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THE EFFECTS OF L-CARNITINE SUPPLEMENTATION DURING CONCURRENT TRAINING ON BODY COMPOSITION AND FUNCTIONAL CAPACITIES IN OBESE MEN

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EFEKTI SUPLEMENTACIJE L-KARNITINA TOKOM ISTOVREMENOG TRENINGA NA SASTAV TELA I FUNKCIONALNE KAPACITETE KOD GOJAZNIH MUŠKARACA

Doktorska disertacija

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The effects of L-carnitine supplementation during concurrent training on body composition and functional capacities in obese men

Abstract

Background: Despite extensive research, the effects of L-carnitine supplementation on obesity treatment remain unclear and inconsistent. L-carnitine is known for transporting fatty acids into mitochondria for oxidation and is marketed as a weight loss supplement. This study aims to investigate the efficacy of L-carnitine supplementation during concurrent training on body composition and functional capacities in obese men.

Methodology: Thirty sedentary, obese males (age = 37.2 ± 1.5 years, body mass index = 33.8 ± 2.5 kg/m²) participated in this study. Participants were randomly assigned to three groups: Experimental group 1 (EXG 1): concurrent training with L-carnitine supplementation, Experimental group 2 (EXG 2): L-carnitine supplementation without training, and a Control group: no training or L-carnitine supplementation. Both experimental groups received 35 mg of L-carnitine per kg of body weight. Concurrent training was conducted for 8 weeks, with three sessions per week, at an intensity ranging from 60% to 75% of maximal heart rate reserve and one-repetition maximum. Various functional and body composition metrics were collected at three time points: pre-test, mid-test, and post-test.

Results: Significant improvements were observed in the EXG 1 group after 4 and 8 weeks in several variables: systolic blood pressure, maximal oxygen consumption, weight, body mass index, and one-repetition maximum. Additional improvements were noted after 8 weeks in diastolic blood pressure, resting heart rate, percentage of body fat, and fat-free mass. No significant changes were observed in the EXG 2 and Control groups.

Conclusion: L-carnitine supplementation combined with concurrent training is an effective approach for improving body composition and enhancing functional capacities in obese men. It is recommended that overweight men incorporate concurrent training into their regimen while taking L-carnitine.

Keywords: L-Carnitine, Bioimpedance, Fat loss, 1RM
Scientific field: Exercise Physiology
Scientific subfield: Science of Physical education, Sport and Recreation
UDK number: 796:613.2 (043.3)

Ефекти суплементације л-карнитина током истовременог тренинга на састав тела и функционалне капацитете код гојазних мушкараца

Сажетак

Uvod: Uprkos opsežnim istraživanjima, efekti suplementacije L karnitinom u lečenju gojaznosti su još uvek nejasni i dvosmisleni. L-karnitin transportuje masne kiseline u mitohondrije radi oksidacije i prodaje se kao dodatak za mršavljenje. Svrha ovog istraživanja je da se ispita efikasnost L-karnitina tokom konkuretnog (mešovitog) treninga na funkcionalne kapacitete i sastav tela gojaznih muškaraca.

Metodologija: U istraživanju je učestvovalo 30 neaktivnih gojaznih muškaraca (starost = 37,2 ± 1,5 godina, indeks telesne mase = 33,8 ± 2,5 kg/m2). Učesnici su nasumično podeljeni u tri grupe: Eksperimentalna grupa 1 (EXG 1): istovremeni trening sa suplementacijom L-karnitina, Eksperimentalna grupa 2 (EXG 2): suplementacija L-karnitinom bez treninga i Kontrolna grupa: bez suplementacije L-karnitinom i treninga. Obe eksperimentalne grupe su suplementirane sa 35 mg L-karnitina po kg telesne težine. Konkurentni trening se izvodio 8 nedelja, tri sesije nedeljno, sa intenzitetom treninga u rasponu od 60% do 75% maksimalne rezerve otkucaja srca i maksimumom od jednog ponavljanja. Različite funkcionalne varijable i varijable telesne kompozicije prikupljene su u tri vremenske tačke (pre-test, sredinom testa i post-test).

Rezultati: Brojne varijable su značajno poboljšane u EXG 1 nakon 4 i 8 nedelja (sistolni krvni pritisak, maksimalna potrošnja kiseonika, težina, indeks telesne mase i maksimum jednog ponavljanja) i tek nakon 8 nedelja (dijastolni krvni pritisak, broj otkucaja srca u mirovanju, procenat telesne masti i masa bez masti). Nisu primećene značajne promene između EXG 2 i kontrolne grupe.

Zaključak: Dodatak L-karnitina, u kombinaciji sa treningom, može biti veoma efikasan pristup za poboljšanje sastava tela i jačanje funkcionalnih kapaciteta kod gojaznih odraslih muškaraca. Zbog toga se preporučuje da muškarci sa prekomernom težinom integrišu istovremeni trening u svoj režim, dok uzimaju L-karnitin.

Ključne reči: L-karnitin, bioimpedansa, gubitak masti, 1RM
Naučna Oblast: Fiziologija vežbanja
Uža Naučna Oblast: Nauke u fizičkom vaspitanju, sportu i rekreaciji
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TABLE OF CONTENTS

TABLES

FIGURES

ABBREVIATIONS

ATP – Adenosine Triphospate	WHO – World Health Organization
CP – Creatine Phosphate	BMI – Body Mass Index
RHR – Resting Heart Rate	VO2max – Maximal Oxygen Consumption
SD – Standard deviation	1 RM – One repetition maximum
min – minimum	BF% – Body Fat Percentage
max – maximum	FFM – Fat-Free Mass
ANOVA – Univariate Analyses of Variance	BIA – Bioelectrical Impedance Analysis
SPSS – Statistical Package for the Social Sciences	CACT - Carnitine Acyl Carnitine Translocase
LCR - L-Carnitine	CPT-I - Carnitine Palmitoyl Transferase -I
EXG 1 - Experimental group 1	DBP - Diastolic Blood Pressure
EXG 1 - Experimental group 2	SBP - Systolic Blood Pressure
C G – Control Group	SpO_2 - Oxygen Saturation
C T - Concurrent Training	mTORC1 - mechanistic Target Of Rapamycin Complex 1
CTE - Concurrent Training Effect	
R T – Ressistant Training	MPB - Muscle Protein Breakdown
S T - Strength Training	CVD - Cardiovascular Disease
E T - Endurance Training	E E - Energy Expenditure
R Q - Respiratory Quotient	BCS - Body Condition Score
D V - Daily Value	TBW - Total Body Water
TMLHE - Trimethyl-Lysine Dioxygenase	MPS - Muscle Protein Synthesis
	MPB - Muscle Protein Breakdown
A F - Atrial Fibrillation	PLC - Propionyl-L-carnitine
FAO - Fatty Acids Oxidation	OZR - Obese Zucker Rats
LDL – Loe Density Lipoprotein	CLA – Conjugated Linoleic Acid
IDF – International Diabetes Federation	NFD – Normal Fat Diet
	HFD - High Fat Diet

1. INTRODUCTION

1.1. Background and rationale

The rapid development of global urbanization and modernization has lasting effects on lifestyle aspects such as unhealthy eating habits, lack of exercise, increased stress and environmental factors. These factors contribute to the alarming growth of obesity (Klein et al., 2022). Overweight and obesity are considered as major health concerns all around the world; in addition, they play a great role in the progression of several non-communicable diseases, including diabetes, cardiovascular diseases, and cancer (Talenezhad et al., 2020). While lifestyle changes and medications are recommended for prevention, they have not been successful in suppressing the increasing incidence conditions. Therefore, it is crucial to gain a deeper understanding of the molecular mechanisms linking obesity and L-Carnitine in order to address this global healthcare challenge effectively (Chandrasekaran and Weiskirchen, 2024). The etiology of obesity is closely related with a reduction in habitual physical activity, physical fitness levels, and everyday mobility. Among the various factors contributing to the excess of body fat over time, significant attention has been directed towards insufficient engagement in physical activity as a behavior that can predispose individuals to a positive energy balance. Additionally, the influence of the physical activity environment, which can either facilitate or limit an active lifestyle, has been properly acknowledged. Consequently, it is important to recognize physical inactivity as an essential determinant in the context of weight gain and the onset of obesity (Oppert et al., 2021).

L-Carnitine is an amino acid-like compound that plays a role in energy metabolism by supporting transport of fatty acids into the mitochondria, where they can be used for energy production through β-oxidation (Virmani and Cirulli, 2022). L-Carnitine is essential for the transfer of long-chain fatty acids across the inner mitochondrial membrane for subsequent β-oxidation (Longo et al., 2016). Therefore, without carnitine most of the dietary lipids cannot be used as an energy source and our body would accumulate fatty-acids promoting obesity (Cha, 2008). This process is particularly important during exercise when the body's demand for energy increases. Consequently, L-carnitine supplementation has been proposed as a means to enhance fat oxidation, improve body composition, and augment physical performance. For all the mentioned reasons, L-Carnitine is marketed as a weight-loss supplement (Villani and Gannon, 2002).

All mammalian species have naturally occurring L-carnitine, which is a quaternary amine (3-hydroxy-4-N-trimethylaminobutyrate). After the discovery of L-carnitine in muscle extracts in 1905 and its structural identification in 1927, the importance of L-carnitine in fatty acid oxidation in the liver and the heart was first described by Fritz in 1959. As mitochondrial membranes are impermeable to coenzyme A (CoA) esters and long-chain fatty acids, binding of L-carnitine to acetyl groups via carnitine acyltransferase is essential for the shuttle of the acetylated fatty acids into the mitochondria and for their subsequent β-oxidation in the matrix (Figure 1.1). The products of the β-oxidation (two carbon molecules) are then used by the Krebs cycle to produce Adenosine triphosphate (ATP) as primary form of energy. L-carnitine has also been recognized for its crucial biological function in buffering the free CoA/acetyl-CoA ratio. Under conditions of stress with excess formation of acyl-CoA, transesterification with L-carnitine potentially promotes the substrate movement in the Krebs cycle (Fielding et al., 2018).

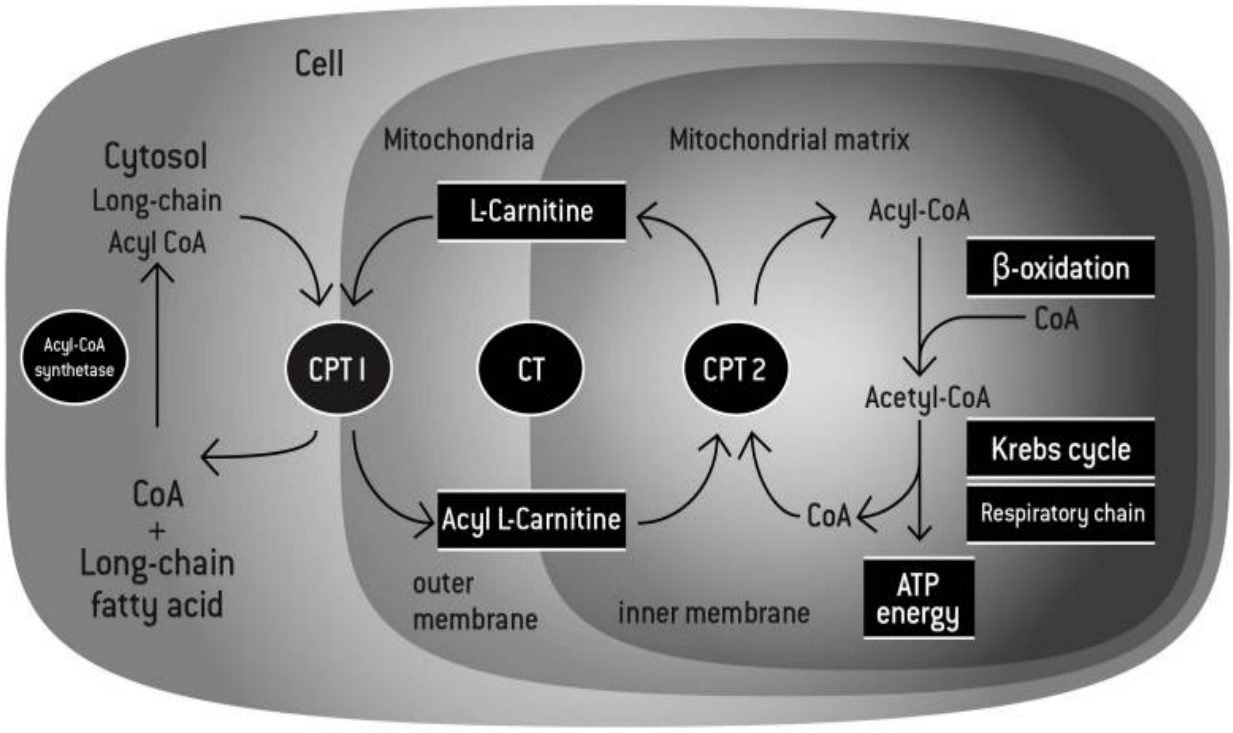

Figure 1.1 L-carnitine shuttles long-chain fatty acids inside the mitochondria by forming a long chain acetyl carnitine ester. The complex is then transported into the mitochondrial matrix by carnitine palmitoyl transferase I (CPT I) and carnitine palmitoyl transferase II (CPT II). The fatty acids are then broken down through the process of β-oxidation to deliver the 2-carbon molecules to the Krebs cycle, leading to the generation of energy under the form of adenosine triphosphate (ATP). In addition, by binding an acetyl group, l-carnitine can maintain the levels of Acetyl-CoA and coenzyme A, playing its buffering role. adopted according Fielding et al., 2018.

Nevertheless, previous clinical studies reported inconsistent data regarding effects of L-carnitine supplementation on obesity-related indexes. L-carnitine supplementation significantly decrease body weight and BMI compared with controls (Pooyandjoo et al., 2016). Similarly, one study reported that L-Carnitine supplementation could lead to significantly increased muscle mass accompanied by a decrease in body weight and reduced physical and mental fatigue (Fielding et al., 2018).

Another study investigated the effect of L-carnitine on weight loss in adults (Talenezhad et al., 2020). The authors reported significant reductions in fat mass, body weight and BMI compared with the control group especially among adults with overweight/obesity.

However, certain authors have reported conflicting outcomes. In a recent comprehensive systematic review and dose-response meta-analysis of randomized controlled trials, the researchers found that L-carnitine supplementation did not ensure a significant impact on body fat percentage or waist circumference among overweight or obese adults (Askarpour et al., 2020). It is essential to acknowledge that the individual response to L-Carnitine supplementation can be influenced by factors such as dietary habits, exercise intensity, and genetic predisposition. The authors proposed that the diversity in study design and the lack to determine the optimal dosage and duration of L-carnitine supplementation may contribute to the inconsistencies in results concerning weight loss and the facilitation of lipid oxidation, primarily involving the transport of long-chain fatty acids into the inner mitochondrial region (Stefan et al., 2021).

The purpose of this study was to assess how an L-carnitine supplement taken in conjunction with a concurrent training program affects the functional abilities and body composition of obese men. This study looked at variables including fat mass, lean muscle mass, and performance metrics in an effort to clarify the possible advantages and real-world uses of supplementing this population with L-carnitine along with structured exercise programs.

