, we examined this dissertation entitled "Cardiovascular Function and Biochemical Biomarkers Response to Concurrent Training: Effect of Exercise Sequence on Type 2 Diabetic Patients: A Randomized Controlled Trial" by Friew Amare. We hereby certify that the dissertation is accepted for fulfilling the requirements for the award of the degree of Doctor of Philosophy (PhD) in Sport Science (Exercise Physiology).

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## ABSTRACT

**Background:** For people with type 2 diabetes, concurrent aerobic and resistance training is recommended because of its benefits for lipid profiles, cardiovascular health, and glucose control; however, the optimal exercise regimen remains unknown. This study examined the effects on metabolic and cardiovascular outcomes in persons with type 2 diabetes mellitus (T2DM) of two concurrent training sequences: aerobic exercise followed by resistance exercise and resistance exercise followed by aerobic exercise.

**Methods:** 39 people with type 2 diabetes were randomized into three groups for a 12-week parallel-group, randomized controlled trial: aerobic-resistance training (CART), resistance-aerobic training (CRAT), or a control group (COG). Anthropometric indices were secondary outcomes, while glycemic control, lipid profile, and cardiovascular function were primary outcome measures. After adjusting for average daily calorie intake, a repeated-measures ANCOVA was used.

**Results:** The findings indicated that both CART and CRAT produced significant improvements in glycemic control, lipid profile, and cardiovascular function compared with the control group ($p < .05$). Significant between-group differences were identified in HbA1c, HOMA-IR, fasting blood sugar, glucose tolerance, LDL, triglycerides, total cholesterol, systolic blood pressure, resting heart rate, oxygen saturation, and $VO_2$ peak, with moderate-to-large effect sizes ($\eta^2 = .258$-$.699$). However, only HbA1c (MD = 0.29%, 95% CI: 0.11–0.70, $p = .041$) and HOMA-IR (MD = 0.30, 95% CI: 0.04–0.57, $p = .022$) demonstrated significant differences between the CART and CRAT groups, favoring CRAT, whereas CART showed relatively greater improvements in resting heart rate, body mass index and $VO_2$ peak.

**Conclusions:** In individuals with type 2 diabetes, both CART and CRAT improved glycemic control, insulin resistance, lipid profile, and cardiovascular function. CRAT showed relatively greater improvements in HbA1c and HOMA-IR, whereas CART demonstrated better improvements in body mass index, maximum oxygen saturation, and resting heart rate. Overall, both concurrent training sequences were beneficial, with only minor outcome-specific differences between exercise orders.



**Keywords:** Type 2 diabetes, concurrent training, exercise sequence, insulin resistance, randomized controlled trial

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## LIST OF SYMBOLS, ABBREVIATIONS, AND ACRONYMS

- %BF: Body Fat Percentage
- 1RM: One Repetition Maximum
- ACSM: American College of Sports Medicine
- ADEi: Average Daily Energy Intake
- AED: Automated External Defibrillator
- AHA: American Heart Association
- ANOVA: Analysis of Variance
- AT: Aerobic Training
- BD: Body Density
- BMI: Body Mass Index
- CAD: Coronary Artery Disease
- CART: Concurrent Aerobic Resistance Training Group
- CoG: Control Group
- CRAT: Concurrent Resistance Aerobic Training Group
- DBP: Diastolic Blood Pressure
- FBG: Fasting Blood Glucose
- GT: Glucose Tolerance
- HbA1c: glycated hemoglobin
- HDL: High-Density Lipoprotein
- HR Max: Maximum Heart Rate
- HRR: Heart Rate Reservoir
- IDF: International Diabetes Federation
- LDL: Low-Density Lipoprotein
- PG-AUC: Plasma Glucose Area Under Curve
- RM-ANCOVA: Repeated Measure Analysis of Covariance
- RT: Resistance Training
- SBP: Systolic Blood Pressure
- $SpO_2$: peripheral capillary oxygen saturation
- T2DM: Type Two Diabetic Mellitus
- TG: Triglycerides
- WC: Waist Circumference
- WHR: Waist Hip Ratio
- $Vo_2$ peak: peak oxygen uptake

# CHAPTER ONE

## 1. INTRODUCTION

This chapter provides an overview of type 2 diabetes mellitus (T2DM) and its clinical and public health significance, emphasizing the role of lifestyle interventions, particularly structured exercise, in disease management. It reviews the pathophysiology of T2DM, associated complications, and the benefits of concurrent training for metabolic and cardiovascular outcomes. The chapter identifies gaps in the current literature, particularly the optimal sequence of aerobic and resistance exercises within concurrent training, and establishes the rationale for the present study. It also presents the research objectives, both general and specific, outlines the research hypotheses, and highlights the study's significance for clinical practice and public health. Additionally, the chapter defines the scope and delimitations of the research. It acknowledges potential limitations and provides a framework for understanding the study's purpose and relevance to improving cardiometabolic health in adults with T2DM.

### 1.1. Background

According to the WHO and ADA diagnostic standards, diabetes is diagnosed by fasting plasma glucose ≥126 mg/dL, 2-hour plasma glucose ≥200 mg/dL after an OGTT, or HbA1c ≥ 6.5% (ACSM, 2020; Jørgensen et al., 2002). It is a chronic disease characterized by impaired insulin production or utilization, leading to the development of diabetes mellitus (Mukhtar et al., 2020).

Type 2 diabetes mellitus (T2DM), which shortens life expectancy and results in costly, severe consequences, is one of the most prevalent and serious chronic illnesses that exists today. It is a global health issue that affects millions of people (Jain & Saraf, 2010). According to the IDF's 10th edition globally, 537 million people are expected to have diabetes in 2021; by 2030, that figure is expected to rise to 643 million, and by 2045, it will reach 783 million (Magliano et al., 2021). In Africa, an estimated 24 million people are currently living with diabetes, and this number is projected to rise by 129%, reaching approximately 55 million by 2045 (WHO, 2023). The countries in the continent with the

highest rates of diabetes cases among people aged 18 to 99 in 2017 were Ethiopia, South Africa, the Democratic Republic of the Congo, Nigeria, and Tanzania (Magliano et al., 2021). In Ethiopia, diabetes and its complications are major contributors to morbidity, mortality, and economic burden. Recent studies have shown that the overall prevalence of diabetes in Ethiopia is 6.5% (Bishu et al., 2019; Zeru et al., 2021)

In terms of age-specific prevalence, a study published in Scientific Reports discovered that diabetes is more common among people over the age of 40, emphasizing the need to focus research and prevention efforts on this age group. This group is also more prone to having chronic diabetes-related problems than younger people (Amsalu et al., 2024; Yang et al., 2019). Although people over the age of 60 face even higher risks, they are more likely to have age-related physical limitations that may prevent them from participating in structured exercise programs at the intensity and frequency required for interventions like the one proposed in this study (Paterson & Warburton, 2010).

These age-related trends are compounded by the rising prevalence of overweight and obesity, which are major contributors to the increasing incidence of type 2 diabetes (Malone & Hansen, 2019; Roglic, 2016), and also type 2 diabetes is a risk factor for both macrovascular diseases (such as myocardial infarction and stroke) and microvascular diseases (such as neuropathy, retinopathy, and nephropathy) (Damaskos et al., 2020; Viigimaa et al., 2020). It is also frequently linked to other risk factors for cardiovascular disease (CVD), such as high blood pressure (BP), dyslipidemia, and obesity (Martín-Timón et al., 2014).

In type 2 diabetes, elevated cardiovascular risk arises not only from systemic metabolic disturbances but also from molecular mechanisms. Hyperglycemia-induced vascular endothelial dysfunction in ischemic limb muscles is largely mediated by increased miR-503 expression, which impairs angiogenesis and vascular repair (Caporali et al., 2011; Zampetaki et al., 2010). Consequently, diabetic patients have a three- to four-fold higher likelihood of developing coronary artery disease compared to non-diabetic individuals (Jahangir et al., 2014).

Excess adipose tissue further contributes to this risk by secreting adipokines such as leptin

and adiponectin, along with pro-inflammatory cytokines (Stern et al., 2016). However, in obesity, leptin resistance develops, and adiponectin production decreases, promoting chronic inflammation and insulin resistance. This pro-inflammatory environment, characterized by elevated Tumor Necrosis Factor-alpha (TNF-α) and Interleukin-6 (IL-6), exacerbates both type 2 diabetes and cardiovascular complications (Bruun et al., 2002; Vilariño-García et al., 2024). Together, these molecular and adipose tissue-related mechanisms underline the interconnected pathophysiology of metabolic and cardiovascular dysfunction in T2DM.

The combination of elevated cytokines, leptin resistance, and reduced adiponectin creates a pro-inflammatory environment that promotes insulin resistance and inflammation. This chronic low-grade inflammation is not only a major contributor to the progression of type 2 diabetes but is also linked to the development of atherosclerosis, a condition characterized by the buildup of plaque in the arteries (Bessueille & Magne, 2015). Additionally, dysfunction in blood pressure regulation may arise from a reduction in nitric oxide (NO) production or an increase in its degradation due to advanced glycation end-products (AGEs) and reactive oxygen species (ROS) (Matsumoto et al., 2021; Ren et al., 2017). Evidence also suggests that the diabetic state exacerbates NO breakdown through Advanced Glycation End Products (AGEs) and oxygen-derived free radicals, further impairing endothelial function and contributing to hypertension (Fatehi-Hassanabad et al., 2010).

On the other hand, insulin resistance impairs normal lipid metabolism in diabetics, resulting in increased LDL cholesterol and triglyceride (TG) (Avramoglu et al., 2006), both of which raise the risk of cardiovascular disease. Adipose tissue releases excess free fatty acids (FFAs) into the bloodstream due to increases lipolysis. The liver then transforms these FFAs into triglycerides and increases the production of very-low-density lipoproteins (VLDL). LDL cholesterol levels rise as a result of these VLDL particles' eventual conversion to LDL (Avramoglu et al., 2006; Ginsberg et al., 2005). Insulin resistance also limits the body's capacity to eliminate arterial cholesterol by lowering HDL cholesterol (Cho, 2022). The development of dense, atherogenic LDL particles that pierce artery walls is encouraged by the combination of high TG, raised LDL, and low HDL, greatly increasing

the risk of atherosclerosis and cardiovascular disease (Welty, 2013). This abnormal fat metabolism is a major contributor to both the severity of type 2 diabetes and increased cardiovascular risk in diabetic patients (Bardini et al., 2012). The clinical advantage of managing LDL-C, TG, and HDL-C is to reduce the risk of CVD (Reiner, 2013). Scientists now recognize that the inflammatory response driven by excess adipose tissue is a key factor in both metabolic and cardiovascular diseases, making it a central target for treatment and prevention strategies (Berg & Scherer, 2005; Chait & Den Hartigh, 2020; Lingvay et al., 2022).

The American Diabetes Association, through a scientific statement, calls for a combined approach of pharmacological and non-pharmacological interventions to manage diabetes. This strategy aims to prevent and reduce the rise of metabolic syndrome, a major risk factor for developing prediabetes to diabetes, both of which increase the likelihood of cardiovascular disease (Joseph et al., 2022). For those with diabetes and prediabetes, applying and maintaining physical activity is essential for blood glucose control and general health (Colberg et al., 2016). Due to the negative effects of medications, physical activity has been given special consideration under new guidelines in recent years (Zanuso et al., 2010). According to research, diabetes mellitus can be effectively managed with a modified lifestyle that emphasizes eating well and increased physical activity/exercise (Oh et al., 2011; Wadden et al., 2012). and can significantly lower the risk of diabetes (Klein et al., 2004).

Exercise can manage body composition and lower blood sugar levels in multiple ways: it increases the ability of muscles to absorb glucose during exercise, improves insulin sensitivity overall, depletes and replenishes glycogen stores, draws more glucose from the blood, and even when at rest, an increased metabolic rate burns more blood sugar for energy (Bassuk et al., 2013). It is the most efficient strategy to increase the expression of GLUT4 in skeletal muscle. This effect can potentially benefit insulin action, muscle glycogen storage following exercise, and glucose clearance (Erik A Richter & Mark Hargreaves, 2013). As a result, there is a reduction in insulin resistance and an increase in muscle fiber hypertrophy, which increases muscle glycogen levels (Ojuka et al., 2012).

Most studies indicate that aerobic exercise training enhances key glucolipid and cardiovascular risk factors, including blood sugar levels, blood lipids (Kolahdouzi et al., 2019), insulin resistance, and insulin sensitivity (Shojaee-Moradie et al., 2007). It also positively affects vascular resistance (Amini Najafabadi et al., 2020; S.-W. Kim et al., 2019) and blood pressure (Cornelissen & Smart, 2013). For middle-aged and older adults, engaging in aerobic exercise leads to significant improvements in waist circumference (WC), fasting glucose, HDL-C, triglycerides (TG), diastolic blood pressure (DBP), and cardiorespiratory fitness (Ingle et al., 2017; Park et al., 2020; Wewege et al., 2018), particularly in diabetic patients (Hayashino et al., 2012; Miele & Headley, 2017). Additionally, resistance training (RT) enhances insulin sensitivity, muscle strength, and glucose oxidation (Hansen et al., 2012a; Lee et al., 2017).

Building on the benefits of single-mode exercise, concurrent training, which combines aerobic and resistance exercises in the same session, has been shown to offer even greater improvements in individuals with diabetes and multiple metabolic syndrome risk factors (Amare et al., 2025; Ambelu & Teferi, 2023; Delgado-Floody et al., 2021). s part of a periodized training program (Shamim et al., 2018; Jacob M Wilson et al., 2012), concurrent training effectively enhances overall physical fitness, reduces cardiovascular risk factors, and improves body composition. Studies report that it lowers insulin resistance, improves glucose tolerance, reduces blood vessel resistance, systolic blood pressure (SBP), total cholesterol (TC), triglycerides (TG), and LDL, while significantly increasing HDL in type 2 diabetic patients compared to non-exercising controls (Doulatyari et al., 2023; Yaowei Sun et al., 2024b). Moreover, a 12-week program of combined aerobic and resistance training has been reported to significantly reduce insulin levels, blood glucose, insulin resistance indices, and body fat percentage in middle-aged men with type 2 diabetes mellitus (Sampath Kumar Amaravadi et al., 2024).

Several researchers have concluded that to enhance the evidence on diabetes mellitus, additional research is required, particularly on the combination of concurrent training and dietary control (Marco Antônio R. Da Silva et al., 2020; Marco Antônio R Da Silva et al., 2020). Concurrent training has been shown to improve metabolic, cardiovascular, and muscular outcomes, but an interference effect has been observed, where simultaneous

aerobic and resistance exercise may compromise certain adaptations, such as strength and hypertrophy (Church et al., 2010; V. G. Coffey & J. A. Hawley, 2017).

Despite these benefits, many studies have not consistently reported key exercise prescription variables, such as intensity and sequence, and have often not controlled for dietary practices. As a result, there remain gaps in understanding how concurrent training affects chronic anthropometric, cardiovascular, and biochemical responses in type 2 diabetic patients. Differences in exercise regimens may elicit distinct metabolic, neuromuscular, and physiological adaptations, highlighting the need for well-controlled studies.

### 1.2. Statement of the Problem

Type 2 diabetes (T2DM) is a growing global health concern and one of the most serious issues impacting human health (Ginter & Simko, 2013). Affecting millions of people, it is recognized as the sixth leading cause of death worldwide (Jain & Saraf, 2010). Weird patterns show that prevalence is increasing not only in developed countries but also worldwide regions (Liu et al., 2020). According to the International Diabetes Federation (IDF), Ethiopia has the largest diabetic population in Sub-Saharan Africa, with 1.96 million adults aged 20 to 79 affected (IDF, 2021). Alarmingly, around 40% of these individuals were unaware of their condition (Solomon et al., 2023). The lack of awareness is largely due to the gradual progression of diabetes, with early-stage symptoms often being unnoticeable, making it challenging to recognize through classic diagnostic signs (Edmonds & Foster, 2014).

Effectively addressing this issue requires a proactive approach to both prevention and treatment. As outlined in the ACSM and ADA guidelines, effective diabetes management involves a comprehensive strategy, combining pharmacological treatments with non-pharmacological methods such as regular physical activity, dietary modifications, and appropriate medication (Colberg et al., 2016; White Jr, 2014).

Considering factors such as efficacy, cost, potential side effects, weight gain, comorbidities, and the risk of hypoglycemia, patients should prefer non-pharmacological

approaches (Chaudhury et al., 2017). Similarly, different researchers demonstrate that regular physical exercise is a fundamental component of T2DM management, demonstrably improving glycemic control and overall well-being (Kanaley et al., 2022; Kirwan et al., 2017; Teixeira-Lemos et al., 2011; Umpierre et al., 2011). Specifically, resistance training (RT) has been shown to promote skeletal muscle growth, which contributes to fat reduction (Hovanec et al., 2012), and improved metabolic outcomes, including lower fasting plasma glucose (FPG), enhanced insulin sensitivity, and better glucose tolerance in diabetic patients (Lee et al., 2017). Additionally, RT benefits lipid regulation by increasing HDL-c levels and reducing triglycerides (TG), making it an effective intervention for T2DM management (Barzegari & Amouzad Mahdirejei, 2014). Similarly, a meta-analysis and systematic review revealed that aerobic exercise has demonstrated positive effects on markers of metabolic syndrome (MetS), including reduced fasting glucose, higher HDL-c levels, and lower TG levels (Kelley & Kelley, 2007; Wewege et al., 2018). Moreover, it helps reduce systolic blood pressure (SBP), diastolic blood pressure (DBP), resting heart rate (RHR), fasting blood sugar (FBS), and body mass index (BMI), while improving oxygen saturation ($SpO_2$) compared to the control group in individuals with T2DM (Ezema et al., 2019).

While both aerobic and resistance exercises independently confer health benefits, concurrent training (CT), which integrates the advantages of both modalities, is widely recommended for managing type 2 diabetes. Substantial evidence supports its effectiveness, with studies reporting significant improvements in glycated hemoglobin (HbA1c), body fat, peak oxygen uptake, cholesterol levels, and insulin resistance (HOMA-IR) following combined aerobic and resistance exercise (Bassi et al., 2016). Similarly, Ambelu and Teferi (2023) demonstrated that an aerobic–strength training program significantly reduced body composition indices, blood pressure, and fasting blood glucose.

Building on this body of evidence, the researcher conducted a systematic review and meta-analysis (Amare et al., 2025), to clarify the effects of concurrent training on health outcomes in individuals with T2DM. The findings provide strong support for the metabolic benefits of a 12-week combined training program performed within the same session, while also highlighting the need for further randomized controlled trials to examine optimal

exercise sequencing, longer intervention durations, and better control of confounding factors. In this context, understanding the molecular mechanisms underlying exercise order is particularly important.

At the molecular level, the order of endurance and resistance exercise in concurrent training significantly influences responses through AMPK-mTORC1 interactions. The aerobic-first sequence (AE-RE) enhances mitochondrial biogenesis, fat oxidation, and cardiovascular efficiency but may leave residual fatigue, impair strength performance, and inhibit mTORC1 (mammalian target of rapamycin complex 1), thereby limiting hypertrophy and strength (Apró et al., 2015). Moreover, glycogen depletion from aerobic exercise reduces the intensity of subsequent resistance training, ultimately diminishing its effectiveness (Fyfe et al., 2014). Conversely, the resistance-first sequence (RE-AE) maximizes strength and hypertrophy gains by preserving mTORC1 activation and neuromuscular efficiency. Research has shown that this sequence has no impact on aerobic capacity (Z. Murlasits et al., 2018; Vikestad & Dalen, 2024); however, Doma et al. (2017) demonstrated that a resistance-first sequence may impair endurance performance due to resistance-induced fatigue and increased cardiovascular strain. Despite these mechanistic insights, the practical implications of exercise sequencing remain inconclusive.

Evidence from applied studies shows inconsistent effects of exercise order on cardiovascular and metabolic outcomes. For instance, Delgado-Floody et al. (2021) displayed (AT + RT) significant decreases in waist circumferences (WC), but not for SBP, DBP, FPG, HDL-c, and TG, all $p>0.05$ compared to RT + AT among in women with severe/morbid obesity. Likewise, Kobayashi et al. (2023) observed no significant changes in HbA1c when concurrent training was performed in an opposite sequence, whereas Church et al. (2010) observed significant changes in HbA1c with aerobic resistance sequence of exercises, despite improvements in VO2 max and fat mass.

With respect to lipid outcomes, among non-diabetic patients, Flores-Moreno et al. (2024) observed significant improvements in BMI, cholesterol, and glucose regulation when resistance training was followed by aerobic exercise among sedentary obese individuals. Conversely, Amare et al. (2024) highlighted that an aerobic-first approach led to significant

enhancements in lipid profiles and glycemic control in overweight and obese adults. Additionally, Azarbayjani et al. (2014) noted improvements were observed in anthropometric measures and insulin resistance when aerobic exercise preceded resistance training, though no significant changes were observed in lipid profiles.

Mechanistic and applied studies further suggest divergent adaptations based on exercise order. Performing resistance training before aerobic exercise has been shown to enhance fat oxidation, muscle glucose uptake, muscular strength, and overall physical fitness in healthy populations (Kang et al., 2009; Zhen Li et al., 2025; Z. Murlasits et al., 2018). In contrast, an aerobic-first approach improves the reduction of visceral fat and induces anabolism after exercise (Wu Min et al., 2022) and potentially induces muscle fatigue (Cadore et al., 2012), which could compromise resistance training performance (Vernon G. Coffey & John A. Hawley, 2017). Nevertheless, a recent systematic review and meta-analysis by Canli and Aldhahi (2024) found no significant effect of exercise order on overall workout effectiveness or physiological adaptations in healthy individuals. Collectively, these conflicting findings, along with results from the Phase I systematic review and meta-analysis, highlight a critical gap in understanding the influence of exercise sequence on health outcomes, particularly in individuals with type 2 diabetes. Accordingly, well-controlled experimental studies are needed to directly compare different concurrent training sequences in this population (Banitalebi et al., 2016; Bassi et al., 2015).

A key unanswered question is: How does the sequence of exercises in a CT program influence metabolic, cardiovascular, and anthropometric outcomes in individuals with Type 2 diabetes? Additionally, previous research on CT for diabetic patients has not sufficiently accounted for diet as a confounding factor, which can greatly influence cardiovascular function and biochemical biomarker outcomes (Tuso, 2014). Understanding how exercise order impacts key anthropometric measures, cardiovascular function, and biochemical biomarkers is essential for optimizing treatment strategies. To ensure accurate assessment of the exercise program's health impacts, participants were adhering to a strict dietary monitoring protocol (Matthews et al., 2012).

Based on the gaps identified in the existing literature and findings from the systematic

review and meta-analysis, this dissertation employed a randomized controlled trial (RCT) to examine and compare the effects of different exercise sequences within concurrent training on anthropometric measures, biochemical markers, and cardiovascular function among middle-aged men with type 2 diabetes.

## 1.3. Objective of the Research

### *1.3.1. General Objective*

The general objective of this study is to evaluate the effects of aerobic-resistance versus resistance-aerobic exercise sequences in concurrent training on cardiovascular function and biochemical biomarkers among patients with Type 2 diabetes.

### *1.3.2. Specific objectives*

The specific objectives for the randomized control trial are organized under the following thematic categories:

**Theme 1:** Cardiovascular Function Outcomes

1. To examine the effect of aerobic followed by resistance exercise order on cardiovascular function (SpO2, RHR, Vo2 peak, SBP, and DBP) in patients with type 2 diabetes.
2. To assess the effect of resistance followed by aerobic exercise order on cardiovascular function in patients with type 2 diabetes.
3. To compare the effects of two concurrent exercise sequences on cardiovascular function in patients with type 2 diabetes.

**Theme** 2: Metabolic (Biochemical Biomarker) Outcomes

1. To examine the effect of aerobic followed by resistance exercise order on biochemical biomarkers (HbA1c, IR, GT, HDL, LDL, and TG) in patients with type 2 diabetes.
2. To examine the effect of resistance followed by aerobic exercise order on biochemical biomarkers in patients with type 2 diabetes.
3. To compare the effects of aerobic-resistance and resistance-aerobic exercise sequences on biochemical biomarkers in patients with type 2 diabetes.

**Theme 3**: Anthropometric Outcomes (as Secondary Outcomes)

1. To examine the effect of aerobic followed by resistance exercise order on anthropometric indices (WHR, BFP, and BMI) in patients with type 2 diabetes.
2. To examine the effect of resistance followed by aerobic exercise order on anthropometric indices in patients with type 2 diabetes.
3. To compare the effects of aerobic-resistance and resistance-aerobic exercise sequences on anthropometric indices in patients with type 2 diabetes.

### 1.4. Research Hypotheses

1. There is a significant change in cardiovascular function levels (SpO2, RHR, Vo2 peak, SBP, and DBP) following a 12-week concurrent training program where aerobic training is performed before resistance training in a single training session, compared to baseline levels, in sedentary type 2 diabetes mellitus patients.
2. There is no significant change in cardiovascular function levels (SpO2, RHR, AS, Vo2 peak, SBP, and DBP) following a 12-week concurrent training program where resistance training is followed by aerobic training in a single session, compared to baseline levels, in sedentary type 2 diabetes mellitus patients.
3. After adjusting for average daily energy intake, there will be no significant differences in cardiovascular function (peripheral capillary oxygen saturation (SpO2), resting heart rate (RHR), maximum oxygen uptake (Vo2 peak), systolic blood pressure (SBP), and diastolic blood pressure (DBP)) among the three groups (aerobic-resistance, resistance-aerobic, and control) in patients with type 2 diabetes.
4. There is a significant difference in biochemical biomarkers (HbA1c, IR, GT, HDL, LDL, and TG) following a 12-week concurrent training program where resistance training is performed after aerobic training in a single training session, in sedentary type 2 diabetes mellitus patients.
5. There is no significant difference in biochemical biomarkers (HbA1c, IR, GT, HDL, LDL, and TG) following a 12-week concurrent training program where resistance training is performed before aerobic training in a single training session, in sedentary type 2 diabetes mellitus patients.

6. After adjusting for average daily energy intake, there will be no significant differences in the biochemical indicators (glycated hemoglobin (HbA1c), insulin resistance (IR), glucose tolerance (GT), high density lipoprotein (HDL), low density lipoprotein (LDL), and triglycerides (TG)) among the three groups (aerobic-resistance, resistance-aerobic, and control) in patients with type 2 diabetes.
7. There is no significant difference in anthropometric indexes (WHR, BFP, and BMI) following a 12-week concurrent training program where resistance training is performed before aerobic training in a single training session, in sedentary type 2 diabetes mellitus patients.
8. There is no significant difference in anthropometric indexes (WHR, BFP, and BMI) following a 12-week concurrent training program where aerobic training is performed before resistance training in a single training session, in sedentary type 2 diabetes mellitus patients.
9. After adjusting for average daily energy intake, there are no significant differences in anthropometric indexes (waist-to-hip ratio (WHR), body fat percentage (BFP), and body mass index (BMI)) among the three groups (aerobic-resistance, resistance-aerobic, and control) in patients with type 2 diabetes.

### 1.5. Scope of the Study

This study was delimited based on geographical area, participant characteristics (sex and age), type of exercise intervention, selected physiological and metabolic variables, and the duration of the intervention.

- Geographical Area: The study was conducted at Debre Markos, Ethiopia.
- Sex of Participants: Both male and female patients with Type 2 diabetes mellitus were included.
- Age Range: The study included participants aged 41 to 60 years.
- Independent Variable (Exercise Type): The study focused on concurrent exercise training, specifically two exercise sequences:

- Concurrent Aerobic Resistance Training (CART)
- Concurrent Resistance Aerobic Training (CRAT)

- Dependent Variables:
  - Cardiovascular function: Systolic and diastolic blood pressure, resting heart rate, and peripheral oxygen saturation ($SpO_2$), maximum $Vo_2$ peak
  - Metabolic variables: Glycated hemoglobin (HbA1c), insulin resistance, glucose tolerance, and lipid profile (LDL, HDL, TG, and TC)
  - Anthropometric indices (Secondary Variables): WHR, BMI, and Body fat percentage
- Study Duration: The study was conducted over a period of 12 weeks

### 1.6. Significance of the Study

- This study examines exercise sequencing in concurrent training to optimize cardiovascular and metabolic health in type 2 diabetes, helping to enhance patient outcomes and overall quality of life through tailored interventions.

- The findings aim to provide actionable insights for healthcare providers, fitness professionals, and exercise physiologists in designing personalized and effective exercise programs.

- This study addresses a literature gap by exploring the impact of exercise sequence, combining aerobic and resistance training, on cardiovascular and metabolic responses in type 2 diabetes.

- Findings may serve as a foundation for further investigations, promoting deeper exploration into exercise prescription for chronic conditions.

### 1.7. Structure of the Dissertation

This dissertation is organized into five chapters, each addressing a distinct aspect of the research process. Chapter One introduces the study background, outlines the problem statement, research objectives, research questions, hypotheses, significance of the study, scope, delimitations, and key operational definitions. Chapter Two presents a

comprehensive review of the relevant literature, focusing on type 2 diabetes mellitus, cardiometabolic risk factors, and the effects of aerobic, resistance, and concurrent exercise training, with particular emphasis on exercise sequence. Chapter Three describes the research methodology, including the study design, participants, sampling procedures, ethical considerations, intervention protocols, data collection instruments, and statistical analysis methods. Chapter Four presents the study results, reporting the findings of the statistical analyses in relation to the research objectives and hypotheses. Chapter Five discusses the results in the context of existing literature, highlighting the implications of the findings, study limitations, and directions for future research. Finally, it provides the study conclusions, summarizes the key findings, and offers practical recommendations for clinical practice and future investigations.

### 1.8. Operational Definition

- **Aerobic Training:** a form of continuous exercise that engages large muscle groups in sustained, rhythmic activity over an extended period. It increases heart rate and respiration, enhancing the body's ability to utilize oxygen efficiently for energy production.

- **Anthropometric index:** is a value that is obtained from one or more anthropometric measurements (measurements of the proportions, size, and composition of the body). It comprises the waist-hip ratio, body fat, and BMI.

- **Biochemical biomarker**: is a measurable indicator of a biological state, condition, or process. These markers are found in blood and provide valuable information about the body's physiological or pathological functions. These include HbA1c, GT, lipid profile (HDL, LDL, and TG), and glucose tolerance, which are biological molecules present in blood that serve as indicators of normal or abnormal processes, conditions, or diseases.

- **Cardiovascular function:** It is the ability of the cardiovascular system, which includes the ability of heart, blood vessels, and lungs, in type 2 diabetic patients to deliver oxygenated blood throughout the body at rest and during exercise.

- **Concurrent Training Sequence:** is a sequence or order of resistance and aerobic exercises done in a single training session.

- **Middle-aged:** Age range defined as 41-60 years old.

- **Resistance Training:** It is a type of exercise aimed at enhancing muscular strength by applying resistance during muscle contractions, typically with brief rest periods between sets.

- **Type 2 Diabetic Patients**: Diagnosed with type 2 diabetes mellitus by a qualified medical doctor. Confirmation was based on medical records or fasting glucose level exceeding a pre-defined cut-off point (126 mg/dL).

# CHAPTER TWO

# 2. RELATED LITERATURE REVIEW

This chapter provides a comprehensive review of the literature relevant to the effects of exercise interventions on type 2 diabetes mellitus (T2DM), focusing on metabolic and cardiovascular health outcomes. It examines key concepts, including the pathophysiology of T2DM, risk factors, and the role of physical activity and structured exercise in disease management. The review also explores different exercise modalities, such as aerobic, resistance, and concurrent training, and their impact on glycemic control, insulin resistance, lipid profiles, and cardiovascular function. Furthermore, the chapter highlights studies investigating the influence of exercise sequence within concurrent training and identifies gaps in the current evidence base that justify the present research. By synthesizing previous findings, this chapter establishes the theoretical and empirical foundation for understanding how the sequence of aerobic and resistance exercises may affect cardiometabolic outcomes in adults with T2DM.

## 2.1. Introduction

The body's inability to produce or effectively use enough insulin results in diabetes, a chronic disease. This insulin deficiency results in hyperglycemia, or high blood glucose levels, along with various metabolic problems. Type 2 diabetes mellitus (T2DM) is an expanding global health issue with rising prevalence worldwide. According to the International Diabetes Federation (IDF), over 537 million adults had diabetes in 2021, and this figure is expected to increase to 643 million by 2030. T2DM makes up about 90-95% of all diabetes cases and is more common in low- and middle-income countries due to factors like rapid urbanization, sedentary lifestyles, and dietary shifts. The prevalence of T2DM rises significantly with age, especially after 45 years. In Sub-Saharan Africa, including Ethiopia, the increasing rate of diabetes is linked to a shift toward Westernized diets, lower physical activity, and an aging population (Ashwal et al., 2015; Assah & Mbanya, 2017).

The pathophysiology of T2DM is complex, involving both genetic and environmental factors (Murea et al., 2012). A central feature of T2DM is insulin resistance, where the body's cells do not respond properly to insulin, the hormone that facilitates glucose uptake. This insulin resistance is often accompanied by β-cell dysfunction, in which the pancreatic β-cells fail to produce sufficient insulin to maintain normal blood glucose levels (Kasuga, 2006; Muoio & Newgard, 2008). As a result, chronic hyperglycemia ensues, leading to the progression of diabetes (Mukhtar et al., 2020). Obesity, especially the accumulation of visceral fat, is closely linked to insulin resistance. Free fatty acids and pro-inflammatory cytokines released by adipose tissue interfere with insulin signaling pathways, while in the liver, insulin resistance leads to excessive glucose production (Al-Mansoori et al., 2022). Over time, persistent high blood glucose levels (hyperglycemia) cause glucotoxicity and lipotoxicity, further impairing β-cell function and worsening diabetes(Kasuga, 2006).

Without proper management, T2DM can lead to a range of microvascular and macrovascular complications. Microvascular complications include diabetic retinopathy, which damages the small blood vessels in the retina and can cause vision loss or blindness (Damaskos et al., 2020; Viigimaa et al., 2020). Diabetic nephropathy, characterized by kidney damage due to persistent hyperglycemia, can lead to chronic kidney disease or end-stage renal failure (Młynarska et al., 2024). Another microvascular problem is diabetic neuropathy, which causes damage to the nerves, especially in the lower extremities. Severe cases of this condition can lead to amputations and loss of sensation (Hicks & Selvin, 2019).

Peripheral arterial disease (PAD) and cardiovascular disease (CVD) are examples of macrovascular consequences. Atherosclerosis, which can cause heart attacks, strokes, and other cardiovascular problems, is greatly increased by type 2 diabetes. Infections, amputations, and foot ulcers are among the risks associated with PAD's reduced blood flow from constricted arteries. In patients with type 2 diabetes, endothelial dysfunction may result from reduced nitric oxide (NO) production, increased NO inactivation, or decreased NO responsiveness. There is now evidence linking diabetes-related endothelial cell damage to a reduction in NO production (Dhananjayan et al., 2016). Comparably, research suggests that having diabetes may accelerate the breakdown of NO by free radicals and

advanced glycation end products, which have several detrimental effects on vascular health (Su et al., 2008). The imbalance between vasodilators and vasoconstrictors caused by this dysfunction significantly increases the risk of atherosclerosis, a condition where plaque builds up in the arteries (Biswas & Khan, 2020).