1.2. Significance of the study

This research point to various advantages of L-carnitine suplementation on body composition and functional capacities in related to concurrent training in obese men.. Numerous studies have shown that maintaining a minimum quantity and quality of exercise decreases the risk of death, prevents the development of certain cancers, and lowers the risk

of osteoporosis and cardiovascular disease in obesity men. L-carnitine has been extensively used in various research activities in relation to obtain the beneficial effects under disease states (Sousa and Costa, 2021). The current study on the effects of L-carnitine supplementation during concurrent training on body composition and functional capacities in obese men holds significant value for several reasons:

- Addressing obesity: Obesity is a major public health concern worldwide, associated with numerous health issues such as cardiovascular diseases, diabetes, and metabolic syndrome. Effective interventions for reducing obesity are crucial for improving public health (Aziz et al., 2024).
- Role of L-Carnitine: L-carnitine plays a vital role in fat metabolism by transporting long-chain fatty acids into the mitochondria for oxidation. Understanding its impact on body composition can provide insights into potential weight management strategies (Schwantje et al., 2024).
- Concurrent training: Combining resistance and aerobic exercises, known as concurrent training, is effective in improving both muscular strength and cardiovascular fitness. Investigating how L-carnitine supplementation enhances the outcomes of such training can lead to optimized exercise protocols for obese individuals (Lee et al., 2024).
- Body composition: Assessing changes in body composition (fat mass and lean mass) helps determine the effectiveness of L-carnitine in promoting fat loss and muscle preservation or growth, which are critical for overall health and physical function in obese individuals (Kruszewski et al., 2024).
- Functional capacities: Improvements in functional capacities, such as strength, endurance, and overall physical performance, are essential for enhancing the quality of life and reducing the risk of obesity-related complications (Vandoni et al., 2024).
- Scientific evidence: This study can contribute to the body of scientific evidence regarding the benefits of dietary supplements in combination with exercise. It can also provide practical recommendations for healthcare providers and fitness professionals working with obese populations.
- Personalized nutrition and exercise: Maximizing health benefits for obese men can be achieved by individualized exercise and nutrition programs that take into account individual responses to concurrent training and L-carnitine supplementation.

- Reduction of Comorbidities: Effective weight management and improved functional capacities can lead to a reduction in obesity-related comorbidities, decreasing healthcare costs and enhancing the overall well-being of individuals.

Overall, this study offered valuable insights into the synergistic effects of L-carnitine supplementation and concurrent training as a potential strategy to improve body composition and functional capacities in obese men. The findings supported the hypothesis that L-carnitine, when combined with concurrent training, could enhance functional capacities and improve body composition. Additionally, the study helped establish optimal timing for L-carnitine administration to maximize its benefits in reducing lipid peroxidation and promoting weight loss. The observed improvements in functional capacities and specific body composition metrics suggested that L-carnitine supplementation, alongside concurrent training, was a promising approach for effective weight management in this population.

2. LITERATURE REVIEW

2.1. Obesity and health implications

Obesity, although recognized millennia ago as an unusual feature and a societal handicap, only since the 1980s has it become a major clinical and public health problem. Originally a disease of affluence it became evident in poorer countries in the 1990s with children then showing increasing evidence of their excess weight gain with all its propensities to premature disease and death. Obesity rates are rising rapidly in poor countries with clear evidence that many societies are more prone to obesity's amplification of diabetes and hypertension rates than in Western Europe and North American. These differences probably relate to the impact of poor fatal and early nutrition as well as infections on development and the epigenetic control of metabolism (Wells, 2006).

Obesity is associated with increased risk of cardiovascular disease (CVD), heart failure, diabetes, cancer, and ultimately all-cause mortality. Obesity is causally related to dyslipidaemia, hypertension, and diabetes, all strong CVD risk factors, and so causally related to CVD risk. In fact, a substantial part of the risk imparted by obesity on CVD outcomes operates via traditional risk factors. Obese men are almost twice as likely and women almost two and half times as likely to develop hypertension. Obese individuals are around 50% more likely to have a stroke and have around 6–12 times higher risks of developing type 2 diabetes compared to those with a normal BMI. Obesity is also linked to greater risk for development of heart failure. Yet, there appears to be an obesity paradox in established heart failure such that the risk of death is lower in overweight and mildly obese individuals than in those with normal weight. Such observations are likely partially driven by reverse causality whereby disease-specific issues drive weight loss rather than higher weight per se being protective (Horwich et al., 2001). While obesity is most commonly defined by BMI, the importance of body fat distribution and markers such as waist circumference, waist: hip ratio, visceral and ectopic fat volumes are becoming better appreciated. The concept of harmful fat distribution is therefore topical and recent evidence suggest those who can store more fat subcutaneously (and so delay their ectopic depot expansions until much heavier) have lesser diabetes and cardiovascular risks. Obesity has also been identified as an independent risk factor for many cancers (Lega and Lipscombe, 2020).

Trials of weight loss add strong support for causal links between adiposity and CVD; for example, the best evidence suggests that losing around 1 kg reduces SBP by around 1 mmHg. Weight loss also improves lipid profiles with reduced total cholesterol, LDL-cholesterol, and in particular triglyceride levels. Weight loss of around 5 kg reduces the risk of obese individuals progressing to impaired glucose tolerance and type 2 diabetes (Stevens et al., 2001).

Obesity is classically defined according to body mass index (BMI), calculated by dividing the person's body mass in kilograms by the square of their height in meters. Normal BMI is defined as 18.5–24.9 kg/m2; overweight, a BMI of 25–29.9 kg/m2; and obesity, a BMI 30 kg/m2. Obesity can be further classified according to severity: obesity grade I: BMI 30–34.9; grade II: BMI 35–39.9; and grade III: BMI 40 kg/m2. However, these thresholds were largely based on White European populations. Consequently, the World Health Organization (WHO) recommend defining overweight as a BMI >23 kg/m2 and obese as a BMI >27.5 kg/m2 in Asian populations and the IDF (International Diabetes Federation) recommend a cut-off waist circumference of 80 cm for Asian women and 90 cm for Asian men. Analysis of UK Biobank data of around 500,000 individuals confirmed the need for lower BMI cut-offs in no white individuals to reflect the higher diabetes prevalence in these groups. A white participant with a BMI of 30 kg/m2 has the equivalent diabetes prevalence as a South Asian individual with a BMI of 22.0 kg/m2, a black individual with a BMI of 26.0 kg/m2, a Chinese woman with a BMI of 24.0 kg/m2, and Chinese man with a BMI of 26.0 kg/m2 (Colao et al., 2021).

2.2. Prevalence and trends of obesity

Obesity is a complex chronic disease in which abnormal or excessive accumulation of body fat impairs health. Adult obesity rates have more than doubled since the 1980s in the U.S. today, obesity affects over 42% of adults and 18% of youth. Obesity and its related complications are major drivers of rising healthcare costs, diminished health-related quality of life, and the recent decline in U.S. life expectancy. This fact sheet is part of a series designed to provide basic information about the science of obesity and current strategies to address it (Hales, 2020).

The prevalence of obesity is a major global concern. In high-income countries, the prevalence of obesity is high and continuing to increase. Whilst the prevalence of obesity is comparatively low in many low and middle income countries, rapid increases have occurred in many countries, driven by a shift away from traditional diets towards diets characterised by nutrient-poor processed foods (Arbel et al., 2024). This section aims to provide a detailed analysis of the prevalence and trends of obesity worldwide, highlighting regional variations, historical changes, and factors contributing to these trends (Asharaf et al., 2024).

The prevalence of obesity has been increasing globally, affecting both developed and developing countries. According to the World Health Organization (WHO), over 1.9 billion adults were overweight in 2016, and more than 650 million were obese. This epidemic affects all regions, with the highest prevalence in North America, the Middle East, and certain Pacific islands, while parts of Asia and Africa are experiencing rapid increases. In the United States, the National Health and Nutrition Examination Survey (NHANES) reported that 42.4% of adults were obese in 2017-2018. Obesity rates among children and adolescents aged 2-19 years were 19.3% during the same period, with higher rates observed in non-Hispanic Black and Hispanic populations (Di Ciaula and Portincasa, 2024).

Obesity rates have significantly increased since the latter half of the 20th century, driven by changes in diet and physical activity. The past few decades have seen a continued rise, with notable acceleration in specific regions. The shift towards high-calorie, low-nutrient foods and sugary beverages is a major contributor to rising obesity rates. Urbanization and economic growth have led to changes in dietary patterns, particularly in developing countries. Obesity is associated with an increased risk of numerous health conditions, including cardiovascular diseases, type 2 diabetes, and certain cancers. The chronic nature of these diseases imposes a significant burden on healthcare systems and reduces life expectancy (Pontzer, 2024).

Unless effective strategies to prevent and treat obesity are implemented, obesity rates will continue to climb. Projections suggest that the U.S. adult obesity rate in 2030 will be around 1 in 2, with severe obesity rates reaching nearly 1 in 4. In Europe, obesity rates have been predicted to grow in 44 countries, despite World Health Organization (WHO) goals to halt the increase of obesity rates by 2025. Globally, obesity rates continue to rise while undernutrition remains a problem in many countries (Donovan and McNulty, 2024).

2.3. Health risks associated with obesity

Obesity is a significant risk factor for numerous health conditions that can affect almost every aspect of physical and mental health for a variety of chronic conditions including diabetes, hypertension, high cholesterol, stroke, heart disease, certain cancers, and arthritis. Higher grades of obesity are associated with excess mortality, primarily from cardiovascular disease, diabetes, and certain cancers. Despite the increases in obesity prevalence, mortality rates and mortality from coronary heart disease and stroke have declined over several decades, possibly due to improvements in public health and medical care and in other cardiovascular risk factors; however, hypertension appears to be increasing (Lee, 2024).

According to the World Health Organization (WHO), being overweight is defined as excessive fat accumulation whereas obesity is defined as excessive fat accumulation to an extent that it may impair health. They are commonly classified according to the body mass index (BMI), a surrogate marker of fatness, with obesity being defined by a BMI $\geq$ 30 kg/m^2, and being overweight by a BMI $\geq$ 25 kg/m^2 . Obesity and being overweight are among the biggest public health problems worldwide, as they can cause premature disability and death by increasing the risk of cardiometabolic diseases (i.e., type 2 diabetes, hypertension, myocardial infarction, stroke, and dyslipidemia), osteoarthritis, dementia, depression, some types of cancers (i.e., breast, ovarian, prostate, colon, among others), and overall mortality (Lima et al., 2024). In addition, psychological, social, and economic complications can result from obesity, overloading public health systems (Apovian, 2016) and decreasing life expectancy (Lung et al., 2019).

The estimated costs attributable to the main chronic diseases associated with inadequate nutrition show how great of an economic burden these diseases are to the Brazilian Unified Health System. The total costs of hypertension, diabetes, and obesity reached USD 890 million in 2018. However, when separately analyzing obesity as a risk factor for hypertension and diabetes, the costs attributable to obesity itself represented 41% of the total costs. These public health costs are higher in women (56%), as well as the levels of hospitalization resulting from obesity (86.5%) . Alarming data from the World Health Organization (WHO) showed that worldwide obesity has nearly tripled since 1975 (Lima et al., 2024).

2.4. Exercise training in obesity management

The prevention and treatment of overweight and obesity on a populationwide basis are challenging. Population-based strategies that improve social and physical environmental contexts for healthful eating and physical activity are complementary to clinical preventive strategies and to treatment programs for those who are already obese (Lee, 2024).

There are two phases to treating obesity: losing weight and preventing it from coming back. The objective of this chapter is to offer evidence-based suggestions for integrating exercise into every phase of the treatment of obesity. It is all too typical to encounter media messages discouraging exercise for people trying to reduce weight. For example, the title of a recent essay was "Public confusion about exercise – why you shouldn't exercise to lose weight, explained with 60 studies. The surprise public messaging that suggests exercise has no role in treating obesity reflects a lack of understanding of how exercise impacts energy balance management, which is the cornerstone of diagnosing and treating obesity (Hall and Kahan, 2018).

Additionally, it shows a disregard for decades' worth of exercise science studies. An important starting point for comprehending the variables that can affect body weight is the control of energy balance. Regulation of energy balance has been reviewed. It is essential to understand that the elements of energy balance are interdependent, meaning that modifications to one might impact adjustments to the others. Provided that the quantity and makeup of energy consumed and expended are equal, body energy reserves and weight stay constant. Changes in this system, such as dietary or exercise modifications, may or may not result in modifications to the body's energy reserves, contingent upon the severity of the disturbance and the compensatory mechanisms in other constituents.

The challenges are different for the active weight loss and weight loss maintenance phases of obesity treatment in related to exercise training. Negative energy balance will produce weight loss in accordance with the extent of the imbalance, but no specific threshold of negative energy balance must be achieved to lose weight. The active weight loss phase of obesity treatment (energy restriction) is also time-limited (usually 6 months or less) (Müller et al., 2016).

Conversely, weight loss maintenance is characterized by a need to exactly match energy intake and energy expenditure during exercise and to maintain balance permanently. The situation is further complicated by the fact that many physiological changes occur with weight loss that tend to promote weight regain. These include reductions in energy expenditure due to declines in resting metabolic rate, the thermic effect of food, and the energy cost of movement, decreases in fat oxidative capacity, changes in hormones associated with appetite, and increases in efficiency of storage of excess energy. Maintaining weight loss requires constantly “pushing back” against these physiological changes. Regular exercise has been shown to counteract many of these compensatory adaptations in response to weight loss, which may help improve long-term weight loss maintenance (Castagneto-Gissey et al., 2022).

2.5. Role of L-Carnitine in metabolism

L-carnitine is a conditionally essential amino acid that plays an important role in cellular energy metabolism. In heart and skeletal muscle, L-carnitine aids the translocation of long chain fatty acids into the mitochondria for subsequent beta-oxidation, which is a major energy source in muscle cells. L-carnitine is absorbed from dietary products and biosynthesized from lysine and methionine; its excretion is efficiently regulated by renal re-absorption. The physiological range of L-carnitine concentrations in various tissues is maintained by complex transporter systems (Liepinsh et al., 2011).

The homeostasis of cellular energy metabolism relies on the availability of two major sources of substrates: fatty acids and carbohydrates. Through catabolic processes, both substrates provide a metabolite, acetyl coenzyme A (acetyl-CoA), which further undergoes oxidation in the mitochondrial machinery to provide cellular metabolism with adenosine triphosphate (ATP) molecules, the "molecular unit of currency" of intracellular energy transfer (Koves et al., 2008). The role of L-carnitine in regulating cellular energy metabolism is schematically summarized in (Fig. 2.1). First, L-carnitine is a substrate of the enzyme L-carnitine palmitoyltransferase-1 (CPT I), which catalysis the rate-limiting reaction in the transfer of FA into the mitochondria. The key mechanism for regulation of CPT I activity is allosteric inhibition by malonyl CoA (Liepinsh et al., 2011).

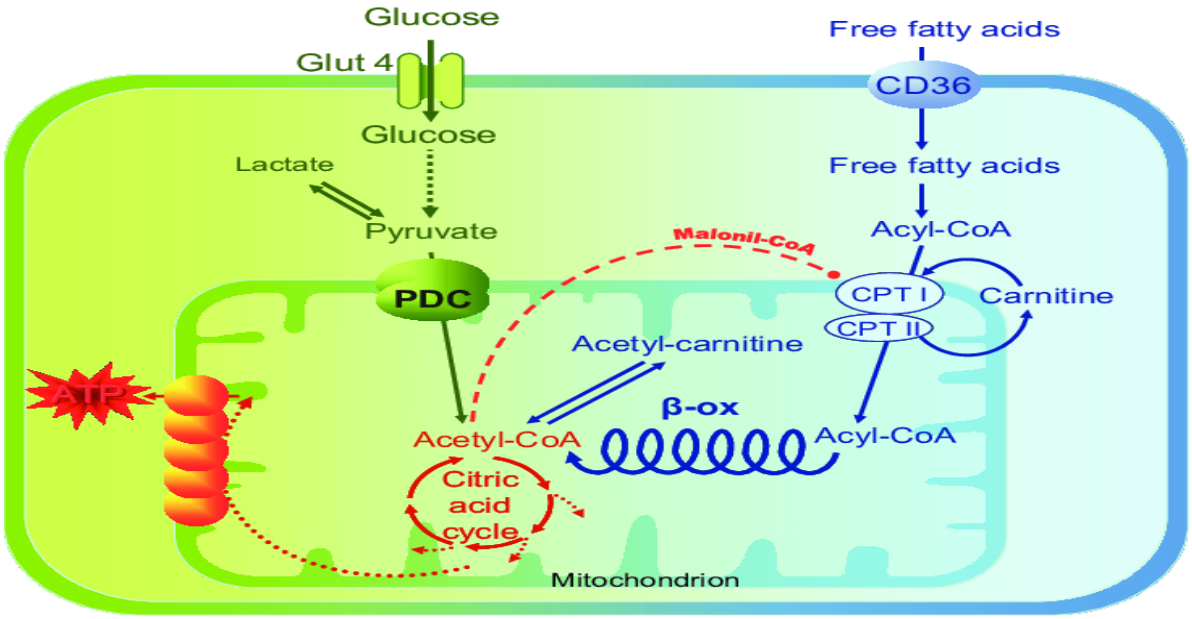

Fig. 2.1. The cellular pathways of energy metabolism. Adapted according Liepinsh et al., 2011.

In the CPT I-catalysed reaction, L-carnitine and acyl-CoA-activated long-chain FA interact to form long-chain acyl-L-carnitine esters that are then shuttled across the mitochondrial membranes by L-carnitine/acyl-L-carnitine translocase (CACT) (Bremer, 1983). Inside the mitochondrial matrix, acyl-L-carnitine is converted back to L-carnitine and long-chain FA by the enzyme CPT II. Thus, L-carnitine aids the import of long-chain FA to the mitochondria for oxidation, which is the major provider of energy for muscle cells. In addition to its role in FA transport pathways, L-carnitine is also involved in the export of acetyl groups out of the mitochondria (Stephens et al., 2007). In the mitochondrial matrix, lumen of the endoplasmic reticulum and peroxisomes, L-carnitine acetyltransferase (CrAT; EC 2.3.1.7) catalysis the reversible transfer of acetyl groups between acetyl-CoA and L-carnitine (Ramsay et al., 2001). By catalysing its reaction in a reversible manner, CrAT regulates the cellular pool of CoA, which serves as a carrier of activated acetyl groups in the oxidation of energy metabolism substrates and in the synthesis of FA and lipids (Liepinsh et al., 2011).

Glucose metabolism pathways are also regulated through the homeostasis of the ratio of acetyl-CoA/CoA. An increase in this ratio is sensed by pyruvate dehydrogenase kinase, which phosphorylates and thereby leads to the inhibition of the pyruvate dehydrogenase complex (PDC), the key rate-limiting step in carbohydrate oxidation (Rebouche, 2004), with L-carnitine being a pivotal regulator of these pathways. For example, during high-intensity exercise, L-carnitine enters the CrAT catalysed reaction and buffers the excess acetyl groups

formed. As a result, a pool of free CoA is maintained for the continuation of the PDC and citric acid cycle reactions (Stephens et al., 2007). It can be concluded that L-carnitine is important for the regulation of both long chain FA and carbohydrate metabolism. L-carnitine-dependent pathways are strongly involved in the regulation of the adaptive responses related to the overall homeostasis of cellular energy metabolism (Liepinsh et al., 2011).

L-carnitine decreases the intramitochondrial acetyl-CoA/CoA ratio through trapping of acetyl groups and activation of the pyruvate dehydrogenase complex. This leads to simultaneous decrease in acetyl-CoA levels in the cytosol contributing to activation of the glycolytic pathway. L-carnitine, thus plays some roles in the glucose metabolism and may increase energy expeniture (Kim et al., 2015).

2.6. L-Carnitine synthesis and function

L-carnitine is synthesized in liver, kidney and in heart muscle because they are highly dependent on energy during aerobic conditions, thereby these tissues contain high concentration of carnitine which is more than seventy percent of plasma. The other tissue where complete enzyme system for carnitine synthesis is lacking needs to obtain it by specific active transport through high affinity plasma membrane bound carnitine transporter from blood. Similarly, in kidney tubular cells also carnitine transport system has high affinity to carnitine to maintain conservation.

In regard to this, carnitine is a carrier molecule of long chain fatty acid across inner mitochondrial membrane in to mitochondrial matrix for oxidation. Long chain fatty acid does not traverse inner mitochondrial membrane freely, oxidative phosphorylation of reducing equivalents released from Krebs cycle, depends on the acetyl CoA pool obtained from oxidation of carbohydrates. Therefore, the acetyl CoA pool from fatty acid oxidation hampering. Thereby, in the light of this, the fatty acid in the cytoplasm gets activated upon binding of CoA with thioester bond catalyzed by Acyl CoA synthetase or thiokinase using ATP as energy molecule. The organic cation transport 2 helps to accumulate carnitine with in cells. L-carnitine traverse activated fatty acid in to matrix across inner mitochondrial membrane. There are four Carnitine Palmitoyl transferase (CPT) isoforms found, they are CPT1a in liver, CPT1b in muscle and other tissues, CPT1c in brain and testis and CPT II.

The two isoenzymes form of carnitine Palmitoyl Transport (CPT) are CPT-I and CPT-II, CPT-I localized in inner side of the outer mitochondrial membrane, where the catalytic site and regulatory domain of enzyme are facing toward the cytosolic site that catalyze esterification of acyl Coa and carnitine in to acyl-carnitine complex.

This CPT–I enzyme also sensitive for malonyl CoA inhibition and allosterically inhibited by malonyl Coa Acyl carnitine complex transported across inner mitochondrial membrane through specific transporter by Carnitine-acyl carnitine translocase (CACT). The inner side of mitochondrial membrane, CPT-II is located; it breaks the acyl bond of acyl-carnitine releases fatty acid. Simultaneously, Coenzyme A recycling takes place and carnitine enters for transport of another molecule of fatty acid. The transported acyl CoA from cytoplasm undergoes B-oxidation for rapid energy release (Fig 2.2).

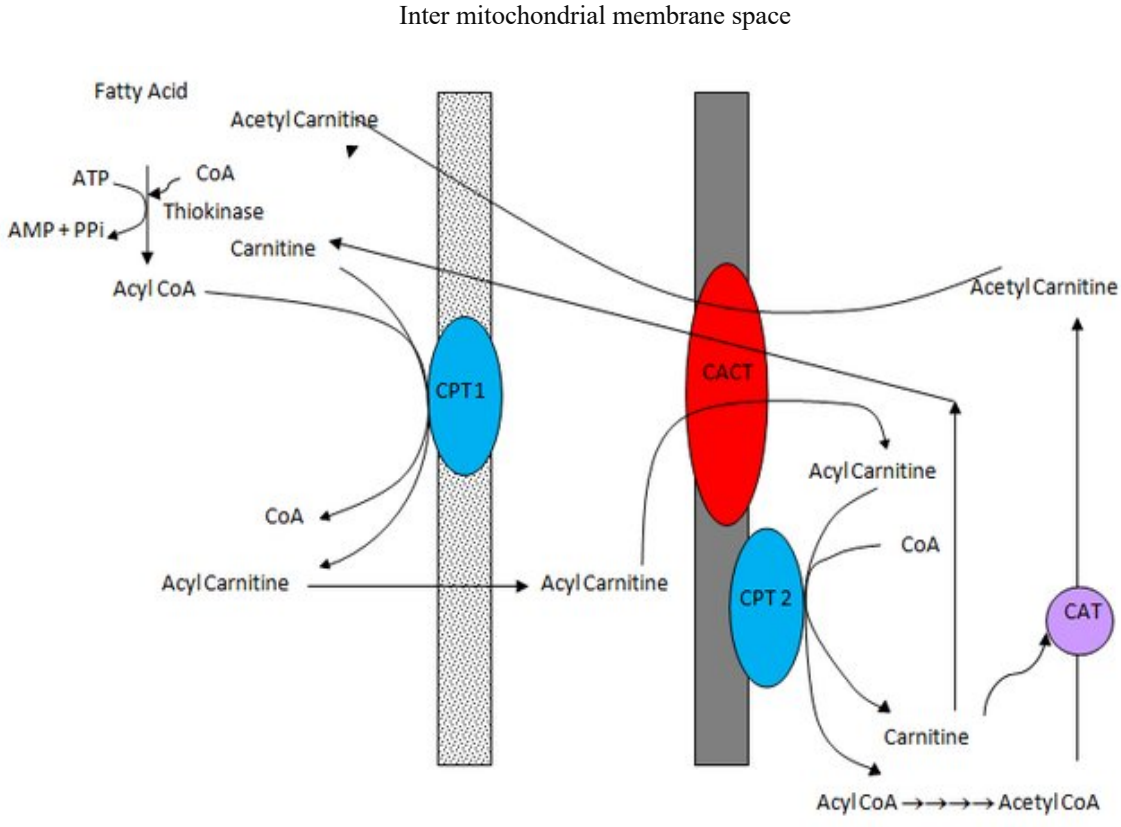

Fig 2.2. Role of L-Carnitine in transport of fatty acid in to matrix CPT-I Carnitine Palmitoyl Transferase -I; CPT-II Carnitine Palmitoyl Transferase-II; CACT Carnitine Acyl Carnitine Translocase; CAT Carnitine Acetyl Transferase. Adpted according Daynanad et al., 2011.

Acetyl carnitine formed by acetyl CoA carboxylase transported in to cytoplasm where it serves as precursor for fatty acid or acetyl choline synthesis. Human genetic defect disorders of enzymes and transporter protein affect the different steps involved in carnitine transport mechanism. The carnitine uptake defect occurs due to the defect in cellular carnitine transporter (CT) that impairs the mechanism of fatty acid transport in to mitochondria for oxidation (Dayanand et al., 2011).

By shuttling fatty acids into the mitochondria for oxidation, L-carnitine supports the generation of ATP, the primary energy currency of cells. This process is especially important during periods of increased energy demand, such as during exercise. L-carnitine exhibits antioxidant properties, helping to neutralize free radicals and reduce oxidative stress, which can damage cells and contribute to various health issues. L-carnitine is known for its role in supporting muscle function. It may reduce muscle damage and soreness following intense exercise, potentially aiding in faster recovery (Pekala et al., 2011).

It's important to note that while L-carnitine plays a role in these metabolic pathways, the body can synthesize it endogenously and obtain it from dietary sources such as meat, fish, poultry, and dairy products. Additionally, individual responses to L-carnitine supplementation can vary based on factors like overall health, diet, and genetic differences. L-carnitine in humans is both endogenously synthesized and obtained through food ingestion.

The biochemical pathway to the endogenous synthesis of L-carnitine in humans has not been well-characterized. Larnitine is synthesized from the substrate 6-N-trimethyl-lysine. Lysine residues in some proteins undergo N-methylation using S-adenosylmethionine as methyl donor, forming 6-N-trimethyl-lysine residues. It is generally assumed that 6-N-trimethyl-lysine is generated by degradation of proteins and converted to L-carnitine in four enzymatic steps, namely hydroxylation at carbon 3, aldol cleavage, oxidation of the aldehyde to 4-butyrobetaine and hydroxylation of 4-butyrobetaine at carbon 3 (Fig. 2.3).

The enzyme trimethyl-lysine dioxygenase (trimethyl-lysine 3-hydroxylase) catalyzes the hydroxylation of trimethyl-lysine at carbon 3 to yield 3-hydroxy-trimethyl-lysine. During this reaction, 2-oxoglutarate (α-ketoglutarate) is converted into succinate, and carbon dioxide is released. The human gene encoding trimethyl-lysine dioxygenase (TMLHE) maps to Xp28, and mutations in this gene have been found in patients with autism disorders, suggesting that the function of the protein is not well-known . The second enzymatic step in

the synthesis of L-carnitine is the aldolytic cleavage of 3-hydroxy-trimethyl-lysine between carbons 2 and 3 to yield glycine and 4-*N*-trimethyl-aminobutyraldehyde. The gene coding the aldolase that catalyzes this reaction has not been identified.