The coexistence of risk factors such as dyslipidemia, obesity, and chronic hyperglycemia, all of which contribute to atherosclerosis, where plaque builds up in the arteries. This plaque buildup can lead to coronary artery disease, myocardial infarction, and stroke (Libby & Theroux, 2005). Cardiovascular complications are the leading cause of death in individuals with T2DM, with nearly 50% of deaths among diabetic patients being attributed to cardiovascular issues (Ma et al., 2022). As such, managing cardiovascular health is of utmost importance in this population. Early interventions, including controlling blood pressure, managing lipids, and adopting lifestyle modifications, are critical in reducing the risk of cardiovascular complications.

Effective glycemic control can be achieved through lifestyle interventions such as diet and exercise, as well as pharmacological treatments like metformin or insulin therapy (Joseph et al., 2022).. Additionally, managing dyslipidemia, which is common in T2DM, is crucial in preventing cardiovascular complications. Dyslipidemia, characterized by elevated triglycerides, low HDL cholesterol, and high LDL cholesterol, accelerates atherosclerosis (Higashi, 2023). Weight management is another important aspect of metabolic control, as obesity exacerbates insulin resistance and worsens both metabolic and cardiovascular health. Regular physical activity, combined with a balanced diet, plays a crucial role in maintaining optimal weight and improving metabolic outcomes.

In conclusion, managing cardiovascular and metabolic health in Type 2 diabetic patients is crucial for reducing complications and improving quality of life. Exercise interventions, alongside pharmacological treatments, play a significant role in mitigating the risks of cardiovascular disease and improving metabolic outcomes in this high-risk population (Brandão et al., 2020). Aerobic exercise enhances insulin sensitivity, increases glucose uptake, and promotes fat oxidation, all of which help maintain glycemic control (Yaribeygi et al., 2019). Resistance training, which improves muscle mass and strength, also contributes to better glucose regulation (Strasser & Pesta, 2013). Combining these two

forms of exercise in a concurrent training regimen has been shown to provide synergistic benefits for cardiovascular and metabolic health in diabetic patients (Ambelu & Teferi, 2023; Saima Zaki, Md Farhan Alam, Saurabh Sharma, Said El-Ashker, et al., 2024). Research suggests that concurrent training not only helps reduce HbA1c levels and improve lipid profiles but also enhances cardiovascular fitness and reduces blood pressure (Saima Zaki, Md Farhan Alam, Saurabh Sharma, Irshad Husain Naqvi, et al., 2024). For diabetic patients, tailored exercise programs that incorporate both aerobic and resistance training can be essential in managing both cardiovascular and metabolic risks effectively.

## 2.2. Cardiovascular Risk in Type 2 Diabetic Patients

### *2.2.1.* Clinical *consequences of cardiovascular disease*

The risk of cardiovascular conditions, such as myocardial infarction, stroke, heart failure, and coronary artery disease (CAD), is significantly raised by type 2 diabetes. Atherosclerosis, a disorder marked by the accumulation of plaque in the artery walls, is accelerated by diabetes and is one of the most direct effects on heart health (Libby & Theroux, 2005). T2DM frequently coexists with hypertension, or high blood pressure, another serious cardiovascular condition in people with diabetes. Because hypertension damages blood vessels and increases the heart's workload, it increases the cardiovascular risk in people with type 2 diabetes and contributes to the development of atherosclerosis (Pavlou et al., 2018). People who have both diabetes and hypertension are far more likely to develop heart disease than people who only have one of the conditions, according to studies. The so-called "diabetic triad" of diabetes, hypertension, and dyslipidemia dramatically raises the risk of cardiovascular events like heart attacks and strokes (Sharabi, 2012).

Diabetic cardiomyopathy is another disorder that results from diabetes that affects the structure and function of the heart. Diastolic dysfunction (impaired heart filling) and left ventricular hypertrophy (enlargement of the heart muscle) are the hallmarks of this disorder, which is unrelated to hypertension and coronary artery disease. Heart failure can develop from diabetic cardiomyopathy, especially in those with inadequate glycemic control (Khavandi et al., 2009; Lee & Kim, 2017). Moreover, type 2 diabetes also causes

arrhythmias because insulin resistance and high blood sugar interfere with the electrical circuitry of the heart, resulting in irregular heartbeats and an increased risk of sudden cardiac death (Vinik et al., 2013).

The underlying cause of type 2 diabetes is insulin resistance, which occurs when the body's cells lose their sensitivity to insulin, raising blood glucose levels. In addition to increased levels of oxidative stress, pro-inflammatory cytokines (Scioli et al., 2020), and free fatty acids, these resistance factors also lead to endothelial dysfunction and vascular inflammation (Theofilis et al., 2021). Atherosclerosis develops as a result of the endothelial lining of blood arteries being harmed by continuously elevated blood levels of fat and glucose. This is primarily caused by dyslipidemia, which is characterized by decreased high-density lipoprotein (HDL) cholesterol and an increase in triglycerides and low-density lipoprotein (LDL) cholesterol (Higashi, 2023), which is frequently brought on by insulin resistance (Bjornstad & Eckel, 2018).

Another important component in the development of cardiovascular problems in people with type 2 diabetes is endothelial dysfunction (Ding & Triggle, 2005). Blood flow, vascular tone, and inflammation are all regulated by the endothelium, a thin layer of cells that lines blood vessels (Sandoo et al., 2010). Insulin resistance and chronic hyperglycemia in type 2 diabetes (T2DM) impair endothelial function by diminishing NO generation, a vasodilator that maintains vascular health by relaxing blood vessels and reducing inflammation. Reduced NO levels lead to vasoconstriction, increased vascular resistance, and elevated blood pressure (Dhananjayan et al., 2016). In addition, T2DM promotes oxidative stress and the release of pro-inflammatory cytokines, which damage the endothelium and progress the early stages of cardiovascular disease (Oguntibeju, 2019; Scioli et al., 2020). By raising the production of reactive oxygen species (ROS) and decreasing the body's antioxidant defenses, chronic hyperglycemia also causes oxidative stress. This oxidative stress causes inflammation, destroys endothelial cells, and makes it easier for advanced glycation end products (AGEs) to occur. By stiffening blood arteries and starting inflammatory processes, AGEs worsen endothelial damage and hasten the accumulation of plaque. Additionally, the buildup of AGEs decreases blood vessel

flexibility, raising the possibility of hypertension and other cardiovascular issues (Kosmopoulos et al., 2019).

Another important element that connects cardiovascular disease and type 2 diabetes is inflammation. An enduring, low-level inflammatory response characterizes both ailments. People with type 2 diabetes (T2DM) who have excess visceral fat emit pro-inflammatory cytokines like interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), which aggravate endothelial dysfunction, insulin resistance, and atherosclerosis. These cytokines enhance vascular inflammation and immunological responses, which increase plaque instability and elevate the risk of cardiovascular events such as strokes and heart attacks (Al-Mansoori et al., 2022). All together, these interrelated processes account for the increased cardiovascular risk in people with type 2 diabetes, highlighting the necessity of all-encompassing risk management techniques.

### *2.2.2. Effect of exercise on cardiovascular function*

Exercise is essential for maintaining and promoting cardiovascular health. A basis for the use of exercise as a non-pharmacological intervention to prevent and treat cardiovascular disease (CVD) has been established by the considerable research on the positive effects of aerobic, resistance, and/or combined training on cardiovascular function (Chudyk & Petrella, 2011; Stewart, 2004).

Aerobic exercise has been widely studied for its effects on cardiovascular function in diabetic patients, with research generally supporting significant improvements in variables such as VO2 max (Najafipour et al., 2017), nitric oxide (NO) production (Wang et al., 2019), systolic and diastolic blood pressure (Whelton et al., 2002), and peripheral oxygen saturation (SpO2) (Ezema et al., 2019). Studies show that regular aerobic exercise can increase VO2 max, improve NO bioavailability, and reduce both systolic and diastolic blood pressure, contributing to better endothelial function and reduced arterial stiffness (Tao et al., 2023; Van Craenenbroeck et al., 2015). However, randomized clinical trials have demonstrated that resistance training significantly affects T2D patients' blood pressure responses (Jorge et al., 2011) and NO bioavailability (Behjati Ardakani et al., 2018; Castaneda et al., 2002).

An alternative form of instruction, studies continually demonstrate the personal advantages that aerobic and resistance training provide for individuals with type 2 diabetes. Nevertheless, a single training session utilizing these two effective tools appears to be an even more successful strategy for T2DM patients' treatment, known as concurrent training, has synergistic advantages that improve cardiovascular health. Concurrent training had a notably good effect on cardiorespiratory fitness, as evidenced by the notable increases in blood pressure (Ambelu & Teferi, 2023; Caminiti et al., 2021) VO2max in diabetic patients with cardiac autonomic neuropathy (CAN) (Saima Zaki, Md Farhan Alam, Saurabh Sharma, Irshad Husain Naqvi, et al., 2024). Concurrent training has several advantages, as recent studies have shown. When compared to aerobic or resistance exercise alone, (Schroeder et al., 2019; Shaw & Shaw, 2009), for instance, showed that concurrent training resulted in higher reductions in cardiovascular risk variables. In order to effectively manage cardiovascular risk in patients with diabetes, this study demonstrated that combining the two exercise modalities increased cardiovascular fitness and decreased inflammatory markers.

### *2.2.3. Methods for assessing cardiovascular function in T2DM patients*

Diabetes mellitus type 2 significantly raises the risk of cardiovascular disease (CVD). Cardiovascular function is evaluated in T2DM patients utilizing techniques other than traditional measures. Non-invasive techniques are the cornerstone, and this measurement is crucial to understanding the load and evaluating the issue.

An easy-to-find and basic marker is the resting heart rate (RHR). Research points to a correlation between higher RHR and more CVD events in T2DM (Martín-Timón et al., 2014). The resting heart rate can be determined using two primary methods. The first is manual palpation, which is the conventional approach and entails feeling the pulse at particular body parts. Regarding the second option heart rate can now be measured more easily and possibly more accurately with the use of electronic equipment (Stone et al., 2021). Chest straps, smart watches, fitness trackers, and pulse oximeters are a few examples of these devices. While manual palpation is simple to use and readily available, each person's accuracy will differ. Electronic devices can be more handy and perhaps more accurate than wristwatches, even though they come in a broad variety and pulse oximeters

may be more accurate for diabetics with circulation issues. With a chest strap, a smart watch or pulse oximeter offers a decent compromise between convenience and precision for the majority of diabetic patients.

Regarding the other variable, brachial blood pressure (BP) measurement remains a crucial technique for assessing cardiovascular health in individuals diagnosed with Type 2 Diabetes Mellitus (T2DM). Traditional auscultatory procedures do have certain drawbacks, too (Stergiou et al., 2014; Vischer & Burkard, 2017). In T2DM, white coat hypertension a disease in which concern raises blood pressure in therapeutic settings, can be common (Pioli et al., 2018). Accuracy can also be compromised by observer bias and the limits of the human ear (Song et al., 2014).

Researchers can use a variety of brachial SphygmoCor XCEL cuff device BP monitoring techniques to examine the effects of exercise order in concurrent training (combining aerobic and resistance exercise) on blood pressure in patients with type 2 diabetes (Ambelu & Teferi, 2023; Dobrosielski et al., 2012). A consistent method is provided with validated SphygmoCor XCEL cuff device (De la Torre Hernández et al., 2021; Shoji et al., 2017), which lowers observer bias and makes numerous blood pressure readings during the study possible (Masding et al., 2001).

Even so, ambulatory blood pressure monitoring (ABPM), which records variations in blood pressure during the day and night, can provide a more complete picture. It may also shed light on how different exercise regimens affect circadian blood pressure patterns (Grossman, 2013). However, ABPM can be costly, uncomfortable, and difficult to interpret (Ringrose et al., 2020). With the development of the arm electronic brachial SphygmoCor XCEL cuff, researchers can better understand how concurrent training regimens affect blood pressure in patients with type 2 diabetes. In order to maximize cardiovascular health in this population, exercise prescription tactics can be informed by this information.

A cautious approach is necessary when measuring VO2 max in people with Type 2 Diabetes Mellitus (T2DM) because of possible cardiovascular restrictions. There are other approaches than standard exercise tests. Although they are non-invasive, indirect techniques, such as the age, weight, and height estimation equations base are not very accurate, particularly when used to individuals with metabolic problems (Harber et al.,

2024). Using a metabolic cart and mouthpiece, cardiopulmonary exercise testing (CPET) evaluates oxygen consumption directly (Glaab & Taube, 2022). However, accessibility is limited since it needs specific tools and individuals with training.

While CPET remains the gold standard, modified Bruce protocols on a treadmill offer a valuable alternative for T2DM patients in research settings (Kozlov et al., 2020; Poirier et al., 2000). These protocols adjust speed and incline increments to a more manageable level, allowing for a maximal effort within a safer zone (Fletcher et al., 2013). This approach balances accurate VO2 peak data collection with patient safety, making it a strong choice for concurrent exercise studies in T2DM populations (Bires et al., 2013; Ellis et al., 2019). In conclusion, a complete approach to measuring cardiovascular function in T2DM is necessary. Combining standard measurements (RHR, BP, SpO2, VO2 max) necessitates Future inclusion of new biomarkers holds the promise to further personalize cardiovascular risk management in T2DM patients.

## 2.3. Biochemical Biomarkers in Type 2 Diabetic Patients

Measurable indicators of the body's internal chemistry are called biochemical markers. Classic examples include glycated hemoglobin (HbA1c), which represents average blood sugar control over a longer period of time, and increased fasting blood sugar levels, which indicate diminished insulin effectiveness or insufficient insulin synthesis (Ortiz-Martínez et al., 2022). Research is looking into new markers outside these conventional ones that can provide better monitoring or early discovery. These include lipid profiles, which can display variations in triglycerides and cholesterol, inflammatory markers that may point to persistent low-grade inflammation linked to type 2 diabetes, and even particular blood metabolite patterns that may suggest early metabolic abnormalities (Sharif et al., 2021).

### *2.3.1. Clinical consequences of abnormal Biochemical biomarkers*

One of the main causes of the series of actions that result in deteriorated biochemical indicators in type 2 diabetes is insulin resistance. Insulin often functions as a key, opening cells to let glucose into them so they can be used as fuel. This "key" loses its effectiveness in people with type 2 diabetes mellitus (T2DM), which leads to an accumulation of glucose

in the blood and elevated fasting plasma glucose levels (Petersen & Shulman, 2018). Increased blood sugar due to insulin resistance has a chain of effect. Hemoglobin, the protein in red blood cells that carries oxygen, attaches to glucose molecules over time to form HbA1c, which is formed at a higher average blood sugar level and provides a long-term window into blood sugar control (Boye et al., 2022).

In addition to glucose, type 2 diabetes affects fat metabolism, which can cause an imbalance in the triglyceride to cholesterol ratio (Bardini et al., 2012). The good cholesterol, or HDL, which is in charge of eliminating LDL from the body, rises as LDL, or bad cholesterol, does. This imbalance makes it more likely for fatty deposits to accumulate in the arteries, which is a significant risk factor for cardiovascular disease in people with type 2 diabetes (Carmena, 2005).

Low-grade inflammation, or a persistent simmering of the immune system, is another condition frequently associated with type 2 diabetes. Elevated levels of inflammatory markers are a reflection of this inflammation and can worsen insulin resistance and the development of the illness (Gratas-Delamarche et al., 2014). Finally, type 2 diabetes affects the intricate biochemical processes known as metabolic pathways, which convert food into energy. Certain metabolite concentrations vary as a result of these alterations, and these fluctuations may reveal information about the state of the disease (Ferrannini et al., 2013). We can better understand the altered metabolic profiles seen in T2DM patients by comprehending these pathways.

While the abnormal blood chemistry profiles in T2DM patients can be explained by comprehending the mechanisms underlying poor biochemical indicators, research on novel biomarkers that are improved without medication is still ongoing. The possibility of a combined approach to improve both established and new markers for a more comprehensive treatment is shown by this ongoing research on the relationship between nutrition and exercise.

Abnormal biochemical markers are important warning signs for prospective health problems in people with Type 2 Diabetes Mellitus (T2DM). The traditional indicators of type 2 diabetes (T2DM), elevated fasting blood sugar and HbA1c, are highly significant. Microvascular consequences, such as nerve damage, eye issues, and renal disease, are

primarily caused by persistently elevated blood sugar levels (Khalil, 2017). High HbA1c, a sign of poor glycemic management, also raises the risk of macrovascular problems like peripheral artery disease, heart disease, kidney problem and stroke (Giannopoulos & Armstrong, 2020; Soyoye et al., 2021).

In addition to blood sugar levels, improper fat metabolism is a problem in type 2 diabetes. A dyslipidemia, or unbalanced lipid profile, increases the risk of cardiovascular disease by accelerating the accumulation of fatty deposits in arteries (Lorenzatti & Toth, 2020; Lucchi, 2021). Additionally, elevated inflammatory markers are a typical indicator of low-grade chronic inflammation, which is associated with type 2 diabetes (Calle & Fernandez, 2012). The body's ability to use insulin is further interfered with by this inflammation, exacerbating hyperglycemia. Moreover, it encourages the growth of atherosclerosis and associated cardiovascular problems (Jellinger, 2007). The effects of T2DM go beyond these recognized indicators. Changes in particular metabolite levels result from the disease's disruption of multiple metabolic pathways. T2DM problems have been associated with abnormal levels of certain amino acids, acylcarnitines, and metabolites generated from gut bacteria (Hameed et al., 2020).

### *2.3.2. Exercise effects on biochemical biomarkers*

Regular physical exercise has a substantial impact on biochemical indicators, such as those pertaining to oxidative stress, inflammation, and the metabolism of fats and blood glucose. Aerobic exercise has significant effects on glucose control (Snowling & Hopkins, 2006), exercise tolerance, fasting glucose level, improve lipid profile (Asuako et al., 2017) and glucose excursion during an OGT in elderly patients with type 2 DM. These modifications help lower the risk of cardiovascular disease, which is especially important for people with type 2 diabetes. In addition resistance training has been shown to significantly improve insulin sensitivity (Hansen et al., 2012b; Ishii et al., 1998), glycemic control, and lipid profiles in individuals with type 2 diabetes (Misra et al., 2008). These improvements highlight the effectiveness of resistance exercises in addressing the metabolic challenges associated with diabetes, such as reduced insulin efficiency and poor blood sugar regulation.

Furthermore resistance exercise has been linked to lower concentrations of pro-inflammatory markers and cytokines, including interleukin-6 (IL-6) and C-reactive protein (CRP) (Kim & Yeun, 2022). Improved insulin sensitivity and a decreased chance of developing metabolic syndrome can result from these reductions. Resistance training has also been demonstrated to improve glucose metabolism and lower insulin levels (Strasser et al., 2010), which in turn have a positive impact on insulin resistance as assessed by the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) (Kolahdouzi et al., 2019).

Studies continually demonstrate the personal advantages that aerobic and resistance training enhances not just muscular strength and cardiovascular fitness (Maiorana et al., 2000) for individuals with type 2 diabetes, but also insulin sensitivity, glucose control, and inflammatory indicators (Ambelu & Teferi, 2023; M. A. R. Da Silva et al., 2020). We call this concurrent training (Methenitis, 2018). By combining the advantages of resistance and aerobic exercise, this creative approach may improve health results even more. According to different studies concurrent training has been linked to better results in lowering blood sugar, changing body composition through fat loss and muscle gain, and even having a good influence on cholesterol levels (Ambelu & Teferi, 2023; Bassi et al., 2015).

Research has demonstrated that concurrent exercise regimens significantly lower hemoglobin A1c (HbA1c) (Bassi et al., 2015; R. J. Sigal et al., 2007), a measure of long-term blood sugar control. This improvement is likely due to increased muscle mass and enhanced insulin sensitivity, allowing the body to utilize blood sugar more effectively (Mavros et al., 2013).

In addition to glycemic management concurrent training has a good impact on body composition (Ambelu & Teferi, 2023; Motahari Rad et al., 2023). This exercise technique helps to regulate blood sugar levels by creating a metabolically healthy profile through the promotion of muscle growth and fat reduction. Concurrent training also improves the cardiovascular system and lowers the risk of heart disease (Atashak et al., 2016; Davis et al., 2008), which is a major cause of type 2 diabetes. Persistent inflammation is another characteristic of type 2 diabetes that concurrent exercise seems to counteract (Annibalini et al., 2017; Yang et al., 2023). Research suggests that it may have the dual benefit of

improving insulin sensitivity and reducing inflammatory markers (Agrawal & Kant, 2014). Additionally, experts feel that concurrent exercise supports the benefit of an exercise program in the management of type 2 diabetes due to the etiology of vascular disease (Maiorana et al., 2001), hear rate and blood pressure (Maiorana et al., 2002). However, careful selection of training modalities is crucial when implementing concurrent training in individuals with T2DM, as the potential for an interference effect between different exercise types may reduce the overall effectiveness of the program. By tailoring the training approach, the balance between aerobic and resistance exercises can be optimized to maximize benefits.

Researchers recommend conducting more research on the protocol used to conduct concurrent training during training sessions. specifically, whether aerobic exercise is performed before or after resistance training, because of the inconsistent effects of concurrent training. This could have an impact on biochemical responses (Banitalebi et al., 2016; Bassi et al., 2015). The physiological processes behind these variations in exercise sequence, such as altered hormone responses, glycogen usage, and metabolic pathways active during different forms of exercise, may be responsible.

### *2.3.3. Methods for assessing biochemical markers in T2DM patients*

Assessing biochemical markers is essential for effective management of Type 2 Diabetes Mellitus (T2DM). Several established methods provide valuable information for researchers and healthcare professionals.

One important test for the diagnosis of type 2 diabetes is fasting blood glucose (FBG). After an overnight fast, the blood sugar level is measured, and elevated readings may indicate possible type 2 diabetes (Fu et al., 2017). FBG does not account for how the human body processes sugar after meals, which is a blind spot. These post-meal surges can be substantial and may eventually lead to health issues (Tang et al., 2020). There are two primary blood sugar testing instruments to obtain a more comprehensive view. Glucometers are handheld instruments that provide a single blood sugar reading by pinching the index finger. They're inexpensive, simple to use, and perfect for routine monitoring—especially if you're not experienced with T2DM management. Conversely,

continuous glucose monitors (CGMs) offer a far more comprehensive view. These minimally invasive devices have a sensor inserted under the skin that continuously tracks blood sugar throughout the day. CGMs are better suited for people with insulin-dependent diabetes or those who need a deeper understanding of their blood sugar patterns, but they're typically more expensive and require a prescription (Kubihal et al., 2021).

Another important blood test that provides insight into the body's insulin production is the fasting insulin test. The pancreas of the body secretes the hormone insulin, which aids in cells' absorption of blood sugar. Like a fasting blood sugar test, fasting insulin levels are determined after abstaining from food and liquids for at least eight hours, except water (Cobb et al., 2013). It can be difficult to interpret insulin values after fasting. Excessive levels could mean that your body is making more insulin to combat insulin resistance, a disease in which cells lose their sensitivity to the effects of insulin. However, a stand-alone test result is less useful because insulin during a fast can be affected by stress, drugs, and other health issues (Borai et al., 2007).

Physicians frequently monitor fasting insulin in addition to fasting blood sugar to obtain a more comprehensive picture. They can compute insulin resistance indices, such as the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), by combining this data. HOMA-IR is a non-invasive method for determining insulin sensitivity (Borai et al., 2011). Based on insulin and fasting glucose levels, it calculates insulin resistance; however, variables including inflammation and obesity may have an impact on accuracy (Gayoso-Diz et al., 2013).

A straightforward blood sample at a clinic or lab is necessary for FPIL testing. It is noteworthy that although fasting insulin has its value, it is not a complete picture. Other procedures, like as an oral glucose tolerance test (OGTT), may be required in specific circumstances to evaluate how the body responds to sugar in terms of insulin (Patarrão et al., 2014). A Glucose Tolerance Test (OGTT) measures the blood sugar response to a standardized glucose drink to provide a more complete picture. It takes longer to diagnose T2DM and prediabetes than a straightforward fasting blood sugar test, despite its value. The total glucose exposure over time is represented by the Area Under the Curve (AUC), which is frequently computed during an OGTT (Bartoli et al., 2011). When compared to

single blood sugar measurements, it yields more information, although an OGTT is necessary.

A blood test can be examining the various lipids, or fats, that are present in the bloodstream. The likelihood of heart disease can be greatly impacted by the quantities of these fats, which are essential to your well-being in general (Schaefer, 2002). The total cholesterol, HDL (good) cholesterol, LDL (bad) cholesterol, and triglycerides are all measured by a standard lipid profile (Arsenault Benoit et al., 2009). Testing for a lipid profile takes several steps instead of a single instrument to obtain a lipid profile. A medical professional will take blood from an arm vein using a sterile syringe and needle. After that, the blood is drawn into a special phlebotomy tube that has anticoagulants in it to stop the blood from clotting. That is not where the journey ends. After that, a laboratory receives this blood sample for examination. Specialized equipment is the main attraction of the lab. Red blood cells and plasma, or the liquid part of the sample, are separated from the other components by high-speed spinning in a centrifuge (Warnick et al., 2008). Ultimately, automated analyzers take over and determine the lipid profile by measuring the various forms of cholesterol and triglycerides in the blood serum through complex chemical reactions (Ferreira et al., 2015).

### 2.4. Anthropometric Index in Type 2 Diabetic Patients

Beyond its effects on blood sugar regulation, type 2 diabetes (T2DM) is linked to notable changes in body composition, as determined by a number of methods. These changes include increased visceral fat accumulation, ectopic fat deposition (fat storage in non-adipose tissues), and decreased muscle mass (sarcopenia) (Lempesis & Georgakopoulou, 2023). This review investigates the mechanisms through which type 2 diabetes leads to these deleterious alterations in body composition, as measured by metrics such as body mass index (BMI), body fat percentage, waist-to-hip ratio, and possibly more specialized evaluations such as muscle mass by dual-energy X-ray absorptiometry (DXA) or bioelectrical impedance analysis.

In type 2 diabetes, persistently high blood sugar levels cause more protein non-enzymatic glycation (NEG). Proteins undergo this process when glucose molecules attach to them,

changing how they function (Wu et al., 2022). Glycated proteins in muscle tissue can hinder protein synthesis, which is the process of gaining new muscle, and encourage protein breakdown, which results in the loss of muscle mass. Further impeding the development of muscle mass is the suppression of the breakdown of amino acids, the building blocks of proteins, for energy by elevated glucose availability (Hipkiss, 2006). Pro-inflammatory cytokine levels are higher in T2DM patients, who have persistent low-grade inflammation. These inflammatory mediators have the potential to worsen insulin signaling in muscle cells and accelerate the breakdown of muscle protein. Inflammation impairs the body's capacity to retain muscle mass by interfering with the mechanisms involved in muscle growth and repair (Dalle & Koppo, 2020; Pérez-Baos et al., 2018).

In the hypothetical case, muscle cells are signaled by the hormone insulin to take in and store glucose from the bloodstream for energy. But in type 2 diabetes (T2DM), the muscle cells become resistant to this signal. This means they take up less glucose, leaving them with less stored energy (like having a low gas tank). Over time, this lack of energy can lead to muscle loss, a condition called sarcopenia (Hou et al., 2023; Petersen & Shulman, 2018).

Chronically elevated blood sugar levels in type 2 diabetes also increase fat accumulation by inhibiting fat breakdown and increasing lipogenesis, or the synthesis of fat (Lewis et al., 2002). Adiponectin, a hormone that encourages fat storage in safe areas like adipose tissue, is similarly suppressed by this. But excess fat spills over and gathers elsewhere when these safe zones are overloaded; this may lead to obesity (Boutcher, 2014). Because of things like insulin resistance and lipotoxicity (the harmful effects of too much lipids), excess fat in T2DM cannot be effectively stored in adipose tissue (fat storage sites) (Defronzo, 2004). This further impairs the function of non-adipose tissues such the liver, muscles, and pancreas by causing fat to accumulate there (Ahmed et al., 2021; van Herpen & Schrauwen-Hinderling, 2008). Insulin sensitivity may be hampered by ectopic fat buildup in muscles, which can worsen muscle loss (da Silva Rosa et al., 2020).

In T2DM, a number of other variables may also impact changes in body composition. Genetic variants may make people more vulnerable to type 2 diabetes and the alterations in body composition that come with it (Murea et al., 2012). Decreased physical activity exacerbates body composition by hastening the loss of muscle mass and impairing insulin

sensitivity. Adopting unhealthful eating habits, especially consuming excessive amounts of processed carbs and harmful fats, can lead to ectopic fat deposition (Della Pepa et al., 2023).

Finally, it should be noted that T2DM alters body composition as a result of a complex interaction of variables, raising the risk of obesity and, in particular, the buildup of visceral fat (Schuster, 2010). Gaining an understanding of these mechanisms is essential to creating strategies that effectively manage T2DM and stop its negative effects on the distribution of body fat. The effects of diet and exercise on body composition and fat distribution in T2DM patients are still being studied. Therapies and researchers targeting inflammation, improving insulin sensitivity, and promoting healthy fat metabolism hold promise for improving body composition and overall health outcomes.

### *2.4.1. Clinical consequences of bad body composition in T2DM patients*

Type 2 diabetes mellitus (T2DM) introduces another complication to health beyond its effects on blood sugar regulation: abnormal body composition. This imbalance exacerbates type 2 diabetes and its symptoms by causing a deleterious cascade that is represented by decreased muscle mass, increased visceral fat (fat surrounding the abdominal organs), and fat development in non-adipose tissues (Marco Antônio R Da Silva et al., 2020; Defronzo, 2004). Less muscle mass impairs the body's capacity to regulate blood sugar since it is a crucial location for glucose absorption (Argilés et al., 2016). On the other way the release of free fatty acids and inflammatory chemicals by visceral and ectopic fat deposits worsens the situation by impairing insulin signaling and creating a vicious loop that deteriorates blood sugar regulation (Ahmed et al., 2021).

Cardiovascular problems are also made more likely by this poor body composition. Peripheral artery disease, heart disease, and stroke are associated with a higher incidence of both ectopic (Lim & Meigs, 2014) and visceral fat accumulation (Lu et al., 2010). This increased risk is influenced by oxidative stress, altered blood lipid profiles, and chronic inflammation. Moreover, the increase of visceral fat closely coexists with hypertension, another significant risk factor for cardiovascular issues (Lu et al., 2010). Visceral fat accumulation can overtax these organs, making them work extra hard to eliminate waste.

The kidneys may eventually suffer harm from this hyperfiltration, which also raises the risk of chronic renal disease. Additionally, kidney function may be directly harmed by the persistent low-grade inflammation linked to an unhealthy body composition (de Vries et al., 2014; Hall et al., 2021).

These serious complications are outweighed by the negative effects. Ectopic fat buildup in the liver, which can culminate in non-alcoholic fatty liver disease (NAFLD), is a frequent outcome of poor body composition in type 2 diabetes (Blackstone, 2016). A poor body composition is also associated with an increased risk of death, which makes it particularly concerning. A strong association has been shown by research to exist between greater death rates in type 2 diabetics, decreased muscle mass, and raised visceral fat (Tancredi et al., 2015).

Generally, poor body composition exacerbates the overall health and progression of type 2 diabetes. It raises the risk of several problems in addition to impeding glycemic management (Lim & Meigs, 2014). Understanding this connection is essential for creating all-encompassing T2DM management plans that take body composition and blood sugar control into account. With the ultimate goal of enhancing long-term health outcomes and lowering the mortality risk in T2DM patients, research is still being conducted to examine the intricate interactions between body composition and comorbidities associated with the disease.

### *2.4.2. Exercise effect on anthropometric index*

Exercise has been widely studied for its potential to improve anthropometric measures and, consequently, reduce the risk of obesity, cardiovascular disease, and other metabolic disorders (Carroll & Dudfield, 2004). Three types of exercise, aerobic exercise, resistance training, and concurrent training, play pivotal roles in improving these indices through different mechanisms.

Aerobic exercise, characterized by activities that elevate heart rate and increase oxygen consumption (e.g., running, cycling, walking), is well-documented for its effects on reducing body fat and improving BMI (Willis et al., 2012). Studies have consistently shown that aerobic training leads to reductions in both visceral and subcutaneous fat

(Hassannejad et al., 2017), which is important for improving body composition and metabolic health. A study by Swift et al. (2014) found that aerobic exercise leads to significant weight loss and reduction in waist circumference (Hassannejad et al., 2017), both of which are critical components of the anthropometric index. The caloric expenditure associated with aerobic activities also helps create a negative energy balance, facilitating fat loss while preserving lean body mass (Donnelly et al., 2004).

In individuals with Type 2 diabetes, the benefits of aerobic exercise extend to improved insulin sensitivity, enhanced glucose control, and better lipid profiles, which are correlated with improved anthropometric measures (Nassis et al., 2005). Ross et al. (2000) demonstrated that aerobic exercise with caloric restriction could reduce abdominal obesity and improve the waist-to-hip ratio, a key marker of cardiovascular risk (Nicklas et al., 2009). This suggests that aerobic exercise is effective not only for general weight management but also for targeted reductions in visceral fat, which is particularly harmful in metabolic disorders.

Resistance training (RT), also known as strength training, involves exercises that improve muscle strength and endurance through resistance, such as weightlifting or body-weight exercises. While its primary focus is on increasing muscle mass and strength, resistance training also exerts significant cardiovascular adaptations and plays a role in body composition changes (Heydarpour et al., 2015), which are reflected in the anthropometric index.

Resistance training has been shown to reduce fat mass, increase lean muscle mass, and improve the overall metabolic rate, leading to favorable changes in BMI and waist circumference (Willis et al., 2012). Beyond changes in body composition, RT induces cardiovascular adaptations that contribute to better vascular health. According to a study by Fagard, regular resistance training reduces blood pressure, improves arterial stiffness, and enhances endothelial function (Fagard, 2006). This indicates that RT not only benefits body composition but also aids cardiovascular health, which is particularly relevant for patients with Type 2 diabetes who are at higher risk of cardiovascular diseases.

Moreover, resistance training can enhance insulin sensitivity, which is closely tied to improvements in anthropometric measures, particularly in reducing central obesity.

Resistance exercise increases glucose uptake in muscles, thereby improving glycemic control and reducing fat storage (Dela & Kjaer, 2006; Hansen et al., 2012b). These effects are harmonious with the metabolic benefits observed with aerobic exercise, leading to comprehensive improvements in body composition and cardiovascular health.

Concurrent exercise is another important form of exercise for people with type 2 diabetes. When aerobic and strength training are combined, body fat decreases more and lean muscle mass increases more than when each type of exercise is done alone (Bouamra et al., 2022). A meta-analysis by García-Hermoso et al demonstrated that individuals who performed both aerobic and resistance training had superior improvements in waist circumference, BMI, and overall body composition than those who engaged in only one type of exercise (García-Hermoso et al., 2018). This is likely since aerobic exercise effectively burns calories and reduces fat (Muscella et al., 2020), while resistance training builds lean muscle mass (Ransdell et al., 2021), which increases the metabolic rate and supports long-term weight management.

### *2.4.3. Methods for assessing body composition in T2DM research*

Research on the changes in body composition associated with type 2 diabetes mellitus (T2DM) is essential. There are various approaches to evaluating this, each with advantages and disadvantages. Although easily accessible, basic and affordable instruments such as the Body Mass Index (BMI) have certain drawbacks. Because BMI just considers height and weight, it may incorrectly identify people who are muscular as overweight or obese (Gutin, 2018). A clearer picture of central fat accumulation a risk factor for problems from type 2 diabetes: can be obtained by measuring waist circumference (WC) and waist-to-hip ratio (WHR). They might not be the best choice for everyone, though, as body forms vary (Zhang et al., 2021).