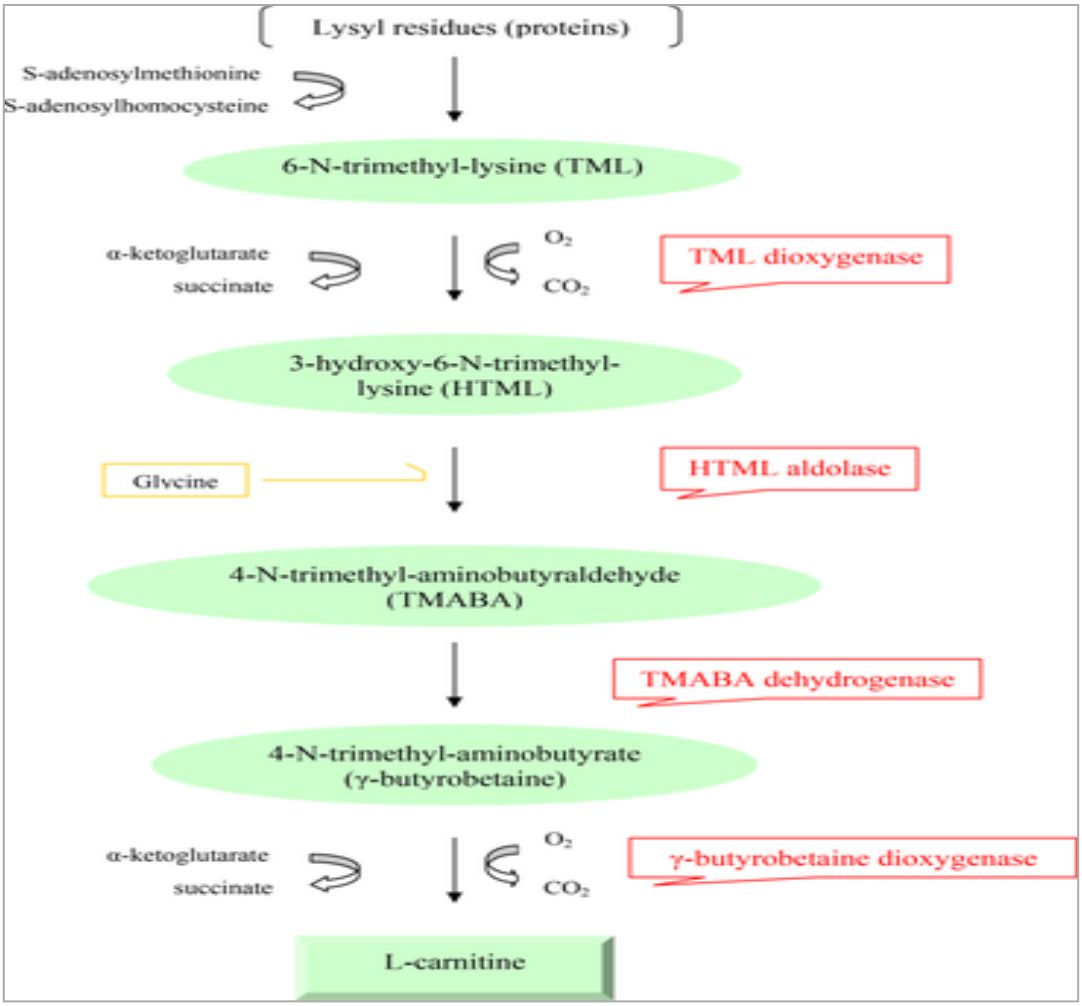

Figure 2.3. Pathway of l-carnitine synthesis. Adapted according Adeva-Andany, Calvo-Castro et al. 2017.

The third step in L-carnitine synthesis is assumed to be the dehydrogenation of the aldehyde 4-N-trimethyl-aminobutyrate to 4-butyrobetaine (4-N-trimethyl-aminobutyrate), but the human gene encoding the enzyme that catalyzes this step has not been identified, and no congenital deficiency has been documented. The last enzymatic step is the hydroxylation of 4-butyrobetaine at carbon 3 by the enzyme 4-butyrobetaine dioxygenase (4-butyrobetaine hydroxylase) to yield L-carnitine. Like the first reaction of the pathway, 2-oxoglutarate (α-ketoglutarate) is converted into succinate, and carbon dioxide is released. The enzyme 4-butyrobetaine dioxygenase adds the hydroxyl group that L-carnitine uses to form ester bonds with acyl moieties. The gene BBOX1 located at 11p14.2 encodes 4-butyrobetaine

dioxygenase. A homozygous deletion containing the BBOX1 gene has been reported in a girl with microcephaly, speech delay, growth retardation and facial anomalies (Kraemer et al., 2008).

Human tissue distribution and subcellular location of the human enzymes involved in the endogenous synthesis of L-carnitine have been barely investigated; therefore, the sites of L-carnitine synthesis have not been elucidated. In autopsy samples, 4-butyrobetaine dioxygenase activity is found in kidney, liver and brain, being absent from skeletal muscle and heart. The highest activity of 4-butyrobetaine dioxygenase in human tissues is detected in the kidney . Besides endogenous synthesis, humans obtain L-carnitine through dietary food. It has been estimated that the average adult diet provides approximately 75% of daily L-carnitine requirement. The bioavailability of dietary L-carnitine ranges from 54% to 87% while the bioavailability of pharmacological doses of L-carnitine is 5–18%. Therefore, intestinal absorption of supplemental L-carnitine is less efficient than that of dietary L-carnitine. Intestinal absorption of L-carnitine occurs via passive and active mechanisms. Studies using human intestinal mucosa have detected passive diffusion of L-carnitine in both the small intestine and the colon and active transport in the duodenum and ileum. Long-chain fatty acids constitute a basic substracts for oxidative energy metabolism in the myocardium. After transport through the cell membrane, they undergo activation to acyl-CoA in the cytoplasm or on the outer mitochondrial membrane. Although some of the activated fatty acids undergo esterification to triglycerides, most become substrates for B-oxidation in the mitochondria.

The primary function of L-carnitine is to allow the entry of esterified fatty acids (source for ATP synthesis) into the mitochondrial matrix, where B-oxidation occurs. The implication of carnitine at this point is critical because it has been shown that disturbances in the uptake of L-carnitine in muscle or heart cells can lead to myopathy and heart disease (Seim et al., 2001). In general, carnitine serves as a carrier for the acyl groups of short- and medium-chain fatty acids are transported into the mitochondrial matrix without any assistance from carnitine in the process. Long-chain acyl groups of fatty acids are transported exclusively as carnitine esters by a carnitine chamber called translocase, which is constituted as a transmembrane protein in the inner mitochondrial membrane. Despite this seemingly large role, this function is active for the oxidation of fatty acids B, as well as for the maintenance of acyl-coenzyme A (acyl-CeA). By themselves, acyl-CoA esters are impermeable to intracellular membranes.

The carnitine system has evolved to allow their transport across membranes and thereby facilitate their specific metabolic roles. This is possible due to the presence of carnitine/acylcarnitine transporters on cell membranes, which move these denatives between intracellular compartments.

The main function of L-carnitine in the body is facilitation lipid oxidation by transporting long-chain fatty acids into the inner mitochondria region where they undergo β-oxidation. In order for fatty acids (from food intake or adipose tissue) to produce energy they must be changed into acyl CoAs prior to β-oxidation; however, since acyl CoAs cannot cross cell walls, carnitine comes into place to help with the transportation through the mitochondrial wall. Therefore, without carnitine, most of the dietary lipids cannot be used as an energy source and our body would accumulate fatty-acids resulting in obesity.

In humans, carnitine is absorbed in the small intestinal mucosa by sodium-dependent active transport and by passive transport. In blood, carnitine does not need protein for a carrier, and is present in the free or acylcarnitine form. Based on carnitine's function as a transporter of fatty acids, early work investigating the effects of carnitine focused on the experimental paradigm that carnitine supplementation would enhance skeletal muscle carnitine concentrations and increase transport (and thus oxidation) of fatty acids (Kraemer et al., 2008).

Also, L-carnitine is important for heart and brain function, muscle movement, and many other body processes. The body can convert L-carnitine to other chemicals called acetyl-L-carnitine and propionyl-L-carnitine and L-carnitine helps preserve muscle glycogen and promote fat oxidation. It also spares the use of amino acids as energy sources during exercise, making them potentially available for new protein synthesis, and decreases the accumulation of lactate. However, research findings on the effectiveness of supplemental carnitine on athletic performance are mixed (Pekala et al., 2011).

2.7. Can L-Carnitine supplementation be useful in physical exercise?

During muscle contraction, aerobic and anaerobic metabolic pathways contribute to the energy supply according to the duration and intensity of muscle effort. There is an inverse relationship between the duration and the intensity of muscle effort, i.e., very intense muscle contractions can be maintained only for a short duration, while less intense contractions can be sustained or repeated for longer periods. Exercise can be classified as low-to-moderate intensity (<70% maximal oxygen consumption, VO2max), or high intensity (>75%, VO2max). At low work rates, muscle aerobic metabolism predominates, lactate does not accumulate, and exercise can be sustained. By contrast, at high work rates, lactate accumulates in muscle and blood, and subjects become rapidly fatigued. Due to the availability of L-carnitine over-the-counter, the use of carnitine as a supplement is often disproportionate among endurance athletes. Furthermore, since it has been suggested that carnitine saves muscle glycogen and promotes fat oxidation, its integration is recommended to lose weight (Pooyandjoo et al., 2016). Carnitine supplementation has been also reported to spare the use of amino acids as energy sources during exercise making them potentially available for new protein synthesis (Fielding et al., 2018). This notion justifies the use of carnitine to increase muscle mass during endurance exercise. Indeed, a study conducted on dogs demonstrated that supplemented carnitine experienced less protein degradation as a result of exercise (Varney et al., 2017).

Despite many years of research on the role of L-carnitine in muscle metabolism, it is yet not completely established whether carnitine supplementation can improve physical performance in healthy subjects. Data on the effect of carnitine supplementation on exercise performance, maximal aerobic capacity, blood lactate response, or substrate utilization during exercise yielded contradictory results . The oral administration of 4 g/day of carnitine for 2 weeks was demonstrated to significantly increase VO2max in competitive walkers (Marconi et al., 1985). The same result was obtained by Dragan and coll. in two different studies, one conducted on 40 and the other on 110 top athletes, both orally supplemented with 3 g carnitine for 3 weeks (Drăgan et al., 1987). Dragan and coll. also reported that 1 g of carnitine for 6 weeks or 2 g carnitine supplementation for 10 days induced higher performances in 7 junior athletes (Drăgan et al., 1989) and 1 g carnitine intravenously furnished ameliorated physical output and muscle contraction (Drăgan et al., 1988). Two

grams of carnitine furnished orally before a high-intensity exercise, in moderately trained males, also demonstrated to increase VO2max (Vecchiet et al., 1990). An effect on mitochondrial respiratory chain enzyme activities was also measured after the oral supplementation of 2 g carnitine for 4 weeks in 14 endurance athletes (Huertas et al., 1992). Vice versa, 6 g carnitine furnished for a couple of weeks in 8 healthy males failed to influence the VO2max and the respiratory exchange ratio (Vukovich et al., 1994). After supplementation, carnitine must be transported from the plasma into tissues. To this respect, it has been reported that muscle, with respect to other tissues, has a much lower net turnover of carnitine; this feature makes muscle, unlike other tissues, particularly refractory to carnitine supplementation (Stephens et al., 2006).

Furthermore, we must consider that, in physiological conditions, carnitine is transported in the muscle against a concentration gradient and that OCTN2 transporter, having a kilometer value (3–5 μM) below plasma carnitine concentrations (30–50 μM), is saturated at the physiological carnitine concentrations. Thus, it is unlikely that an increased plasma concentration of carnitine can cause higher transport of carnitine in the muscle (Longo et al., 2016, Fielding et al., 2018). Based on these considerations, it is conceivable to predict that oral carnitine supplementation would have little if any effect on muscle carnitine content in humans, and thus on muscle metabolism. Indeed, studies have demonstrated that even if long-term carnitine administration in humans increases plasma carnitine concentrations, but it does not increase muscle carnitine content (Evans and Fornasini, 2003).

Fats and carbohydrates represent the two major energy sources for physical exercise. Either source can predominate, depending upon the duration and intensity of exercise, degree of prior physical conditioning, and the composition of the diet consumed in the days before the exercise. To guarantee a high delivery of these substrates to the muscle, during the passage from a moderate to maximal exercise intensity a higher blood flow to legs has been demonstrated in steady-state 1-leg kicking performed for several minutes (Gnoni et al., 2020).

Exercise-induced muscle damage, and the subsequent pain, can have a significant impact on exercise performance by limiting training activity and decreasing the quality of life. Indeed, exercise itself leads to a depletion of L-carnitine in the muscle (Fielding et al., 2018). The link between L-carnitine levels, particularly in the plasma and the muscle, and enhanced exercise capacity have been reported in many trials. With the commercial availability of l-

carnitine in the early 1980s, studies were initiated to examine the effect of l-carnitine supplementation on metabolism during exercise. In light of its fundamental role in the β-oxidation of fatty acids for the purpose of energy production, and its role in the regulation of the acetyl-CoA pool, studies on l-carnitine as an ergogenic aid initially focused on of its interaction with exercise. Arenas et al. first reported that dietary supplementation of 1 g of l-carnitine given twice daily during 6 months of exercise training led to an increase in muscle l-carnitine levels (total and free) compared to placebo. Endurance runners and to a lesser extent sprinters showed a significant decrease in muscle free L-carnitine as a result of exercise only. These levels were reversed by L-carnitine supplementation (Arenas et al., 1991).

2.8. Concurrent training: benefits and mechanism of action

Concurrent training (CT) refers to a workout regimen that combines both resistance or strength training and endurance or aerobic training within the same overall training program. Both strength and endurance training regimens induce distinct skeletal muscle adaptations. It has been suggested that when performed in conjunction with a high frequency, volume, and intensity, conflicting adaptations may occur. If not implemented properly, concurrent strength and endurance training may result in reduced strength training (ST) adaptations. The negative interaction between strength training (ST) and endurance training (ET) has been defined as the interference effect. The advancements in technology have increased our understanding of the molecular mechanisms behind the exercise-induced adaptations to both strength and endurance stimuli. The molecular basis of muscular adaptation in response to different training regimens is very complex. It involves increases in the expression or activity of genes and proteins in order to increase contractile tissue (i.e., muscle hypertrophy) or mitochondrial content. Furthermore, there is considerable cross-talking and redundancy between signaling pathways that control exercise induced adaptations (Spurway and MacLaren, 2006). Hickson, with his pioneering work in early 1980s, reported that after a concurrent training (CT; e.g., the simultaneous training of strength and endurance) intervention, resistance training-induced adaptions were lower compared to those that occurred when individuals perform only resistance training. Hickson referred to this phenomenon as the “Interference effect”, however, it is now known as the “Concurrent training effect” (CTE) (Hickson, 1980).

In contrast to the experimental settings, in the “real” world and for the general population, the combination of both resistance and endurance exercise in a training program leads to superior adaptations in health-related and body function variables, independent of age or sex, including increases and/or improvements of basal metabolic rates, insulin sensitivity, glucose/lipids metabolism, lipidemic profile and body composition, while both muscular hypertrophy/strength/power and endurance capacities are increased. Additionally, the majority of sports are neither “endurance-based” nor “strength–power-based”, but of a mixed type, with performance to be determined by the specific contribution of muscle strength/power and endurance, which varies between sports. Thus, it is aim to maximize training adaptations from both training modules by what is known as “concurrent training” (e.g., simultaneously training for both strength and endurance regiment) (Methenitis, 2018).
Both resistance and endurance exercises activate different types of muscle fibers. Resistance training primarily targets fast-twitch muscle fibers for strength and power, while aerobic exercise engages slow-twitch muscle fibers for endurance. Concurrent training recruits and stimulates a broader spectrum of muscle fibers, leading to comprehensive muscle adaptations. Different exercise modalities activate distinct molecular signaling pathways within muscles. For instance, resistance training activates pathways related to muscle protein synthesis (mTOR pathway), promoting muscle hypertrophy and strength gains. On the other hand, aerobic exercise activates pathways involved in mitochondrial biogenesis and fat oxidation (AMPK pathway). Concurrent training, by combining both modalities, triggers a complex interplay of these pathways, potentially enhancing multiple aspects of cellular adaptation (Knuttgen, 2007).

Understanding these mechanisms helps in designing effective concurrent training programs by optimizing exercise selection, volume, intensity, and sequencing to maximize the benefits while mitigating potential interference between resistance and aerobic training adaptations. Individualizing training plans based on goals, fitness levels, and balancing recovery is crucial to achieve desired outcomes from concurrent training (Lee, 2019).