The other measurement tool is called a Bioelectrical Impedance Analysis (BIA), which uses electrical currents to determine body composition accurately and non-invasively (Marini et al., 2013). Body temperature, recent meals, and hydration levels can influence the results of BIA, despite its portability and ease of use (Stahn et al., 2012). Measurements of skinfold thickness, provide a more targeted assessment of fat distribution (Jayawardena

et al., 2020). However, this process might be affected by the experience and technique of the individual taking the measurements, necessitating the use of skilled personnel (Hume & Ackland, 2017).

When determining body composition, Dual-Energy X-ray Absorptiometry (DXA) is regarded as the gold standard. It provides precise measurements of bone mineral density, muscle mass and fat mass using dual-energy X-rays, providing comprehensive body composition data. However, in comparison to other techniques, DXA is usually more costly and less available (Brownbill & Ilich, 2005). However, innovative techniques such as Bioelectrical Impedance Spectroscopy (BIS) provide even more information than lean mass and total body fat (Jaffrin & Morel, 2008). The most accurate image is produced using magnetic resonance imaging (MRI), but it is costly, time-consuming, and not commonly accessible for research (Rashmi & Snekhalatha, 2019).

The ideal approach for a given T2DM research project will vary depending on the objectives of the study, the available funds, the availability of participants, and the required level of information (Paulweber et al., 2010). For a more thorough evaluation, combining various techniques may be required, particularly when concentrating on particular components of body composition. For T2DM research to advance, a precise assessment of body composition is essential. A multitude of instruments are available to researchers, each with unique benefits and drawbacks. It is vital to carefully weigh these considerations when choosing the best approach or methods to address certain research topics.

## 2.5. Concurrent Training and Exercise Sequence

### *2.5.1. Concurrent training overview*

Concurrent training, defined as the combination of aerobic exercise (AE) and resistance exercise (RE) in a single program, is designed to enhance both cardiovascular and muscular fitness simultaneously (Shamim et al., 2018; Jacob M Wilson et al., 2012). Aerobic exercise primarily improves cardiorespiratory endurance, while resistance training focuses on increasing muscular strength, hypertrophy, and endurance (Muscella et al., 2020; Ransdell et al., 2021). The physiological adaptations induced by these two exercise modes are distinct; aerobic exercise promotes mitochondrial biogenesis and enhances oxidative

capacity through pathways like AMPK (adenosine monophosphate-activated protein kinase) (Ihsan et al., 2015), whereas resistance training activates the mTOR (mammalian target of rapamycin) pathway, stimulating muscle protein synthesis (Ogasawara et al., 2016). Even though these pathways may interfere, a phenomenon known as the interference effect (J. J. Fyfe et al., 2014), concurrent training is still a useful tactic for enhancing general health since it combines the advantages of resistance and aerobic exercise (Bouamra et al., 2022).

In diabetic populations, particularly those with Type 2 diabetes, concurrent training provides significant health benefits. One of the key advantages is improved glycemic control (Ambelu & Teferi, 2023; Motahari Rad et al., 2023). Studies have demonstrated that concurrent training can lead to greater reductions in HbA1c levels and fasting glucose compared to aerobic or resistance training alone (Hou et al., 2015). This dual modality of training, therefore, plays a crucial role in improving insulin sensitivity (Zheng & Cai, 2019) and controlling blood sugar levels (Ambelu & Teferi, 2023) in individuals with Type 2 diabetes.

Concurrent training also contributes significantly to cardiovascular health, which is often compromised in individuals with diabetes (Saima Zaki, Md Farhan Alam, Saurabh Sharma, Irshad Husain Naqvi, et al., 2024). Additionally, this type of training modality positively impacts lipid profiles by increasing high-density lipoprotein (HDL) and reducing low-density lipoprotein (LDL) cholesterol (Mann et al., 2014; Saima Zaki, Saurabh Sharma, et al., 2024). These cardiovascular adaptations are critical in reducing the risk of heart disease, a major complication in diabetic patients. However, there were no statistically significant variations in the groups' lipid profiles or blood pressure. Blood pressure and lipid measurements, including triglycerides and cholesterol, did not alter significantly between the concurrent, aerobic, and resistance training groups in spite of the intervention (Ronald J. Sigal et al., 2007).

Moreover, concurrent training has been shown to positively impact body composition and weight management (Bouamra et al., 2022), both of which are closely linked to Type 2 diabetes. Regular participation in concurrent training leads to an increase in lean muscle mass and a reduction in fat mass, particularly visceral fat (Wilhelm & Pinto, 2019), which

plays a pivotal role in insulin resistance (Bardini et al., 2012). The combination of aerobic fat oxidation and muscle hypertrophy from resistance training supports long-term metabolic health, reducing the risk of obesity-related complications. A combined AT and RT regimen, on the other hand, did not produce noticeably greater reductions in body mass or fat mass than AT alone, while needing twice as much time (Willis et al., 2012; Zhang et al., 2017).

While the synergistic effects of concurrent training offer a powerful intervention for improving the anthropometric index in individuals with type 2 diabetes, the contradictory results observed may be attributed to the sequence of exercises performed within the training regimen. Adjusting the order of exercises could play a critical role in maximizing the desired outcomes.

### *2.5.2. Molecular basis for concurrent training adaptation specificity*

In terms of their innate stimuli and the adaptations that persistent training induces in skeletal muscle, resistance and endurance exercise constitute distinct exercise modalities. Understanding the molecular mechanisms behind skeletal muscle adaptations to various exercise modalities has emerged in recent years (Atherton et al., 2005; Bodine et al., 2001; Pilegaard et al., 2003). The cumulative effect of acute molecular signaling responses and subsequent gene expression triggered after repeated exercise bouts is thought to be the cause of exercise-induced adaptations in skeletal muscle. Over time, this accumulation of particular proteins results in an altered muscle phenotype (Flück & Hoppeler, 2003; Perry et al., 2010). Resistance and endurance training have been hypothesized to cause nearly different activation of particular gene networks and molecular signaling pathways that mediate the mode-specific adaptations to long-term exercise training (Shamim, 2020).

Fiber hypertrophy resulting from resistance exercise is driven by the anabolic mTORC1 signaling cascade (Gonzalez et al., 2016). This pathway integrates mechanical stimuli, growth factors, and nutrient signals to enhance net protein synthesis. It achieves this by phosphorylating downstream targets involved in initiating translation, thereby promoting muscle protein synthesis in response to acute resistance exercise in humans (Drummond et al., 2009; Egan & Sharples, 2022).

Unlike resistance training, aerobic exercise usually involves longer-duration, lower-intensity contractile activity that produces far less physical stress on the working muscle fibers (J. J. Fyfe et al., 2014). Instead, it imposes a substantial metabolic challenge, leading to disruptions in intracellular concentrations of calcium ($Ca^{2+}$), oxygen, lactate, and reactive oxygen species (ROS), as well as shifts in AMP:ATP and $NAD^{+}$:NADH ratios (Bouviere et al., 2021; De Nicolo et al., 2023). These changes activate key intracellular signaling pathways, such as AMPK and $Ca^{2+}$/CaMKII, which drive mitochondrial biogenesis through PGC-1α and promote adaptations like enhanced substrate utilization and capillary density, ultimately improving oxidative capacity (Coffey & Hawley, 2007; Craig et al., 2015).

Endurance-type stimulation suppresses the Akt/mTOR pathway and its downstream targets (Apró et al., 2013; Ogasawara et al., 2014). This suggests that the distinct activation of either Akt/mTOR or AMPK/PGC-1α pathways may account for the contrasting adaptations observed with resistance and endurance training, aligning with the concept known as the 'AMPK/Akt master switch' hypothesis (de Souza et al., 2013).

In concurrent training, the sequence of exercises plays a crucial role at the molecular level. When endurance training precedes resistance training, the activation of AMPK can suppress mTOR signaling, potentially hindering strength gains and muscle hypertrophy (Atherton et al., 2005; Bolster et al., 2002). Conversely, starting with resistance training optimizes mTOR activation, promoting strength and hypertrophic adaptations, while the subsequent endurance exercise preserves aerobic benefits (Solsona et al., 2021). This interaction highlights the significance of exercise order in aligning training outcomes with specific goals.

### *2.5.3. Impact of concurrent training exercise sequence on outcomes*

Because it may have an impact on training results, the order in which aerobic and resistance exercises are performed during concurrent training has generated interest. Particularly in populations like Type 2 diabetic patients, the interaction of these two modalities within a single session might result in a variety of physiological reactions that may affect performance (Z. Murlasits et al., 2018), biochemical adaptations (Z. Murlasits et al., 2018),

and health consequences. However, to understand the optimal interference effect on variables related to patients with type 2 diabetes, researchers advise that more research be done on the best order to perform resistance and aerobic training when completing combination training (Bassi et al., 2015).

When CT with distinct exercise orders affect one another's adaptation either AT or RT comes first, this is known as the interference effect (V. G. Coffey & J. A. Hawley, 2017). The order in which resistance and aerobic exercises are performed during a concurrent workout may theoretically have an impact on the physiological responses that occur immediately afterward (Zsolt Murlasits et al., 2018). While acute signaling responses affect long-term adaptations, the order of exercise modalities in concurrent training sessions has an impact. Resistance and aerobic exercise start separate pathways. Resistance training stimulates the mTOR pathway, which encourages muscle protein synthesis, whereas aerobic exercise mainly activates the AMPK-PGC-1α axis, which increases mitochondrial biogenesis and oxidative capacity (Vernon G. Coffey & John A. Hawley, 2017). The sequence in which both forms of exercise are undertaken may have an impact on the magnitude and nature of these signaling pathways. Studies suggest that performing aerobic exercise before resistance training may suppress the mTOR pathway due to the activation of AMPK, thereby limiting muscle hypertrophy (Coffey et al., 2009). Conversely, resistance training before aerobic exercise may prevent this interference and allow for better muscle adaptation. The cumulative effect of these acute signaling responses could alter gene expression patterns over time, impacting muscle growth, endurance capacity, and overall metabolic health (De Souza, 2019).

In addition to acute molecular adaptation to concurrent training order, the majority of research have demonstrated its impact on physiological measures that concurrent aerobic-resistance based training compromises increases in muscle hypertrophy and strength (Häkkinen et al., 2003; Jones et al., 2013; Lee et al., 2020). Researchers found that performing aerobic exercise before resistance exercise resulted in considerably higher post-exercise VO2 (Drummond et al., 2005). In contrast to aerobic exercise prior to resistance exercise; resistance exercise before aerobic exercise, improves lower and upper limb strength (Silva et al., 2022), optimize hypertrophy (Pinto et al., 2014). Another researcher

results suggest that although vascular function is not improved by AT before RT (Okamoto et al., 2007).

Even though studies have shown interferences in aerobic adaptations and performance-related muscular hypertrophy without regulating participants' dietary practices, there are still gaps in the literature regarding the effects of the sequence of stimuli on the chronic response of anthropometric index, physiological, and biochemical biomarker response on type 2 diabetic patients while controlling dietary practice.

## 2.6. Summary of the Researcher's Systematic Review and Meta-Analysis

### *2.6.1. Purpose of the review*

The purpose of this systematic review and meta-analysis is to provide a more refined assessment of the effects of concurrent training (CT), specifically the combination of continuous aerobic and short-rest resistance exercises in a single session, on metabolic biomarkers in patients with Type 2 Diabetes Mellitus. The study intends to overcome the shortcomings of previous reviews by applying firm inclusion criteria and focusing on programs that last exactly 12 weeks. These limitations included varied demographics, uneven training procedures, and vast differences in intervention duration. The ultimate goal is to create more clinically relevant, standardized, and usable evidence for advising exercise prescription and enhancing metabolic health outcomes in T2DM patients.

### *2.6.2. Search strategy and databases used*

Up to January 30, 2025, an electronic search was performed across databases such as Google Scholar, PubMed, Web of Science, Science Direct, and Cochrane to uncover randomized controlled trials (RCTs) on concurrent training effects in type 2 diabetes mellitus. Search terms included "Diabetes" AND ("Exercise" OR "Training"), following the PICOS framework: population (T2DM), intervention (concurrent training), comparator (no exercise or standard care), outcomes (HbA1c, HOMA-IR, HDL, total cholesterol, triglycerides), and study type (RCTs). The reference lists for selected research and relevant reviews were also examined. The intervention consisted of combined aerobic and

resistance workouts performed three times weekly on non-consecutive days, whereas controls received usual medical treatment without exercise.

### *2.6.3. Inclusion/exclusion criteria*

Studies were included if they involved participants diagnosed with Type 2 Diabetes Mellitus (T2DM) and tested a concurrent training intervention combining continuous aerobic exercise (50-85% $VO_2$ max or heart rate reserve) with resistance training (50–80% 1RM) using short rest intervals (30-90 seconds), performed 40-60 minutes per session, three times weekly. Included studies had to measure at least one primary outcome related to glycemic control (HbA1c), insulin resistance (HOMA-IR), or lipid profiles (TC, TG, HDL), be published in English in peer-reviewed journals, and be randomized controlled trials (RCTs).

Studies were excluded if they involved mixed participant samples, combined interventions like diet and exercise, control groups that exercised, lacked specified outcomes, had intervention durations other than 12 weeks, or were reviews, case reports, or had unclear data.

### *2.6.4. Summary of key findings*

A meta-analysis of six studies involving 378 participants demonstrated that concurrent training significantly reduced HbA1c levels, with a moderate effect size (pooled effect = -0.53, 95% CI: -0.98 to -0.07, p = 0.03), although considerable heterogeneity was present ($I^2$ = 65.69%). Similarly, five trials including 255 participants showed a significant and clinically meaningful reduction in insulin resistance as measured by HOMA-IR (SMD = -0.80, 95% CI: -1.24 to -0.35, p = 0.001), indicating a moderate to large effect size, despite moderate heterogeneity across studies ($I^2$ = 56.41%). Regarding lipid profiles, eight studies with 217 participants found a moderate but statistically significant increase in high-density lipoprotein (HDL) levels following concurrent training (Hedges' g = 0.30, 95% CI: 0.03 to 0.57, p = 0.03), with moderate heterogeneity ($I^2$ = 46.40%). Triglyceride (TG) levels were moderately to largely reduced in seven studies comprising 191 participants (SMD = -0.78, 95% CI: -1.33 to -0.23, p = 0.01), though high heterogeneity was observed ($I^2$ = 70.63%).

Finally, total cholesterol (TC) levels showed a moderate but significant reduction across eight studies involving 221 participants (SMD = -0.37, 95% CI: -0.63 to -0.10, p = 0.01), with moderate heterogeneity ($I^2 = 48.97\%$). Overall, these findings indicate that concurrent training combining continuous aerobic exercise with short-rest resistance training effectively improves glycemic control and lipid profiles in patients with Type 2 Diabetes Mellitus, although variability across studies suggests the need for further research to understand influencing factors.

## 2.7. Gaps in the Literature

### *2.7.1. Lack of research on exercise sequence impact*

Regarding the impact of concurrent training, combining aerobic and resistance exercises on cardiovascular and metabolic health in individuals with Type 2 diabetes, there is a significant study gap. Exercise is beneficial for diabetes, but little is known about how the sequence of aerobic and resistance training influences certain health outcomes. To the best of the researcher's knowledge, no research has yet shown how the order of exercises affects these results in people with Type 2 diabetes. The majority of studies have ignored the special potential of exercise sequencing in favor of general exercise. Researchers have suggested that in order to develop evidence-based exercise recommendations, randomized controlled trials (RCTs) that specifically examine the sequence of concurrent training are required. To determine the best exercise sequence for this group of people, focused RCTs are necessary.

### *2.7.2. Lack of research on controlling dietary practice*

There is a notable research gap regarding the impact of exercise sequence, combining aerobic and resistance training, on specific health outcomes in people with Type 2 diabetes, particularly when controlling for dietary practices. While numerous studies have explored the benefits of concurrent exercise on diabetes management (Ambelu & Teferi, 2023; Azmand et al., 2024; Saima Zaki, Md Farhan Alam, Saurabh Sharma, Said El-Ashker, et al., 2024; Saima Zaki, Saurabh Sharma, et al., 2024), no research has yet demonstrated how the order of aerobic and resistance training influences these outcomes while accounting for

the dietary habits of participants. Most existing studies tend to focus on the effects of exercise alone, without considering how diet might modulate the impact of exercise. Knowing the importance of diet to managing the levels of glucose and metabolic health, it is critical to investigate the potential differential effects of exercise and controlled dietary practices on variables like insulin sensitivity, lipid profiles, cardiovascular risk markers, and glycemic control. This lack of controlled, comprehensive studies calls for further research to provide evidence-based exercise prescriptions for Type 2 diabetic patients, considering both exercise sequence and dietary management.

### *2.7.3. Focus on the special population*

Most studies on exercise sequencing have been conducted on healthy individuals, athletes, or recreationally active people, whose responses may not directly apply to Type 2 diabetics, who face unique metabolic challenges such as insulin resistance, chronic inflammation, and altered lipid metabolism. Given the growing global burden of Type 2 diabetes, this population needs special attention, as their exercise responses differ significantly from healthy individuals. Factors like impaired glucose uptake, reduced mitochondrial function, and the presence of comorbid conditions (e.g., hypertension, obesity) can influence how they respond to different exercise sequences. Therefore, it is crucial to focus on how the sequence of aerobic and resistance exercise affects key health outcomes, such as HbA1c, blood glucose, and lipid levels, to provide targeted, evidence-based exercise prescriptions for managing Type 2 diabetes.

## 2.8. Theoretical Framework

The present study is theoretically grounded in the Stimulus-Recovery-Adaptation (SRA) theory, an applied training model that evolved from Hans Selye's General Adaptation Syndrome (GAS) theory of stress (Campbell et al., 2013). While GAS explains biological responses to stress in general, the SRA framework was subsequently adapted within exercise physiology and training science to describe how the body responds specifically to repeated exercise stimuli. This model has been widely articulated and applied in the training literature by scholars such as (Bompa & Buzzichelli, 2019; Zatsiorsky et al., 2020), who emphasized the cyclic interaction between training stimulus, fatigue, recovery, and

long-term adaptation.

According to the SRA theory, each bout of exercise acts as a training stimulus that disrupts physiological homeostasis and induces acute fatigue. In the context of concurrent aerobic and resistance training, this stimulus imposes substantial metabolic, cardiovascular, and neuromuscular stress, particularly in individuals with chronic metabolic disorders such as type 2 diabetes mellitus. The magnitude of this stimulus is determined by training variables, including intensity, volume, frequency, dietary practice, and exercise sequence, all of which are central components of the present study.

Following the application of the training stimulus, the body enters the recovery phase, during which physiological systems repair and restore functional capacity. As emphasized by Zatsiorsky et al. (2020), recovery is a crucial element of the SRA cycle, as adaptations occur not during the exercise bout itself, but rather during the post-exercise recovery period. In clinical populations, recovery processes such as glycogen replenishment, vascular regulation, and neuromuscular repair may be compromised, making recovery management essential for achieving positive adaptations.

When recovery is sufficient, the organism progresses to the adaptation phase, characterized by an enhanced capacity to tolerate subsequent training stress. This phenomenon, often described as supercompensation, has been extensively discussed by Bompa and Buzzichelli (2019) within the framework of training periodization. Recent studies have shown that repeated stimulus-recovery cycles are expected to result in favorable cardiometabolic adaptations, including improved glycemic control, enhanced lipid metabolism, improved blood pressure regulation, increased cardiorespiratory fitness, and beneficial changes in body composition.

The SRA framework also provides a strong theoretical basis for examining the effects of exercise sequence in concurrent training. As proposed by Robineau et al. (2016), the order in which different exercise modalities are performed can influence the magnitude of fatigue and the quality of recovery, thereby modifying long-term adaptations. Performing aerobic exercise before resistance training or vice versa may differentially affect metabolic and cardiovascular stress, ultimately influencing adaptive outcomes (Jacob M. Wilson et al.,

2012).

Furthermore, the SRA theory underscores the importance of progressive overload and recovery balance to prevent excessive fatigue and maladaptation. In line with this framework, the present study incorporates supervised training, controlled progression, and adherence monitoring to ensure that participants remain within the adaptive range of the SRA continuum. This approach is particularly important when applying concurrent training interventions in populations with elevated cardiometabolic risk.

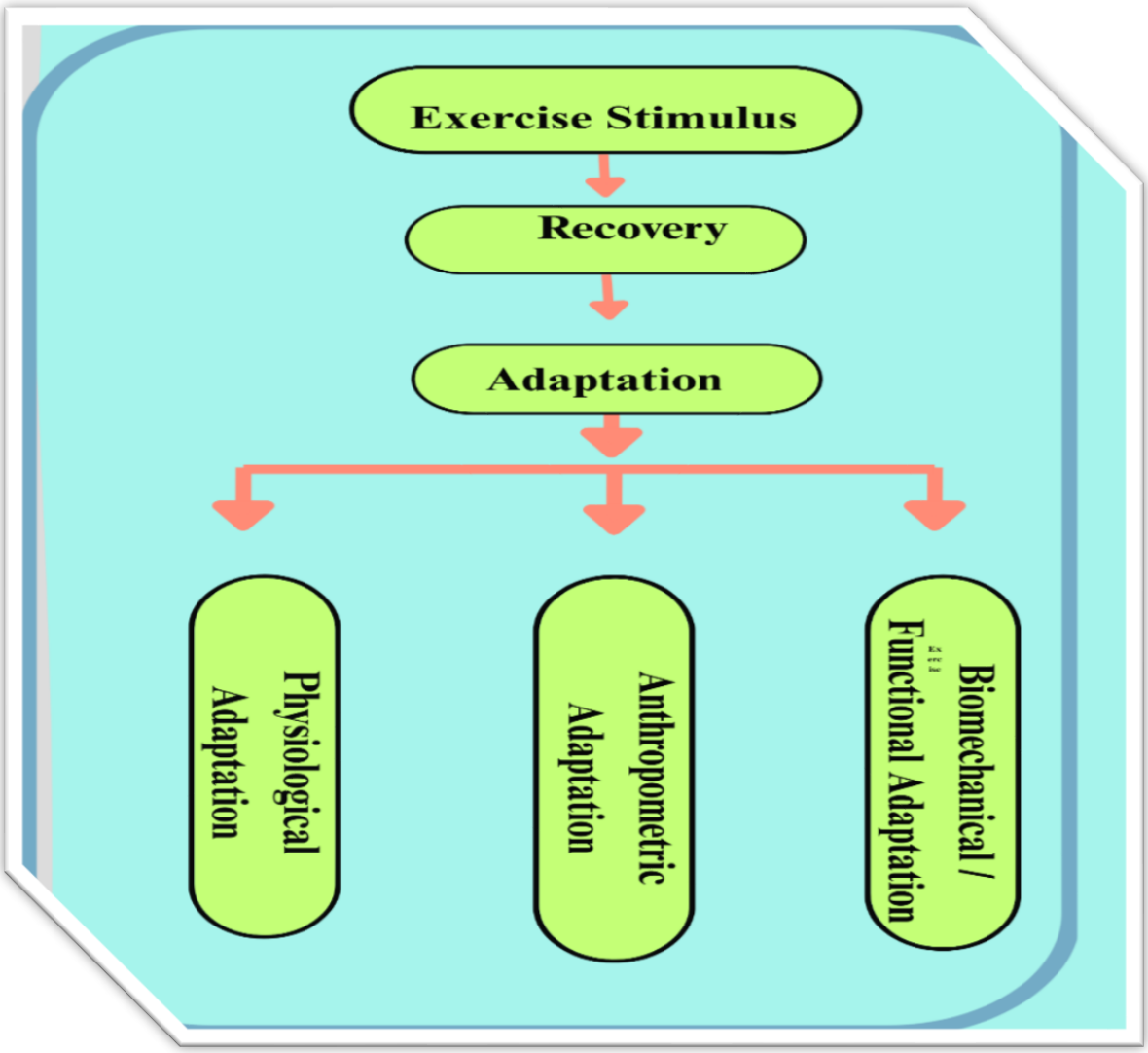


*Figure 1. Exercise-Induced Adaptations Based on the Stimulus-Recovery-Adaptation (SRA) Theory*

## 2.9. Conceptual Framework

This conceptual framework aims to explain the effects of concurrent training on cardiovascular function, anthropometric indices, and biochemical biomarkers in Type 2 diabetic patients while controlling the dietary practice of patients. Specifically, it addresses the importance of exercise sequence (i.e., whether aerobic or resistance training is performed first) in influencing these outcomes. The framework builds on the **e**xercise hypothesis, offering insights into how exercise interventions can optimize cardiovascular health and metabolic control in diabetic populations while controlling the dietary practices of patients.

The exercise sequence hypothesis explores the order in which aerobic and resistance exercises are performed and how this affects health outcomes, particularly in diabetic patients. The sequence of exercise may modulate factors such as fatigue, substrate utilization, and hormone release, impacting both short- and long-term health effects. Exercise sequence hypothesis in concurrent training incorporates aerobic first hypothesis and resistance first hypothesis.

The arrangement of aerobic and resistance training sessions affects VO2 Peak, blood pressure, and peripheral oxygen saturation. It is postulated in this study that the exercise sequence influences cardiovascular function, along with influence anthropometric metrics such as body fat percentage, BMI, and WHR. Furthermore, biochemical indicators that are critical to comprehending metabolic responses in Type 2 diabetic patients, such as glucose metabolism and lipid profiles may be impacted by the exercise regimen. On the other hand, dietary practices have a significant impact on cardiovascular function, directly altering blood pressure and heart health as well as the anthropometric index through modifications to body composition, including percentage of body fat and BMI. Additionally, it is anticipated that food decisions will affect biochemical indicators, controlling metabolic markers such as cholesterol and glucose levels. Additionally, it will be expected that food decisions may affect anthropometric indices, cardiovascular function, and biochemical indicators. Changes in the anthropometric index may correlate with improvements in cardiovascular health markers, while alterations in body composition can significantly impact metabolic markers.

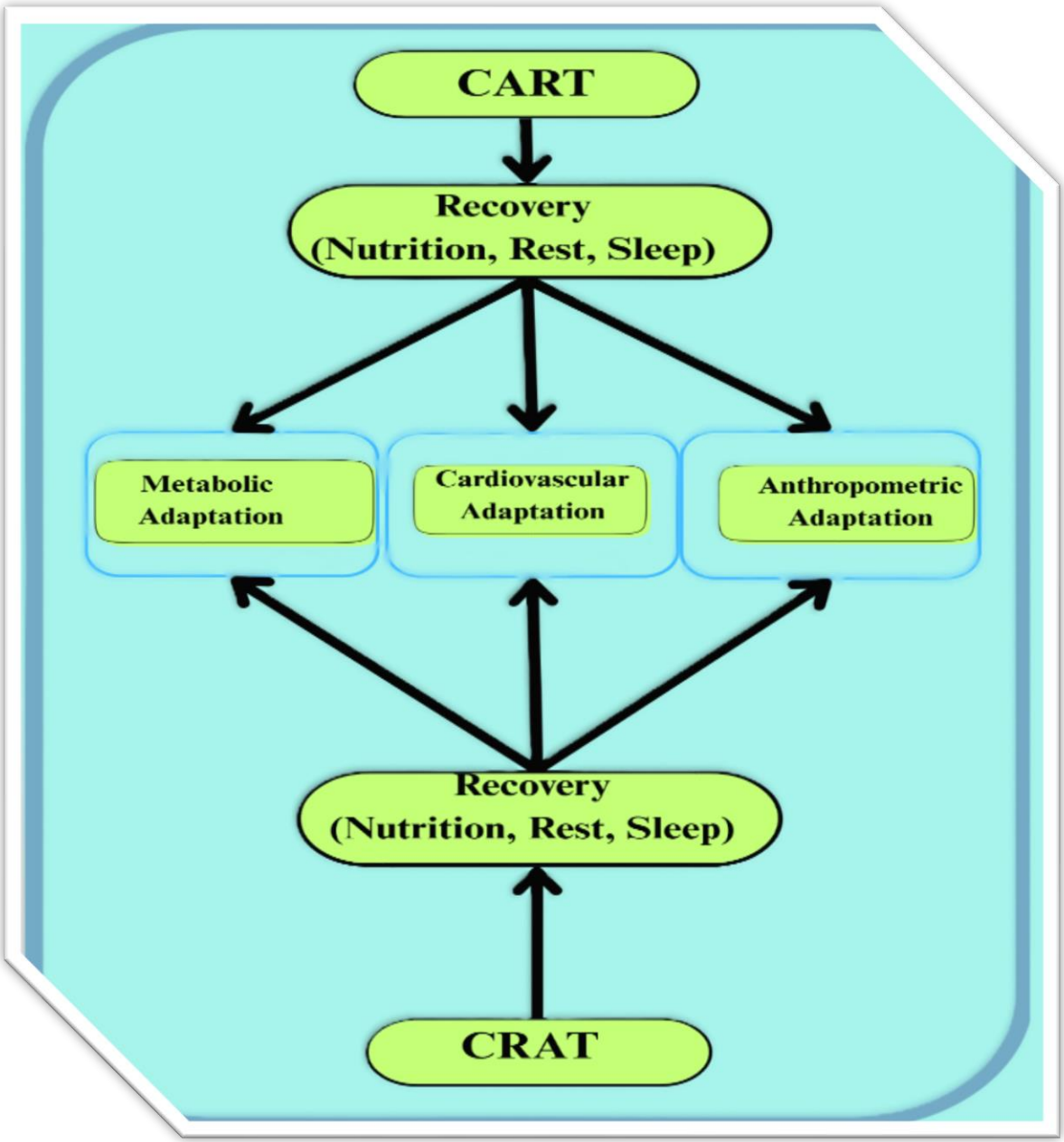


*Figure 2. Visual representation of the conceptual framework*

# CHAPTER THREE

# 3. MATERIAL AND METHODS

This chapter describes the research design and methodology employed to investigate the effects of different sequences of concurrent aerobic and resistance training on metabolic and cardiovascular outcomes in adults with type 2 diabetes mellitus (T2DM). It includes details on the study design, participant selection criteria, sampling procedures, and ethical considerations, ensuring that participants provided informed consent and voluntarily adhered to the intervention. The chapter also outlines the intervention protocols, including the frequency, intensity, duration, and sequence of aerobic and resistance exercises, as well as the monitoring of adherence and safety. Additionally, it covers the measurement procedures for anthropometric, metabolic, and cardiovascular variables, including glycemic control, insulin resistance, lipid profile, blood pressure, and aerobic capacity. Data collection instruments, laboratory analyses, and standardized procedures are described, followed by the statistical methods used to analyze the data, ensuring that the study findings are valid, reliable, and reproducible.

## 3.1. Setting of the Study

This research was conducted at Debre Markos, Ethiopia, a metropolitan city within the Amhara National Regional State, roughly 300 kilometers northwest of the capital, Addis Ababa. The city sits at a high elevation of 2,446 meters (8,025 feet) above sea level (Uhlig, 2003).

The exercise program was conducted at the Center for Fitness and Health at Debre Markos University Sport Science Academy Gymnasium, providing a controlled and safe environment. This facility offers several key advantages, including a variety of training machines, a spacious and well-maintained setting, and a strong focus on safety, making it an ideal location for the exercise program. A variety of equipment, including treadmills (12), Bic (9), cross fit training (5), leg press (4), chest press (5), multi gym (4), dual adjustable pulley (4), biceps/triceps machines (4), barbel and dumbbells with adjustable weights and different type of adjustable benches are available to accommodate different

training needs and fitness levels. This diverse type of equipment, ranging from cardio, weight machines to free weights, ensures that participants can engage in a comprehensive training regimen tailored to their individual requirements. Certified trainers are available throughout the program to assist participants with proper exercise techniques, offer support, and help maintain motivation. The research team prioritizes participant well-being by offering bottled water for hydration during workouts. Additionally, a dedicated health care assistant with first-aid equipment, like an AED and oxygen, was on hand to address any potential safety concerns. This controlled setting with qualified personnel and appropriate equipment ensures a safe and effective exercise intervention for all participants in the study.

### 3.2. Study Design

This study employed a three-arm parallel-group randomized controlled trial (RCT) design to compare the effects of exercise sequence in concurrent training on patients with type 2 diabetes. Participants were randomly assigned to one of three groups: CART (Aerobic Training + Resistance Training), CRAT (Resistance + Aerobic Training), or a wait-list control group (COG).

Participants were randomly assigned in equal numbers to the CART, CRAT, and COG groups, with stratification by sex and by four age categories: 41-45 years, 46-50 years, 51-55 years, and 56-60 years. Randomization was performed in a 1:1:1 ratio using a computer-generated sequence, and group assignments were placed in sealed, opaque envelopes. To minimize bias, the randomization process was overseen by the personal trainer and researcher rather than the data collectors.

Both groups participated in a one-hour concurrent training program held at 5:00 PM on Tuesdays, Thursdays, and Sundays. While the exercises were the same for both groups, the sequence of aerobic and resistance training differed. The researcher tracked changes within each group by assessing anthropometric, cardiovascular, and biochemical parameters at baseline and after the intervention.

### 3.3. Population of the Study

The study population comprised adult patients diagnosed with type 2 diabetes mellitus from the outpatient department of Debre Markos Referral Hospital, as well as individuals diagnosed with diabetes mellitus within Debre Markos town. Participants were recruited through voluntary enrollment, facilitated by local radio announcements and brochures posted on notice boards throughout the town. Additionally, hospital patient records were reviewed to identify eligible individuals for participation in the study. This approach aims to ensure a diverse and representative sample of middle-aged adults with type 2 diabetes from the region. Working with hospital staff also helps ensure accurate participant information, eases recruitment, and increases study credibility for participants unfamiliar with the research.

After obtaining informed consent, participants' eligibility is assessed based on the study's inclusion and exclusion criteria. The recruitment process strictly adhered to ethical guidelines, including securing informed consent, maintaining confidentiality, and safeguarding participants' privacy.

### 3.4. Inclusion and Exclusion Criteria

#### *3.4.1. Inclusion criteria*

Participants who fit the following requirements were recruited for this study:

- Established diagnosis of T2DM confirmed by a physician
- Participants must be between 41 and 60 years old
- Participants should be physically inactive based on the International Physical Activity Questionnaire-Short Form (IPAQ-SF) (Craig et al., 2003). (Appendix E and F)
- Participants should be managing their condition through dietary changes and/or lifestyle modifications.
- Participants must voluntarily choose to take part in the study and provide written informed consent after receiving a full explanation of the study procedures, including

any potential risks and benefits. (Appendix A and B)

- Participants must be medically cleared for exercise participation through the physical activity readiness questionnaire (PARQ) based on ACSM exercise prescription guidelines (Pescatello, 2014). (Appendix C and D)

### *3.4.2. Exclusion criteria*

Participants were excluded when:

- Individuals experiencing diabetes-related complications, including diabetic retinopathy, autonomic or peripheral neuropathy, and nephropathy, as identified using the Diabetes-Related Complications Questionnaire adapted from Fincke et al. (2005) (Appendix K)
- When they have uncontrolled hypertension > 220/105 mmHg), uncontrolled hyperglycemia (blood glucose > 250 mg/dl or less than 70 mg/dL), or other uncontrolled cardiovascular conditions (ACSM's, 2013).
- They have musculoskeletal conditions that may severely impair their ability to safely complete the prescribed exercise routines.
- Individuals with other chronic health conditions that, according to the physicians' judgment, may pose safety risks or hinder their full participation in the study were excluded.
- Participants were excluded if they completed less than 70% of the prescribed exercise protocol (S. K. Amaravadi et al., 2024).