Adaptations due to concurrent training can be either acute or long-term in nature. The former includes homeostatic regulatory responses, activation of oxygen transport and use of energy reserves with the main aim being to optimize ATP resynthesis. Structural and functional changes occurring during prolonged periods of training are associated with long-term adaptations, which, in turn, are founded on adaptive protein synthesis. For instance, endurance (i.e., aerobic) training results in an increased concentration of myoglobin,

mitochondrial enzyme activity, mitochondrial density, increased respiratory capacity and oxygen transport, as well as enhanced cardiac output. On the other hand, strength and power training results in increased muscle cross-sectional areas, or hypertrophy. However, these training-induced adaptations at the muscle cell level are also associated with concomitant adaptations in myocardial, hepatic, renal, endocrine and other cells. Bone growth is also affected by exercise. It has been found that low- and high-intensity exercise training may respectively enhance and hinder bone growth in children (Matsuda et al., 1986).

Induced muscle hypertrophy is the cumulative effect of resistance training sessions that have resulted in a net positive balance between the rate of muscle protein synthesis (MPS) and muscle protein breakdown (MPB). Despite the complexity of the protein synthesis process, it is regulated through signaling pathways that enhance mRNA translation. The mammalian or mechanistic target of rapamycin complex 1 (mTORC1) is a key kinase controlling protein synthesis and muscle hypertrophy. On the other hand, ET-induced adaptions are attributed to increases in mitochondrial function and content within the skeletal muscles that ultimately results in improved oxidative capacity and endurance performance. Even though ET has been shown to activate multiple signals. The peroxisome-proliferator-activated receptor γ co-activator-1α (PGC-1α) has been referred to as a key driver of mitochondrial biogenesis. PGC-1α is a transcriptional co-activator that induces mitochondrial biogenesis. It activates different transcription factors that modulate gene expression resulting in the encoding of mitochondrial proteins.

Even though multiple signals can modulate PGC-1α, it has been suggested that AMP-activated protein kinase (AMPK) is one of the major contributors as it controls the transcription and activity of PGC-1α. AMPK also plays an important role in cellular energy metabolism during exercise and nutrient deprivation. Furthermore, AMPK has been referred to as a sensor for cellular energy status as it is activated by increases in cellular AMP:ATP ratio. Once activated, AMPK blunts the biosynthetic process that demands ATP consumption and stimulates an energy generating process in order to re-establish cellular energy levels. In fact, animal model studies have demonstrated that AMPK activation can inhibit mTORC1 activity, its downstream and blunts MPS and skeletal muscle hypertrophy. In this regard, the greater energy demands and the different signalling pathways involved with CT compared to a single mode regimen create a conflicting environment within the skeletal muscle. Therefore, a molecular hypothesis has been put forward to explain the reduced training adaptation after CT. In this hypothetical model referred to AMPK-Akt

switch hypothesis, the AMPK phosphorylates tuberous sclerosis complex−2 (TSC2). TSC2 switches off the mTORC1-signaling cascade, ultimately decreasing the potential for muscle fibber hypertrophy after CT regimen (Fig. 2.4) (Schumann and Rønnestad, 2019).

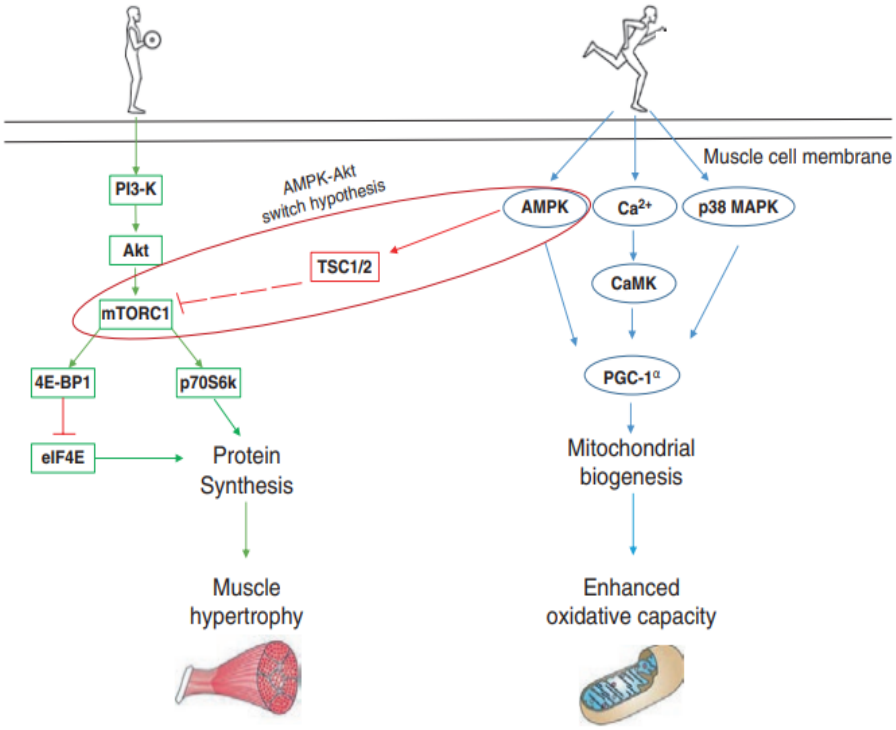

Fig. 2.4. Schematic diagram summarizing signaling pathways activated by strength (ST) and endurance training (ET) and the AMPK-Akt switch hypothesis. ST induces an increase in the activity of protein kinase B (Akt), mammalian target of rapamycin complex 1 (mTORC1), that modulates rates of protein synthesis though phosphorylation of eukaryotic initiation factor 4E-binding protein (4E-BP1) that promotes dissociation between 4E-BP1 and eukaryotic initiation factor 4E- (eIF4E) and activation of 70 kDa ribosomal protein kinase (p70S6K). ET activates signaling cascade that regulates metabolic process and mitochondrial biogenesis that comprises adenosine-monophosphate-activated protein kinase (AMPK), p38 mitogen-activated protein kinase (MAPK), calmodulin-dependent protein kinase (CaMK) and proliferator-activated receptorgamma coactivator 1-alpha (PGC-1α). In the Akt-AMPK switch hypothesis model, AMPK activated by ET may inhibit mTORC1 signaling cascade through tuberous sclerosis complex (TSC) blunting ST-induced protein synthesis. Figure was adapted from: Hawley, JA. 2009.

2.9. Definition and components of concurrent training

Concurrent training is a program that combines resistance and endurance training to maximize all aspects of physical performance (Rubin et al., 2024). Resistance (strength) training involves exercises that cause muscles to contract against an external resistance with the expectation of increases in strength, tone, mass, and/or endurance. Examples include weightlifting, bodyweight exercises (like push-ups and pull-ups), and resistance band exercises. It is among the most important components for almost every sport. Strength

training aims to increase the athlete's competition performance by: (a) enhancing the neural component of muscle contraction, and (b) augmenting the muscle-fibre size (Fig 2.5).

The latter has been based on the hypothesis that exercise training causes an accumulation of metabolites which specifically induce the adaptive synthesis of structural and enzyme proteins resulting in larger and more efficient muscle (Viru, 2001). Consequently, muscle hypertrophy is the result of a cumulative effect of several training sessions arranged in particular training cycles. Resistance training induces hypertrophy in muscle fibers of all types, particularly those designated as fast-twitch or type II fibers, the area occupied by which may increase by as much as 90%, mainly due to increased rates of protein synthesis and the associated augmentation in myofibrillar size. However, speed or power training results in a selective hypertrophy of fast-twitch glycolytic (type IIb) or fast twitch oxidative (type IIa) fibers. It should be stressed here that stretching exercise can increase protein synthesis in the exercised muscle through a chain of events which involve satellite cell multiplication (Spurway and MacLaren, 2006).

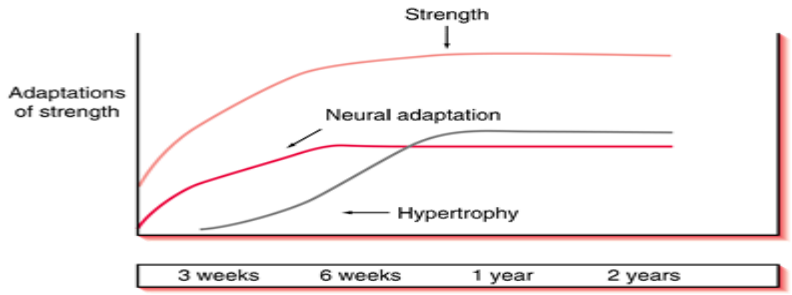

Figure 2.5. Strength training adaptations. adopted according Spurway et al., 2006.

Aerobic (endurance) training: Also known as endurance or cardiovascular training, this involves exercises that improve the efficiency of the cardiovascular system in absorbing and transporting oxygen. Examples include running, cycling, swimming, and rowing (Wilson et al., 2012). Endurance training, also known as aerobic or cardiovascular training, focuses on improving the efficiency and performance of the cardiovascular and respiratory systems. It enhances the body's ability to sustain prolonged physical activity by increasing the efficiency of oxygen uptake, transportation, and utilization (Jones and Carter, 2000). Aerobic training brings about adaptations that influence the processes of energy transportation and use by the working muscle. Major cell and anatomical adaptations include increases in the size and number of mitochondria, density of capillaries, hemoglobin concentration, and left

ventricular enlargement. These directly contribute to increments in maximum oxygen uptake (VO2 max), providing the foundation for improved physical performance. VO2 max is a major indicator of endurance as it represents the maximum ability of an athlete to utilize oxygen. Improved aerobic endurance requires enhanced oxidative potential of muscle fibres, which is founded in an increased number and volume of mitochondria (increased mitochondrial density) and elevated activity of oxidative enzymes (Spurway and MacLaren 2006).

2.10. Physiological adaptations of concurrent training

Concurrent training can stimulate muscle hypertrophy and strength gains due to resistance training. Simultaneously, endurance exercise can enhance mitochondrial density and oxidative capacity within muscle fibers, improving endurance performance. Concurrent training affects the nervous system by improving coordination, motor control, and the recruitment of muscle fibers, leading to better overall performance. Combining both types of exercises may increase the risk of overtraining due to higher cumulative stress on the body. Adequate rest and recovery periods are crucial to prevent overtraining and maximize adaptations. This kind of training influence body composition positively by reducing body fat percentage while simultaneously increasing muscle mass.

While it can enhance multiple aspects of fitness, the interference effect suggests that combining endurance and resistance training in the same session may slightly attenuate strength or muscle gains compared to focusing solely on one type of training. However, the degree of interference might vary based on factors like training volume, intensity, and individual differences (Furrer et al., 2023).

The aerobic component of concurrent training (e.g., running, cycling) improves cardiovascular endurance by enhancing heart function, increasing stroke volume, and improving the efficiency of oxygen utilization. It can impact metabolic adaptations, such as increased fat oxidation and improved insulin sensitivity. Resistance training can lead to enhanced muscle glycogen storage and utilization, while aerobic exercise improves fat metabolism. Both resistance and endurance exercises can impact hormonal levels. Resistance training tends to elevate hormones like testosterone, which supports muscle

growth, while endurance exercise can influence hormones like cortisol and adrenaline, impacting metabolism and stress responses (Hughes et al., 2018).

These physiological changes resulting from concurrent training are influenced by various factors including the frequency, intensity, duration, and order of exercises within the training program, as well as an individual's genetics, nutrition, and overall health status. Balancing these components is key to maximizing the benefits of concurrent training while minimizing potential drawbacks.

The adaptive responses of muscle to exercise are specific to the training mode Endurance training induces increases in mitochondrial density and enzymes of the TCA cycle (tricarboxylic acid) and electron transport chain as well as increases in capillary density, myoglobin, and VO2max. These adaptations also may be responsible for decreases in lactate production and reduced lactate accumulation as well as elevated clearance rates (Gravelle and Blesssing, 2000).

2.11. Adoption for concurrent training in obese people

Globally, obesity has reached epidemic proportions in the current 21st century and is associated with higher risk of premature mortality (Lavie et al., 2018). Indeed, obesity is an independent risk factor for cardiovascular disease, including hypertension, coronary heart disease, heart failure, and sudden cardiac death. Health care spending derived from obesity related diseases has exponentially increased during the last decade and is expected to continue rising. Therefore, the application of cost-effective measures to reduce obesity and its related health burden are of clinical and scientific interest. Over the past years, different strategies have been found to improve cardiometabolic health in individuals with obesity. Physical activity is considered an integral approach for obese individuals, not only for weight loss goals but also for reducing the risk of CVD, type 2 DM, and all-cause mortality (Ma et al., 2017).

Although physical inactivity is a key factor in the etiologic and progression of chronic and cardiovascular and metabolic disease, the precise mechanisms through which physical inactivity increases cardio vascular disease risk factors are incompletely understood. In

reverse, both aerobic and resistance training have been shown to improve lipid profiles, body composition and blood pressure in obese people (Atashak et al., 2016).

The combination of aerobic and resistance training (i.e., concurrent training) has been positioned as a promising tool to improve cardiovascular and metabolic profiles in both healthy individuals (Bennie et al., 2020) and patients with cardiometabolic diseases. Concretely, previous studies have reported that concurrent training is an effective antihypertensive and anti-inflammatory therapy, improving in turn the glycaemic and lipid profiles as well as hepatic function. Nevertheless, these previous studies included individuals with different biological characteristics making it necessary for further investigations attaining patients with cardiometabolic disturbances (Amaro-Gahete et al., 2021).

Concurrent training is effective in promoting weight loss and reducing body fat in obese individuals. Aerobic exercise helps burn calories during the workout, while resistance training helps build muscle mass, which can increase resting metabolic rate and aid in fat loss over time (Medeiros et al., 2015). It helps in improving body composition by reducing body fat percentage while increasing lean muscle mass. This can lead to better overall health and metabolic function. Obese individuals often have metabolic disturbances, such as insulin resistance (Wu and Ballantyne, 2020).
Concurrent training has been shown to improve insulin sensitivity and glucose regulation, which can reduce the risk of type 2 diabetes and other metabolic conditions. The aerobic component of concurrent training improves cardiovascular fitness, reducing the risk of heart disease and other cardiovascular complications commonly associated with obesity. Resistance training in concurrent training can help obese individuals increase muscle strength and enhance muscular endurance, leading to improved functional capacity and better ability to perform daily activities. Regular participation in concurrent training can help reduce obesity-related health risks such as hypertension, high cholesterol levels, and metabolic syndrome (Atashak et al., 2016).

2.12. Previous Studies on L-Carnitine Supplementation

2.12.1. Human studies

Zhang et al. (2021) revealed that enhancing fatty acids oxidation via L-Carnitine attenuates obesity-related atrial fibrillation and structural remodeling by activating AMPK signaling and

alleviating cardiac lip toxicity. Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in clinical setting. Its pathogenesis was associated with metabolic disorder, especially defective fatty acids oxidation (FAO). Taken together, results demonstrated that FAO promotion via LCA attenuated obesity-mediated AF and structural remodeling by activating AMPK signaling and alleviating atrial lip toxicity. Thus, enhancing FAO may be a potential therapeutic target for AF (Zhang et al., 2021).