## 3.5. Sample Size and Sampling Technique

### *3.5.1. Sample size determination*

Acceptable statistical power would be provided by recruiting a sufficient number of patients in each group. Based on a previous similar population study on the effect of concurrent exercise on diabetic patients, we chose the main outcome (i.e., change in total cholesterol) to determine a sufficient sample size from previous research outcome (S. Zaki et al., 2024). Power (80%) at an α-level of 0.05 was employed to identify a significant

difference in TC of 0.41 effect size among the groups.

The ideal sample size for this study was calculated using G*Power software (latest ver. 3.1.9.7; Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany), considering the ANOVA repeated measures between-factor statistical test. In academic research, this popular, easy-to-use, and open-source software is well-known for its accurate sample size estimations. Even without a specified population size, it accomplishes this by taking into account important criteria, including effect size, statistical power, alpha level, and the number of groups (Abt et al., 2020; Kang, 2021).

From the final software analysis, the required sample size was determined to be 36 participants. To account for an estimated 10% dropout rate, the final sample size was adjusted to 39 participants, with 13 individuals per group.

### *3.5.2. Sampling technique and procedures*

For participant selection in the study, a simple random sampling technique was employed to ensure that each individual in the target population had an equal opportunity of being chosen. The process begins by creating a sampling frame from the list of registered diabetic patients, which includes all potential participants. Eligibility for the study was then verified using specific inclusion criteria, ensuring only those who meet the criteria were included in the sampling frame. Finally, a simple random sample was drawn by entering the names or identification numbers of all eligible participants into a system that randomly selected individuals, similar to a lottery. This system included the use of online random number generators, ensuring that each participant had an equal chance of selection and minimizing selection bias by preventing researcher influence. Overall, this approach enhances the external validity of the study, allowing for more reliable generalization of the findings to the broader population.

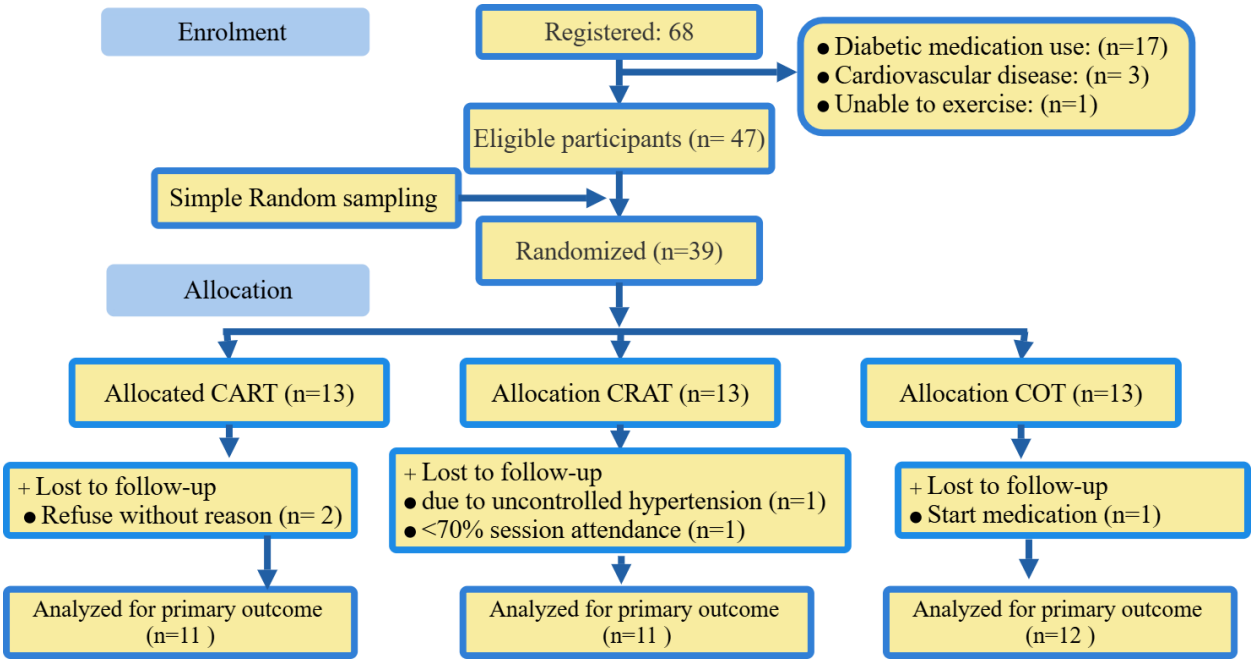


*Figure 3. Description of participants' flow chart*

### 3.6. Variables

In this research, a primary outcome was to measure the change in cardiovascular function and biochemical analyses in T2DM patients after a 12-week concurrent exercise training program. And also, a secondary outcome measure, the researcher analyzed changes in anthropometric indices following a 12-week concurrent exercise training program. And also, CART and CRAT are considered as independent variables; additionally, average daily energy intake was considered as a covariate variable.

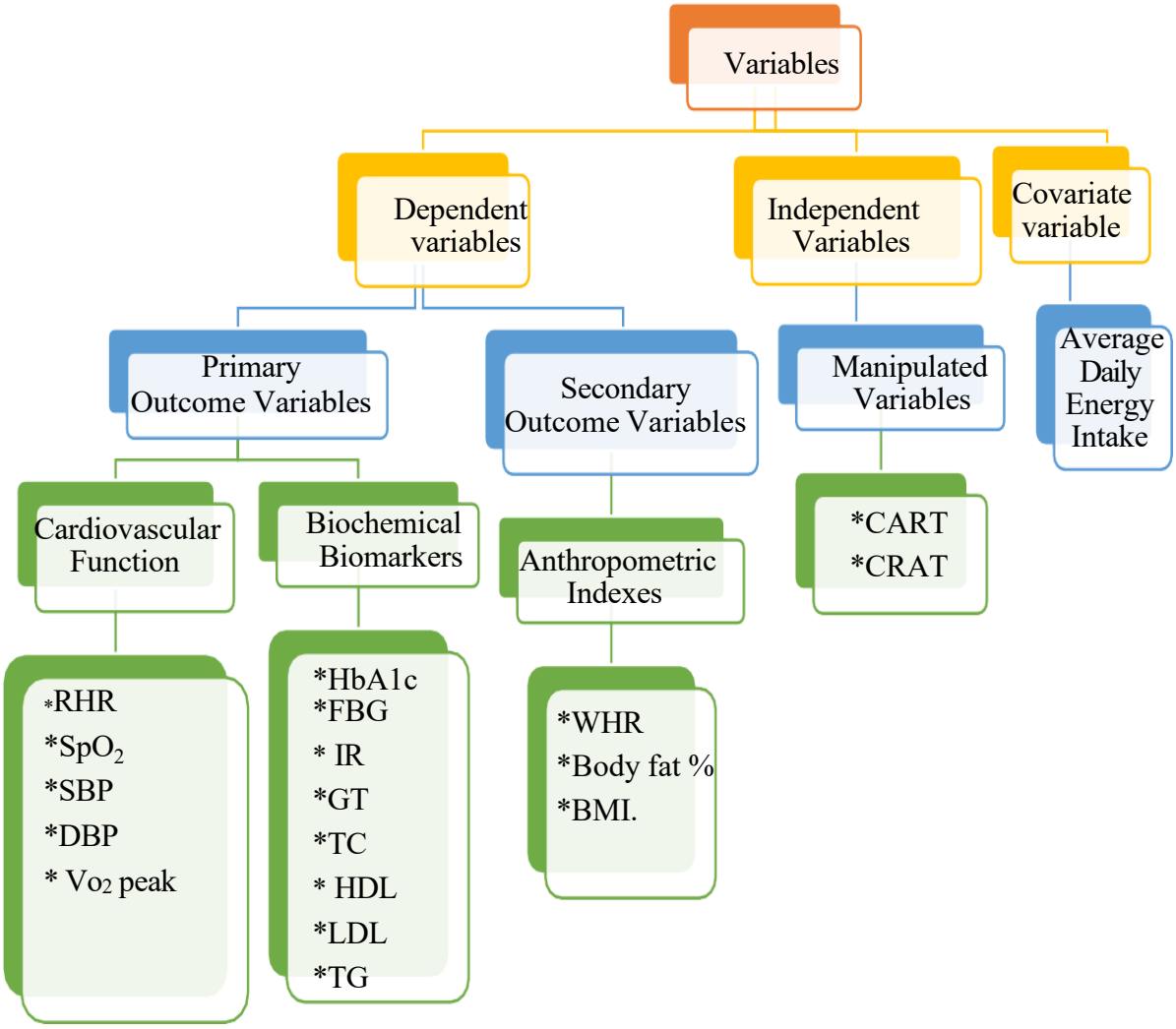


*Figure 4. Illustrates all variables involved in this research.*

### 3.7. Method and Procedures of Data Collection

Data collection for this study was conducted under carefully controlled environmental and procedural conditions to ensure the consistency and accuracy of results. Every subject was assessed for the same variables at the same time of day to minimize variations that can significantly influence physiological responses, including cardiovascular function and biochemical biomarkers. The experimental room was maintained at a relatively constant air humidity and temperature to prevent external factors, such as fluctuating environmental conditions, from affecting participants' responses. This consistency in timing and environment is crucial for reducing potential variability in the data and ensuring that any

observed effects can be attributed to the exercise interventions rather than external factors.

Additionally, all research and laboratory staff involved in data collection were rigorously trained and instructed to follow specific protocols to avoid influencing participants during the assessments. They were required to remain still and silent throughout the procedures, minimizing any potential distractions or stressors for the participants.

### *3.7.1. Anthropometric and body composition tests*

**Body Fat Percentage**

Body fat percentage can be accurately determined by a trained professional using a Lange skinfold caliper (Cambridge Scientific Industries, Cambridge, MD) (Khan et al., 2009). This applies to the three-site measurements on the male (chest, abdomen, and thigh) and female (triceps, suprailium, and thigh) groups.

All measurements were conducted on the right side of the body. The caliper must be positioned perpendicular to the site being assessed. The participant should ensure the muscle group being evaluated is fully relaxed. During the skinfold measurement, the practitioner was to record the reading at the midpoint of the pinched skinfold, avoiding the apex or base of the pinch. After releasing the caliper, the reading was noted within 1 to 2 seconds, rounding to the nearest 0.5 mm (Heyward, 1998). The test is adapted from the exercise testing and prescription guidelines of the American College of Sports Medicine (ACSM, 2020).

**Male measurements:**

- Chest: diagonal fold, half the distance between the anterior axillary line and the nipple.
- Abdominal: vertical fold 5 cm to the right of the navel.
- Thigh: vertical fold on the midpoint of the anterior side of the upper leg between the patella and the top of the thigh. This measurement was taken with the subject sitting and the knee bent at a right angle.

**Female participants' measurements:**

- Triceps: vertical fold at the midpoint of the posterior side of triceps between the shoulder (bony tip of shoulder) and elbow, with the arm relaxed, with the palm facing forward.

- Suprailia: The site is located where a horizontal line parallel to the iliac crest and a line from the anterior point of the iliac crest to the anterior part of the axilla (armpit) intersection point. The skinfold is taken diagonally, paralleling the iliac crest and just above it.

- Thigh: vertical fold on the midpoint of the anterior side of the upper leg between the patella and the top of the thigh. This measurement was taken with the subject sitting and the knee bent at a right angle.

  The Jackson-Pollock 3-Site Skinfold formula for Body Density J-P 3-Site (Jackson & Pollock, 1985) was utilized for this investigation in accordance with the particular guidelines validated by (Baranauskas et al., 2017).

$$\mathrm{BD} = 1.10938 - 0.008267\ (sum\ of\ skinfolds) + 0.0000016\ (sum\ of\ three\ skinfolds)^2 - 0.0002574\ (age)$$

*Equation 1. Three-site generalized body density equations for men*

$$\mathrm{BD} = 1.0994921 - 0.0009929\ (sum\ of\ skinfolds) + 0.0000023\ (sum\ of\ three\ skinfolds)^2 - 0.0001392\ (age)$$

*Equation 2. Three-site generalized body density equations for women*

Body Density (BD) can be used to calculate the percentage of body fat, as per the Siri Equation (Siri, 1993).

$$\%\ Body\ Fat = \frac{495}{BD} - 450$$

*Equation 3. Body fat percentage equations*

**Waist to hip ratio**

Using a Sammons Preston Tape (Narang Medical Limited, New Delhi), the circumferences of the waist and hips were measured to the nearest 0.01 cm (Khan et al., 2009). When measuring waist circumference, the participants were instructed to breathe normally and wear lightweight clothing to ensure accurate measurement. The measurement was taken at the narrowest point of the waist, usually located just above the navel. For hip circumference, the measurements were taken at the site of the greatest circumference around the buttocks (Hu et al., 2010). This ensures that the widest part of the hips is accurately captured.

Each site (waist and hips) was measured three times to ensure precision. The average of these three measurements was calculated for each site to minimize variability and enhance data reliability. Waist-to-hip ratio was calculated as waist circumference divided by hip circumference (Bredella et al., 2009).

**Body mass index**

Participants were measured in the morning after an overnight fast to ensure they hadn't eaten or drunk anything. They should wear light clothing and avoid shoes to minimize any additional weight. An electronic digital scale (Omron Ultrasonic Weight Meter HNH-219, Dalian, China) was utilized for the measurements. Participants are required to stand upright on the scale, positioning their head, hips, and heels close to the measuring device. To ensure accurate readings, participants should maintain a neutral posture by looking straight ahead. They should avoid tilting their heads upwards, raising their heels, or standing on their toes (Jiang et al., 2020).

Once the participant was properly positioned, the height and weight measurements were recorded by the assessor as indicated on the digital LED display of the scale. Body mass index (BMI) is then determined by dividing weight by height squared ($kg/m^2$) (Frankenfield et al., 2001).

### *3.7.2. Measurement of biochemical variables*

Blood samples were collected from the antecubital vein both before and after the 12-week exercise training. 48 hours after the last training session, blood samples were taken to reduce the influence of recent exercise and ensure accurate results. Additionally, participants were required to fast for 12 hours before the blood draw and to avoid alcohol consumption or a high-fat diet.

A qualified medical laboratory technician from Debre Markos Referral Hospital collected blood samples. Trained technicians performed venipuncture to draw blood from the antecubital vein while the participants were seated. These samples were analyzed to assess various biochemical parameters. With careful planning and preparation, a single blood draw was used to obtain the samples needed to evaluate all biomarkers (HbA1c, Insulin Sensitivity, Glucose Tolerance, HDL, LDL, TC, and Triglycerides) based on pre-established standard operating procedures (APPENDIX J).

**Blood collection tools**

- Blood collection tubes (e.g., EDTA, serum separator tubes).
- Sterile needles and syringes
- Alcohol swabs
- Tourniquet
- Cotton balls
- Sharps disposal container

**Venipuncture Procedure**

Position the patient comfortably in a seated position, with the arm fully extended and the palm facing upward. Select an accessible vein, typically in the antecubital fossa, while avoiding areas with bruises, scars, or inflammation. Apply a tourniquet 3- 4 inches above the venipuncture site and check for an easily accessible vein. Clean the site thoroughly using an alcohol swab in a circular motion, starting from the center and moving outward, and allow it to air dry completely. Press the vein by holding the skin with a thumb below

the puncture site, and insert the needle bevel side up at a 15-30-degree angle.

For sample collection, follow the correct order of draw to prevent cross-contamination by collecting blood in a serum separator tube (SST) for fasting insulin, blood glucose level, and lipid profile, and in an EDTA tube for HbA1c. Make sure to collect enough blood for all tests, usually 5 mL per tube for serum tests and 2-3 mL for HbA1c. To avoid multiple blood draws, schedule the collection of fasting insulin and HbA1c on the same day. On the next day, perform the lipid profile and glucose tolerance test by first collecting a fasting glucose sample, then giving the patient a 75g glucose solution, and collecting blood samples at specified times (e.g., 30, 60, 120 minutes after glucose intake). Gently invert the tubes as needed to mix the additives properly, and immediately label each tube with the patient's name, date of birth, date, and time of collection.

Since Debre Markos lacks a facility for fasting insulin level tests, the blood samples were securely transported to the Wudassie Diagnostic Center in Addis Ababa for analysis. After collection, the fasting insulin samples were placed in a serum separator tube (SST) and immediately labeled with the patient's information, date of birth, and time of collection. The samples were stored in a cool, insulated container with an ice pack to maintain their integrity during transport. The sample should be delivered promptly to the diagnostic center to ensure accurate results, ideally within 24 hours. Upon arrival at the laboratory, the sample was processed according to standard procedures for insulin level testing.

For the HbA1c test, two to three milliliters of blood should be placed into an EDTA tube, and blood samples were processed using a validated Glycosylated Hemoglobin Kit (Ion Exchange Resin Method, Coral Clinical Systems, Verna, India) and analyzed for HbA1c levels through High-Performance Liquid Chromatography (HPLC) (Biobase Meihua Trading Co., Ltd., China) (Wang et al., 2018). Whereas the Enzyme-Linked Immunosorbent Assay (ELISA) assay type, which is the product of China (Shakil-Ur-Rehman et al., 2017) was used for the fasting insulin test assays.

For lipid profile tests that require serum, collect blood in a Serum Separator Tube (SST). This volume provides sufficient serum for the tests needed to assess lipid profile, including HDL, LDL, triglycerides, and glucose at 0 time. After centrifugation and rapid cooling to

4°C, the SST creates a clear serum layer that can be separated into individual portions for each test. The samples were analyzed within 24 hours. The enzymatic colorimetric method was used to measure glucose, low-density lipoprotein (LDL), high- density lipoprotein cholesterol (HDL-C), and total cholesterol (TC) according to the manufacturer's instructions, using an Alpha X autoanalyzer (Hitachi, Tokyo, Japan) with E2HL-100 kits, providing a sensitivity of 0.1 mmol/dL (Ngayimbesha et al., 2019).

The homeostasis model of insulin resistance (HOMA-IR index), which is the product of glucose and insulin concentrations divided by a factor, was used to quantify insulin resistance (Vogeser et al., 2007).

The HOMA-IR index was calculated as:

$$HOMA - IR = \frac{\text{fasting serum glucose (mmol. L}^{-1}) * \text{fasting serum insulin}(\mu U. mL^{-1})}{22.5}$$

*Equation 4. Homeostasis model of insulin resistance equation*

Glucose concentrations were determined at 30, 60, 90, and 120 minutes following the administration of a standard 75 g oral glucose solution dissolved in 300 ml of water drink within 5 minutes (Yassine et al., 2009). Assign skilled personnel to supervise the oral glucose tolerance test (OGTT) in order to guarantee that participants successfully swallow the glucose solution within the allotted test period. The OGTT assesses the body's ability to utilize glucose and break it down, as well as remove it from the bloodstream (Bano, 2013).

The trapezoidal rule was used to compute and compare the area under the glucose curve. The trapezoidal approximation of PG levels was used to compute the plasma glucose area under the curve (PG-AUCs) (Sakaguchi et al., 2016). PG levels at *x* min were defined as PG(*x*), and the PG-AUC was calculated (Yassine et al., 2009).

The AUC was calculated as:

$$\text{AUC (mgh/dl)} = \frac{PG(0) + PG(30) * 2 + PG(60) * 3 + PG(120) * 2}{4}$$

*Equation 5. Trapezoidal approximation of the area under the curve of glucose*

### *3.7.3. Measurement of cardiovascular function variables*

**Peripheral oxygen saturation and Resting Heart rate**

Ascertain that the patient can rest comfortably on their back for a minimum of 10 minutes to obtain a blood oxygen saturation ($SpO_2$) and resting heart rate value. Make sure their thumb is free to move and free of any jewelry, bandages, or nail polish. The pulse oximeter (MQ3200; manufactured in China) was applied to the patient's thumb to measure the SpO2 and RHR (Ezema et al., 2019). A probe was usually composed of two parts that clipped onto the fingertip before resting on the nail bed. Modify the probe to make sure it fits snugly, but don't squeeze the thumb too much. After several seconds, the pulse oximeter's screen showed the RHR and SpO2 levels as a percentage (Ezema et al., 2019).

**Blood pressure**

The procedure for accurately measuring blood pressure using an automated Sphygmocor XCEL device (AtCor Medical, CardieX, Sydney, Australia) (De la Torre Hernández et al., 2021), was adapted from Mengistu et al. (2025).

**Materials Required**

- SphygmoCor XCEL device
- The appropriate brachial cuff was selected based on arm circumference: dark blue for 22-33 cm, maroon for 31-40 cm, and brown for 38-50 cm.
- A stable and flat table and a comfortable bench.

**Preparation**

**Participant Preparation:**

- Instruct the participant to avoid caffeine, alcohol, and strenuous exercise for at least 30 minutes before measurement.
- Make sure the participant has been positioned and lying on the catheterization laboratory table for at least 5 minutes before starting the procedure.

- Ask the participant to remove any clothing that may obstruct the placement of the cuff on the upper arm.

**Procedure**

**Cuff Placement:**

- Place the cuff on the participant's left upper arm, positioning it so that the artery marker aligns with the brachial artery.
- Ensure the cuff is snug but not excessively tight, and the lower edge is approximately 2-3 cm above the elbow crease.

**Positioning:**

- Position the arm with the cuff at heart level for accurate readings. Use cushioning if needed to maintain proper positioning.

**Initiating the Measurement:**

- Begin the measurement by activating the SphygmoCor XCEL system.
- The device automatically records the brachial blood pressure (SBP and DBP) during cuff inflation and deflation.

**Instructions During Measurement:**

- Instruct the participant to remain still and refrain from speaking or moving during the cuff inflation and waveform measurement phases.

**Post-Measurement**

- Remove the cuff and assist the participant to sit up if needed.
- Record the measurements displayed by the device:
- Brachial SBP and DBP
- Resting heart rate
- Conduct the measurement three times to ensure accuracy, adhering to standard protocols, and use the average of the remaining two readings.

**Cardiopulmonary Exercise Test**

The Modified Bruce Protocol was used to determine the peak aerobic power of type 2 diabetic individuals (Thompson et al., 2013; Vergès et al., 2004). It remains the gold standard; modified Bruce protocols on a treadmill offer a valuable option for T2DM patients in research settings (Kozlov et al., 2020; Poirier et al., 2000). These protocols adjust speed and incline increments to a more manageable level, allowing for a maximal effort within a safer zone (Fletcher et al., 2013). This approach was valid and an accurate VO2 peak measurement tool with patient safety, making it a strong choice for T2DM populations (ACSM, 2020; Bires et al., 2013). Begin the test with a 2 to 3-minute warm-up to familiarize clients with the exercise equipment and prepare them for the first stage of the exercise test.

Before their submaximal exertion testing, participants shall adhere to the following guidelines:

- avoid caffeine consumption at least 2 h before testing;
- if a diabetic patient, to have eaten or ensure adequate blood glucose levels before testing; it should be (90 - 250 mg · $dL^{-1}$) (ACSM, 2020)
- To reschedule tests if participants felt unwell due to respiratory, gastrointestinal, or illness within 48 h of their appointments.

Participants in the Modified Bruce Treadmill Test approach walked on a motorized treadmill (Precor C954i, Woodinville, Washington, United States) at increasing speeds and grades for three-minute intervals (Table 1). Participants exercised until symptoms forced them to stop. There are three main reasons why a test could end: firstly, if the patient feels tired, has cramping in his legs, chest pain, shortness of breath, dizziness, or any other discomfort. Second, because patient safety comes first, the test was also ended if the monitor displayed an irregular cardiac rhythm or blood pressure reading. Lastly, if the patient meets a target heart rate or workload set by their physician (Equation 6), the test may be terminated (Colberg et al., 2010). Clearly stated common indicators for termination $VO_2$ peak assessment are in Appendix L.

$$\text{THR} = \text{HR rest} + [(\text{HR max} - \text{HR rest}) \times \text{Intensity}]$$

*Equation 6. Target heart rate estimation*

Heart rate was continuously monitored during all submaximal exercise tests using Polar heart rate monitors (FT1, Polar Electro, Kempele, Finland), with heart rate values recorded at the end of each 3-minute stage of the Modified Bruce treadmill protocol. The speed and grade of the last completed stage were used to estimate VO2 peak, adapted from the ACSM walking equation (ACSM, 2020).

$$\mathbf{VO2peak} = [\boldsymbol{speed}\ (\boldsymbol{m \cdot min - 1}) \times \mathbf{0.1}] + [\boldsymbol{grade}\ (\boldsymbol{decimal}) \times \boldsymbol{speed}\ (\boldsymbol{m \cdot min - 1}) \times \mathbf{1.8}] + \mathbf{3.5}$$

*Equation 7. Estimate VO2 peak adapted from the ACSM walking equation*

Successful tests were defined as a participant completing at least two stages (to extrapolate ˙ VO2peak) and reaching 85% of HR peak upon completion of the final stage (Colberg et al., 2010; Fletcher et al., 2013).

*Table 1.Modified Bruce Treadmill Test approach*

| Stage | Speed (mph) | Grade (%) | Duration (Minutes) |
|---|---|---|---|
| **0** | **1.7** | **0** | **3** |
| **0.5** | **1.7** | **5** | **3** |
| **1** | **1.7** | **10** | **3** |
| **2** | **2.5** | **12** | **3** |
| **3** | **3.4** | **14** | **3** |
| **4** | **4.2** | **16** | **3** |
| **5** | **5.0** | **18** | **3** |
| **6** | **5.5** | **20** | **3** |
| **7** | **6.0** | **22** | **3** |

*Table 1 Modified Bruce Treadmill Test approach*

### *3.7.4. Covariate variable (dietary assessment)*

While nutrition is not a primary focus of the study, it should be monitored due to its potential impact on the dependent variable. Therefore, we tracked the average daily calorie intake through face-to-face interviews. We utilized a 24-hour interactive personal interview with multiple passes (Quick list, forgotten foods, Time & occasion, Detail cycle, and Final probe) that was developed and validated for use in developing countries (Blanton et al., 2006; Gibson & Ferguson, 2008) (Appendix H, I). This approach employs five steps:

- Step 1: Quick list (a list is made of foods and drinks consumed in the last 24 hours)
- Step 2: Forgotten foods (questions are asked to identify any foods that may have been overlooked in Step 1)
- Step 3: Time & occasion (the time and occasion of each food item are recorded)
- Step 4: Detail cycle (each food's detailed description, quantity, and any additions are documented)
- Step 5: Final probe (a last check is done to ensure no other foods or drinks were consumed in the past 24 hours)

The 24-hour food frequency data was collected on three non-consecutive days (Baranowski, 2012; Buttriss et al., 2017): from Monday 6 p.m. to Tuesday 5 p.m., Wednesday 6 p.m. to Thursday 5 p.m., and Saturday 6 p.m. to Sunday 5 p.m. It is better to choose non-consecutive days, as this helps to capture a broader range of variability in an individual's diet (FAO, 2018). We applied the Ethiopian food composition table (EHNRI, 1981; EHNRI, 1998) to estimate nutrient and energy levels from dietary data. The names of foods and drinks, their descriptions, cooking methods, and amounts from 24-hour periods were coded and submitted to the NutriSurvey200 (Feyesa et al., 2020). After determining the daily frequency of consumption, we used the product-sum approach to estimate daily food intake. Daily food intake = ∑ (food item's stated consumption frequency, translated to times per day) * (portion size ingested of that food). The daily average energy intake was also determined as follows: ADEi = ∑daily food intake/number of data collection days.

### 3.8. Exercise Training Protocol

The concurrent training program consisted of 36 individually supervised sessions conducted three times per week over 12 weeks on alternate days (Tuesday, Thursday, and Sunday). Detailed descriptions of the training protocol are provided in Appendix VII. Every training session was conducted under the strict observation of fitness experts. Each 70-minute session had a 5-minute warm-up, a 60-minute main training session (30 aerobic and 30 resistance), and a 5-minute cool-down. We used the American College of Sports Medicine's recommendation for type 2 diabetic individuals as the basis for the exercise programs (ACSM, 2020).

To minimize biased influence during the main training process, a one-week familiarization period was implemented beforehand. This familiarization involved adjustable-intensity aerobic exercises on a treadmill, such as walking and jogging, as well as low-load resistance exercises that participants could perform for 10-15 repetitions without fatigue.

The RT program focused on the body's major muscle groups in accordance with recommendations from the American Diabetes Association (Sigal et al., 2006). Exercises that were done include abdominal curl, standing plantar flexion, and squatting with body weight and free weights, machine leg press, neutral rowing, machine bicep curl, triceps pulley, and machine bench press (vertical press) exercise using a multi-gym, leg press machine, and dual adjustable pulley (Cybex International, Medway, Massachusetts). They performed 50- 85 % of the estimated 1-RM in line with (ACSM, 2020; Mager et al., 2008). Workouts using the circuit form of resistance training (RT) were employed with intervals, consisting of one to three sets of 10-15 repetitions to near fatigue per set, with a 30 to 90-second break in between to improve muscle mass and strength (ACSM, 2020). To ensure steady repetitions throughout the training program, the weight lifted was increased gradually.

To determine protocol loads, the 1-RM test was used, with resistance gradually increased until the volunteer could perform no more than 1 repetition. Start with a warm-up using a small weight, roughly 40-60% of the perceived maximum load, to calculate each individual's 1-RM. To make sure the muscles are prepared for the subsequent section of the

test, give everyone a minute to relax after finishing the warm-up. Provide the individual 12-15 repetitions after increasing the weight to a moderate load (60-80% of the perceived maximum). This set should be difficult, but not impossible. Rest for one to two minutes after finishing this set.

After establishing a reasonable weight, encourage the subject to do up to 10 repetitions with a 10% increase in load. Allow the individual an additional one to two minutes of break before continuing if they can perform ten or more repetitions with the new weight. Keep an eye on the participant throughout this rest period to make sure they aren't exerting themselves excessively. Increase the weight by 10% again and have them try repetition with the larger load if they can finish the set of 10 or more reps. After that, the resistance was gradually raised until the individuals could only complete each exercise nine repetitions or fewer. Reaching the target number of repetitions in between 3 and 6 tries is the aim of increasing the resistance. Three minutes of rest are permitted between each particular exercise, and two minutes are permitted between each try. Brzycki 1-RM prediction equation (Brzycki, 1993) was used to estimate the 1-RM based on the resistance and repetitions recorded on the last try. The mathematical expression for the equation is 1RM = W/ [1.0278 - 0.0278(R)], where R is the maximum number of repetitions and W is the weight used (Abdul-Hameed et al., 2012).

The aerobic workout involved using a Cybex treadmill (Cybex Corporation, Ronkonkoma, New York) (McNamara & Stearne, 2013) at moderate intensity (40 -59% HRR) to vigorous intensity (60-89% HRR) (ACSM, 2020).

We used the heart rate reserve (HRR) approach, which was based on the Karvonen formula, to determine the target heart rate (THR) to manage the intensity of the exercise (Yabe et al., 2021). This approach is appropriate for a broad spectrum of adult fitness levels (ACSM's, 2013). The following is the formula:

$$\mathrm{THR} = \mathrm{HR\ rest} + [(\mathrm{HR\ max} - \mathrm{HR\ rest}) \times \mathrm{Intensity}]$$

*Equation 8. HRR approach Karvonen target heart rate formula*

Whereas:

- HR max = 220 – age
- RH: expressed as the number of beats per minute (bpm) at rest.
- Intensity: the decimal representation of the desired level of exercise intensity (e.g., 0.40 for 40%, 0.60 for 60%).

The Polar H7 heart rate monitor (Polar Electro, Kempele, Finland) (Hernández-Vicente et al., 2021) was used to continually track the participants' target heart rates as they exercise. To give real-time feedback, this device makes sure that the intensity of the workout stays within the predetermined target heart rate range. The detailed monitoring protocol is fully described in Appendix N.

There were resistance and aerobic workouts within the concurrent resistance-aerobic (CRAT) and concurrent aerobic-resistance (CART) groups. The sequence in which the resistance or aerobic components were done first and second is the only distinction between the two training regimens (CRAT and CART). The two training programs (aerobic and resistance components) are separated by a five-minute recuperation and transition interval throughout each training session.

To ensure the detection of any adverse events, heart rate, blood pressure, and blood glucose levels were monitored before and after each exercise session, particularly if a medical professional observes unusual or concerning patterns (APPENDIX M).

### 3.9. Quality Control Mechanism

This study's quality control method includes a number of crucial steps to guarantee correctness and dependability. Participants in each group were first thoroughly matched to the intervention groups and control group according to important clinical and demographic traits, like gender and age. To guarantee comparability across all groups, stratification was used. The International Physical Activity Questionnaire (IPAQ) was utilized to assess physical activity levels among control group participants. Data were collected through interviewer-administered IPAQ during weekly check-ins. Participants in the control group

who reported engaging in over 150 minutes of moderate physical activity per week were excluded from the study.

Before every test session, the equipment was calibrated, and established testing protocols were adhered to for all biochemical, cardiovascular, and anthropometric index measurements. All participants were given tests at the same time of day to reduce variability. To avoid measurement bias, the test data collector and analyst were masked to group assignments. All testing personnel also received extensive training to guarantee the capability to follow the set procedures.

In order to ensure that participants complete exercises with the right form and intensity, trained exercise physiologists were overseeing all training sessions. Both attendance and any sessions that were missed were noted. Lastly, weekly progress checks were conducted to make sure participants were performing the exercises at the recommended volume and intensity.

To facilitate participation and reduce barriers related to travel, a modest transport settlement was provided to participants to cover actual travel expenses. This reimbursement was clearly communicated as compensation for costs incurred, not as an inducement to participate. The process for distributing the reimbursement was standardized, documented, and monitored to ensure transparency and fairness.

All individuals approached for the study were systematically recorded, including whether they chose to enroll or decline participation. This monitoring ensures equitable access to the study and helps detect any potential coercion or undue influence on participants.

### 3.10. Data Analysis

SPSS version 27 was used to analyze the data (SPSS Inc., Chicago, IL). For each group (CART, CRAT, and COG), compute the means, standard deviations (SDs), and normality tests for all variables at baseline. Applying a Bonferroni correction for multiple comparisons in their RM-ANCOVA, with average daily energy intake as the covariate, helps the researchers ensure that the between-group comparisons. This correction was used for WHR, %BF, BMI, HbA1c, IR, HDL, LDL, TG, GT, peripheral oxygen saturation,

blood pressure, and resting heart rate. Participants' changes over time and groups' variations in exercise techniques were compared. Interactions between these factors were also investigated. All the statistical tests were two-tailed, and a p-value of 0.05 or less was considered statistically significant.

### 3.11. Ethical Consideration

Before deciding to participate, participants will receive a thorough explanation of all procedures, risks, and protocols, and will sign an informed consent form. The study team will clearly outline the steps it will take to protect patient privacy and confidentiality, including removing patient names and data. Health professionals should give special consideration to the requirements and safety of diabetic patients during the study, as they are a vulnerable population. Furthermore, I obtained ethical clearance from two sources: Debre Markos University Sport Science Academy, representing the research site (SpSc.IRC/03/25), and the Natural and Computational Sciences Research Ethics Committee at Addis Ababa University, representing my academic institution (EDRE/04/2017/25). In addition, the trial was prospectively registered with the Pan African Clinical Trials Registry (PACTR202509591505325), ensuring transparency and adherence to international research standards (Appendix O). Additionally, adherence to the 2000 revision of the Helsinki Declaration ensures that the study prioritizes participant welfare and upholds their rights.

To address the ethical concern of withholding exercise from the control group during the intervention period, the researcher provided a tailored and supervised exercise program for these participants after the study was completed. This program was designed to meet their specific needs and promote improvements in cardiovascular and metabolic health.

### 3.12. Declaration of Potential Conflicts of Interest

The investigator declares that there are no potential conflicts of interest related to this research. The study was conducted purely for academic and scientific purposes as part of the doctoral research project at Addis Ababa University, Sport Sciences and Physical Education Department. No financial, personal, or professional interests exist that could inappropriately influence the design, conduct, or reporting of the study.

# CHAPTER FOUR

# 4. RESULTS

This chapter presents results from a randomized controlled experiment comparing two concurrent training sequences, CRAT (resistance followed by aerobic) and CART (aerobic followed by resistance), against a control group. The Results section comprises participant flow, baseline characteristics, and primary and secondary outcomes. Repeated-measures ANCOVA (RM-ANCOVA) is used to evaluate outcomes, with dietary practice included as a covariate to adjust for it. 39 participants were successfully randomized into three groups: 13 were assigned to CART, 13 to CRAT, and 13 to COG. After attrition during the intervention period, 12 participants from the COG group, 11 from the CRAT group, and 11 from the CART group completed the study and were included in the final analysis; the remaining participants were considered dropouts. A comprehensive CONSORT flow diagram (Figure 1) illustrates the study's recruitment procedure, group assignment, attrition, and ultimate participant inclusion.

## 4.1. Demographic, Baseline, and Follow-up Characteristics

Table 3 summarizes the subjects' baseline anthropometric, metabolic, and demographic data. There were no significant age differences among the groups at baseline, with CART at 48.73 ± 2.05 years, CRAT at 49.73 ± 2.92 years, and COG 49.00 ± 2.97 years. Males made up 81.8% of the CART group, 72.7% of the CRAT group, and 83.3% of the COG group, indicating a similar sex distribution. Daily caloric intake (ADEi) showed minimal variances, with CART individuals ingesting 2,381.15 ± 147.52 kcal, CRAT 2,389.18 ± 116.85 kcal, and COG somewhat higher at 2,515.29 ± 72.96 kcal, suggesting very similar dietary energy intake.

Baseline glycemic indicators were consistent across groups. HOMA-IR values showed insulin resistance in all groups (CART: 3.93 ± 0.39, CRAT: 4.07 ± 0.27, COG: 4.09 ± 0.29). All subjects exhibited mild hyperglycemia based on HbA1c readings (CART: 6.74 ± 0.26%, CRAT: 6.76 ± 0.38%, COG: 6.68 ± 0.28%).

Cardiovascular function markers suggested that participants presented with borderline

hypertension at baseline. The systolic blood pressure (SBP) readings were 131.37 ± 0.54 mmHg in COG, 132.91 ± 4.40 mmHg in CRAT, and 130.73 ± 2.13 mmHg in CART. Diastolic blood pressure (DBP) averaged 85.70 ± 1.92 mmHg, 87.25 ± 5.02 mmHg, and 84.82 ± 3.97 mmHg, IN CART, CRAT, and COG, respectively. Resting heart rate (RHR) ranged from 74.33 to 75.63 beats/min, and peripheral oxygen saturation ($SpO_2$) values were 94.62 ± 0.80% (CART), 95.03 ± 1.25% (CRAT), and 94.54 ± 0.48% (COG). Low cardiorespiratory fitness was indicated by baseline $VO_2$ peak values of 23.45 ± 1.74 mL/kg/min, 22.54 ± 2.63 mL/kg/min, and 22.38 ± 1.19 mL/kg/min for CART, CRAT, and COG, respectively.

Anthropometric indicators showed that participants in all three groups were overweight at baseline. For CART, CRAT, and COG, the mean BMI values were 27.55 ± 0.99 kg/m², 27.52 ± 0.67 kg/m², and 27.69 ± 0.88 kg/m². Body fat percentage (BFP) was likewise comparable, with CART at 28.39 ± 0.94%, CRAT at 28.69 ± 0.75%, and COG at 28.60 ± 0.92%. Similarly, the waist-to-hip ratio (WHR) suggested central obesity across the groups: 1.02 ± 0.039 in CART, 0.99 ± 0.03 in CRAT, and 1.01 ± 0.026 in COG. These anthropometric results reveal a homogenous overweight profile across all groups before the intervention.

Overall, participants in the three groups demonstrated comparable demographic characteristics and similar baseline values for anthropometric indices, glycemic markers, lipid profiles, and cardiovascular parameters. These similarities suggest that the randomization process was effective and that subsequent changes observed at follow-up are likely attributable to the intervention. However, the covariate variable related to dietary practice during the intervention period showed a statistically significant difference between groups.

*Table 2. Demographic, baseline, and follow-up characteristics of the participants by group.*

| VARIABLES | CART | | CRAT | | COG | | p-value |
|---|---|---|---|---|---|---|---|
| | Baseline | Follow-up | Baseline | Follow-up | Baseline | Follow-up | |
| **Age (years)** | 48.73 ± 2.054 | | 49.73 ± 2.970 | | 49.00 ± 2.923 | | NS |
| **Sex (Male), n (%)** | 9 (81.8%) | | 8 (72.7%) | | 10 (83.3%) | | NS |
| **ADEi (kcal)** | 2381.15 ± 147.52 | | 2389.1845 ± 116.85 | | 2515.29 ± 72.96 | | 0.04 |
| **Glycemic control** | | | | | | | |
| **IR** | 3.89 ± .09[a] | 3.39 ± .076[a] | 4.03 ± .09[a] | 2.63 ± .69[a] | 4.17 ± .1[a] | 4.09 ± .07[a] | NS |
| **HbA1c (%)** | 6.74 ± .1[a] | 5.47 ± .19[a] | 6.76 ± .09[a] | 4.86 ± .18[a] | 6.69 ± .1[a] | 6.53 ± .19[a] | NS |
| **FBS (mg/ dL)** | 131.33 ± 1.7[s] | 118.08 ±1.78[s] | 134.00 ± 1.68[s] | 113.98 ± 1.76[a] | 135.61 ± 1.73[a] | 135.29 ± 1.81[a] | NS |
| **GT (AUC) (mg·h/dl)** | 443.17 ± 1.68[a] | 420.89 ± 1.74[a] | 443.62 ± 1.66[a] | 413.95 ± 1.73[a] | 443.49 ± 1.71[a] | 443.69 ± 1.77[a] | NS |
| **Lipid Profile** | | | | | | | |
| **HDL (mg/dL)** | 39.52 ± 0.58[a] | 46.75 ± 0.81[a] | 40.17 ± .57[a] | 46.93 ± 0.81[a] | 41.75 ± 0.59[a] | 40.90 ± 0.83[a] | NS |
| **LDL (mg/dL)** | 123.25 ± 1.56[a] | 92.59 ± 2.27[a] | 123.85 ± 1.54[a] | 96.26 ± 2.25[a] | 122.93 ± 1.59[a] | 126.68 ± 2.31[a] | NS |
| **TG (mg/dL)** | 168.62 ± 3.70[a] | 138.95 ± 3.04[a] | 167.41 ± 3.67[a] | 146.68 ± 3.01[a] | 170.41 ± 3.77[a] | 168.46 ± 3.10[a] | NS |
| **TC (mg/dL)** | 233.26 ± 1.49[a] | 208.35 ± 1.48[a] | 232.42 ± 1.48[a] | 207.42 ± 1.47[a] | 231.94 ± 1.52[a] | 233.12 ± 1.51[a] | NS |
| **Cardiovascular Function** | | | | | | | |
| **SBP (mm Hg)** | 130.63 ± 1.22[a] | 125.02 ± 1.17[a] | 132.82 ± 1.21[a] | 121.25 ± 1.16[a] | 131.54 ± 1.24[a] | 133.89 ± 1.19[a] | NS |
| **DBP (mm Hg)** | 85.44 ± 1.20[a] | 82.71 ± 1.06[a] | 87.03 ± 1.19[a] | 80.91 ± 1.05[a] | 85.26 ± 1.23[a] | 85.13 ± 1.08[a] | NS |
| **RHR (bpm)** | 74.52 ± 0.64[a] | 67.56 ± 0.97[a] | 75.62 ± 0.64[a] | 71.04 ± 0.96[a] | 74.36 ± 0.66[a] | 74.44 ± 0.98[a] | NS |
| **$SPO_2$ (%)** | 94.82 ± 0.25[a] | 97.02 ± 0.27[a] | 94.89 ± 0.25[a] | 97.01 ± 0.26[a] | 94.49 ± 0.23[a] | 94.61 ± 0.24[a] | NS |
| **$Vo_2$ peak (mL/kg/min)** | 23.43 ± 0.61[a] | 26.36 ± 0.45[a] | 22.53 ± 0.60[a] | 25.56 ± 0.44[a] | 22.40 ± 0.62[a] | 22.31 ± 0.46[a] | NS |
| **Anthropometric Indices** | | | | | | | |
| **BFP (%)** | 28.31 ± 0.27[a] | 26.80 ± 0.31[a] | 28.63 ± 0.27[a] | 26.79 ± 0.31[a] | 28.72 ± 0.27[a] | 29.22 ± 0.31[a] | NS |
| **WHR** | 1.03 ± 0.01[a] | 0.92 ± 0.019[a] | 0.99 ± 0.01[a] | 0.95 ± 0.03[a] | 0.99 ± 0.09[a] | 1.04 ± 0.019[a] | NS |
| **BMI ($kg/M^2$)** | 27.53 ± 0.27[a] | 25.37 ± 0.31[a] | 27.50 ± 0.27[a] | 25.85 ± 0.31[a] | 27.73 ± 0.27[a] | 27.66 ± 0.32[a] | NS |

Note: [a] =*The data were corrected for confounders, which were examined at an average daily energy intake (ADEi) of 2431.0959 kcal. Values are presented as mean ± standard error (SE). CART = Concurrent Aerobic-Resistance Training; CRAT = Concurrent Resistance-Aerobic Training; COG = Control group; NS = no significance difference between groups at baseline; ADEi (kcal)= Average Daily Energy Intake; IR = Insulin Resistance Measured by Homeostatic Model Assessment of Insulin Resistance; HbA1c (%) = Glycated Hemoglobin; FBS (mg/ dL) = Fasting Blood Sugar; GT (AUC) (mg·h/dl)= Glucose Tolerance Area Under Curve; HDL (mg/dL)= High Density Lipoprotein; LDL (mg/dL)=Low Density Lipoprotein; TG (mg/dL)=Triglycerides; TC (mg/dL)=Total Cholesterol; SBP (mm Hg)=Systolic Blood Pressure; DBP (mm Hg)=Diastolic Blood Pressure; RHR (b/m) =Resting Heart Rate; SPO2 (%)=Peripheral Oxygen Saturation; Vo2 peak (mL/kg/min) Peak Oxygen Consumption; BFP (%)=Body Fat Percentage; WHR=Waist To Hip Ratio*

## 4.2. Primary Outcomes Results

### *4.2.1. Glycemic Control*

As demonstrated in Table 3 and Figure 5, the analysis showed meaningful within-subject improvements across multiple glycemic control indicators, particularly in the CART group, where HbA1c demonstrated a statistically significant time effect ($F = 4.91$, $p = .034$) with a moderate effect size ($\eta^2 = .141$), indicating that approximately 14% of the variance in HbA1c change was attributable to the intervention. According to pairwise comparisons, CART resulted in a clinically significant reduction of 1.267% (p =.011), with a 95% CI ranging from 0.871 to 1.662. CRAT likewise demonstrated a reduction (mean diff = 1.896%), with a 95% CI ranging from 1.503 to 2.288. There was no significant difference in the COG group (mean diff = –.156%, NS).

HOMA-IR revealed the largest intervention effect, especially in CRAT, which demonstrated a very significant within-subject change ($F = 21.91$, $p = .001$) with a substantial effect size ($\eta^2 = .422$), implying almost 42% of the reduction in insulin resistance was related to the intervention. Pairwise comparisons indicated major reductions in CART (mean diff = 0.497, p = .001, CI 0.347–0.648) and CRAT (mean diff = 1.401, p

= .001, CI 1.252–1.550), but COG exhibited no significant change.

Fasting blood glucose demonstrated a similar pattern, with a significant within-subject impact over time (F = 5.76, p = .023, $\eta^2$ = .161), indicating a considerable effect of the intervention. Pairwise comparisons revealed that the CART group saw a substantial reduction of 13.25 mg/dL (p = .001, 95% CI: 9.47–17.02), while the CRAT group achieved an even higher decrease of 20.03 mg/dL (p = .001, 95% CI: 16.29–23.77). In contrast, the control group exhibited no significant decrease (−3.53 mg/dL, NS). Similarly, glucose tolerance, assessed by AUC, exhibited a significant within-subject impact (F = 6.28, p = .018, $\eta^2$ = .173), again reflecting a considerable effect. The CRAT group demonstrated an even greater improvement of 29.67 units (p =.001, 95% CI: 26.38–32.95), whereas the CART group showed a decrease of 22.28 units (p =.001, 95% CI: 18.96–25.60). The control group, however, revealed no significant change.

Overall, the pattern suggests that both CART and CRAT significantly improved HbA1c, insulin resistance, fasting glucose, and glucose tolerance, with CRAT showing the greatest magnitude of change in most variables, while the control group showed no meaningful improvement in any of the outcomes.

*Table 3. Within-subject changes in glycemic control outcomes across intervention time points*

| **Variables** | **Group** | **Within-Subjects Effects** | | | **Pairwise Comparison** | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | F | Sig.[b] | $\eta^2$ | Mean Diff. | Std. Error | Sig.[b] | 95% CID | |
| | | | | | | | | Lower Bound | Upper Bound |
| **HbA1c (%)** | CART | 4.91 | .034 | .141 | 1.267 | .194 | .011 | .871 | 1.662 |
| | CRAT | | | | 1.896 | .192 | .001 | 1.503 | 2.288 |
| | COG | | | | .156 | .197 | NS | -.247 | .559 |
| **IR** | CART | 21.91 | .001 | .422 | .497 | .074 | .001 | .347 | .648 |
| | CRAT | | | | 1.401 | .073 | .001 | 1.252 | 1.550 |
| | COG | | | | .073 | .075 | NS | -.081 | .226 |
| **FBS (mg/ dL)** | CART | 5.76 | .023 | .161 | 13.249 | 1.84 | .001 | 9.474 | 17.024 |
| | CRAT | | | | 20.027 | 1.83 | .001 | 16.287 | 23.767 |
| | COG | | | | .311 | 1.88 | NS | -3.533 | 4.155 |
| **GT AUC (mg/dL·min)** | CART | 6.28 | .018 | .173 | 22.281 | 1.62 | .001 | 18.96 | 25.595 |
| | CRAT | | | | 29.669 | 1.60 | .001 | 26.38 | 32.952 |
| | COG | | | | -.199 | 1.65 | NS | -3.574 | 3.175 |

Note: *Values are presented as means difference ± SE, with significant differences between groups at $p < 0.05$; [b]=Adjustment for multiple comparisons: Bonferroni; CART = Concurrent Aerobic - Resistance Training; CRAT = Concurrent Resistance - Aerobic Training; COG = Control group; IR = Insulin Resistance Measured by Homeostatic Model Assessment of Insulin Resistance; HbA1c (%) = Glycated Hemoglobin; FBS (mg/ dL) = Fasting Blood Sugar; GT (AUC) (mg·h/dl) = Glucose Tolerance Area Under Curve*

Table 4 and Figure 5 revealed that the between-subjects analysis of glycemic control outcomes indicated significant differences between treatment groups across all glycemic control variables, with large effect sizes, showing that the kind of intervention had a significant impact on outcomes. There was a significant overall group effect (F = 10.65, p =.001, $\eta^2$ =.41) for HbA1c, with pairwise comparisons showing that the CRAT group had significantly lower HbA1c than the control group (mean difference = - 0.796%, p =.001, 95% CI: -1.234 to - 0.358) and that CART also had lower HbA1c than the control group (mean difference = -0.503%, p =.022, 95% CI: - 0.947- -0.06). A smaller yet significant difference was discovered between CART and CRAT (mean difference = 0.293%, p =.041, 95% confidence interval: 0.113 to 0.698).

The therapies significantly affected insulin resistance (F = 24.46, p = .001, $\eta^2$ = .62), as measured by HOMA-IR. CRAT showed the greatest reduction in HOMA-IR compared to the control group (mean difference = -0.796, p = .001, 95% CI: -1.085 to -0.507), while CART also significantly improved insulin resistance relative to the control (mean difference = -0.493, p = .001, 95% CI: -0.785 to -0.201). Additionally, a significant difference was observed between CART and CRAT (mean difference = 0.303, p = .022, 95% confidence interval: 0.036 to 0.571).

*Table 4. Test between-subject effect changes in glycemic control outcomes within treatment groups*

| Variables | Between-Subjects Effects | | | Pairwise Comparison | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | F | Sig.[b] | $\eta^2$ | Treatment groups | Mean Diff. | Std. Erro | Sig.[b] | 95% CID | |
| | | | | | | | | Lower Bound | Upper Bound |
| **HbA1c (%)** | 10.649 | .001 | .41 | CART-CRAT | .293 | .160 | .041 | .113 | .698 |
| | | | | CART-COG | -.503 | .175 | .022 | -.947 | -.060 |
| | | | | CRAT-COG | -.796 | .173 | .001 | -1.234 | -.358 |
| **IR** | 24.46 | .001 | .620 | CART-CRAT | .303 | .105 | .022 | .036 | .571 |
| | | | | CART-COG | -.493 | .115 | .001 | -.785 | -.201 |
| | | | | CRAT-COG | -.796 | .114 | .001 | -1.085 | -.507 |
| **FBS (mg/ dL)** | 16.20 | .001 | .519 | CART-CRAT | .712 | 2.025 | NS | -4.422 | 5.846 |
| | | | | CART-COG | -10.74 | 2.215 | .001 | -16.36 | -5.129 |
| | | | | CRAT-COG | -11.45 | 2.189 | .001 | -17.01 | -5.907 |
| **GT** | 23.124 | .000 | .607 | CART-CRAT | 3.248 | 2.070 | NS | -2.000 | 8.496 |
| | | | | CART-COG | -11.55 | 2.264 | .001 | -17.30 | -5.817 |
| | | | | CRAT-COG | -14.80 | 2.238 | .001 | -20.48 | -9.132 |

*Note: The data were corrected for confounders, which were examined at an average daily energy intake (ADEi) of 2431.0959 kcal. Values are presented as means difference ± SE, with significant differences between groups at $p < 0.05$; [b]=Adjustment for multiple comparisons: Bonferroni; CART = Concurrent Aerobic - Resistance Training; CRAT = Concurrent Resistance - Aerobic Training; COG = Control group; IR = Insulin Resistance Measured by Homeostatic Model Assessment of Insulin Resistance; HbA1c (%) = Glycated Hemoglobin; FBS (mg/ dL) = Fasting Blood Sugar; GT (AUC) (mg·h/dl) = Glucose Tolerance Area Under Curve*

Fasting blood glucose showed a significant overall group effect ($F = 16.20$, $p = .001$, $\eta^2 = .519$), indicating a strong impact. CART (mean difference = -10.74 mg/dL, $p = .001$, 95% CI: -16.36 to -5.13) and CRAT (mean difference = -11.45 mg/dL, $p = .001$, 95% CI: -17.01 to -5.91) were significantly lower than the control group, while the difference between CART and CRAT was not significant (mean difference = 0.712 mg/dL, NS).

Glucose tolerance (GT AUC) had a significant between-group effect ($F = 23.12$, $p < .001$, $\eta^2 = .607$), indicating important practical implications. CRAT showed the greatest improvement compared to control (mean difference = -14.80, $p = .001$, 95% CI: -20.48 to -9.13), followed by CART (mean difference = -11.55, $p = .001$, 95% CI: -17.30 to -5.82).

However, the difference between CART and CRAT was not statistically significant (mean difference = 3.25, NS). Generally, both exercise regimens significantly improved glycemic control relative to the control group. Although CRAT reduced HbA1c and insulin resistance more than CART, the sequence of exercise did not result in significant differences between the two regimens for the other variables. substantial to very substantial effect sizes ($\eta^2$ =.41-.62) emphasize the therapies' practical and clinical value.

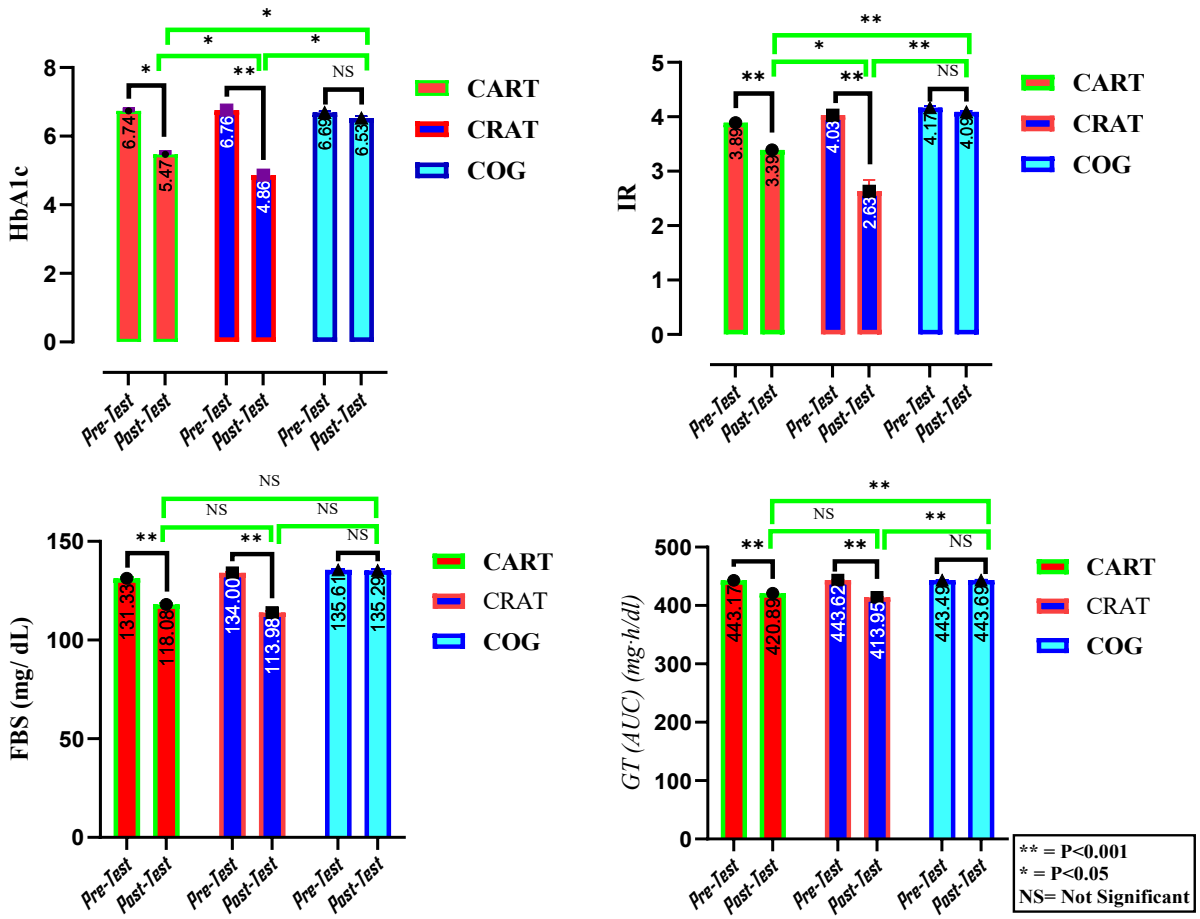


*Figure 5. Pre–Post Changes and Between-Group Differences in Glycemic Control Indicators (HbA1c, IR, FBS, and GT AUC) Across CART, CRAT, and COG Groups.*

### *4.2.2. Lipid profile*

Table 5 and Figure 6 display the within-subject effects and pairwise comparisons of the lipid profile variables HDL, LDL, TG, and TC among the three study groups (CART, CRAT, and COG). The CART group showed a significant within-subject effect on HDL levels ($F = 5.24$, $p = .029$, $\eta^2 = .149$), indicating improvement over time. Both CART and CRAT significantly increased HDL levels, with mean differences of -7.24 mg/dL and -6.76 mg/dL, respectively ($p < .001$). These confidence intervals do not include zero, signifying a consistent change. In contrast, the control group experienced no significant change. This suggests that both exercise interventions effectively boosted HDL levels, while the lack of significance in the control group indicates no spontaneous improvement without planned exercise.

LDL had a significant within-subjects impact in the CART group ($F = 7.80$, $p = .009$, $\eta^2 = .206$). Both CART and CRAT significantly reduced LDL levels, with mean decreases of 30.66 mg/dL and 27.60 mg/dL, respectively ($p < .001$). Again, the control group showed no significant difference. These findings demonstrate that both exercise orders significantly improved LDL. Although the drop in triglycerides in the CART group did not approach statistical significance ($F = 2.32$, $p = .138$), pairwise comparisons show substantial reductions in TG for both CART (29.67 mg/dL, $p < .001$) and CRAT (20.73 mg/dL, $p < .001$). The control group showed no significant difference. Thus, both concurrent training procedures significantly reduced TG, even though the aggregate time effect was not statistically significant for CART.

The CART group saw a significant within-subjects impact of TC ($F = 4.44$, $p = .043$, $\eta^2 = .129$). Significant decreases were observed in both CART (24.91 mg/dL, $p < .001$) and CRAT (25.00 mg/dL, $p < .001$), with narrow confidence intervals indicating consistent effects. The control group showed a minor, non-significant change ($p = .086$). This demonstrates that exercise programs, regardless of sequencing, were equally beneficial in lowering total cholesterol levels. Across all lipid variables, both concurrent training sequences (CART and CRAT) achieved significant and clinically relevant improvements, whereas the control group showed no discernible changes.

Table 5. Within-subject changes in lipid profile outcomes across intervention time points

| Variables | Group | Within-Subjects Effects | | | Pairwise Comparison | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | F | Sig.[b] | $\eta^2$ | Mean Diff. | Std. Error | Sig.[b] | 95% CID | |
| | | | | | | | | Lower Bound | Upper Bound |
| **HDL (mg/dL)** | CART | 5.24 | .029 | .149 | -7.240 | .748 | .001 | -8.767 | -5.713 |
| | CRAT | | | | -6.760 | .741 | .001 | -8.272 | -5.247 |
| | COG | | | | .843 | .761 | NS | -.712 | 2.397 |
| **LDL (mg/dL)** | CART | 7.80 | .009 | .206 | 30.656 | 1.83 | .001 | 26.906 | 34.407 |
| | CRAT | | | | 27.595 | 1.81 | .001 | 23.879 | 31.310 |
| | COG | | | | -3.749 | 1.87 | NS | -7.567 | .170 |
| **TG (mg/dL)** | CART | 2.32 | .138 | .072 | 29.670 | 3.31 | .001 | 22.903 | 36.438 |
| | CRAT | | | | 20.726 | 3.28 | .001 | 14.021 | 27.431 |
| | COG | | | | 1.945 | 3.37 | NS | -4.945 | 8.835 |
| **TC (mg/dL)** | CART | 4.44 | .043 | .129 | 24.909 | .555 | .001 | 23.776 | 26.042 |
| | CRAT | | | | 24.999 | .550 | .001 | 23.877 | 26.122 |
| | COG | | | | -1.178 | .565 | NS | -2.332 | .125 |

*Note: The data were corrected for confounders, which were examined at an average daily energy intake (ADEi) of 2431.0959 kcal. Values are presented as means difference ± SE, with significant differences between groups at $p < 0.05$; [b]=Adjustment for multiple comparisons: Bonferroni; CART = Concurrent Aerobic - Resistance Training; CRAT = Concurrent Resistance - Aerobic Training; COG = Control group; HDL (mg/dL) = High Density Lipoprotein; LDL (mg/dL) =Low Density Lipoprotein; TG (mg/dL) =Triglycerides; TC (mg/dL) =Total Cholesterol*

Table 6 and Figure 6 summarize the between-group effects of interventions on lipid profile indicators (HDL, LDL, TG, and TC) and compare the three groups (CART, CRAT, and COG). Overall, significant differences are observed among the groups for LDL, TG, and TC, while HDL is only marginally significant. The between-subjects effect for HDL approached statistical significance ($F = 3.313$, $p = .050$, $\eta^2 = .181$), indicating a small-to-moderate effect size. However, no pairwise group comparisons reached statistical significance. The differences between CART and CRAT (mean difference = -0.414) and CART and COG (1.810) were both within large, overlapping confidence intervals. Conversely, CRAT and COG (2.224, P=0.047) showed a significant difference compared

to the control group. This suggests that HDL levels did not differ significantly between the intervention groups, implying that the order of exercise in concurrent training had no meaningful impact on HDL outcomes.

LDL had a significant between-group effect ($F = 24.425$, $p < .001$, $\eta^2 = .620$), indicating a large effect size. Pairwise comparisons found no significant difference between CART and CRAT (mean difference = -2.133, not significant). However, CART and CRAT considerably exceeded the control group, with mean reductions of -16.88 and -14.74 mg/dL, respectively (both $p < .001$). this implies that concurrent exercise interventions substantially reduced LDL levels compared to the control, but the order of exercise (CART vs. CRAT) did not create a meaningful difference.

The group effect for TG was significant ($F = 6.685$, $p = .004$, $\eta^2 = .308$) with a moderate effect size. No significant difference was found between CART and CRAT (mean difference = -3.263, NS). However, both intervention groups demonstrated considerably higher decreases than the control: CART-COG (-15.65 mg/dL, $p = .004$) and CRAT-COG (-12.38 mg/dL, $p = .025$). This suggests that both exercise routines efficiently reduced triglycerides, although the order of aerobic and resistance training made no meaningful difference in the level of improvement.

A significant between-group effect was reported for TC ($F = 19.869$, $p < .001$, $\eta^2 = .570$), indicating a large effect size. The CART-CRAT comparison was not significant (mean difference = 0.884, NS). CART (-11.72 mg/dL) and CRAT (-12.61 mg/dL) had considerably higher decreases than the control group ($p < .001$). As a result, TC improved significantly in both intervention groups compared to the control group, but the level of change was unaffected by exercise sequence.

Overall, the data show that both exercise therapies (CART and CRAT) led to significant improvements in LDL, TG, and TC compared to the control group, supporting the strong clinical value of exercise training in enhancing patients' lipid profiles. Importantly, no significant differences were observed between CART and CRAT across all cholesterol variables, indicating that exercise sequence did not significantly affect lipid outcomes, even though both regimens proved beneficial.

*Table 6. Test between-subject effect changes in lipid profile outcomes within treatment groups*

| Variables | Between-Subjects Effects | | | Pairwise Comparison | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | F | Sig.[b] | $\eta^2$ | Treatment groups | Mean Diff. | Std. Error | Sig.[b] | 95% CID | |
| | | | | | | | | Lower Bound | Upper Bound |
| **HDL (mg/dL)** | 3.313 | .050 | .181 | CART-CRAT | -.414 | .829 | NS | -2.516 | 1.689 |
| | | | | CART-COG | 1.810 | .907 | NS | -.491 | 4.110 |
| | | | | CRAT-COG | 2.224 | .897 | 0.047 | .050 | 4.497 |
| **LDL (mg/dL)** | 24.42 | .000 | .620 | CART-CRAT | -2.133 | 2.358 | NS | -8.112 | 3.846 |
| | | | | CART-COG | -16.88 | 2.580 | .001 | -23.422 | -10.33 |
| | | | | CRAT-COG | -14.74 | 2.550 | .001 | -21.213 | -8.282 |
| **TG (mg/dL)** | 6.68 | .004 | .308 | CART-CRAT | -3.263 | 4.056 | NS | -13.548 | 7.021 |
| | | | | CART-COG | -15.65 | 4.438 | .004 | -26.903 | -4.398 |
| | | | | CRAT-COG | -12.38 | 4.386 | .025 | -23.508 | -1.266 |
| **TC (mg/dL)** | 19.86 | .000 | .570 | CART-CRAT | .884 | 2.005 | NS | -4.200 | 5.969 |
| | | | | CART-COG | -11.72 | 2.194 | .001 | -17.289 | -6.162 |
| | | | | CRAT-COG | -12.61 | 2.168 | .001 | -18.108 | -7.111 |

*Note: The data were corrected for confounders, which were examined at an average daily energy intake (ADEi) of 2431.0959 kcal. Values are presented as means difference ± SE, with significant differences between groups at $p < 0.05$; [b]=Adjustment for multiple comparisons: Bonferroni; CART = Concurrent Aerobic - Resistance Training; CRAT = Concurrent Resistance - Aerobic Training; COG = Control group; HDL (mg/dL)= High Density Lipoprotein; LDL (mg/dL)=Low Density Lipoprotein; TG (mg/dL)=Triglycerides; TC (mg/dL)=Total Cholesterol*

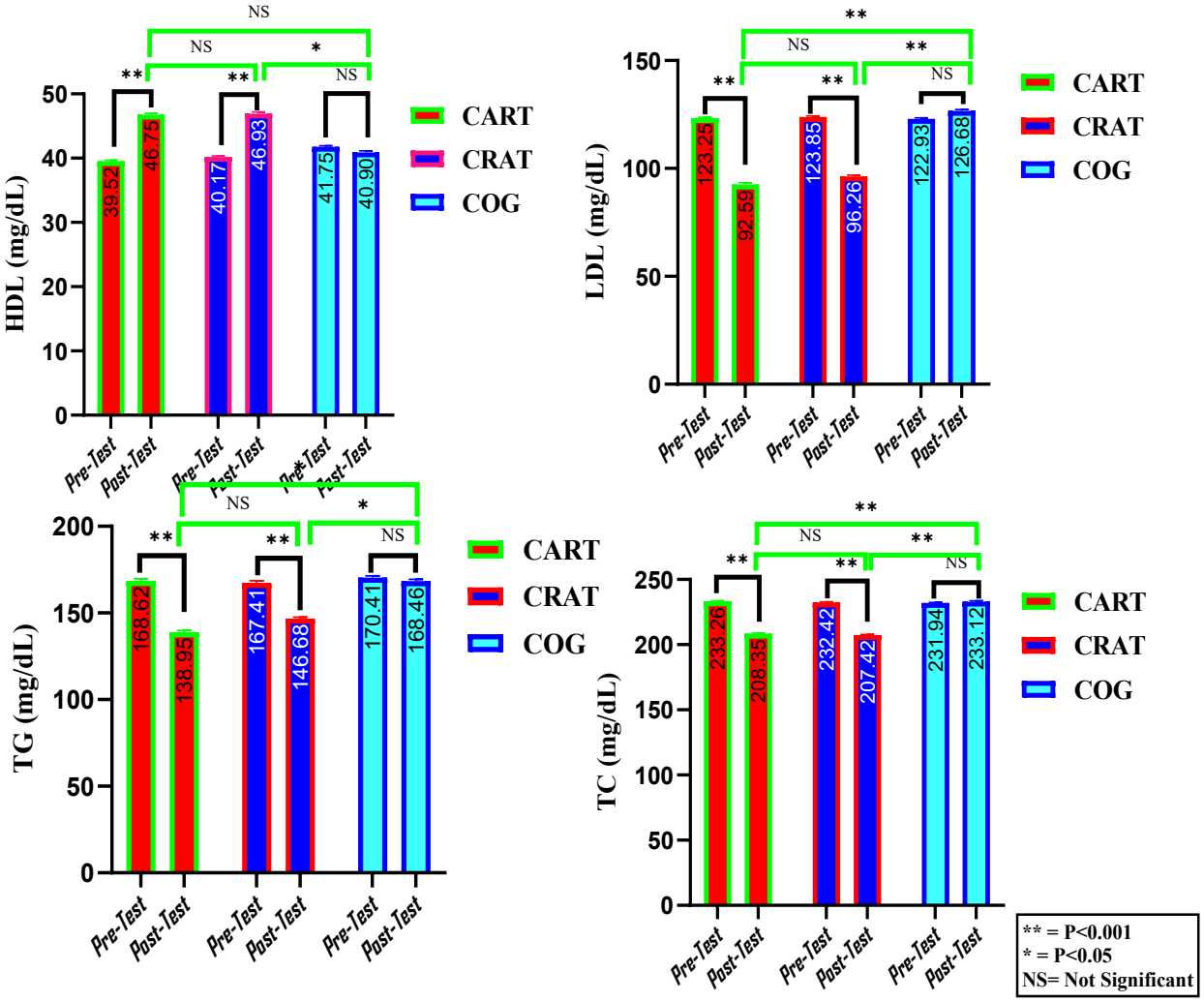


*Figure 6. Pre–Post Changes and Between-Group Differences in Lipid Profile Markers (HDL, LDL, TG, and TC) Across CART, CRAT, and COG Groups.*

### *4.2.3. Cardiovascular Function*

Table 7 and Figure 7 compare systolic blood pressure (SBP), diastolic blood pressure (DBP), resting heart rate (RHR), oxygen saturation ($SpO_2$), and $VO_2$ Peak within three study groups: CART, CRAT, and COG. A substantial within-subjects effect was identified in the CART group ($F = 3.621$, $p = .007$, $\eta^2 = .208$), showing noteworthy progress over time. Pairwise comparisons reveal a substantial reduction in SBP for CART (mean difference = 5.61 mmHg, $p = .001$). The CRAT group also exhibited a considerable and significant

improvement (mean difference = 11.58 mmHg, p =.001), marking the biggest drop among the groups. In comparison, the control group experienced no significant change in SBP. These findings suggest that both exercise regimens significantly lowered SBP, with CRAT showing the greatest improvement.