Vecchio et al. (2021) studied on the effects of L-Carnitine supplementation on physical performance in healthy subjects. The aim of this study was to identify the correct dosage of supplementation to obtain improvements in physical performance and evaluate the changes related to L-carnitine supplementation in specific metabolic parameters, such as VO2 at rest and after physical activities in healthy subjects. Based on thier study VO2 at rest could be used to clinically follow individuals during physical activity. Moreover, the supplementation should have a correct dosage to have maximum effect and L-carnitine supplementation improves body strength, sports endurance and exercise capacity (Vecchio et al., 2021).

L-carnitine supplementation vs cycle ergometer exercise for physical activity and muscle status in hemodialysis patients: Twenty patients were divided into L-carnitine and cycle ergometer groups and were followed for 3 months. Muscle and fat mass, physical activities, and muscle status were evaluated by an impedance, physical function test, and magnetic resonance imaging, respectively. The L-carnitine significantly increased muscle mass (P = .023) and thigh circumference (P = .027), decreased fat mass (P = .007), and shortened chair stand-up time (P = .002) and 10-m walk test (P = .037). The fat fraction was improved by the l-carnitine (P = .047). Compared with the exercise group, L-carnitine improved the changes in 10-m walk test (P = .026), chair stand-up time (P = .014), and thigh circumference (P = .022). Baseline fibroblast growth factor-21 and myostatin levels predicted the L-carnitine-associated changes in exercise activities. L-carnitine, rather than exercise, improved physical activity and muscle status in hemodialysis patients (Yano et al., 2021).

Askarpour and et al. (2020), in one study demonstrated about beneficial effects of L-carnitine supplementation for weight management in overweight and obese adults. Interestingly subgroup analysis revealed that L-carnitine showed anti-obesity effects only in overweight and obese subjects; L-carnitine decreased weight, and BMI alone when combined with other lifestyle modifications. Anthropometric indexes were not changed following L-carnitine supplementation among patients' undergoing hemodialysis. Thier study revealed that L-

carnitine supplementation might have a positive effect in achieving an improved body weight and BMI especially in overweight and obese subjects (Askarpour et al., 2020).

This study aimed to examine the 9-weeks effects of L-carnitine supplementation on exercise performance, anaerobic capacity, and exercise-induced oxidative stress markers in resistance-trained males. In a double-blind, randomized, and placebo-controlled treatment, 23 men (age, 25±2y; weight, 81.2±8.31 kg; body fat, 17.1±5.9%) ingested either a placebo (2 g/d, n=11) or L-carnitine (2 g/d, n=12) for 9 weeks in conjunction with resistance training. L-carnitine supplementation enhances exercise performance while attenuating blood lactate and oxidative stress responses to resistance training (Koozehchian et al., 2018).

The effect of L-carnitine on weight loss in adults: a systematic review and meta-analysis of randomized controlled trials. The results of meta-regression analysis of duration of consumption revealed that the magnitude of weight loss resulted by carnitine supplementation significantly decreased over time ($p = 0.002$). We conclude that receiving the carnitine resulted in weight loss. Using multiple-treatments meta-analysis of the drugs and non-pharmacotherapy options seem to be insightful areas for research (Pooyandjoo et al., 2016).

In a research, exercises were performed interval for four weeks and three 60-minute sessions each week with an intensity of 65-80% of maximum heart rate. Before the start of training and supplementation and after four weeks, aerobic capacity was measured using Bruce test and blood lactate level by lactometer and resting blood pressure and maximum and resting and maximum heart rate. L-carnitine supplementation improves aerobic capacity and increases fatigue time $P < 0.01$ (and decreased lactic acid content was rested ($P = 0.01$), but had no significant effect on the amount of active lactic acid .Supplement along with exercise improved aerobic capacity ($P < 0.001$) and reduced resting lactic acid content ($P = 0.01$), but had no significant effect on the amount of active lactic acid. Also, the effect of exercise and supplementation and exercise There was no significant difference with aerobic supplementation and resting and active lactate levels in the blood, so carnitine supplementation with exercise could be used to improve athletic performance and increase aerobic capacity (Kashef and Saei, 2017).

Arazi and et al. (2013), The effect of acute L-carnitine supplementation on the blood lactate, glucose, VO2max and power in trained men: a brief report. These findings indicate that acute

oral supplementation of L-carnitine can induce fatigue decreasing and improvement of aerobic and anaerobic performance (Arazi et al., 2013).

L-carnitine supplementation in humans has demonstrated a wide range of health benefits, particularly in cardiovascular health, athletic performance, metabolic health, cognitive function, and certain medical conditions. L-carnitine, a naturally occurring compound involved in mitochondrial fatty acid transport, has been widely studied for its potential benefits in exercise performance, fat metabolism, and recovery. The effectiveness of L-carnitine supplementation varies significantly depending on factors such as dosage, baseline fitness levels, and whether it is combined with exercise. While its roles in fat metabolism, recovery, and metabolic health are supported by numerous studies, the overall evidence suggests that L-carnitine holds considerable potential as a supplement to enhance both health and performance.

2.12.2. Animal studies

Nazari and et al. (2023) investigated the combined effects of L-Carnitine and Conjugated Linoleic Acid (CLA) on weight loss and adipose tissue microRNA levels. Forty male Wistar rats weighing 150–200 g and about 8 weeks old were fed either a normal fat diet (NFD) or a high-fat diet (HFD) for 8 weeks. Afterwards, the HFD group was randomly divided into four subgroups: control, LC (200 mg kg−1), CLA (500 mg kg−1), and both (n = 8 in each group). The study lasted for an additional 4 weeks. The animals' weights were recorded regularly, and after 12 weeks, miRNAs were extracted from epididymal adipose tissue and analysed using real-time PCR. CLA and LC, which are considered weight loss supplements, can potentially regulate metabolism and cellular pathways. However, their combination did not show a synergistic effect on weight loss, possibly due to the reduction in miR-27a expression. Further studies are needed to evaluate the effects of combined fat burners on obesity treatment (Nazari et al., 2023).

Demirdag and et al. (2004) investigated the protective effect of L-carnitine in experimental acute liver damage induced by CCl. Fifty rats were allocated to five equal groups. The first group was the control (group 1), the second group received an intraperitoneal CCl4 injection for 3 days (group 2), and the third group received a 50 mg/kg subcutaneous L-carnitine injection for 4 days, beginning a day before CCl4 injection. It appears that L-carnitine has a

protective effect in the early stage of experimental acute liver damage induced by CCl4. As the toxic effect or damage continues, its effect lessens (Demirdag et al., 2004).

In another study by Brandsch and Eder (2002) showed effect of L-Carnitine on weight Loss and body composition of rats fed a hypocaloric diet. An experiment was conducted with 36 rats with an initial body weight of about 460 g. One-third of the rats were killed, the remainder were divided into two groups (control group, treated group) and fed a semi synthetic diet at an energy level of about half of the rats' maintenance requirement. The basal diet was essentially carnitine-free. The diet of the treated group was supplemented with L-carnitine (5 g/kg). he rat model used here did not show a positive effect of L-carnitine supplementation on weight loss and body composition of rats fed an energy-deficient diet. The animals' endogenous carnitine synthesis was obviously adequate to ensure efficient β-oxidation of fatty acids during the catabolic phase (Brandsch and Eder, 2002).

Oral supplementation of propiony l-L-carnitine reduces body weight and hyperinsulinaemia in obese Zucker rats was another research about this supplemet in rlated to animal studies. This work was by Carmen Mingorance and et al. (2009). Propiony l-L-carnitine (PLC) is an SCFA esterified to carnitine that plays an important role in fatty acid oxidation and energy expenditure, in addition to having a protective effect on the endothelium. In order to evaluate the effect of PLC on an animal model of obesity, insulin resistance and, consequently, endothelial dysfunction, lean and obese zucker rats (OZR) received either vehicle- or PLC-supplemented drinking water (200 mg/kg per d) for 20 weeks. Body weight, food intake, systolic blood pressure and heart rate were controlled weekly and an oral glucose tolerance test was performed. The protection of vascular function found after treatment with PLC in an animal model of insulin resistance supports the necessity of clinical trials showing the effect of L-carnitine supplements on metabolic disorders (Mingorance et al., 2009).

Finally, in a work oabout the effects of L-carnitine on obesity. They investigated the separate and combined effects of L-carnitine and antioxidant supplementation on carnitine and lipid concentrations in trained and nontrained animal. Supplementation of L-carnitine and antioxidants improve lipid profiles and exercise ability in exercise-trained rats. Also, both exercise training and supplementation of carnitine and antioxidants improved lipid profiles and carnitine metabolism in humans, suggesting that carnitine and antioxidant supplementation may improve exercise performance (Cha, 2008).

L-carnitine supplementation was used in this study to enhance fatty acid oxidation so as to ameliorate diet-induced disturbances in lipid metabolism. Male wistar rats (8–9 weeks old) were fed with either corn starch or high-carbohydrate, high-fat diets for 16 weeks. Separate groups were supplemented with L-carnitine (1.2% in food) on either diet for the last 8 weeks of the protocol. High-carbohydrate, high-fat diet-fed rats showed central obesity, dyslipidaemia, hypertension, impaired glucose tolerance, hyperinsulinaemia, cardiovascular remodelling and non-alcoholic fatty liver disease. L-carnitine supplementation attenuated these high-carbohydrate, high-fat diet-induced changes, together with modifications in lipid metabolism including the inhibition of stearoyl-CoA desaturase-1 activity, reduced storage of short-chain monounsaturated fatty acids in the tissues with decreased linoleic acid content and trans fatty acids stored in retroperitoneal fat. Thus, L-carnitine supplementation attenuated the signs of metabolic syndrome through inhibition of stearoyl-CoA desaturase-1 activity, preferential β-oxidation of some fatty acids and increased storage of saturated fatty acids and relatively inert oleic acid in the tissues (Panchal et al., 2015).

L-carnitine has been included in feline diets to enhance weight loss and reduce risk of hepatic lipidosis. However, many overweight cats are fed maintenance diets and are not undergoing weight loss. The objective of this study was to investigate how feeding lean and overweight adult cats dietary LC (100 mg/kg) during weight maintenance affected resting energy expenditure (EE), respiratory quotient (RQ), and play motivation. Twenty healthy adult cats were stratified by gender and body condition score (BCS) and randomly assigned to receive either a control food or the same food supplemented with 100 mg/kg LC (LC+) for 42 days. These results suggest that dietary LC fed at a low level of supplementation results in greater EE, lower RQ, and greater motivation to play in overweight, but not lean, cats fed to maintain weight. Future research should investigate whether a similar mechanism is present in cats fed ad libitum, the feeding management strategy commonly used (Shoveller et al., 2014).

Rivero and et al. (2002) showed to determine whether oral L-carnitine supplementation enhances the responses of skeletal muscle to training in seven 2-year-old Standardbreds. Four horses were supplemented with 10 g/day L-carnitine for 10 weeks and 3 horses served as controls. All horses were exercised regularly every second day on a treadmill for 5 weeks (training period) and housed in individual boxes for 5 additional weeks (detraining period). The training period consisted of 8 high- and 8 low-speed exercises carried out in alternating sequence. After detraining, most of these adaptations reverted towards the pretraining

situation. Therefore, exogenous carnitine has an additive effect on muscular responses to training and this should be favourable to improve athletic performance. Nevertheless, further studies are necessary to show whether muscle carnitine content is a limiting factor for fatty acid oxidation (Rivero et al., 2002).

Also, Carlson and et al. (2006) in a diferrent study reviewd that L-carnitine is required for mitochondrial fatty acid oxidation, but the effects of carnitine supplementation on nutrient metabolism during dry matter intake depression have not been determined in dairy cows. Studies in other species have revealed responses to l-carnitine that may be of specific benefit to dairy cows during the periparturient period. Eight lactating Holstein cows (132 ± 36 d in milk) were used in a replicated 4 × 4 Latin square experiment with 14-d periods. Treatments were factorial combinations of abomasal infusion of either water or l-carnitine (20 g/d; d 5 to 14) and either ad libitum or restricted intake (50% of previous 5-d dry matter intake; d 10 to 14) of a balanced lactation diet. Liver and muscle biopsies were obtained on d 14 of each period (Carlson et al., 2006). Research on L-carnitine in animals demonstrates a range of benefits, including enhanced fat metabolism, improved athletic performance, better reproductive health, and neuroprotection.

These findings suggest that L-carnitine can be a valuable supplement for various animal species, though the specific effects and optimal dosages may vary depending on the animal's needs and conditions.

2.13. Gaps in Literature

Identifying gaps in literature about the effect of L-carnitine supplementation during concurrent training on functional capacities and body composition in obese men involves a comprehensive review of existing studies. Here are some potential gaps you might explore:

- Limited studies on obese populations: Most research on L-carnitine supplementation has been conducted on athletes or non-obese individuals. There is a lack of studies focusing specifically on obese adult men. Many studies include mixed populations or do not specifically target obese individuals, which can obscure specific effects in this demographic.

- Concurrent training research: While there are studies on L-carnitine supplementation in conjunction with either resistance or aerobic training, research combining both (concurrent training) is scarce.

- Functional capacities measurement: The impact of L-carnitine on various functional capacities (e.g., strength, resting heart rate, blood pressure, oxygen saturation, maximal oxygen consumption) in obese men during concurrent training is not well-documented. Comprehensive evaluation of functional capacities over multiple time points during an 8-weeks intervention is rare. Existing studies may not use a broad range of functional tests to capture overall physical performance.

- Duration and dosage: There is a lack of consensus on the optimal duration and dosage of L-carnitine supplementation for achieving significant changes in body composition and functional capacities during concurrent training. The 8-week duration with consistent pre-, mid-, and post-testing intervals is not commonly explored. Most studies have varied durations and do not follow a strict testing schedule. Most studies have focused on short-term interventions. The long-term effects of L-carnitine supplementation combined with concurrent training on functional capacities and body composition in obese men remain unclear.

- Body composition changes: Although some studies have examined the effect of L-carnitine on body composition, comprehensive analyses involving fat free mass, body fat percentage, body mass index changes during concurrent training in obese men are limited.

Addressing these gaps can provide a more thorough understanding of how L-Carnitine supplementation and concurrent training interact to affect functional capacities and body composition in obese men, offering valuable insights for optimizing interventions.

2.14. Importance and potential contribution of current Study

To our knowledge, this is the first reported case that simultaneously analyses for factors of LCR, functional capacities, body composition for obesity male in both resistance and endurance trainings and also it would be a reduced cost and effect factor in non-pharmacological. In short, the important and contribution of the study is expected to be in field of:

- Advancements in obesity management: Insight into whether L-carnitine supplementation enhances concurrent training outcomes could lead to more effective and personalized interventions for obesity management in men. Understanding the potential synergistic effects may help tailor exercise programs by incorporating L-carnitine supplementation, potentially improving outcomes for obese individuals and improvement of the testing procedures and study methodology with specific tests in the most researched in related to supplements.