CART had no significant influence on DBP within participants (F = 1.846, ns, $\eta^2$ =.058), and a pairwise analysis confirmed this. However, CRAT resulted in a significant reduction in DBP (mean difference = 6.11 mmHg, p =.001), demonstrating a definite training effect. The control group showed no significant difference. Thus, only CRAT resulted in significant DBP improvements. Both CART (F = 9.125, p =.02, $\eta^2$ =.241) and CRAT had significant decreases in RHR. CART exhibited a greater reduction (mean difference = 6.97 bpm, p =.001), and also CRAT showed a substantial drop (mean difference = 4.58 bpm, p =.001). The control group exhibited no meaningful difference. These findings suggest that both training programs effectively reduced resting heart rate, with CART achieving a little higher reduction.

CART had significant within-subject effects (F = 5.461, p =.026, $\eta^2$ =.154), and paired results showed a substantial decrease in $SpO_2$ (mean difference = -2.20%, p =.001). Similarly, CRAT was significantly reduced (mean difference = -2.12%, p =.001). The control group experienced no significant change. Although $SpO_2$ declined somewhat in both training groups, it remained within physiological limits and may indicate enhanced oxygen extraction efficiency.

$VO_2$ Peak did not exhibit a significant within-subjects effect for CART (F = 1.287, ns, $\eta^2$ =.041), but the pairwise comparison revealed a significant increase (Mean Diff = -2.92 ml/kg/min, p =.001; negative value implies improvement owing to coding direction). CRAT also demonstrated a substantial improvement (mean difference = -3.04 ml/kg/min, p =.001). The control group exhibited no meaningful difference. These findings indicate that both workout sequences considerably increased aerobic capacity, with CRAT exhibiting a modest advantage.

Both CART and CRAT resulted in significant improvements in key cardiovascular markers when compared to the control group. CRAT resulted in the greatest decreases in SBP and

DBP, while CART showed a slightly greater improvement in resting heart rate. Both interventions significantly increased $VO_2$ Peak while decreasing $SpO_2$ within normal physiological limits. The control group revealed no significant improvements in any variable, demonstrating the effectiveness of the exercise programs.

*Table 7. Within-subject changes in cardiovascular function outcomes across intervention time points*

| Variables | Group | Within-Subjects Effects | | | Pairwise Comparison | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | F | Sig.[b] | $\eta^2$ | Mean Diff. | Std. Error | Sig.[b] | 95% CID | |
| | | | | | | | | Lower Bound | Upper Bound |
| **SBP (mm Hg)** | CART | 3.621 | .007 | .208 | 5.613 | 1.45 | .001 | 2.651 | 8.574 |
| | CRAT | | | | 11.576 | 1.43 | .001 | 8.642 | 14.510 |
| | COG | | | | -2.352 | 1.47 | NS | -5.367 | .664 |
| **DBP (mm Hg)** | CART | 1.846 | NS | .058 | 2.736 | 1.60 | NS | -.539 | 6.011 |
| | CRAT | | | | 6.114 | 1.58 | .001 | 2.870 | 9.359 |
| | COG | | | | .132 | 1.63 | NS | -3.203 | 3.466 |
| **RHR (bpm)** | CART | 9.125 | .02 | .241 | 6.965 | .776 | .001 | 5.380 | 8.551 |
| | CRAT | | | | 4.578 | .769 | .001 | 3.007 | 6.149 |
| | COG | | | | -.081 | .790 | NS | -1.695 | 1.533 |
| **$SPO_2$ (%)** | CART | 5.461 | .026 | .154 | -2.197 | .441 | .001 | -3.098 | -1.297 |
| | CRAT | | | | -2.120 | .432 | .001 | -3.003 | -1.237 |
| | COG | | | | -.117 | .406 | NS | -.946 | .711 |
| **VO2 Peak (mL/kg/min)** | CART | 1.287 | .266 | .041 | -2.924 | .580 | .001 | -4.108 | -1.739 |
| | CRAT | | | | -3.036 | .575 | .001 | -4.210 | -1.863 |
| | COG | | | | .095 | .590 | NS | -1.111 | 1.301 |

*Note: The data were corrected for confounders, which were examined at an average daily energy intake (ADEi) of 2431.0959 kcal. Values are presented as means difference ± SE, with significant differences between groups at $p < 0.05$; [b]=Adjustment for multiple comparisons: Bonferroni; CART = Concurrent Aerobic - Resistance Training; CRAT = Concurrent Resistance - Aerobic Training; COG = Control group; SBP (mm Hg)=Systolic Blood Pressure; DBP (mm Hg)=Diastolic Blood Pressure; RHR (b/m) =Resting Heart Rate; SPO2 (%)=Peripheral Oxygen Saturation; Vo2 peak (mL/kg/min) Peak Oxygen Consumption*

The between-subjects study found substantial differences in several cardiovascular outcomes after the intervention period. The therapies had a significant influence on systolic blood pressure (SBP) ($F = 8.968$, $p = .001$, $\eta^2 = .374$). Both CART and CRAT significantly lowered SBP compared to the control group, with CRAT demonstrating a slightly higher reduction (mean difference = -5.681 mmHg, $p < .001$) than CART (mean difference = -4.896 mmHg, $p = .005$). However, the difference between CART and CRAT was not statistically significant, indicating that the order of aerobic and resistance training had no relevant effect on SBP results.

There were no significant differences in diastolic blood pressure (DBP) between the groups ($F = .610$, NS, $\eta^2 = .039$), and no pairwise comparisons reached significance, showing that neither intervention had a meaningful effect on DBP. The between-subjects analysis for resting heart rate (RHR) showed a significant group effect ($F = 5.202$, $p = .011$, $\eta^2 = .258$), indicating a moderate influence of the interventions. CART significantly reduced RHR relative to the control group (Mean Diff. = -3.358 bpm, $p = .013$), but CRAT did not differ significantly (Mean Diff. = -1.071 bpm, NS) or from CART (Mean Diff. = -2.287 bpm, NS). These findings suggest that concurrent training can effectively reduce resting heart rate, although the sequence of aerobic and resistance exercises (CART vs. CRAT) does appear to influence the outcome.

A strong and highly significant between-group effect was observed for oxygen saturation ($SpO_2$) ($F = 34.82$, $p < .001$, $\eta^2 = .699$). Both CART and CRAT significantly improved $SpO_2$ compared to the control group, with no notable differences between the two exercise sequences, emphasizing the clear benefit of concurrent training on oxygenation. Likewise, maximal oxygen uptake ($VO_2$ Peak) showed significant group differences ($F = 7.112$, $p = .003$, $\eta^2 = .322$). CART resulted in a significant increase in $VO_2$ Peak compared to the control group (Mean Diff. = 2.542 $mL \cdot kg^{-1} \cdot min^{-1}$, $p = .002$), while the difference between CRAT and control was not significant. The comparison between CART and CRAT also did not reach significance, indicating that the order of aerobic and resistance exercise has minimal impact on improvements in aerobic capacity.

Concurrent training significantly improved SBP, RHR, $SpO_2$, and $VO_2$ Peak compared to the control group. However, differences between the two workout sequences (CART vs. CRAT) were generally not statistically significant across variables, except that CRAT showed slightly greater reductions in SBP and CART demonstrated clearer improvements in $VO_2$ Peak and RHR. This suggests that, although concurrent training is effective, the order of aerobic and resistance exercises does not affect cardiovascular outcomes (Table 8).

*Table 8. Test between-subject effect changes in cardiovascular function outcomes within treatment groups*

| **Variables** | **Between-Subjects Effects** | | | **Pairwise Comparison** | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | F | Sig.[b] | $\eta^2$ | Treatment groups | Mean Diff. | Std. Error | Sig.[b] | 95% CID | |
| | | | | | | | | Lower Bound | Upper Bound |
| **SBP (mm Hg)** | 8.968 | .001 | .374 | CART-CRAT | .785 | 1.309 | NS | -2.534 | 4.104 |
| | | | | CART-COG | -4.896 | 1.432 | .005 | -8.527 | -1.265 |
| | | | | CRAT-COG | -5.681 | 1.415 | .001 | -9.270 | -2.093 |
| **DBP (mm Hg)** | .610 | NS | .039 | CART-CRAT | .104 | 1.108 | NS | -2.706 | 2.913 |
| | | | | CART-COG | -1.125 | 1.212 | NS | -4.198 | 1.949 |
| | | | | CRAT-COG | -1.228 | 1.198 | NS | -4.266 | 1.810 |
| **RHR (bpm)** | 5.202 | .011 | .258 | CART-CRAT | -2.287 | .997 | NS | -4.815 | .240 |
| | | | | CART-COG | -3.358 | 1.091 | .013 | -6.124 | -.593 |
| | | | | CRAT-COG | -1.071 | .078 | NS | -3.804 | 1.662 |
| **SPO2 (%)** | 34.82 | .000 | .699 | CART-CRAT | -.033 | .209 | NS | -.564 | .498 |
| | | | | CART-COG | 1.369 | .199 | .001 | .863 | 1.875 |
| | | | | CRAT-COG | 1.402 | .194 | .001 | .911 | 1.893 |
| **VO2 Peak (mL/kg/min)** | 7.112 | .003 | .322 | CART-CRAT | .850 | .620 | NS | -.723 | 2.423 |
| | | | | CART-COG | 2.542 | .679 | .002 | .821 | 4.262 |
| | | | | CRAT-COG | 1.692 | .671 | NS | -.009 | 3.392 |

*Note: The data were corrected for confounders, which were examined at an average daily energy intake (ADEi) of 2431.0959 kcal. Values are presented as means difference ± SE, with significant differences between groups at $p < 0.05$; [b]=Adjustment for multiple comparisons: Bonferroni; CART = Concurrent Aerobic - Resistance Training; CRAT = Concurrent Resistance - Aerobic Training; COG = Control group; SBP (mm Hg)=Systolic Blood Pressure; DBP (mm Hg) =Diastolic Blood Pressure; RHR (b/m) =Resting Heart Rate; SPO2 (%) =Peripheral Oxygen Saturation; Vo2 peak (mL/kg/min) Peak Oxygen Consumption*

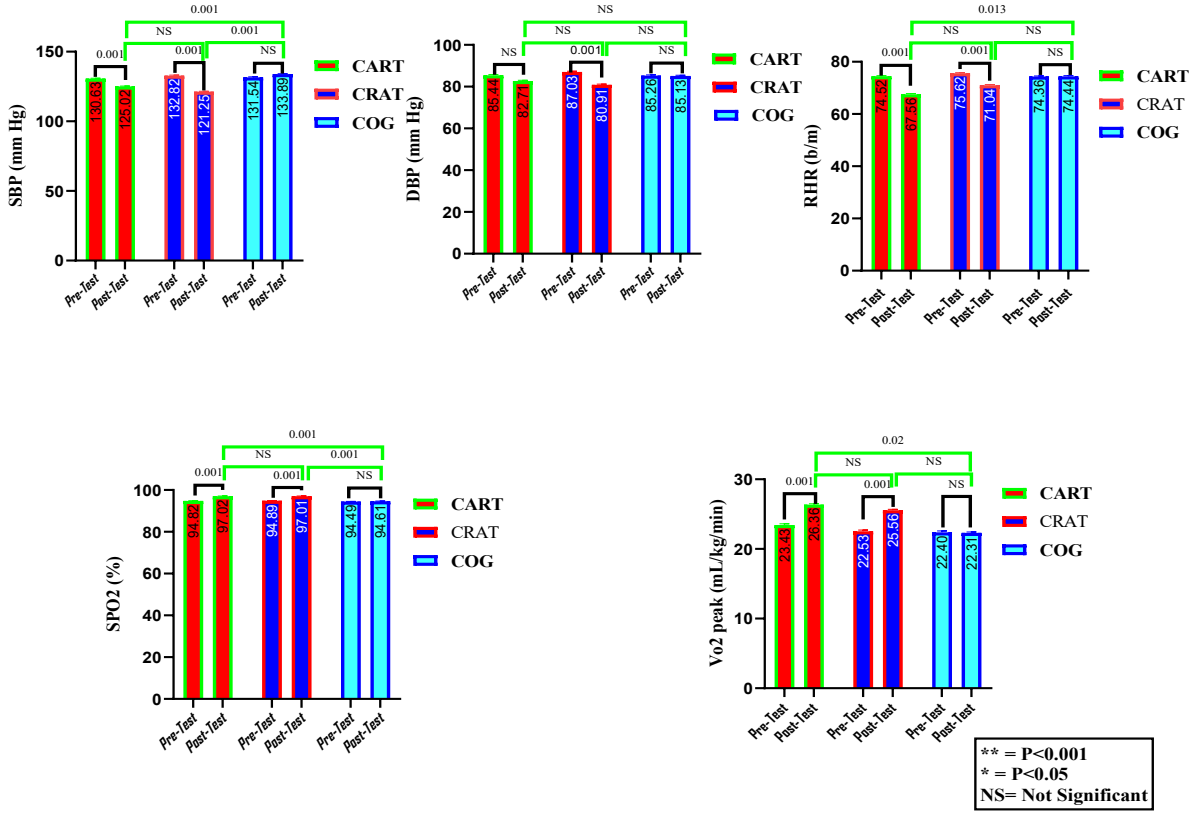


*Figure 7. Between-Group Differences and Pre–Post Changes in SBP, DBP, RHR, $SpO_2$, and $VO_2$ Peak Across CART, CRAT, and Control Groups*

### *4.2.4. Anthropometric Indices*

According to the findings in Table 9 and Figure 8, analysis of body composition variables such as body fat percentage (BFP), waist-to-hip ratio (WHR), and body mass index (BMI) revealed significant within-subject improvements in both the CART and CRAT groups, while the control group (COG) showed no significant changes. For BFP (%), the within-group effect demonstrated a significant reduction over time ($F = 6.480$, $p = .022$, $\eta^2 = .204$), CART with a mean difference of 1.516% (95% CI: 0.943–2.088, $p = .001$). The CRAT group had an even larger mean reduction of 1.837%, although the standard error was higher (.278), showing variability. In contrast, the COG group did not show a significant change. This suggests that both exercise interventions effectively reduced body fat, with CRAT achieving slightly greater reductions than CART, while no change occurred in the control group.

CART resulted in a substantial decrease in WHR (F = 4.688, p =.038, $\eta^2$ =.135), with a mean reduction of 0.107 (95% CI: 0.065-0.150, p =.001). CRAT also resulted in a significant but smaller reduction of 0.049 (95% CI: 0.006-0.091, p =.026). Conversely, WHR increased marginally in the control group (-0.047, p =.035), demonstrating that exercise interventions helped to reduce central adiposity, with CART having a greater effect.

For BMI (kg/m2), CART participants experienced a substantial decrease (F = 6.301, p =.018, 2 =.274), with a mean reduction of 2.161 kg/m2 (95% CI: 1.890-2.431, p =.001). The CRAT group showed a significant reduction of 1.647 kg/m² (95% CI: 1.379-1.915, p =.001), while the control group did not change significantly (0.071 kg/m², p = NS). These findings show that both exercise regimens are effective at lowering BMI, with CART producing a slightly bigger drop than CRAT. Overall, the CART and CRAT therapies resulted in significant changes in body composition parameters when compared to the control group. CART resulted in slightly higher decreases in WHR and BMI, but CRAT had a significantly stronger effect on BFP. The absence of significant changes in the control group emphasizes the efficacy of the exercise regimens.

*Table 9. Within-subject changes in anthropometric indices outcomes across intervention time points*

| **Variables** | **Group** | **Within-Subjects Effects** | | | **Pairwise Comparison** | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | F | Sig.[b] | $\eta^2$ | Mean Diff. | Std. Error | Sig.[b] | 95% CID | |
| | | | | | | | | Lower Bound | Upper Bound |
| **BFP (%)** | CART | 6.480 | .022 | .204 | 1.516 | .280 | .001 | .943 | 2.088 |
| | CRAT | | | | 1.837 | .278 | .001 | 1.270 | 2.404 |
| | COG | | | | -.498 | .285 | NS | -1.081 | .085 |
| **WHR** | CART | 4.688 | .038 | .135 | .107 | .021 | .001 | .065 | .150 |
| | CRAT | | | | .049 | .021 | .026 | .006 | .091 |
| | COG | | | | -.047 | .021 | .035 | -.091 | -.004 |
| **BMI (kg/m²)** | CART | 6.301 | .018 | .274 | 2.161 | .132 | .001 | 1.890 | 2.431 |
| | CRAT | | | | 1.647 | .131 | .001 | 1.379 | 1.915 |
| | COG | | | | .071 | .135 | NS | -.205 | .346 |

*Note: The data were corrected for confounders, which were examined at an average daily energy intake (ADEi) of 2431.0959 kcal. Values are presented as means difference ± SE, with significant differences between groups at p < 0.05; [b]=Adjustment for multiple comparisons: Bonferroni; CART = Concurrent Aerobic - Resistance Training; CRAT = Concurrent Resistance - Aerobic Training; COG = Control group; BFP (%) =Body Fat Percentage; WHR=Waist To Hip Ratio*

Body fat percentage (BFP), waist-to-hip ratio (WHR), and body mass index (BMI) all showed significant differences between the treatment groups after the intervention, according to Table 11, between-subjects analysis. Significant practical and clinical significance of the interventions was demonstrated by the considerable effect sizes for BFP ($\eta^2$ =.340), WHR ($\eta^2$ =.263), and BMI ($\eta^2$ =.661).

For BFP (%), pairwise comparisons showed that both CART and CRAT reduced BFP compared to the control group (COG), with CART-COG (mean difference = -1.416, p = .003) and CRAT-COG (mean difference = -1.263, p = .008) achieving statistically significant reductions. There was no significant difference between CART and CRAT (mean difference = -0.153, NS), indicating that the sequence of concurrent training did not significantly affect body fat reduction. Although the difference between CART and CRAT was not significant (mean difference = 0.002, NS), both exercise methods significantly lowered WHR compared to the control group (CART-COG mean difference = -0.046, p =.025; CRAT-COG mean difference = -0.048, p =.017). This demonstrates that concurrent training significantly reduced central adiposity, regardless of exercise order.

In terms of BMI (kg/m2), there were significant decreases in CART compared to control (mean difference = -1.246, p =.021), but there was no significant trend in CRAT compared to control (mean difference = -1.019, NS). The difference between CART and CRAT was not significant (mean difference = -0.227, NS), indicating that both therapies had a comparable effect on overall body mass, with CART somewhat more effective in this cohort. Taken together, these findings indicate that concurrent exercise training, regardless of order, is successful in changing key body composition indices in Type 2 diabetic individuals, with both therapies outperforming the non-exercising control group.

*Table 10. Test between-subject effect changes in lipid profile outcomes within treatment groups*

| Variables | Between-Subjects Effects | | | Pairwise Comparison | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | F | Sig.[b] | $\eta^2$ | Treatment groups | Mean Diff. | Std. Error | Sig.[b] | 95% CID | |
| | | | | | | | | Lower Bound | Upper Bound |
| **BFP (%)** | 7.717 | .002 | .340 | CART-CRAT | -.153 | .355 | NS | -1.053 | .746 |
| | | | | CART-COG | -1.416 | .388 | .003 | -2.400 | -.432 |
| | | | | CRAT-COG | -1.263 | .384 | .008 | -2.236 | -.291 |
| **WHR** | 5.354 | .010 | .263 | CART-CRAT | .002 | .015 | NS | -.035 | .040 |
| | | | | CART-COG | -.046 | .016 | .025 | -.087 | -.005 |
| | | | | CRAT-COG | -.048 | .016 | .017 | -.089 | -.007 |
| **BMI ($kg/m^2$)** | 58.503 | .000 | .661 | CART-CRAT | -.227 | .394 | NS | -1.226 | .771 |
| | | | | CART-COG | -1.246 | .431 | .021 | -2.338 | -.154 |
| | | | | CRAT-COG | -1.019 | .426 | NS | -2.098 | .061 |

*Note: The data were corrected for confounders, which were examined at an average daily energy intake (ADEi) of 2431.0959 kcal. Values are presented as means difference ± SE, with significant differences between groups at $p < 0.05$; [b]=Adjustment for multiple comparisons: Bonferroni; CART = Concurrent Aerobic - Resistance Training; CRAT = Concurrent Resistance - Aerobic Training; COG = Control group; BFP (%) =Body Fat Percentage; WHR=Waist To Hip Ratio*

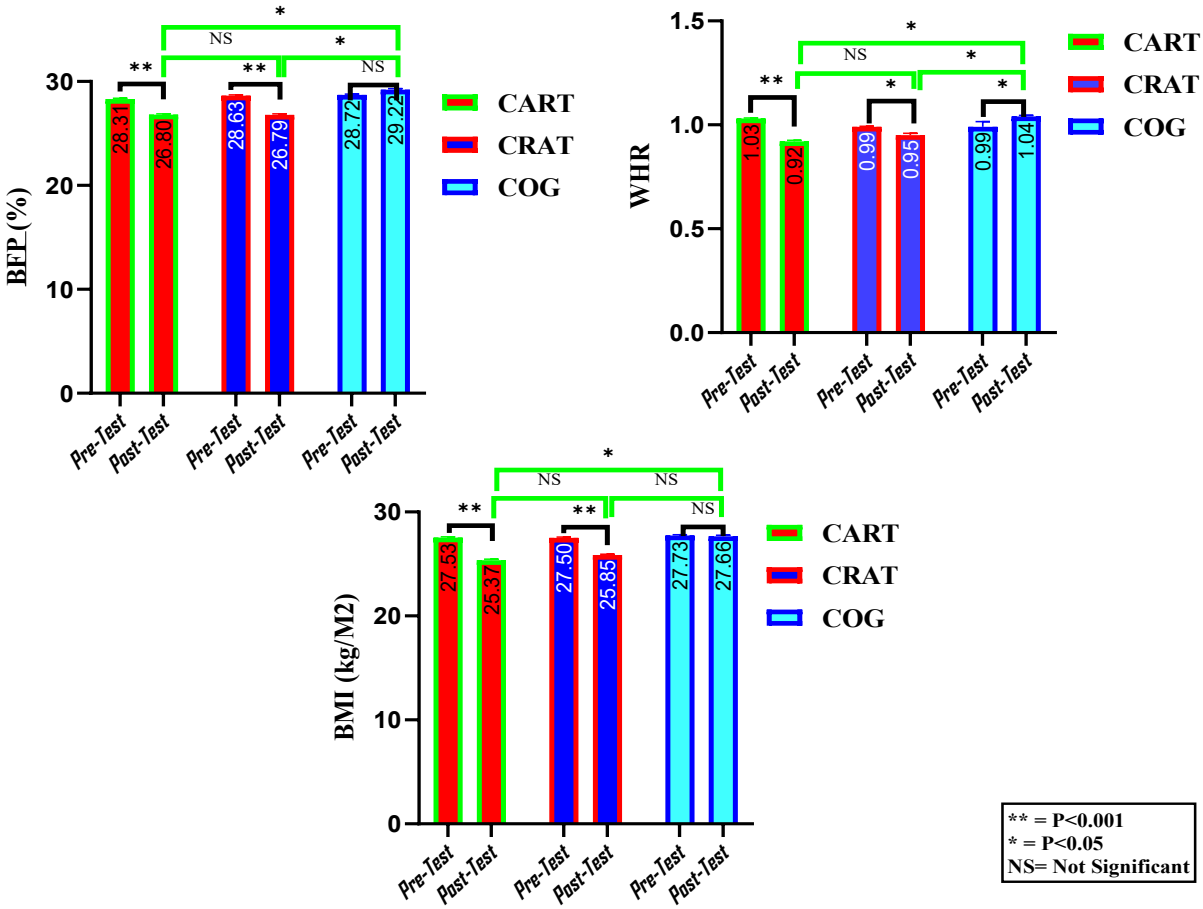


*Figure 8. Pre–Post Changes and Between-Group Differences in Anthropometric indices (BFP, WHR and BMI) Across CART, CRAT, and COG Groups.*

# CHAPTER FIVE

# 5. DISCUSSION

This chapter provides a critical interpretation of the findings of the present doctoral research, which was conducted in two sequential and complementary phases: a systematic review and meta-analysis and a randomized controlled trial. The two-phase approach was deliberately employed to combine evidence synthesis with experimental investigation, thereby strengthening the scientific and clinical relevance of the study.

Informed by these findings from systematic review and meta-analysis, the RCT was designed to advance the investigation by determining whether altering the order of aerobic and resistance exercise within a concurrent training session affects the magnitude of cardio-metabolic and anthropometric adaptations. Whereas Phase I established the general effectiveness of concurrent training, Phase II refined exercise prescription by enabling causal inference on sequence-specific effects under rigorously controlled experimental conditions.

Accordingly, the discussion is structured to first interpret the findings of the systematic review and meta-analysis, followed by an integrated analysis of the randomized controlled trial results across metabolic biomarkers, cardiovascular function, and anthropometric indices. Throughout the chapter, findings from Phase I are used to contextualize and support the Phase II results, thereby demonstrating conceptual continuity between the two phases and highlighting the original contribution of this dissertation to exercise prescription research in Type 2 diabetes mellitus.

## 5.1. Discussion of systematic review and meta-analysis

The objective of this meta-analysis was to objectively assess the therapeutic benefits of a 12-week program combining continuous aerobic and short rest resistance exercise training, conducted within a single session, on lipid profiles (HDL, TG, and total cholesterol) and glycemic indices (HbA1c and HOMA-IR) in patients with Type 2 Diabetes Mellitus (T2DM). The analysis included data from 11 randomized controlled trials involving 438

participants who performed both exercise modalities in the same session. Notably, variations in training intensity ranging from 50 - 85% HRmax for aerobic exercise and 50 - 80% 1RM for resistance training with short rest (30-90 seconds) between sets may have significantly influenced metabolic outcomes (Willardson, 2006).

The key findings indicated significant reductions in glycemic and lipid profile parameters, suggesting that such structured interventions offer clinically meaningful improvements for individuals with T2DM. The included studies showed significant heterogeneity in effect estimates for key outcomes, including triglycerides, HbA1c, and HOMA-IR. Several key elements are believed to have contributed to this variability. Differences in sample sizes were significant, with smaller studies frequently providing less stable effect sizes that increased heterogeneity, whereas larger trials with more exact estimates altered the pooled effects differently, sometimes attenuating overall impact (Holzmeister et al., 2024).

Our findings revealed that the concurrent training combining continuous aerobic exercise and short-rest resistance training program significantly reduced HbA1c and HOMA-IR levels, reflecting enhanced glycemic control through mechanisms such as improved insulin sensitivity, increased muscle glucose uptake, and reduced adiposity. These effects are consistent with previous studies (Afshounpour et al., 2016; Keshel & Coker, 2015), highlighting the metabolic advantages of multi-modal training in T2DM management.

These results are consistent with previous meta-analyses evaluating the effects of concurrent training combining continuous aerobic exercise and short-rest resistance training exercise program on glucose metabolism in individuals with T2DM (Al-Mhanna et al., 2024; Schwingshackl et al., 2014). Additionally, Zhao et al. (2021) systematic reviews and meta-analyses demonstrated that, 12 weeks combining continuous aerobic exercise and short-rest resistance training exercise program has been recognized as an optimal exercise strategy for inducing beneficial changes in glycemic control among individuals with Type 2 Diabetes and concurrent overweight/obesity. Notably, a 12-week multi-modal exercise program demonstrated greater efficacy in improving glycemic control and postprandial glucose responses than shorter interventions (≤12 weeks) (Teo et al., 2020). highlighting the sustained benefits of structured concurrent exercise in managing glycemia among individuals with T2DM.

The HOMA-IR index estimates insulin resistance based on fasting glucose and insulin

levels. Individuals with metabolic diseases, particularly type 2 diabetes, are likely to have elevated HOMA-IR levels. Type 2 diabetes is caused by insulin resistance and β-cell malfunction, leading to hyperglycemia and poor metabolic control. Our findings demonstrated that combined exercise significantly reduced insulin resistance in T2D patients, which was consistent with the findings of Yaowei Sun et al. (2024a) and Zhao et al. (2021). Studies have shown that during a 12-week concurrent exercise program, insulin in skeletal muscle plays a key role in upregulating glucose transporter protein expression (Donges et al., 2013) and enhancing glycogen synthase activity (Christ-Roberts et al., 2003). These adaptations improve glucose uptake efficiency in muscle tissue, thereby contributing to changes in HOMA-IR.

Individuals with diabetes frequently exhibit disruptions in lipid metabolism, characterized by elevated levels of total cholesterol (TC) and triglycerides (TG), alongside reduced levels of high-density lipoprotein cholesterol (HDL-C) (Bardini et al., 2012; Pan et al., 2024). These imbalances not only contribute to an increased risk of cardiovascular complications but also reflect underlying metabolic dysfunction associated with insulin resistance and impaired lipid clearance (Du & Qin, 2023). Managing these lipid abnormalities is crucial for reducing the risk of atherosclerosis and improving overall metabolic health in diabetic patients.

This study demonstrated that combining resistance and aerobic training significantly improved HDL-C levels and reduced TC and TG. HDL-C plays a protective role in cardiovascular health by aiding in the metabolism of excess lipids in the bloodstream (Rysz et al., 2020). A recent meta-analysis revealed that combining aerobic and resistance training significantly enhanced HDL-C and reduced the total cholesterol level and TG. Yaowei Sun et al. (2024a) reported that 81 % increase in HDL-C and a 46 % reduction in TG. Similarly, Tambalis et al. (2009), Y. Sun et al. (2024), and K. B. Kim et al. (2019) systematic review and meta-analysis reported that there is a significant improvement in HDL-C and reduced TC and TG levels after combined exercise intervention in individuals with obesity. These results align with the findings of our study.

There are several limitations when interpreting these findings, including considerable variations in the number of participants between studies, which may have an impact on the study's heterogeneity. The generalizability of the results may be influenced by

heterogeneity caused by differences in the number of participants in each article (Holzmeister et al., 2024). Outlier studies, which had very low or high standard deviations, notably for total cholesterol, disproportionately influenced the pooled estimates and skewed the results, were another source of heterogeneity (Lijmer et al., 2002). Although the interventions were all 12 weeks long, changes in the structure of concurrent training protocols, such as circuit versus non-circuit formats or the order of resistance and aerobic workouts, are likely to have contributed to extra variation. Specifically, concurrent resistance-endurance (CRE) training, where resistance exercises are performed before endurance training, is more effective in managing body fat metabolism compared to concurrent endurance-resistance (CER) training, where endurance exercises are performed first (Hakimi & Ali-Mohammadi, 2019; Z. Li et al., 2025). This finding highlights the importance of exercise order in optimizing the metabolic benefits of concurrent training, suggesting that the sequencing of resistance and endurance exercises can significantly influence outcomes, particularly in fat metabolism regulation.

## 5.2. Integrated Discussion of Randomized Controlled Trial

### *5.2.1. Glycemic and Lipid Biomarker Adaptations Following CART and CRAT*

The present study demonstrated that concurrent aerobic and resistance training produces significant and clinically meaningful improvements in key metabolic biomarkers associated with Type 2 diabetes mellitus. These biomarkers include long-term glycemic control (HbA1c), insulin resistance (IR), fasting and post-prandial glucose regulation (FPG and AUC-GT), and lipid profile indices (HDL-C, LDL-C, TG, and TC). The findings are consistent with the objectives of Phase I, which established the overall efficacy of concurrent training for metabolic regulation, and are further extended by Phase II through experimental evaluation of exercise sequence effects.

The RCT demonstrated that both concurrent aerobic-resistance training sequences (CART and CRAT) significantly improved long-term and short-term glycemic control, as evidenced by reductions in HbA1c and fasting plasma glucose (FPG) levels compared with the control group (see Tables 3 and 4; Figure 5). These findings confirm the efficacy of

concurrent training as a non-pharmacological strategy to improve metabolic regulation in individuals with type 2 diabetes mellitus (T2DM).

With respect to HbA1c, both exercise sequences produced clinically meaningful reductions; however, the CRAT protocol induced comparatively greater improvements. This finding suggests that although continuous training in itself is beneficial, the order in which exercise modalities are performed may influence the degree of long-term glycemic adaptation. Similar reductions in HbA1c following combined aerobic and resistance exercise have been consistently reported in recent clinical trials and systematic reviews involving individuals with T2DM (Amare et al., 2025; Y. Sun et al., 2024). Moreover, both training sequences were beneficial; the CRAT produced somewhat greater reductions in HbA1c, suggesting that the order of exercise may influence the magnitude of adaptation (Zarei et al., 2021).

In contrast, some studies have reported superior or comparable cardiometabolic benefits when aerobic exercise precedes resistance training. For example, Al-Mhanna et al. (2024) observed favorable metabolic adaptations following CART in individuals with T2DM and concurrent overweight or obesity. These discrepancies may be attributable to differences in participant characteristics, training volume and intensity, intervention duration, or baseline metabolic status. Importantly, such variability underscores the need to consider exercise sequencing within the broader context of individualized exercise prescription rather than as an isolated determinant of outcome.

From a mechanistic perspective, the relatively greater HbA1c reduction observed in the CRAT group may be explained by the well-documented interference effect associated with concurrent training. When aerobic exercise precedes resistance exercise, as in CART, residual fatigue and preferential activation of AMP-activated protein kinase (AMPK) may attenuate resistance-exercise-induced anabolic signaling pathways, particularly those involving the mammalian target of rapamycin (mTOR) (Vernon G. Coffey & John A. Hawley, 2017; Fyfe et al., 2014). Conversely, initiating training sessions with resistance exercise may enhance motor unit recruitment and muscle fiber activation (Cadore et al., 2010; Coffey & Hawley, 2017), leading to greater glycogen depletion and, consequently, augmented glucose uptake during the aerobic component (Richter et al., 2011). These

adaptations collectively contribute to improved skeletal muscle glucose disposal, increased GLUT-4 translocation, and enhanced insulin signaling efficiency (McGee & Hargreaves, 2006; Erik A. Richter & Mark Hargreaves, 2013), thereby exerting a more pronounced effect on long-term glycemic markers such as HbA1c.

Regarding fasting plasma glucose, both CART and CRAT resulted in significant reductions compared with the control group, with no statistically meaningful difference between the two exercise sequences. This finding indicates that the acute glucose-lowering effect of concurrent training is largely sequence-independent. The absence of a differential sequence effect on FPG suggests that both aerobic and resistance exercise activate complementary molecular pathways involved in glucose regulation, including AMPK-mediated GLUT-4 translocation, enhanced insulin receptor sensitivity, and improved mitochondrial function (Chen et al., 2021; Pereira et al., 2017; Perez, 2021). These mechanisms are sufficient to improve basal glucose homeostasis regardless of exercise order.

The present results are consistent with previous evidence demonstrating that combined aerobic and resistance exercise is superior to single-mode training for improving glycemic control in T2DM (AminiLari et al., 2017; Kang & Huh, 2021). Additionally, studies examining exercise sequence have reported comparable reductions in fasting glucose when resistance exercise precedes aerobic training (Saeidi et al., 2021; Zarei et al., 2021), further corroborating the current findings.

Overall, the findings indicate that concurrent training, irrespective of sequence, is effective in improving fasting glucose levels, while resistance-first sequencing may confer additional advantages for long-term glycemic control as reflected by greater HbA1c reductions. These results have important clinical implications, suggesting that while flexibility in exercise sequencing may be acceptable for improving short-term glycemic outcomes, prioritizing resistance exercise before aerobic exercise may optimize chronic metabolic adaptations in individuals with T2DM.

Between-group analyses revealed that both CART and CRAT significantly improved insulin resistance, as reflected by reductions in HOMA-IR, compared with the control group. These findings reinforce existing evidence that concurrent exercise training, irrespective of sequence, is an effective intervention for enhancing insulin sensitivity in

individuals with type 2 diabetes mellitus. Previous studies have consistently demonstrated that both aerobic-first and resistance-first training sequences improve insulin action through enhanced glucose uptake and increased insulin receptor activity (Amare et al., 2025; Amin et al., 2024; Bassi et al., 2015)

Notably, although both exercise sequences were effective, the CRAT protocol elicited a modestly greater reduction in insulin resistance than CART. This observation suggests that initiating exercise sessions with resistance training may optimize insulin sensitivity adaptations. Similar findings have been reported in recent clinical trials examining combined resistance and aerobic exercise in individuals with T2DM, where resistance-first sequencing resulted in superior glycemic improvements (Y. Sun et al., 2024; Zarei et al., 2021). The enhanced effect observed with CRAT may be attributed to greater skeletal muscle engagement and adaptations induced by resistance exercise, including increased muscle fiber recruitment and improved glucose disposal capacity (Denadai & Greco, 2025).

Mechanistically, resistance training performed before aerobic exercise may attenuate the interference effect commonly observed in concurrent training, thereby allowing more effective activation of resistance-induced signaling pathways such as the mammalian target of rapamycin (mTOR). This facilitates greater improvements in muscle glucose uptake and insulin signaling efficiency (Vernon G. Coffey & John A. Hawley, 2017; Fyfe et al., 2014). Furthermore, resistance exercise is known to promote GLUT-4 translocation and enhance insulin receptor sensitivity, processes that are central to improved insulin responsiveness (Merz & Thurmond, 2020; Sjøberg et al., 2017). When followed by aerobic exercise, these adaptations may be further amplified, contributing to the greater reduction in insulin resistance observed in the CRAT group.

In terms of glucose tolerance, assessed by the area under the glucose curve (AUC-GT), no statistically significant differences were observed between CART and CRAT. However, both intervention groups demonstrated substantial improvements compared with the control group, indicating that concurrent training markedly enhances post-prandial glucose handling regardless of exercise order. The significant time × group interaction observed in

both training groups, but not in the control group, further underscores the metabolic benefit of combined exercise interventions over sedentary behavior.

The lack of a sequence-specific effect on glucose tolerance may be explained by the complementary physiological adaptations elicited by aerobic and resistance exercise. Aerobic exercise enhances skeletal muscle glucose utilization through increased GLUT-4 expression, mitochondrial density, and oxidative enzyme activity (Bajpeyi et al., 2023; Erik A. Richter & Mark Hargreaves, 2013). Resistance training augments these effects by increasing muscle mass and glycogen storage capacity, thereby expanding the reservoir for glucose clearance (LeBrasseur et al., 2010; Stotzer et al., 2018). When combined, these modalities exert additive effects that improve overall glycemic regulation, as reflected by reduced AUC-GT values (Amare et al., 2024; Y. Sun et al., 2024).

Consistent with the present findings, previous studies and meta-analyses have reported that the sequence of aerobic and resistance exercise does not significantly influence glucose tolerance outcomes, suggesting that cumulative training volume and intensity are more critical determinants of post-prandial glucose regulation than exercise order alone (S. Zaki et al., 2024). These results support the notion that flexibility in exercise sequencing can be permitted without compromising improvements in glucose tolerance, thereby facilitating individualized and sustainable exercise prescriptions.

Overall, the present findings demonstrate that concurrent training significantly improves both insulin resistance and glucose tolerance in individuals with T2DM. While both exercise sequences were effective, resistance-first training elicited a greater reduction in insulin resistance, indicating that exercise order may modulate the magnitude of insulin sensitivity adaptations. Improvements in glucose tolerance, however, were comparable between sequences, highlighting that the primary determinant of post-prandial glucose control is participation in combined training rather than the specific order of modalities. Importantly, these results extend the Phase I evidence by confirming that concurrent training is efficacious in improving glucose regulation and that exercise sequence may selectively influence specific metabolic outcomes, particularly insulin resistance.

In our outcome, the pattern, which includes significant TG drops and reductions in LDL-

C and TC (Table 5; Figure 6) in both groups, is consistent with the current exercise-lipid literature. However, there is no significant change in the HDL index. It should be noted that although HDL-C did not differ between sequences, within-group increases were observed, indicating that both exercise modalities improved HDL over time, even if sequence-specific effects were not evident. Consistent with the findings of the present study, Hojati, et al. in a study of 21 diabetic women, reported the acute effect of combined aerobic and resistance exercise with a significant decrease in TG and TC levels 24 hours after exercise (Hojjati Zidashti & Shahsavari, 2015). Sillanpää et al. (2009) in a study of 62 female (middle-aged and old) subjects, reported that endurance, strength, and combined strength and endurance training significantly decreased blood cholesterol and LDL-c levels, and in contrast to our finding, significantly increased HDL levels, which may reflect longer intervention duration, higher aerobic dose, or population differences**.** Recent meta-analyses indicate that combined aerobic and resistance training is particularly effective at lowering TC and LDL, and that HDL is less responsive to sustained aerobic volume/intensity; resistance training contributes to reductions in LDL and TG but has a smaller variable effect on HDL (Amare et al., 2025; Y. Sun et al., 2024).

Additionally, in individuals with Type 2 diabetes, impaired insulin signaling, altered CETP activity, and glycation of apolipoproteins may limit HDL responsiveness to short-term interventions (Walke et al., 2021). Exercise improves lipid metabolism through multiple mechanisms: enhanced skeletal muscle lipoprotein lipase (LPL) activity increases TG clearance; increased expression of LDL receptors and improved hepatic lipid handling reduce circulating LDL; and increased reverse cholesterol transport and enzyme activity (e.g., LCAT) can raise HDL, particularly when aerobic dose is sufficient (Nomikos et al., 2022; Zhu & Guo, 2025). That both CART and CRAT produced large LDL and TC reductions suggests that the concurrent format (irrespective of exact order) provides enough aerobic stimulus (and muscle mass activation) to improve hepatic and peripheral lipid handling (Zheng & Cai, 2019). However, these findings suggest that lipid parameters, unlike AIx, may be less sensitive to exercise sequence in short-term interventions. The absence of between-sequence differences in HDL-C in the present study, despite significant increases in both training sequences, contrasts with randomized controlled trials reporting greater HDL-C improvements following resistance-to-aerobic training over

extended intervention periods (e.g., 24 months) (Zarei et al., 2021). This discrepancy may reflect both the shorter duration of our intervention and the need for sufficient aerobic dose to elicit robust HDL-specific adaptations in diabetic populations.

Although the overall main effect of time for TG did not reach significance, the significant Time × Group interaction and large within-group reductions in CART and CRAT indicate clinically relevant improvements in TG metabolism with exercise. Mechanistically, post-exercise increases in skeletal muscle LPL activity and greater fatty acid oxidation lower fasting TG (Al Mulla et al., 2000; Bittel et al., 2020; Lundsgaard et al., 2020); repeated sessions produce cumulative adaptations. Consequently, an increase in caloric expenditure and positive effects on the lipid profile are two benefits of combined exercise. It should be noted that caloric expenditure was not directly measured; therefore, this explanation is plausible but should be interpreted cautiously. Thus, calorie expenditure and subsequent lipid oxidation may be the cause of these effects in the current investigation. However, there was no discernible difference between the two combined exercise modes' effects on the lipid profile. This may be because both sequences had comparable training volume, intensity, and duration, and because short-term interventions may not capture subtle sequence-specific lipid effects.

From a clinical perspective, the observed improvements in metabolic biomarkers underscore the importance of incorporating concurrent aerobic and resistance training into lifestyle management strategies for Type 2 diabetes. The enhanced glycemic benefits associated with the resistance-before-aerobic sequence suggest that exercise order may be strategically manipulated to optimize metabolic outcomes, particularly in individuals with poor baseline insulin sensitivity. However, both sequences were effective, indicating that flexibility in exercise prescription can be maintained to support long-term adherence.

### *5.2.2. Cardiovascular Function Responses to CART and CRAT*

The present study demonstrated that concurrent aerobic and resistance training elicits significant improvements in multiple indices of cardiovascular function in individuals with type 2 diabetes mellitus (T2DM) (Table 7 and 8; Figure 7). These improvements were evident in blood pressure and cardiorespiratory fitness, confirming the cardiovascular

efficacy of concurrent training and extending the findings of Phase I by examining the influence of exercise sequence on cardiovascular adaptations.

Consistent with these overall improvements, systolic blood pressure was significantly reduced in both the CART and CRAT groups compared with the control group, with no significant difference between the two exercise sequences. This finding suggests that the blood pressure-lowering effect of concurrent training is robust and largely independent of exercise order. A plausible explanation for this effect is that both aerobic and resistance exercise induce complementary vascular adaptations, including improvements in endothelial function (Oliveira et al., 2021), reductions in arterial stiffness (Li et al., 2015; Montero et al., 2015), and enhanced nitric oxide bioavailability (Braga et al., 2015; Macedo et al., 2016), all of which contribute to reductions in peripheral vascular resistance and systolic pressure.

The observed reductions in SBP are consistent with previous studies reporting significant blood pressure improvements following combined aerobic and resistance training in individuals with T2DM (Kang et al., 2016). Moreover, similar SBP reductions have been reported when resistance exercise precedes aerobic training, suggesting that resistance-first sequencing does not diminish the antihypertensive benefits of concurrent exercise (Bassi et al., 2015). In contrast, Fernandes et al. (2022) demonstrated that aerobic exercise followed by resistance training can induce post-exercise hypotension regardless of exercise order in hypertensive older adults, highlighting that acute and chronic blood pressure responses may vary according to population characteristics and study design.

Regarding diastolic blood pressure, significant within-group reductions were observed in the exercise groups after the intervention; however, no significant between-group differences were detected. This finding aligns with prior research showing that 12-week exercise interventions often yield limited or inconsistent effects on DBP, particularly among individuals with T2DM (Marco Antônio R. Da Silva et al., 2020; Hale et al., 2022; Kang et al., 2016). One potential explanation is that DBP is less responsive to exercise-induced vascular adaptations than SBP, especially in populations with longstanding metabolic dysfunction (Carpio-Rivera et al., 2016; Kelley et al., 2001).

From a mechanistic perspective, concurrent training may reduce circulating levels of endothelin-1, a potent vasoconstrictor and established risk factor for hypertension, thereby contributing to the observed reductions in SBP (Ghassemiyan & Salesi, 2014). Collectively, these findings suggest that concurrent aerobic and resistance training is an effective non-pharmacological strategy for improving blood pressure regulation in individuals with T2DM, and that exercise sequence does not substantially influence chronic blood pressure outcomes when training volume and intensity are matched.

Extending beyond blood pressure, concurrent training also produced notable cardiovascular adaptations. Peripheral oxygen saturation levels increased in both the CART and CRAT groups, again with no sequence-specific effect, consistent with recent evidence that concurrent training enhances vascular function and oxygen utilization in T2D patients (Canli & Aldhahi, 2024; Chen et al., 2023). Interestingly, RHR was reduced significantly only in CART, but CRAT did not vary from COG. This finding supports the findings of Hellsten and Nyberg (2016) and Teixeira et al. (2011), who reported that prioritizing aerobic work improved central cardiovascular adaptations such as vagal tone and stroke volume. Resistance-first sequencing may result in rapid sympathetic activation or muscular fatigue, reducing the effectiveness of the subsequent aerobic component (Docherty & Sporer, 2000; Richter et al., 2011). Thus, our findings add to current research by demonstrating that CART may be more successful than CRAT in generating autonomic cardiovascular adjustments.

Both exercise modalities, CART and CRAT, led to significant increases in $VO_2$ Peak from pre- to post-intervention, as evidenced by the current study's significant Group × Time interaction. Both methods were more effective than the control condition, underscoring the value of structured exercise in enhancing cardiovascular fitness, even though the between-group comparison did not reveal a statistically significant difference between the two exercise groups.

Notably, the CART group demonstrated a greater improvement than the control group, confirming earlier research by Church et al. (2010) and others (Drummond et al., 2005), who observed significant increases in $VO_2$ max and reductions in fat mass following

combined aerobic and resistance training. These improvements likely stem from various physiological adaptations, such as increased cardiac output and stroke volume, higher skeletal muscle capillary density, and greater mitochondrial content, all of which enhance oxygen delivery and utilization during exercise (Nystoriak & Bhatnagar, 2018). Additionally, the resistance component promotes effective oxygen extraction during aerobic activity by increasing muscle size and muscular endurance (Hughes et al., 2018).

The CRAT group's progress was less than that of the control group, despite also showing notable improvements over time. One possible explanation is that doing resistance training first could limit the intensity of the subsequent aerobic session or cause early fatigue, which would reduce the stimulus needed for optimal aerobic adaptation (Gao & Yu, 2023). This aligns with studies showing how cumulative tiredness can influence cardiovascular strain during concurrent sessions.

The lack of a significant difference between CART and CRAT is in line with meta-analytic data that indicates adult aerobic improvements are typically not very sensitive to the sequence in which resistance and aerobic workouts are conducted (Gao & Yu, 2023). Concurrent training, independent of sequence, helps improve cardiometabolic function in adult populations, as evidenced by the fact that both modalities showed notable pre-post improvements. The benefit of combining different exercise modalities is further supported by CART's better effect over the control group.

It's interesting to note that the effect of sequence seems to vary with duration of training and developmental physiology. Aerobic exercise before resistance training increased oxygen uptake in prepubescent children compared to the opposite order, according to a 24-week program (Alves et al., 2016). Exercise tolerance, developmental physiology, or the extended duration of interventions commonly employed in pediatric studies could all be contributing factors to these variations.

Practically speaking, the discovery that both CART and CRAT considerably increased $VO_2$ Peak implies that concurrent training is a versatile and adaptive approach to enhancing cardiovascular fitness. Exercise order did not significantly affect adult outcomes; therefore, training regimens can be modified to accommodate individual preferences, time

constraints, or facility limitations without sacrificing aerobic advantages. This flexibility enhances the feasibility of implementing concurrent training in clinical and community settings while ensuring meaningful improvements in cardiovascular health.

### *5.2.3. Anthropometric Adaptations Following CART and CRAT*

The present study demonstrated that concurrent aerobic and resistance training elicited favorable changes in key anthropometric indices in individuals with type 2 diabetes mellitus (T2DM), indicating meaningful improvements in body composition and central adiposity (Table 9 and 10; Figure 8). Reductions in body mass index (BMI), waist circumference, waist-to-hip ratio (WHR), and percentage body fat (%BF) were observed in the exercise groups compared with the control group, confirming the effectiveness of concurrent training as a non-pharmacological strategy for improving anthropometric health in this population. These findings are clinically relevant, given the strong association between excess adiposity, particularly central fat accumulation, and insulin resistance, cardiometabolic risk, and cardiovascular morbidity in T2DM.

Both CART and CRAT resulted in considerable reductions in body fat percentage compared with COG, with no sequence differences. These findings are consistent with prior research demonstrating that concurrent training, regardless of sequence, improves fat mass loss in persons with metabolic diseases in the resistance-first training group (Zarei et al., 2021) and in the aerobic first group (Saima Zaki, Md Farhan Alam, Saurabh Sharma, Irshad Husain Naqvi, et al., 2024). Meta-analyses have also revealed that the effect on adiposity is mostly determined by total exercise volume and energy expenditure rather than by order (Sheikholeslami-Vatani et al., 2015). As a result, while our study revealed that exercise sequence did not affect fat loss, our findings add to the growing body of data indicating that concurrent training is a viable and effective method for altering body composition in individuals with type 2 diabetes.

Similarly, exercise order did not affect central adiposity outcomes, since this study observed no significant differences in WHR reduction between the CART and CRAT groups. The lack of a sequencing effect indicates that the physiological mechanisms responsible for lowering WHR are triggered similarly regardless of whether aerobic or

weight training is finished first, even though both exercise modalities exhibited notable improvements in comparison to the control group. This result is in line with reported in prior studies where concurrent training decreased waist circumference and WHR (Amaro-Gahete et al., 2021; Shi et al., 2017; Saima Zaki, Md Farhan Alam, Saurabh Sharma, Irshad Husain Naqvi, et al., 2024). Long-term metabolic adaptations, including higher energy expenditure, greater fat oxidation, improved insulin sensitivity, and positive hormonal alterations, are the primary cause of reductions in WHR (Theodorakis et al., 2024) in a 12-week intervention like the current study. Because both training groups completed equivalent total training loads, they experienced similar cumulative metabolic stress, resulting in comparable reductions in central adiposity (Amaro-Gahete et al., 2021). Importantly, this finding highlights the practical flexibility of concurrent training, allowing exercise sessions to be structured according to individual preference or logistical considerations without compromising improvements in central adiposity, thereby enhancing feasibility and long-term adherence.

In contrast to fat percentage and WHR, a significant difference between the CART and CRAT groups was observed for BMI reduction, indicating that exercise sequence influenced the magnitude of weight-related adaptations. The greater BMI decrease observed in the CART group may be explained by physiological mechanisms: performing aerobic exercise before resistance work preserves aerobic performance, allowing participants to train at higher intensities and expend more calories, and enhances fat oxidation due to fresher glycogen stores, resulting in greater reliance on fat as a fuel source (Kang & Ratamess, 2014). In contrast, beginning with resistance exercise in the CRAT group may induce early muscular fatigue, limiting the intensity and efficiency of the subsequent aerobic session (Apró et al., 2015). Additionally, CRAT may increase muscle mass (Pinto et al., 2014), which could offset reductions in body weight, leading to smaller changes in BMI. Despite this, both the CART and CRAT groups demonstrated significant improvements relative to the control group, confirming the effectiveness of concurrent training for improving obesity indices. The significant Group × Time interaction further indicates that both exercise modalities produced meaningful pre- to post-intervention reductions driven by chronic metabolic adaptations such as increased energy expenditure, improved insulin sensitivity, enhanced lean mass, and elevated post-exercise oxygen

consumption. This result contrasts with (Saima Zaki, Md Farhan Alam, Saurabh Sharma, Irshad Husain Naqvi, et al., 2024), who were done on diabetic patients with CAN. Notably, decreased adiposity enhances insulin sensitivity and lowers inflammation, both of which are critical for controlling diabetes and lowering the risk of cardiovascular problems (Rohm et al., 2022). Overall, while both exercise sequences were beneficial, the superior BMI reduction observed in the CART group suggests a potential advantage of prioritizing aerobic exercise when body mass reduction is a primary intervention goal.

In summary, concurrent aerobic and resistance training effectively improves anthropometric indices in individuals with T2DM, with comparable benefits observed across exercise sequences. These results reinforce the role of concurrent training as a practical and comprehensive intervention for reducing adiposity and improving body composition, thereby supporting its inclusion in exercise prescriptions aimed at mitigating cardiometabolic risk in T2DM populations.

### 5.3. Limitations of the study

Despite the valuable findings of the present study, several limitations should be acknowledged. First, the duration of the intervention was limited to a moderate-term training period. While this timeframe was sufficient to elicit significant cardiometabolic and anthropometric adaptations, longer intervention and follow-up periods are needed to determine the sustainability of these adaptations and to assess long-term clinical outcomes such as disease progression, medication dependency, and cardiovascular events.

Secondly, although exercise intensity and volume were carefully matched between groups, variations in individual adherence, habitual physical activity outside the intervention, and dietary intake were not fully controlled. Dietary intake was assessed using a 24-hour dietary recall; however, this self-reported method is subject to recall bias and may not accurately reflect usual intake. These factors may have influenced the observed outcomes. Future studies should incorporate more rigorous and objective monitoring of lifestyle behaviors, including accelerometer-based assessment of habitual physical activity and objectively measured or tightly controlled dietary intake.

Furthermore, the study did not thoroughly evaluate psychosocial factors such as motivation, quality of life; instead, it focused primarily on physiological and biochemical outcomes. Moreover, changes at the molecular level in insulin signaling pathways, glucose transporter (GLUT4) expression, mitochondrial biogenesis, and inflammatory markers that underlie the observed adaptations were not assessed.

### 5.4. Implications of the Study

The findings of this study have important clinical, practical, and research implications for the management of type 2 diabetes mellitus (T2DM). Clinically, the demonstrated effectiveness of both CART and CRAT in improving glycemic control, insulin resistance, lipid profile, and cardiovascular function supports the inclusion of concurrent aerobic and resistance training as a core component of non-pharmacological T2DM management. The slightly superior glycemic improvements observed with CRAT suggest that resistance-first sequencing may be prioritized when glycemic regulation is the primary therapeutic goal, particularly for individuals with poor baseline glycemic control. Conversely, the minimal cardiovascular advantage associated with CART indicates that aerobic-first sequencing may be beneficial for patients with elevated cardiovascular risk or hypertension. In practice, these findings provide exercise professionals and clinicians with flexibility in exercise prescription, allowing training programs to be tailored to individual clinical priorities, preferences, and physical capacity, thereby potentially improving adherence and long-term participation. From a research perspective, the study highlights the need for longer-term interventions, objective monitoring of lifestyle behaviors, and exploration of underlying physiological mechanisms to further clarify sequence-specific adaptations. Overall, the results contribute to evidence-based exercise programming and support personalized exercise strategies to optimize cardiometabolic health outcomes in adults with T2DM.

### 5.5. Conclusions

The present study investigated the effects of concurrent aerobic and resistance training and the influence of exercise sequence on cardiometabolic, and anthropometric outcomes in individuals with type 2 diabetes mellitus. The findings clearly demonstrate that concurrent

training is an effective non-pharmacological intervention for improving overall cardiometabolic health in this population.

Both concurrent aerobic-resistance training and concurrent resistance-aerobic training produced significant improvements in glycemic control, lipid profile, cardiovascular function, and anthropometric indices compared with the control group. These results confirm that combining aerobic and resistance exercise within a single training program elicits broad and clinically meaningful health benefits for individuals with type 2 diabetes, independent of exercise sequence when training volume and intensity are matched.

Regarding exercise sequence, most outcome variables, including blood pressure, lipid profile, peripheral oxygen saturation, body fat percentage, and waist-to-hip ratio, did not differ significantly between CART and CRAT. This suggests that chronic adaptations associated with concurrent training are largely driven by total training load and metabolic demand rather than by the order of exercise modalities.

Despite the overall effectiveness of both training sequences, sequence-dependent differences were evident for specific outcomes. The CART protocol produced greater reductions in resting heart rate and body mass index than CRAT, indicating more favorable adaptations in autonomic cardiovascular regulation and body-weight-related parameters when aerobic exercise is performed first. This suggests that prioritizing aerobic exercise before resistance training may confer additional advantages for improving central cardiovascular control and reducing body mass. In contrast, CRAT elicited slightly greater improvements in glycemic regulation, as reflected by larger reductions in HbA1c and HOMA-IR.

In conclusion, concurrent aerobic and resistance training is an effective, clinically applicable strategy for improving cardiometabolic health in individuals with type 2 diabetes mellitus. Although the exercise sequence did not substantially influence most long-term adaptations, modest sequence-specific effects were observed. Prioritizing aerobic exercise before resistance training favored improvements in resting heart rate and body mass, whereas performing resistance exercise first yielded slightly greater benefits in glycemic regulation. Collectively, these findings provide evidence-based guidance for

optimizing exercise prescription while preserving flexibility in program design, which may enhance adherence and support sustainable implementation in clinical and community settings.

### 5.6. Recommendations

Drawing on the key findings of this study and their relevance to clinical application and scientific advancement, the following recommendations are proposed to inform practice and future research in the management of type 2 diabetes mellitus (T2DM):

1. Concurrent aerobic and resistance training should be incorporated into routine clinical management for individuals with type 2 diabetes mellitus (T2DM), as it significantly improves cardiovascular, metabolic, and anthropometric outcomes.

2. Exercise professionals may structure concurrent training programs flexibly according to individual preferences, facility availability, and time constraints, as most health benefits appear to be independent of exercise sequence.

3. Health professionals, including clinicians and exercise physiologists, should tailor concurrent exercise prescriptions based on individual patient goals, functional capacity, and likelihood of adherence to maximize intervention effectiveness.

4. Future investigations should explore long time intervention duration with a variety of exercise modalities, including high-intensity interval training (HIIT), circuit training, isometric and dynamic resistance exercises, and combined approaches to determine whether sequence effects differ by training type.

5. Researchers should integrate molecular, physiological, and psychosocial determinants, while also ensuring rigorous control and objective measurement of dietary intake and physical activity outside the intervention. In addition, evaluating long-term adherence outcomes is essential to deepen understanding and facilitate the development of more precise, personalized exercise prescriptions for individuals with T2DM.

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# 8. APPENDICES

*Appendix A. Consent Form: (English Version)*

*Introduction:*

You are invited to participate in a research study investigating the effects of concurrent training order on cardiovascular function and biochemical markers in type 2 diabetic patients. This study aims to understand how different exercise sequences within concurrent training programs might impact your body's response to cardiovascular function and biochemical biomarkers.

**Procedures:**

- If you agree to participate, you will be asked to complete a medical screening to ensure your safety for the exercise program.
- You will be divided into groups and assigned a specific exercise sequence for concurrent training. This training will combine different types of exercise, like aerobic and resistance training for 12 weeks.
- Throughout the study, researchers will gather cardiovascular data (e.g., heart rate, blood pressure, and maximum oxygen uptake), biochemical biomarkers from blood samples (e.g., blood sugar, insulin levels, and lipid profiles), as well as anthropometric measurements (e.g., body weight, height, and body circumference) at two points: before and after the training program, to monitor participants' health and their response to the intervention.
- The entire study protocol will be explained by the researchers in detail, and you will have ample opportunity to ask questions before deciding to participate.
- If you are placed in the control group, which requires maintaining your usual physical activity routine throughout the intervention period, we understand the concern about potentially missing out on the benefits of exercise. To address this, a personalized exercise program will be offered to you after the study concludes. This program will be designed to

support your cardiovascular and metabolic health. Details about this opportunity will be shared with you during the recruitment process.

**Confidentiality:**

All your personal information and medical data will remain confidential. A coding system will be used to de-identify your data during analysis and reporting to protect your privacy. Additionally, any blood samples collected for this study will only be used for this research. Once the analysis is complete, these samples will be disposed of to address confidentiality concerns.

**Potential Risks and Benefits Risks:**

- Exercise-related injuries (muscle soreness, strains)
- Potential discomfort during or following exercise sessions and assessments
- Hypoglycemia

If the above risks occur during testing, a trained clinician will be present on-site, and rapid on-call access to the physician is ensured. Emergency equipment, including an AED and oxygen, will be available at all sessions. The nearest hospital, Debre Markos Referral Hospital, has been identified, and the expected transfer time in case of severe events is documented to ensure timely medical intervention. And also, if those risks will be reported to the Natural and Computational Science College, Addis Ababa University, Institutional Review Board

**Benefits:**

- Improved overall fitness and metabolic health
- Increased knowledge about the effects of exercise order on concurrent training
- Free health assessments
- Contribution to scientific research

**Voluntary Participation:**

Your participation in this study is entirely voluntary. You have the right to withdraw from the study at any point without any penalty.

**Contact Information:**

If you have any questions about the research or your participation, please do not hesitate to contact the lead researcher.


| | |
|---|---|
| Name | Friew Amare |
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If you have any questions, concerns, or complaints about this study, you may contact the Institutional Review Board (IRB) at the College of Natural and Computational Sciences, Addis Ababa University.

- **Main Campus Address**: Addis Ababa University, 4 Kilo Campus, Addis Ababa, Ethiopia
- **Phone**:
- **Website**: www.aau.edu.et
- Email: irb.cncs@aau.edu.et

**Note:** ***By signing this consent form, you acknowledge that you have read and understood the information provided above. If you decide to participate, you will be asked to sign this form.***

***Name of participant:*** _____

***Date:*** _____ ***Signature:*** .

***Name of Researcher:*** _____ ***Date:***____

***Signature:*** _____

*Appendix B. Consent Form: (Amharic Version)*

**መግቢያ:**

ይህ ጥናት የኮንኮረንት አካላዊ ስልጠና በውስጡ የያዛቸዉ የስዉነት እንቅሰቃሴ የስልጠና ቅደም ተከተል ማለትም ኤሮቢክ እና ሪዚስታንስ የልብ እና የደም ዝውውር ተለዋዋጮች እንዲሁም የባዮኬሚስትሪ ምልክቶችን ላይ የሚያመጡትን ለዉጥ ለማጥናት የተዘጋጀ ነዉ። እርስዎም ይዚህ ጥናት ተሳታፊ እንዲሁኑ ትምርጠዋል።

**የጥናቱ ሂደት:**

- በጥናቱ ውስጥ ለመሳተፍ ፍቃደኛ ከሆኑ ድረስ ለስዉነት እንቅሰቃሴ ስልጠና ብቁ ስለመሆንዎ በጤና ምርምራ ልየታ ይደረግልዎታል።

- ተሳታፊዎቹ የተለያዩ የስልጠና ቅደም ተከተሎች እንዲሁም ክሁለቱ ዉጭ ልዩ ክትትል የሚደረግለት ከአካላዊ እንቅስቃሴ ነጻ (አካላዊ እንቅስቃሴ የማይሰሩ) ቡድኖች ውስጥ ሊመደቡ ይችላሉ።

- በጥናቱ ውስጥ የልብ የደም ዝዉውር ብቃት ምልክቶች (እንደ የልብ ምት ፣ የደም ግፊት እና ከፍተኛ የኦክሲጅን ጥልቅ ልቀት) ፣ የደም ምልክቶች (እንደ ደም ስኳር፣ ኢንሱሊን ሙግደት እና የሊፒድ መጠን) ፣ እንዲሁም የሰውነት መለኪያዎች (እንደ ክብደት፣ ቁመት እና የሰውነት ስብ ስሪት) በስልጠናዉ የመጀመሪያ እና የመጨረሻ ጊዜያት ውስጥ ከዕርስዎ ይሰበሰባል።

- የጥናቱ ሙሉ ሂደት በምርምር ቡድኑ ዝርዝር ማብራሪያ ይሰጣችኋል። ይህን ሲያደርጉ ማንኛውም ጥያቄ ለማድረግ ዕድል ይኖራችኋል።

- ልዩ ቁጥጥር በሚደረግበት ቡድን ውስጥ ማለትም (አካላዊ እንቅስቃሴ ከማይሰራዉ ቡድን) የተመደቡ ተሳታፊዎች መረመሩ እስከ ሚጥናቀቅ ድረስ መደበኛ የተለመደዉን እንቅስቃሴ ማስቀጠለ ይጠበቅባችዋል። ይህ ቡድን የምርምር

ጊዜዉ እንዳልቀ ያልሰሩበትን ጊዜ ሊያካክስ በሚችል መንገድ የስልጠና ፕሮግራም የሚዘጋጂላቸዉ ይሆናል። ይህ ዕድል በምርምሩ ውስጥ ለተሳታፊንት በሚመለመሉበት ጊዜ በሰፊዉ ይብራራልዎታል።

**ሚስጢራዊነት፡**

ሁሉም የግል መረጃዎት እና የሕክምና መረጃዎች በሚስጥር ይያዛሉ። ምርምር ሲካሄድ የተሳተፉ ሰዎች መረጃ ማንነት በማይታወቅበት መንገድ መሆኑን ለማረጋገጥ ይጠቀማል። የደም ናሙናዎቹ ለምርምር ብቻ በመጠቀም ምርምሩ ከተጠናቀቀ በኋላ እንዲወግዱ ይደረጋል።

**የምርምር መሳተፍ ያለዉ ስጋትና ጥቅሞች:**

**ስጋቶች፡**

- በስልጠና ወቅት ሊክሰቱ የሚችሉ አካላዊ ጉዳቶች
    - በስልጠና ጊዜም ይሁን በኋላ ላጭር ጊዜ የሚቆይ ምቾት የሌለዉ ሁኔታ መሰማት
    - የስኳር በድንገት መዉረድ

ከላይ የተጠቀሱት አደጋዎች በፈተና ሂደት ወቅት ከሆነ፣ በስልጠና ጊዜ የሕክምና ባለሙያ በቦታ ስለሚኖሩ ከባለሙያዉ/ዋ ጋር ፈጣን መገናኘት ይደረጋል። አደጋ ሲፈጥር የሚያገለግል መሳሪያ እንደ AED እና ኦክሲጅን በሁሉም በአካል ብቃት መስሪያ ቦታዉ ላይ ይገኛል። ከቅርብ የሆነው ሆስፒታል፤ ደብረ ማርቆስ ሆስፒታልእና በከባድ ክስተቶች የሚደረገው ትራንስፈር ጊዜ እንዲሁም በጊዜያዊ ሕክምና ሥርዓት እንዲያገለግል ትስስር እንዲኖረው ይረጋል። እንዲሁም እነዚህ አደጋዎች ወደ አዲስ አበባ ዩኒቨርሲቲ የተፈጥሮና የኮምፒውተር ሳይንስ ኮሌጅ ተቋማዊ የጥናት ክስተት ሰብስ ቦርድ (Institutional Review Board) ሪፖርት ይደረጋል።

**ጥቅሞች:**

- የአካል ብቃት እና ሁሉን እቅፍ የጤና ሁኔታን ማሻሻል
- የስልጠና ቅደም ተከተል በልብ እና በደም ምልክቶች ላይ ያለው ተፅእኖ ላይ ግንዛቤ እንዲኖራቸዉ ያደርጋል
- የነጻ የጤና ምርመራ
    - ለሳይንስ ምርምር የራሰን አስተዋፆ እነደማድረግ ይቆጥራል የተሳታፊነት በጎ ፈቃድ:

በዚህ ጥናት የሚሳተፉተ ያለምንም አስገዳጂነት በፍጹም ፍቃኝነት ነው። እንዲሁም ክምርምሩ በማንኛውም ጊዜ መዉጣት ውይም ማቋርጥ ይችላሉ።

| | | |
|---|---|---|
| የምርምር አዘጋጅ:ስም: ፍሬው አማረ | የተመራማሪ ስም:_____ | የተሳታፊው ስም: _____ |
| ኢሜይል: firewa6070@gmail.com | ቀን: _____ | ቀን: _____ |
| ስልክ ቁጥር: +251913912776 | ፊርማ: ____ | ፊርማ: ____ |

*Appendix C. Physical Activity Readiness Questionnaire (PAR-Q) (English version)*

Engaging in regular physical activity is both enjoyable and beneficial for your health, and more people are adopting active lifestyles every day. For most individuals, becoming more active is very safe. However, certain individuals should consult their doctor before significantly increasing their physical activity levels.