- Scientific understanding: Contribution to the existing body of knowledge by elucidating the effects and mechanisms of L-carnitine supplementation within the context of concurrent training specifically in obese populations. Investigating the potential metabolic and physiological mechanisms underlying the observed effects could uncover novel pathways for obesity management and exercise performance enhancement. Combining L-carnitine supplementation with concurrent training could lead to more effective fat loss and muscle preservation, essential components of a healthy body composition.

- Healthcare and clinical implications: Findings provided evidence-based guidance for healthcare practitioners in recommending adjunctive measures like L-carnitine to optimize exercise-based interventions for obese men and a novel methodology for measuring of L-carnitine along with concurrent training. Understanding whether L-carnitine supplementation positively impacts functional capacities and body composition may aid in mitigating obesity-related health risks in affected populations.

- Public Health impact: If proven effective and safe, the study outcomes might influence public health recommendations, potentially impacting policy

development in obesity management. Application of findings might lead to improved health outcomes for obese individuals, reducing the burden of obesity-related complications in the long term. Obesity is a major public health concern linked to numerous chronic diseases, including cardiovascular disease, diabetes, and metabolic syndrome. Understanding how supplements like L-carnitine can aid in managing obesity is critical for developing effective interventions.

The potential contributions of a study examining L-carnitine supplementation during concurrent training in obese men extend from refining obesity management strategies to advancing scientific knowledge and informing clinical practice. By addressing gaps in understanding the impacts of supplementation within specific exercise, the study offered valuable insights into optimizing interventions for obese individuals, ultimately contributing to improved health outcomes and enhanced strategies for obesity management. In summary, the study's importance lies in its potential to enhance understanding and management of obesity, improve exercise performance and adherence, inform evidence-based recommendations, optimize training programs, and guide future research, all of which contribute to better health outcomes for obese individuals.

3. RESAERCH PROBLEM, AIMS AND HYPOTHESE

3.1. Reserch problem

Despite extensive research, the effects of L carnitine supplementation in treating obesity are still unclear and equivocal. In spite of advancements in obesity management through exercise, optimizing functional capacities and body composition in obese individuals remains a challenge. The potential role of L-carnitine supplementation, known for its involvement in fatty acid metabolism and energy production, in enhancing the effects of concurrent training on functional capacities and body composition in obese men warrants investigation.

The primary problem addressed by this research is to investigate the isolated and combined effects with concurrent training of L-Carnitine supplementation on body composition and functional capacities in obese men. By exploring the potential synergies or additive effects of these interventions, the study aims to provide a comprehensive understanding of their impact on metabolic and physical outcomes, contributing valuable insights to the field of obesity management and exercise physiology.

Addressing this study problem will not only enhance our understanding of the physiological mechanisms underlying the response to concurrent training and L-carnitine supplementation but also inform the development of personalized and effective strategies for the treatment and prevention of obesity-related complications.

A trial by Roger Fielding et al (Fielding et al., 2018) could not demonstrate a protective effect of L-carnitine in exercise. But the study by Pooyandjoo et al (Pooyandjoo et al., 2016) found that L-carnitine might be an effective supplementation for weight loss in adults. Majid S. Koozehchian et al (Koozehchian et al., 2018) showed that L-carnitine might be suitable to enhance exercise performances.

While individual studies have explored the effects of L-carnitine or concurrent training in obesity, there is a noticeable gap in the literature concerning the combined impact of L-carnitine supplementation during concurrent training on functional capacities and body composition specifically in obese men. Understanding the potential synergistic effects of L-carnitine supplementation and exercise training in this demographic is essential for devising comprehensive obesity management strategies.

With regard to the above facts, it is important to clarify the effect of L-carnitine as a supplement on the functional capacities of obesity men during a Concurrent training. A training program may be used as a non-pharmacological treatment to improve these factors and energy balance.

Findings from this study could contribute to the development of more effective and tailored interventions for obese men, potentially improving their functional capacities and body composition. Identifying whether L-carnitine supplementation enhances concurrent training outcomes could have implications for healthcare practitioners in recommending personalized approaches for obesity management. Bridging the gap in current knowledge regarding the synergistic effects of L-carnitine supplementation and concurrent training in obese men could pave the way for further research in this area.

In summary, the lack of comprehensive studies exploring the impact of L-carnitine supplementation in combination with concurrent training on functional capacities and body composition in obese men necessitates further investigation. Addressing this gap could provide valuable insights into optimizing obesity management strategies. Remember to use scholarly references to support the importance of the problem and the potential significance of the proposed study. This structure provides a framework to introduce the problem, justify the need for the research, highlight the gap in current literature, and emphasize the study's potential contributions.

3.2. Aims of the study

The primary aim of this study is to investigate the efficacy of L-carnitine supplementation on enhancing functional capacities and optimizing body composition in obese men undergoing concurrent training .

The additional aims are to:

- Determine effects of L-carnitine supplementation on the body composition in obese men during a concurrent training.
- Determine effects of L-carnitine supplementation on the development functional capacities in obese men during a concurrent training.

3.3. Hypotheses

Based on the literature overview and literature analysis as well as on defined problem, purpose, aim and tasks of the dissertation, the following hypotheses are defined:

A] General hypotheses;

H_g – It is possible to define effect of L-carnitine along with concurrent training based on functional capacities and body composition characteristics in obesity men.

B] Supporting hypotheses;

H1 – Hypotheses for body composition;

H_{1-1} - Weight loss in obese men is significantly affected by L-carnitine along with concurrent training.

H_{1-2} – Body mass index **(**BMI) in obese men is significantly affected by L-carnitine along with concurrent training.

H_{1-3} – Body fat percentage **(**BF%) in obese men is significantly affected by L-carnitine along with concurrent training.

H_{1-4} – Fat free mass **(**FFM) in obese men is significantly affected by L-carnitine along with concurrent training.

H2 – Hypotheses for functional capacities;

H_{2-1} – One Repetitions Maximum **(**1RM) in obese men is significantly affected by L-carnitine along with concurrent training.

H_{2-2} – Maximal Oxygen Consumption **(**VO2max) in obese men is significantly affected by L-carnitine along with concurrent training.

H_{2-3} – Resting heart rate **(**RHR) in obese men is significantly affected by L-carnitine along with concurrent training.

H_{2-4} – Systolic Blood Pressure **(**SBP) in obese men is significantly affected by L-carnitine along with concurrent training.

H_{2-5} – Diastolic Blood Pressure **(**DBP) in obese men is significantly affected by L-carnitine along with concurrent training.

H_{2-6} – Oxygen Saturation **(**SpO2) in obese men is significantly affected by L-carnitine along with concurrent training.

4. METHODOLOGY

4.1. Research Design

This experimental research study utilized purposive sampling to select its sample based on specific criteria. The participants were then divided into three groups using a systematic random grouping method, ensuring an equal distribution of male subjects across each group. This research was characterized as both fundamental and applied, as it provided a novel approach within the existing body of knowledge in training technology, while also having practical applications for obese men.

4.2. Participants

Initially, 35 sedentary males were recruited based on the sampling technique and criteria. However, five individuals withdrawn from the study for reasons unrelated to the research. Consequently, a cohort of 30 males, with a mean weight of 106.48 ± 11.78 kg, height of 1.77 ± 0.08 m, BMI of 33.83 ± 2.52 kg/m², and an average age of 37.22 ± 1.49 years, were enrolled. These participants were randomly assigned to one of three groups: Experimental Group 1 (L-Carnitine + 8 weeks of training), Experimental Group 2 (L-Carnitine + no training) and Control Group (No L-Carnitine + no training). The subjects were familiar with the concurrent training, characteristics of research, measuring the variables, training protocol, pretest, midtest and posttest, instructions for participants, possibilities and limitations of time and place research.

4.3. Inclusion and Exclusion Criteria

The study employed the purposive sampling technique to select participants based on predetermined criteria. Inclusion criteria specified sedentary males aged between 35 and 40 years with a body mass index (BMI) within the range of 30–35 kg/m². Recruitment occurred in the Behshahr city area in Iran through direct outreach and advertising. Exclusion criteria included allergies to L-carnitine, a lack of recent physical activity, chronic illnesses, and

medication use. Prospective participants were also required to have refrained from engaging in conditioning exercises exceeding 2 hours per week for the six months preceding the study. Obtaining a consent from study participants was a crucial step, involving a comprehensive explanation of the research's objectives and methods. This process aimed to ensure participants' thorough comprehension of the study, enabling an inform decision regarding their involvement. Participants familiarized with various aspects, including concurrent training, research characteristics, variable measurement, training protocol, pretest, midtest, and posttest procedures, as well as instructions, possibilities, and limitations related to the research's time and location.

4.4. Intervention

4.4.1. L-Carnitine supplementation protocol

The experimental groups received L-carnitine supplementation (BIOTECH USA, L-CARNITINE 1000 MG) 30 minutes prior to each exercise session, administer at a dosage of 35 mg/kg of body weight. This supplementation occured three times per week over an eight-week period, with the L-carnitine dissolve in distilled water (table 3.1) (Amiri et al., 2014).

Tables 4.1. The combination of nutrients in the supplements L-Carnitine

Supplement Facts Serving Size; 2 Tablet		
	Amount per serving	% DV
Calcium	330 mg	25%
L-Carnitine Tartrate	1000 mg	¥
¥ Daily Value (DV) not established		
Other ingredients: Calcium carbonate, microcrystalline cellulose, stearic acid, croscarmellose sodium, film coat (Hypromellose, polyethylene glycol, hydroxypropyl cellulose), silica and magnesium stearate.		

4.4.2. Concurrent training program

The researcher introduced the study's objectives and procedure to each participant, and after discussing any questions. The participant then completed a training which demonstrated the low and high demand tasks. Subjects engaged in both strength and endurance programs on the same day, with aerobic sessions preceding strength sessions.

Training sessions occured on Mondays, Wednesdays, and Fridays or Saturdays. All meticulously supervised by a minimum of two experienced personal trainers. Variable measurements conducted for all groups before the study initiation, at the 4-weeks mark, and at the conclusion of the 8-week period. The study protocol comprisesed three sessions per week, each lasting 70-85 minutes, maintaining an intensity of 60-75 percent of maximal reserve heart rate and one repetition maximum.

The concurrent training protocol, integrating strength and endurance training, commence in the first week at 60% HRR and 1RM for 70 minutes, progressively increasing to 85 minutes with 75% maximum heart rate reserve and 1RM by the study's conclusion. This progression involves the addition of 5 minutes to the duration and a 5% intensity increase every two weeks (table 4.2 and 4.3).

Table 4.2. Training Protocol (Concurrent Training)

Week	**First**	**Second**	**Third**	**Fourth**	**Fifth**	**Sixth**	**Seventh**	**Eighth**
Warm-up	5 Min	5 Min	5 Min	5 Min	5 Min	5 Min	5 Min	5 Min
CT	30 Min, R + 30 Min, RT	30 Min, R + 30 Min, RT	30 Min, R + 35 Min, RT	30 Min, R + 35 Min, RT	35 Min, R + 35 Min, RT	35 Min, R + 35 Min, RT	35 Min, R + 40 Min, RT	35 Min, R + 40 Min, RT
Duration	60 Min	60 Min	65 Min	65 Min	70 Min	70 Min	75 Min	75 Min
Intensity	60 %	60 %	65 %	65 %	70 %	70 %	75 %	75 %
Cool-Down	5 Min	5 Min	5 Min	5 Min	5 Min	5 Min	5 Min	5 Min
Total	70 Min	70 Min	75 Min	75 Min	80 Min	80 Min	85 Min	85 Min

Table note: Abbreviations: CT; Concurrent Training; R, Running; RT, Resistance Training; Min, Minutes

Table 4.3. Resistance Training

Training sessions	**Training movements**			
Chest, Biceps, Triceps (First Session)	Bench Press, Incline barbell bench press, Machine fly, Triceps push-down, Biceps Barbell curl			
Shoulder, back (Second Session)	Lateral dumbbell raises, Dumbbell shoulder press, Lift dumbbell, Lat pull-down, Seated pulley row			
Leg, Abdominal (Third Session)	45-degree leg press, Machine leg extension, Machine leg flexion, ball crunch, Side bend			
Week	Set	Repeat	1RM	Rest between set
First and second	3	12-14	60 %	30 s – 1 min
Third and fourth	3	12-14	65 %	30 s – 1 min
Fifth and sixth	3	12-14	70%	30 s – 1 min
Seventh and eighth	4	13-15	75 %	1 min – 2 min

4.5. Variables, Instruments and tools

In research, variables, instruments, and tools play crucial roles in shaping the design, data collection, and interpretation of a study. Here's a detailed explanation of each:

Variables are the measurable factors or characteristics that are studied in research. They can take different forms, and their manipulation or measurement is what enables the researcher to answer research questions. Variables are categorized based on their roles in the research design.

Instruments are the tools or devices used to collect data on the variables. They are designed to accurately and reliably measure the variables that researchers are interested in.

Tools refer to the broader resources used in the research process, including devices, methods, and techniques that aid in collecting, analyzing, and interpreting data.

Here's a detailed representation of the Variables, Instruments, and Tools in this research, as you may want to present them in (Table 4.4).

Table 4.4. Variables, Instruments, and Tools in Research

Category	Variable	Instrument/Tool	Measurement Method
Independent Variables	L-Carnitine Supplement	L-CARNITINE 1000 MG BIOTECH USA,	dosage of 35 mg/kg of body weight
	Concurrent Training	Strength and Endurance training	60-75 percent of maximal reserve heart rate
Dependent Variables	Body Composition (Weight, BMI, Body Fat percentage (BF%), Fat-Free Mass (FFM))	TANITA Body Composition Analyzer TBF-300	Bioelectrical Impedance Analysis (BIA)
	Strength	1RM (One-Rep Max)	Bench Press and Leg Press machine
	Endurance	Treadmill Modified Bruce Protocol	Maximal Oxygen Uptake (VO2max) testing
	Other Functional Capacities Variables	Polar RS400 Heart Rate Monitor	Resting Heart Rate (RHR)
		Omron M6 Comfort Blood Pressure Monitor	Blood Pressure Systolic and Diastolic Blood Pressure (SBP/DBP)
		Zacurate 500C Elite Fingertip Pulse Oximeter	Blood Oxygen Saturation (SpO2)
Categorical Variables	Gender	driver's license, or ID card	Self-Reported
	Age	Passport	Self-Reported
	BMI	Tandis Sport Systems	Weight (kg) / Height (m^2)
Control Variables	Nutrition		
Extraneous Variables	Lack of Awareness from Concurrent Training		

4.6. Data Collection

4.6.1. Body composition measurements

Bioelectrical impedance analysis (BIA) is a method for estimating body composition, in particular body fat and muscle mass, where a weak electric current flows through the body and the voltage is measure in order to calculate impedance (resistance) of the body. Most body water is stored in muscle. Therefore, if a person is more muscular there is a high chance that the person will also have more body water, which leads to lower impedance. Since the advent of the first commercially available devices in the mid-1980s the method has become popular owing to its ease of use and portability of the equipment. It is familiar in the consumer market as a simple instrument for estimating body fat. BIA actually determines the electrical impedance, or opposition to the flow of an electric current through body tissues which can then be used to estimate total body water (TBW), which can be used to estimate fat-free body mass and, by difference with body weight, body fat (Kalantar-Zadeh and Fouque, 2017).