Before starting the physical activity portion of our research program, please begin by answering the seven questions provided below. If you are between the ages of 15 and 69, the PAR-Q will help determine whether you should seek medical advice before beginning. Use common sense as your guide and answer each question carefully and honestly.

| Yes | NO | Q no | Questions |
|---|---|---|---|
| ☐ | ☐ | **1.** | Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor? |
| ☐ | ☐ | **2.** | Do you feel pain in your chest when you do physical activity? |
| ☐ | ☐ | **3.** | In the past month, have you had chest pain when you were not doing physical activity? |
| ☐ | ☐ | **4.** | Do you lose your balance because of dizziness or do you ever lose consciousness? |
| ☐ | ☐ | **5.** | Do you have a bone or joint problem that could be made worse by a change in your physical activity? |
| ☐ | ☐ | **6.** | Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition? |
| ☐ | ☐ | **7.** | Do you know of any other reason why you should not do physical activity? |

If you answered NO to all of the questions above, you are cleared for physical activity.

Please sign the PARTICIPANT DECLARATION.

I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. I acknowledge that this physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes.

Participant's

Name: _____

Date: _____

Signature: _____

*Appendix D. Physical Activity Readiness Questionnaire (PAR-Q) (Amharic version)*

መደበኛ የአካል ብቃት እንቅስቃሴ መሳተፍ ሁሉም ሰው የሚወደውና ለጤናዎ ጠቃሚ የሆነ እና የሚመክር ነው። በየቀኑም በርካታ ሰዎች ይህን ንቁ ዘይቤ እየተከተሉ ነው። ለብዙም ሰዎች የተጨማሪ እንቅስቃሴ ማከናወን እጅግ ጠቃሚ ነው፣ ነገር ግን ለአንዳንድ ግለሰቦች የአካል ብቃት እንቅስቃሴያቸውን ደረጃ በከፍተኛ ሁኔታ ሲጨምሩ ሀኪማቸውን ማማከር ይኖርባቸዋል።

በመሆኑም በዚህ ምርምር ፕሮግራም ውስጥ የእንቅስቃሴ ክፍሉን ለማስጀመር ስለተፈለገ፣ እባኮትን ከታች የቀረቡትን ሰባት ጥያቄዎች መልስ ይመልሱ። የአካላዊ እንቅስቃሴ ዝግጁነት መጠይቅ (PAR-Q)፤ ከአካል ብቃት እንቅስቃሴ መሳተፍ በፊት የሕክምና ምክር ማስፈለጉን ወይም አልማስፈለጉን ለመወሰን ይረዳናል። አስቀድመዉ የራስዎን ሁኔታ በመረዳት እያንዳንዱን ጥያቄ በትክክል እና በቅንነት ይመልሱ።

| አዎ | አይደለም | ቁጥር | ጥያቄ |
|---|---|---|---|
| ☐ | ☐ | 1. | ዶክተርዎ ከዚህ በፊት የልብ ችግር እንዳለብዎ አስታውቆዎታል እና የምታደርጉትን እንቅስቃሴ በሀኪሙ ምክር መሰረት ብቻ እንዲሰሩ ተነግርዎታል? |
| ☐ | ☐ | 2 | እንቅስቃሴ ሲያደርጉ በደረትዎ ላይ ህመም ተሰምተዎት ይዉቃል? |
| ☐ | ☐ | 3 | ባለፈው ወር ምንም እንቅስቃሴ ሳይደርጉ የደረት ህመም ሰምተዋል? |
| ☐ | ☐ | 4. | በህመም ምክንያት ሆነ በሌላ ሚዛንዎን ስተዉ ይውደቃሉ? ወይንም ንቃትዎን ይስታሉ? |
| ☐ | ☐ | 5. | እንቅስቃሴ በመስራት ሊባባስ የሚችል የአጥንት ወይም የመገጣጠሚያ ችግር አለብዎት? |
| ☐ | ☐ | 6 | ዶክተርዎ በአሁኑ ጊዜ ለደም ግፊት ወይም ልብ ችግርዎ የሕክምና መድሃኒት አዝዞለዎታል? |
| ☐ | ☐ | 7 | እርስዎ እንቅስቃሴ ማድረግ የሚከለክልዎት ሌላ ምክንያት አለዎት? |

እስከ አሁን ድረስ ላሉት ጥያቄዎች ሁሉ "አይ" ብለው ክመለሱ፣ በአካላዊ እንቅስቃሴ ፕሮግራም ለመሳተፍ ዝግጁ መሆንዎ ተረግጧል።

እባኮትን ፎርም ስለመሙላትዎ ማረጋገጫ ይፈርሙ፤

እኔ _____ (ስሜ)፣ ይህን መጠየቂያ በጥልቀት አንብቤ እና ተገንዝቤ መሙላቴን ብፈርማየ አረጋግጣለሁ። ይህ የእንቅስቃሴ ከሊራንስ ከተሞላበት ቀን ጀምሮ እስከ 12 ወር ድረስ የሚያገለግል ሆኖ የጤናዬ ሁኔታ ቢለወጥ ዋጋውን የሚያጣ እንደሆነ አውቃለሁ።

የተሳታፊ ስም፡ _____

ቀን፡ ____

ፊርማ፡ __

*Appendix E. International Physical Activity Questionnaire Short Form (IPAQ-SF) (English version)*

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the last 7 days. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the vigorous activities that you did in the last 7 days. Vigorous physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

1. During the last 7 days, on how many days did you do vigorous physical activities like heavy lifting, digging, aerobics, or fast bicycling?

   _____days per week

   ◯ No vigorous physical activities → Skip to question 3

2. How much time did you usually spend doing vigorous physical activities on one of those days?

   _____hours per day

   _____minutes per day ◯ Don't know/Not sure

Think about all the moderate activities that you did in the **last 7 days**. Moderate activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the last 7 days, on how many days did you do moderate physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking

. _____days per week

○ No moderate physical activities → Skip to question 5

4. How much time did you usually spend doing **moderate** physical activities on one of those days?

**_____hours per day**

**_____minutes per day**

○ Don't know/Not sure

Think about the time you spent walking in the last 7 days. This includes at work and at home, walking to travel from place to place, and any other walking that you have done solely for recreation, sport, exercise, or leisure.

5. During the last 7 days, on how many days did you walk for at least 10 minutes at a time?

_____days per week

○ No walking → Skip to question 7

6. How much time did you usually spend walking on one of those days?

_____hours per day

_____minutes per day

○ Don't know/Not sure

The last question is about the time you spent sitting on weekdays during the last 7 days. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the last 7 days, how much time did you spend sitting on a week day?

_____hours per day

_____minutes per day

○ Don't know/Not sure

**This is the end of the questionnaire, thank you for participating**

*Appendix F. Appendix G. International Physical Activity Questionnaire Short Form (IPAQ-SF) (Amharic version)t Form (IPAQ-SF) (Amharic version)*

ተሳታፊዎች በዕለት ተዕለት ሕይወታቸው ምን ዓይነት አካላዊ እንቅስቃሴዎች እንደሚያከናውኑ ለማወቅ እንፈልጋለን ። ጥያቄዎቹ ባለፉት 7 ቀናት ውስጥ አካላዊ እንቅስቃሴ በማድረግ ስላሳለፋችሁት ጊዜ ይጠይቃል ። ራስዎትን ንቁ አድርገዉ ባይመለከቱም እንኳ ለእያንዳንዱ ጥያቄ መልስ ይስጡ ።እባክዎ በቤትዎ እና በስራዎ ውስጥ የምታከናውኗቸውን እንቅስቃሴዎች፣ ከቦታ ቦታ ለመድረስ፣ እንዲሁም ለመዝናኛ፣ ለአካል ብቃት እንቅስቃሴ ወይም ለስፖርት በትርፍ ጊዜአችሁ ያሳለፉትን አስቡ።

በመጨረሻዎቹ 7 ቀናት ውስጥ ያደረጉትን ከፊተኛ ጫና ያለዉ እንቅስቃሴ ያአስቡ ። ጠንካራ አካላዊ እንቅስቃሴ ማለት ከባድ ጥረት የሚጠይቅና ከወትሮው የበለጠ መተንፈስ የሚያስችግርዎ እንቅስቃሴዎችን ያመለክታል ።እስቲ በአንድ ጊዜ ቢያንስ ለ**10** ደቂቃ ያህል ስላደረጉት አካላዊ እንቅስቃሴ ብቻ ያስቡ።

**1.** ባለፉት 7 ቀናት ውስጥ እንደ ከባድ ክብደት ማንሳት, ቁፋሮ, ኤሮቢክስ, ወይም በፍጥነት ብስክሌት ማሽከርከር የመሳሰሉ ጠንካራ ጫና ያላቸዉን አካላዊ እንቅስቃሴዎችን ለስንት ቀናት አከናውነዉ ነበር?

_____ቀን በሳምንት

አልሰራሁም → ወደ ጥያቄ **3** ይለፉ

**2.** ከእነዚያ ቀናት በአንዱ ላይ ጠንካራ ጫና ያላቸዉን አካላዊ እንቅስቃሴዎችበማድረግ ምን ያህል ጊዜ ያሳልፍ ነበር?

_____ሰአት በቅን

_____ደቂቃ በቀን

እርግጠኛ አይደለሁም/ አላቀዉም

ባለፉት 7 ቀናት ውስጥ ያደረጉትን መካከለኛ ጫና ያለዉ እንቅስቃሴ ያስቡ ። መካከለኛ ጫና ያለዉ እንቅስቃሴ ማድረግ ሲባል መጠነኛ የሆነ አካላዊ እንቅስቃሴ ማድረግና መተንፈስ ከወትሮው የበለጠ ከባድ እንዲሆንብዎ የሚያደርጉ እንቅስቃሴዎችን ያመለክታል። እስቲ አንድ ጊዜ ቢያንስ ለ**10** ደቂቃ ያህል ስላደረጉት አካላዊ እንቅስቃሴ ብቻ ያስቡ።

**3.** ባለፉት 7 ቀናት ውስጥ, ለስንት ቀናት እንደ ቀላል ጭነት መሸከም, በመደበኛ ፍጥነት ብስክሌት መንዳት, ወይም

የቡድን ቴኒስ መጫወትን ያሉ መካከለኛ ጫና ያለዉ እንቅስቃሴን አከናውናችኋል? በእግር መሄድን አይጨምርም

_____ቀን በሰምንት

◯አልሰራሁም ⟶ ወደ ጥያቄ **5** ይለፉ

**4.** ከእነዚያ ቀናት በአንዱ ላይ መካከለኛ ጫና ያላቸዉን አካላዊ እንቅስቃሴዎች በማድረግ ምን ያህል ጊዜ ያሳልፍ ነበር?

_____ሰአት በቅን

_____ደቂቃ በቀን

◯ እርግጠኛ አይደለሁም/ አላቀዉም

ባለፉት 7 ቀናት ውስጥ በእግር በመጓዝ ያሳለፍትን ጊዜ ያስቡ ። ይህም በሥራ ቦታም ሆነ በቤት ውስጥ መጓዝን፣ ከቦታ ወደ ቦታ መጓዝን እንዲሁም ለመዝናኛ፣ ለስፖርት፣ ለአካል ብቃት እንቅስቃሴ ወይም ለመዝናናት እንዲሁም ማንኛውንም የእግር ጉዞ ይጨምራል።.

**5.** ባለፉት 7 ቀናት ውስጥ በስንት ቀናት ውስጥ ቢያንስ ለ**10** ደቂቃ በአንድ ጊዜ በእግር ተጉዘዋል?

_____ቀን በሰምንት

◯አልሰራሁም ⟶ ወደ ጥያቄ **7** ይለፉ

**6.** ከነዚህ ቀናት በአንዱ ላይ በእግር በመጓዝ አብዛኛውን ጊዜ ምን ያህል ጊዜ ያሳልፍ ነበር?

_____ሰአት በቀን

_____ደቂቃ በቀን

◯ እርግጠኛ አይደለሁም/ አላቀዉም

የመጨረሻው ጥያቄ ባለፉት 7 ቀናት ውስጥ በሳምንት ቀናት ቁጭ ብለዉ ስላሳለፍት ጊዜ የሚጠይቅ ነው ። በሥራ ቦታ፣ በቤት፣ በትምህርት ቤትና በመዝናኛ ጊዜ ያሳለፉትን ጊዜ ያስቀምጡ። ይህ ደግሞ ጠረጴዛ ላይ ቁጭ ብሎ ጓደኞችን በመጠየቅ፣ በማንበብ ወይም ቴሌቪዥን ለመመልከት ቁጭ ብሎ ወይም ጋደም ብሎ ማሳለፍን ይጨምራል።.

**7.** ባለፉት 7 ቀናት ውስጥ በሳምንት ቀን ቁጭ ብለዉ ምን ያህል ጊዜ አሳለፉ?_____ሰአት በቅን

_____ደቂቃ በቀን

እርግጠኛ አይደለሁም/ አላቀዉም

◯

የጥያቄው መጨረሻ ይህ ነው, ስለተሳተፉ እናመሰግናለን

*Appendix H. Dietary assessment questionnaire*

**Unstructured 24-Hour Dietary Recall**

**Date ___/____/____**

**Identification No: _**

**Instructions:**

Thank you for participating in this important research study! Recall everything you consumed yesterday, from the moment you woke up to the time you went to sleep, including all snacks and beverages. To gain valuable insights into your daily energy consumption, this questionnaire will ask you to recall everything you ate and drank in the past 24 hours. Your participation is crucial in helping us understand your dietary patterns. Don't hesitate if you face a problem regarding to a questionnaire, a seasoned interviewer, fluent in your native language (Amharic) and well-versed in dietary data collection, is here to guide you. Don't hesitate to ask questions or seek clarification, their expertise ensures the accuracy and completeness of your dietary recall.

Note:

- Think about all the foods and beverages you typically consume in a specific day.
- Start with the first thing eaten in the morning until the last food item consumed before waking up the next morning, reporting for each meal the time along with the place consumed.
- Be as specific as possible when describing the food items (e.g., brand name, type of cut, cooking method…).
- Report for each meal consumed: name of food, food description, household measures (e.g.

slices, teaspoons, etc.), unit of measure, if possible (e.g. grams, oz. and ml etc.), and finally the kind of preparation methods used and/or ingredients

| Time of day | | | What did you eat? | | | | |
|---|---|---|---|---|---|---|---|
| | | | Name of food/ beverage item | preparation/ Ingredients | Cooked method (Optional) | Household amount | Amou (g or m |
| **DINNER** | _____ | AM PM | | | | | |
| | _____ | AM PM | | | | | |
| | _____ | AM PM | | | | | |
| **BREAKFAST** | _____ | AM PM | | | | | |
| | _____ | AM PM | | | | | |
| | _____ | AM PM | | | | | |
| **SNACK (mid - morning)** | _____ | AM PM | | | | | |
| | _____ | AM PM | | | | | |
| | _____ | AM PM | | | | | |
| **LUNCH** | _____ | AM PM | | | | | |
| | _____ | AM PM | | | | | |

**Additional Notes:**

- Please feel free to list any additional food or beverage items you consume that were not mentioned previously.

- If you have difficulty estimating portion sizes, ask the data collector to provide pictures of common household utensils for reference.

**Thank you for your participation**

*Appendix I.* *Dietary assessment questionnaire (Amharic Version)*

**24-ሰዓታት የአመጋገብ ምርመራ/ሁኔታ**

ቀን___/__/__

መለያ ቁጥር: _____

መመሪያ:

በዚህ አስፈላጊ የምርምር ጥናት ላይ ስለተሳተፉ እናመሰግናለን! ከእንቅልፋችሁ ከነቃችሁበት ጊዜ አንስቶ ሁሉንም ምግቦችና መጠጦች ጨምሮ እስከተኛችሁበት ጊዜ ድረስ ትናንት የበላችሁትን ሁሉ አስታውስ። የዕለት ተዕለት የእመጋገብ ልምድዎን ጠቃሚ ግንዛቤ ለማግኘት, ይህ ጥያቄ ባለፉት 24 ሰዓታት ውስጥ የበላችሁን እና የጠጣችሁትን ሁሉ እንድታስታውሱ ይጠይቃችኋል። የአመጋገብ ልማድዎን እንድንረዳ በመርዳት ረገድ የእርስዎ ተሳትፎ ወሳኝ ነው ። ጥያቄ ጋር በተያያዘ ችግር ቢያጋጥምዎት, በማርኛ አቀላጥፎ/ፋ የሚናገር/ምትናገር እና የአመጋገብ መረጃ የመሰብሰብ ልምድ ያልዉ/ያላት ባለሙያ፣ እርስዎ ለማገዝ ክጎንዎ ስለሚገኝ ፤ ጥያቄዎችን ከመጠየቅ ወይም ማብራሪያ ከመፈለግ ወደኋላ አየበሉ።

ማሰታወሻ

- ባለፉት 24 ሰዓታት ውስጥ በአብዛኛው የምትመገበውን ምግብና መጠጥ አስቡ ።
- በማግስቱ ጠዋት ከእንቅልፍ በፊት የመጨረሻው ምግብ እስኪበላ ድረስ በመጀመሪያ ከተመገቡት ምግብ ይጀምሩና ከተመገቡት ቦታ ጋር ለእያንዳንዱ ምግብ ሪፖርት ያድርጉ።
- የምግብ እቃዎችን (ለምሳሌ፣ የምልክት ስም፣ ዓይነት መቁረጥ፣ የምግብ ማብሰያ ዘዴ...) ሲገልጹ በተቻለ መጠን ታሳቢ ማድረግ ይሞክሩ።
- ለእያንዳንዱ ምግብ ሪፖርት፡- የምግብ ስም፣ የምግብ መገለጫ፣ የቤት ውስጥ መለኪያ (ለምሳሌ ቁርጥ፣ የሻይ ማንኪያ ወዘተ)፣ ከተቻለ የመለኪያ ዩኒት (ለምሳሌ ግራም፣ oz. እና ml ወዘተ)፣ በመጨረሻም የሚጠቀሙባቸው የዝግጅት ዘዴዎች እና/ወይም ቅመሞች።

| ሰአት | ምን በሉ? |
|---|---|

| | | የምግብ እና የመጠጥ ስም | ዝግጅት/ በዉስጡ የያዛቸዉ ንጥረ ምግቦች | የአበሳሰል ዘዴ (አማራጭ) | የቤት ውስጥ መጠን | መጠን (g or **ml**) |
|---|---|---|---|---|---|---|
| እራት | AM PM | | | | | |
| | AM PM | | | | | |
| | AM PM | | | | | |
| ቁርስ | AM PM | | | | | |
| | AM PM | | | | | |
| | AM PM | | | | | |
| መክሰስ (ክቁርስ ብኋላ) **(mid-morning)** | AM PM | | | | | |
| | AM PM | | | | | |
| | AM PM | | | | | |
| ምሳ | AM PM | | | | | |
| | AM PM | | | | | |
| | AM PM | | | | | |
| መክሰስ (ከምሳ በኋላ) **(mid-afternoon)** | AM PM | | | | | |
| | AM PM | | | | | |
| ሌሎች | AM PM | | | | | |
| | AM PM | | | | | |

*Appendix J. Standard Operating Procedures (SOPs)*

**Title:** SOPs for Blood Sampling and Biomarker Analysis in the Trial

**Study Title:** *Cardiovascular Function and Biochemical Biomarkers Response to Concurrent Training: Effect of Exercise Sequence on Type 2 Diabetic Patients: A Randomized Control Trial*

**Objective**

To outline standardized procedures for blood collection, processing, analysis, and data recording to ensure consistency, reliability, and participant safety during the trial.

**Scope**

This SOP applies to all research personnel involved in blood sample collection, processing, analysis, and data handling in the trial.

Responsibilities

**Principal Investigator (PI):**

- Ensure adherence to SOPs and oversee all processes.
- Medical Laboratory Technicians:
- Collect, handle, and process blood samples according to protocol.

**Research Assistants:**

- Assist with participant preparation and documentation.
- Data Analysts:
- Analyze data according to validated methods and maintain accuracy in reporting.
- Materials and Equipment

**Collection Materials:**

- EDTA tubes (2-3 mL for HbA1c).
- Serum Separator Tubes (SST, 8-10 mL for serum tests).
- Sterile needles and syringes.
- Tourniquets, alcohol swabs, and gauze pads.
- Labels and markers.
- Glucose Solution (75 g in 300 mL water)

- Processing and Storage:
- Centrifuge.
- Refrigerators (4°C).
- Biohazard disposal containers.
- Analytical Equipment:
- HPLC (for HbA1c).
- Autoanalyzer (for glucose, lipids).
- ELISA kits and analyzer (for insulin).

**Procedures**

**Participant Preparation**

Instruct participants to:

- Avoid alcohol, caffeine, and high-fat foods for 12 hours before blood collection.ast for at least 12 hours before the test.
- Ensure participants have completed their last exercise session at least 48 hours prior.
- Confirm adherence to fasting and other pre-test requirements upon arrival.

**Blood Collection**

- Verify participant identity using the trial ID number.
- Apply a tourniquet and clean the antecubital area with an alcohol swab.
- Use a sterile needle and syringe to draw blood:
  - EDTA Tube (2-3 mL): For HbA1c.
  - SST Tube (8-10 mL): For glucose, lipids, and insulin analysis.
- Label each tube immediately with the participant's ID, date, and time of collection.
- Apply gauze and ensure participant comfort post-draw.

**Sample Processing**

**Centrifugation (for SST):**

- Centrifuge samples at 2,000–3,000 g for 10 minutes at 4°C.
- Transfer the serum layer into labeled aliquot tubes.

**Storage**:

- Store EDTA samples at 4°C for HbA1c analysis.
- Freeze serum samples at -80°C for lipid and insulin analysis if not analyzed within 24 hours.

**Analysis Protocols**

**HbA1c Analysis:**

- Use the Ion Exchange Resin Method and analyze using HPLC.
- Insulin Analysis:
- Perform using ELISA kits according to manufacturer guidelines.

**Glucose and Lipids:**

- Use enzymatic colorimetric methods with an autoanalyzer.
- Analyze fasting glucose, LDL, HDL, and total cholesterol.

**OGTT (Oral Glucose Tolerance Test):**

- Administer a 75 g glucose solution after fasting glucose collection.
- Measure glucose levels at 0-, 30-, 60-, and 120-minutes post-consumption.

**Data Recording**

- Record raw results immediately into the laboratory logbook and the electronic database.
- Double-check all entries for accuracy.

**Quality Control**

- Perform regular calibration of equipment (HPLC, autoanalyzer, centrifuge).
- Use control samples during each analysis batch to verify reliability.
- Review data for inconsistencies or outliers and resolve them with the lab team.

**Safety Measures**

- Follow universal precautions for bloodborne pathogens.
- Dispose of all biohazardous waste in approved containers
- Monitor participants for adverse events during and after blood collection (e.g., dizziness, nausea).

**Deviations and Corrective Actions**

- Document any deviations from the protocol in a deviation log.
- Investigate and resolve issues promptly to prevent recurrence.

*Appendix K.* *Diabetes-Related Complications Questionnaire*

Kindly respond to all the interviewer's questions to the best of your ability. If you are uncertain about any question, please don't hesitate to ask your interviewer, who is a medical doctor with experience working with diabetic patients, for clarification. The information you provide will assist us in gaining a better understanding of diabetic patients, both with and without diabetes- related complications.

Demographic Information Age: _____

Gender: □ Male □ Female □ Other
Duration of diabetes diagnosis: _____years
**Section 1**: Diabetic Retinopathy (Eye Complications)
Please answer the following questions based on your experience.

- Have you noticed any changes in your vision, such as:
- Blurry vision?
- Difficulty seeing at night?
- Sudden loss of vision in one or both eyes?
- Spots or floaters in your vision? Have you been diagnosed with any eye problems or referred to an eye specialist for diabetes-related issues?

If yes, please specify:
_____

_____

_____

**Section 2:** Autonomic Neuropathy (Nerve Damage Affecting Internal Organs) Please indicate if you experience any of the following symptoms.

- Do you experience any unexplained dizziness or lightheadedness, especially when standing up?
- Do you have trouble with digestion, such as nausea, bloating, or constipation?
- Have you noticed any changes in your ability to sweat, such as excessive sweating or an

inability to sweat?

- Do you experience any difficulties with sexual function, such as erectile dysfunction or vaginal dryness?
- Have you been diagnosed with autonomic neuropathy by a healthcare provider?

**Section 3**: Peripheral Neuropathy (Nerve Damage in the Limbs)
Please indicate if you have experienced any of the following symptoms in your hands or feet.

- Do you experience tingling, numbness, or a "pins and needles" sensation in your hands or feet?
- Do you experience sharp, burning, or stabbing pain in your extremities?
- Have you noticed weakness or loss of balance when walking or standing?
- Do you have trouble feeling hot or cold temperatures in your hands or feet?
- Have you been diagnosed with peripheral neuropathy by a healthcare provider?

**Section 4:** Nephropathy (kidney disease)
Please answer the following questions related to kidney function.

- Have you noticed any changes in your urination, such as:
  Frequent urination, especially at night? /Reduced amount of urine? /Swelling in your legs, ankles, or feet? /Have you been diagnosed with kidney disease or nephropathy by a healthcare provider?
- Have you had any tests for kidney function, such as urine tests for protein or blood tests for creatinine or eGFR?
- If yes, what were the results (if known)? ___

*Appendix L: Common Indicators for Termination $VO_2$ peak Assessment*

1. Onset of angina or angina-like symptoms
2. Drop in systolic BP of >10 mmHg from baseline BP despite an increase in workload
3. Excessive rise in BP: systolic pressure >250 mmHg or diastolic pressure >115 mmHg
4. Shortness of breath, wheezing, leg cramps, or claudication
5. Signs of poor perfusion (e.g., ataxia, dizziness, pallor, cyanosis, cold or clammy skin, or nausea)
6. Failure of HR to rise with increased exercise intensity
7. Noticeable change in heart rhythm
8. Client's request to stop
9. Physical or verbal manifestations of severe fatigue
10. Failure of the testing equipment

*Appendix M. Adverse Events (AE) and Serious Adverse Events (SAE) for Diabetic Participants*

1. Definitions

- Adverse Event (AE):

  Any unfavorable medical occurrence in a participant during the study, whether or not it is causally related to the exercise intervention. Common examples in diabetic adults include:

  - Mild hypoglycemia (blood glucose <70 mg/dL)
  - Transient fatigue, dizziness, or muscle soreness
  - Minor joint or muscle pain

- Serious Adverse Event (SAE):

  Any AE that:

  - Results in death,
  - Is life-threatening (e.g., severe hypoglycemia with loss of consciousness, acute cardiovascular event),
  - Requires hospitalization or prolongs an existing hospitalization,
  - Causes persistent or significant disability, or
  - Leads to a congenital anomaly/birth defect (if relevant).

2. Documentation

All AEs and SAEs will be recorded in a standardized AE/SAE reporting form, including:

- Participant ID and age
- Date, time, and duration of the event
- Description of the event and symptoms (e.g., hypoglycemia, dizziness, chest pain)
- Severity (mild, moderate, severe)
- Relationship to the intervention (related, possibly related, unrelated)
- Action taken (intervention stopped, medical treatment provided, hospital visit)
- Outcome (resolved, ongoing, resolved with sequelae)

Special monitoring for diabetic participants:

- Blood glucose will be measured pre- and post-exercise sessions to detect hypoglycemia early.
- Cardiovascular symptoms (chest pain, palpitations) will be immediately assessed.

3. IRB Reporting Timelines

- SAEs: Must be reported to the IRB within 24 hours of occurrence. A full written report should follow within 7 days.
- Non-serious AEs: Recorded for each session and summarized for periodic IRB reports (e.g., quarterly or annual continuing review).
- Confidentiality of all participants will be strictly maintained.

4. Stopping Rules

The study may be temporarily or permanently stopped if:

1. Any unexpected SAE related to exercise occurs (e.g., severe hypoglycemia requiring hospitalization, myocardial infarction).
2. Multiple participants experience the same SAE, suggesting systemic risk.
3. Interim monitoring shows exercise-related harm outweighs benefits.
4. The IRB or DSMB recommends suspension due to safety concerns.

**Note**: During exercise sessions, a trained professional will monitor participants' vital signs, symptoms, and glucose levels to minimize risk.

*Appendix N. Detailed Training Plan*

**Plan Overview Session Structure**

1. **Warm-Up** (5–10 minutes) and **Cool-Down: 5-10 minutes** will be applied in floor aerobics room with light aerobic activity and stretching activities for major muscle group.

2. **Main Exercises**

- Perform the exercises in the order below to ensures balanced development of cardiovascular fitness, strength, and endurance, with a progression over time with different sequence of exercise.

| Weeks | Days | Aerobic Training (AT) | | Resistance Training (RT) | | | |
|---|---|---|---|---|---|---|---|
| | | **Intensity** | **Duration** | **Types of exercise** | **en:** | **Freq:** | **Set** |
| **Familiari zation weeks** | **Tuesday** | Walking for 2 m | 10 minutes | | 40% - )% 1- RM | 10 - 15 | 1-3 |
| | **Thursday** | Walking for 6 m | 12 minutes | | | | |
| | **Saturday** | Jogging for 5 m | 15 minutes | | | | |
| **Week 1** | **Tuesday** | 50 % - 55 % THR | 15 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | 50 % - 55 % 1RM | 10 | 2 |
| | **Thursday** | 50 % - 55 % THR | 16 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 12 | 2 |
| | **Sunday** | 50 % - 55 % THR | 17 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 15 | 3 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Week 2** | **Tuesday** | 56 % – 60 % THR | 15 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | 56 % – 60 % 1RM | 10 | 2 |
| | **Thursday** | 56 % – 60 % THR | 16 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 12 | 2 |
| | **Sunday** | 56 % – 60 % THR | 17 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands),Triceps Pulley, Standing Plantar Flexion | | 15 | 3 |
| **Week 3** | **Tuesday** | 56 % - 60 % THR | 18 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | 56 % - 60 % 1RM | 10 | 2 |
| | **Thursday** | 56 % - 60 % THR | 19 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 12 | 2 |
| | **Sunday** | 56 % - 60 % THR | 20 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 15 | 3 |
| **Week 4** | **Tuesday** | 60 % - 65 % THR | 18 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | 60 % - 65 % 1RM | 10 | 2 |
| | **Thursday** | 60 % - 65 % THR | 19 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 12 | 2 |
| | **Sunday** | 60 % - 65 % THR | 20 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 15 | 3 |
| **Week 5** | **Tuesday** | 60 % - 65% THR | 21 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | 60 % - 65 % 1RM | 10 | 2 |
| | **Thursday** | 60 % - 65% THR | 22 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 12 | 2 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | **Sunday** | 60 % - 65% THR | 23 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 15 | 3 |
| **Week 6** | **Tuesday** | 66 % – 70 % THR | 21 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | 66 % – 70 % 1RM | 10 | 2 |
| | **Thursday** | 66 % – 70 % THR | 22 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 12 | 2 |
| | **Sunday** | 66 % – 70 % THR | 23 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 15 | 3 |
| **Week 7** | **Tuesday** | 66 % - 70 % THR | 24 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | 66 % - 70 % 1RM | 10 | 2 |
| | **Thursday** | 66 % - 70 % THR | 25 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 12 | 2 |
| | **Sunday** | 66 % - 70 % THR | 26 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 15 | 3 |
| **Week 8** | **Tuesday** | 71 % - 75 % THR | 24 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | 71 % - 75 % 1RM | 10 | 2 |
| | **Thursday** | 71 % - 75 % THR | 25 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 12 | 2 |
| | **Sunday** | 71 % - 75 % THR | 26 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 15 | 3 |
| **Week 9** | **Tuesday** | 71 % - 75 % THR | 27 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | 71 % - 75 % 1RM | 10 | 2 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | **Thursday** | 71 % - 75 % THR | 28 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 12 | 2 |
| | **Sunday** | 71 % - 75 % THR | 29 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 15 | 3 |
| **Week 10** | **Tuesday** | 76 % - 85 % THR | 27 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | 76 % - 80 % 1RM | 10 | 2 |
| | **Thursday** | 76 % - 85 % THR | 28 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 12 | 2 |
| | **Sunday** | 76 % - 85 % THR | 29 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 15 | 3 |
| **Week 11** | **Tuesday** | 80 % - 89 % THR | 30 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | 81 % - 85 % 1RM | 10 | 2 |
| | **Thursday** | 80 % - 89 % THR | 30 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 12 | 2 |
| | **Sunday** | 80 % - 89 % THR | 30 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 15 | 3 |
| **Week 12** | **Tuesday** | 85 % - 89 % THR | 30 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | 81 % - 85 % 1RM | 10 | 2 |
| | **Thursday** | 85 % - 89 % THR | 30 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 12 | 2 |
| | **Sunday** | 85 % - 89 % THR | 30 minutes | Machine Leg Press, Abdominal Curl, Rowing (Machine or Cable), Bench press, Biceps Curl (Dumbbells or Bands), Triceps Pulley, Standing Plantar Flexion | | 15 | 3 |

*Appendix O. Trial registration*

02 September 2025

To Whom It May Concern:

**RE: Cardiovascular Function and Biochemical Biomarkers Response to Concurrent Training: Effect of Exercise Sequence on Type II Diabetic Patients: A Randomized Control Trial**

As project manager for the Pan African Clinical Trial Registry (pactr.samrc.ac.za) database, it is my pleasure to inform you that your application to our registry has been accepted. Your unique identification number for the registry is **PACTR202509591505325**.

Please be advised that your trial is registered under an initiative within our system that allow us to capture data of trials that are already in progress or completed. As such, your trial registration may not adhere to the mandates set forth by the International Committee of Medical Journal Editors for registration requirements, and it is your duty to be transparent to any journal that may ask about the retrospective status of your registration.

Please note you are responsible for updating your trial, or for informing us of changes to your trial. Additionally, please provide us with copies of your ethical clearance letters as we must have these on file (via email or post or by uploading online) at your earliest convenience if you have not already done so.

Please do not hesitate to contact us at +27 21 938 0835 or email pactradmin@mrc.ac.za should you have any questions.

Yours faithfully,

PACTR Admin
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