Bioelectrical impedance analysis is a method for estimating body composition where a weak electric current flows through the body and the voltage is measured in order to calculate impedance (resistance) of the body. Different types of BIA can be used to assess different components of body composition such as hydration status, muscle mass, and percentage of body fat.

Figure 4.1. Tanita TBF-300 measurement method

Bioelectrical impedance analysis (BIA) scales are a common technique that estimate Height, Weight, body mass index (BMI), body fat ppercentage (BF%) and fat free mass (FFM) by using bioelectrical impedance analysis (Fig 4.1). Body composition variables were measured three times, before training protocol as a pretest, after four as midtest and eight weeks as a posttest by (Tanita TBF-300A Body Composition Analyzer Digital Scale Body Composition Analyzer) (Kalantar-Zadeh and Fouque, 2017, Kyle et al., 2004) and the height of the subjects was measured with by stadiometer (Huang et al., 2020).

4.6.2. Functional Capacity Assessments

The functional Capacity variables were measured in three times, before training protocol as a pretest, after four as midtest and eight weeks as a posttest. Resting heart rate (RHR) measured by (Polar RS400 Heart Rate Monitor) after 10 min of rest in the supine position using standard procedures. Subjects relaxed for a few minutes to ensure their heart rate stabilizes (Sima et al., 2020).

Systolic blood pressure (SBP) is the top number and refers to the amount of pressure experienced by the arteries while the heart is beating. Diastolic blood pressure (DBP) is the bottom number and refers to the amount of pressure in the arteries while the heart is resting in between heartbeats. Then, SBP and DBP determined by auscultation of the brachial artery and a mercurial sphygmomanometer, based on standard clinical procedures. Blood pressure was measured by (M6 Comfort Omron M6 Comfort Blood Pressure Monitor) in barometers in millimeters of mercury. For this purpose, the person sat on a chair and put his hand on the table at an angle of 90 degrees, and after resting about 15 minutes, then the measurement was performed (Huang et al., 2020).

Oxygen saturation measure by Zacurate 500C Elite Fingertip Pulse Oximeter Blood Oxygen Saturation Monitor with Silicon Cover, Batteries and Lanyard (Mystic Black) also known as (SpO2), is a measure of the amount of oxygen-carrying hemoglobin in the blood relative to the amount of hemoglobin not carrying oxygen. The body needs there to be a certain level of oxygen in the blood or it will not function as efficiently. In fact, very low levels of SpO2 can result in very serious symptoms. This condition is known as hypoxemia.

There is a visible effect on the skin, known as cyanosis due to the blue (cyan) tint it takes on. Hypoxemia (low levels of oxygen in the blood) can turn into hypoxia (low levels of oxygen in the tissue). This progression and the difference between the two conditions is important to understand. There are many ways that the blood can be tested to ensure it contains normal oxygen levels. The most common way is to use a pulse oximeter to measure the SpO2 levels in the blood. Pulse oximeters are relatively easy to use, and are common in health care facilities and at home. Pulse oximetry was ubiquitously used for monitoring oxygenation in the critical care setting. By forewarning the clinicians about the presence of hypoxemia, pulse oximeters may lead to a quicker treatment of serious hypoxemia and possibly circumvent serious complications. To used a pulse oximeter, simply place it on your finger. A percentage displayed on the screen. This percentage should be between 94 percent and 100 percent, which indicates a healthy level of hemoglobin carrying oxygen through the blood (Perkins et al., 2003, Jubran, 1999).

For measurement of estimate strength one repetition maximum (1RM), subjects warmed up for eight to ten minutes. In this test, subjects were under researcher and trainer took two records (bench press and leg press by machine) with estimated by the formula of Brzycki (Zahabi, 2015).

Maximal oxygen consumption (VO2 max) was measured during a continuous treadmill test to exhaustion on a motorized treadmill using the modified Bruce protocol. The treadmill speed was adjusted during the warm-up period elicit a heart rate that was approximately 70% of age predicted maximal heart rate. The speed of the treadmill held constant during the test and the grade of the treadmill was increased two percent every two minutes until volitional fatigue. Objective evidence that maximal rate of oxygen uptake had been achieved was the attainment of at least two of the following: plateau in oxygen consumption with increased exercise intensity, heart rate within 10 beats per min of age-predicted maximal heart rate and respiratory exchange ratio exceeding 1.10 (Ilic et al., 2015).

4.7. Dietary and physical activity monitoring

Accurate assessment of dietary intake and physical activity is a vital component for quality research in public health, nutrition, and exercise science. However, accurate and consistent methodology for the assessment of these components remains a major challenge. Classic methods use self-report to capture dietary intake and physical activity in healthy adult populations. However, these tools, such as questionnaires or food and activity records and recalls, have been shown to underestimate energy intake and expenditure as compared with direct measures like doubly labeled water (McClung et al., 2018).

The primary objective of dietary monitoring in this study was to accurately track participants' nutritional intake to assess the impact of L-Carnitine supplementation on body composition and functional capacities during concurrent training in obese men. Participants were instructed to maintain a detailed food diary, recording all meals, snacks, and beverages consumed throughout the day. Adherence to L-Carnitine supplementation, including dosage and timing, was meticulously tracked, with participants reporting their intake daily. This is typically done through interviews. Dietary data were collected daily and reviewed weekly to ensure accuracy. Participants received regular feedback and guidance to improve compliance. Any discrepancies or gaps in data were addressed promptly through follow-up communications. Also, Food Frequency Questionnaires assess habitual food intake over a longer period, usually the past month or year. Digital Tools: Apps like MyFitnessPal, Cronometer, or specific research tools can help participants log their food intake easily and provide detailed nutritional information. Similar to food diaries, participants log their physical activities, including type, duration, and intensity.

Also, Dietary and physical activity monitoring involves tracking what you eat and your physical activity levels to help manage weight, improve health, and optimize performance. By systematically monitoring and analyzing dietary intake and physical activity, you can accurately assess the impact of L-Carnitine supplementation during concurrent training on the functional capacities and body composition of obese men.

4.8. Statistical analysis

All variables were analyzed descriptively first by using measures of central tendency and data dispersion such as:

- Mean,
- Standard deviation (SD),

The Kolmogorov-Smirnov test examined if variables are normally distributed. For the data analysis, with use of inferential statistics (3 groups × 3 times factorial ANOVA between-within design) with the post-hoc analysis of variance (LSD test) was used, at significance level set on $p \leq 0.05$. All data is processed using SPSS software (IBM SPSS Statistics 22) (Guruhan et al., 2021).

5. RESULTS

5.1. Participant Characteristics

Consequently, a cohort of 30 males, with a mean weight of 106.48 ± 11.78 kg, height of 1.77 ± 0.08 m, BMI of 33.83 ± 2.52 kg/m², and an average age of 37.22 ± 1.49 years, were enrolled. These participants were randomly assigned to one of three groups: Experimental Group 1 (L-Carnitine + 8 weeks of training), Experimental Group 2 (L-Carnitine + no training), and Control Group (No L-Carnitine + no training). Participant demographics and characteristics are detailed in (Table 5.1).

Table 5.1. Participant characteristics

Participant characteristics	**EXG 1**	**EXG 2**	**C G**
Sample Size	10	10	10
Age (years)	37.34 ± 1.44	37.38 ± 1.59	36.94 ± 1.55
Height (m)	1.78 ± 0.83	1.75 ± 0.92	1.78 ± 0.87
Weight (kg)	104.86 ± 12.66	104.73 ± 12.04	109.85 ± 11.1
BMI (kg/m$^{2)}$	32.85 ± 1.93	33.93 ± 1.76	34.73 ± 3.41
1RM	153.4 ± 4.14	155.6 ± 5.29	152.4 ± 5.16

Table note: * significant effects differences between groups. Abbreviations: EXG 1, Experimental Group 1; EXG 2, Experimental Group 2; C G, Control Group; BMI, Body Mass Index; 1RM; One Repetition Maximum. All values are presented as Mean ± Standard deviation.

5.2. Effects on Body Composition

5.2.1. Body Weight and BMI

Null hypothesis; Weight loss in obese men isn't significantly affected by L-carnitine along with concurrent training

Research hypothesis; Weight loss in obese men is significantly affected by L-carnitine along with concurrent training

The analysis of data for weight in the groups in three stages after the training protocol showed that there was a significant main effect in the Experimental group 1 than the Experimental group 2 and control group (Table 5.2). ($F(2, 54) = 239.35$, $p = .000$, $\eta p^2 = .89$).

For this reason, the Null hypothesis rejected and the research hypothesis is accepted. So, we can conclude: Eight weeks L-Carnitine supplementation during Concurrent training in EXG 1 has decreased weight more than EXG 2 and CG at both midtest and posttest for obese men.

Table 5.2. Descriptive Statistics, ANOVA between-within design for Weight

Groups	Weight (kg)		
	Pre-test	**Mid-test**	**Post-test**
EXG 1	104.86±12.66	100.59±12.12*¥	94.46±12.01*¥
EXG 2	104.73±12.04	104.04±11.87	102.70±12.08
C G	109.85±11.10	110.10±11.79	110.03±10.45

Note: * significant differences compared to pre-test; ¥ Significant difference compared to the control group; Abbreviations: EXG 1, Experimental Group 1; EXG 2, Experimental Group 2; C G, Control Group; All values are presented as Mean ± Standard deviation.

Null hypothesis; BMI in obese men isn't significantly affected by L-carnitine along with concurrent training.

Research hypothesis; BMI in obese men is significantly affected by L-carnitine along with concurrent training.

The analysis of data for BMI in the groups in three stages after the training protocol showed that there was a significant main effect in the Experimental group 1 than the Experimental group 2 and control group (Table 5.3). ($F (2, 54) = 235.15$, $p = .000$, $\eta p^2 = .89$). For this reason, the Null hypothesis rejected and the research hypothesis is accepted. So, we can conclude: Eight weeks L-Carnitine supplementation during Concurrent training in EXG 1 has decreased BMI more than EXG 2 and CG at both midtest and posttest for obese men.

Table 5.3. Descriptive Statistics, ANOVA between-within design for BMI

Groups	BMI (Kg/m^2)		
	Pre-test	**Mid-test**	**Post-test**
EXG 1	32.85±1.92	31.51±1.75*¥	29.58±1.88*¥
EXG 2	33.93±1.76	33.71±1.76	33.26±1.68
C G	34.73±3.41	34.83±3.40	34.80±3.36

Note: * significant differences compared to pre-test; ¥ Significant difference compared to the control group; Abbreviations: EXG 1, Experimental Group 1; EXG 2, Experimental Group 2; C G, Control Group; BMI, Body Mass Index; All values are presented as Mean ± Standard deviation.

5.2.2. Body fat and Fat free Mass

Null hypothesis; BF% in obese men isn't significantly affected by L-carnitine along with concurrent training.

Research hypothesis; BF% in obese men is significantly affected by L-carnitine along with concurrent training.

The analysis of data for BF% in the groups in three stages after the training protocol showed that there was a significant main effect in the Experimental group 1 than the Experimental group 2 and control group (Table 5.4). ($F(2, 54) = 235.92$, $p = .000$, $\eta p^2 = .88$).

For this reason, the Null hypothesis rejected and the research hypothesis is accepted. So, we can conclude: Eight weeks L-Carnitine supplementation during Concurrent training in EXG 1 has decreased value of BF% more than EXG 2 and CG at only posttest for obese men.

Table 5.4. Descriptive Statistics, ANOVA between-within design BF%

Groups	BF (%)		
	Pre-test	**Mid-test**	**Post-test**
EXG 1	31.81±2.51	30.02±2.34	27.89±2.48*¥
EXG 2	33.11±2.10	32.85±2.11	32.31±2.02
C G	33.97±3.98	34.09±3.95	34.06±3.90

Note: * significant differences compared to pre-test; ¥ Significant difference compared to the control group; Abbreviations: EXG 1, Experimental Group 1; EXG 2, Experimental Group 2; C G, Control Group; BF %, Body Fat Percentage; All values are presented as Mean ± Standard deviation.

Null hypothesis; FFM in obese men isn't significantly affected by L-carnitine along with concurrent training.

Research hypothesis; FFM in obese men is significantly affected by L-carnitine along with concurrent training.

The analysis of data for FFM in the groups in three stages after the training protocol showed that there was a significant main effect in the Experimental group 1 than the Experimental group 2 and control group (Table 5.5). ($F(2, 54) = 208.55$, $p = .000$, $\eta p^2 = .88$).

For this reason, the Null hypothesis rejected and the research hypothesis is accepted. So, we can conclude: Eight weeks L-Carnitine supplementation during Concurrent training in EXG 1 has decreased value of FFM more than EXG 2 and CG at only posttest for obese men.

Table 5.5. Descriptive Statistics, ANOVA between-within design FFM

Groups	FFM (Kg)		
	Pre-test	**Mid-test**	**Post-test**
EXG 1	71.31±7.10	70.04±7.08	67.93±7.09*¥
EXG 2	69.95±7.73	69.77±7.28	69.41±7.36
C G	72.32±6.28	72.38±6.03	72.37±6.04

Note: * significant differences compared to pre-test; ¥ Significant difference compared to the control group; Abbreviations: EXG 1, Experimental Group 1; EXG 2, Experimental Group 2; C G, Control Group; FFM, Fat Free Mass. All values are presented as Mean ± Standard deviation.

5.3. Effects on Functional Capacities

5.3.1. Strength

Null hypothesis; 1RM (bench press and leg press) in obese men isn't significantly affected by L-carnitine along with concurrent training.

Research hypothesis; 1RM (bench press and leg press) in obese men is significantly affected by L-carnitine along with concurrent training.

The analysis of data for 1RM were for bench press and leg press in the groups in three stages after the training protocol showed that there was a significant main effect (improved) in the Experimental group1 than the Experimental group 2 and control group (Table 5.6). ($F(2, 54) = 209.73$, $p = .000$, $\eta p^2 = .88$) and (Table 5.7). ($F(2, 54) = 301.8$, $p = .000$, $\eta p 2 = .39$).

For this reason, the Null hypothesis rejected and the research hypothesis is accepted. So, we can conclude: Eight weeks L-Carnitine supplementation during Concurrent training in EXG 1 has increased value of 1RM (bench press and leg press) more than EXG 2 and CG at both midtest and posttest for obese men.

Table 5.6. Descriptive Statistics, ANOVA between-within design 1RM (Bench Press)

Groups	1RM (Kg)		
	Pre-test	**Mid-test**	**Post-test**
EXG 1	65.8±6.46	71.2±6.28*¥	75.9±6.13*¥
EXG 2	67.2±8.33	67.6±8.44	67.9±8.25
C G	66.8±7.37	66.7±7.54	66.7±7.54

Note: * significant differences compared to pre-test; ¥ Significant difference compared to the control group; Abbreviations: EXG 1, Experimental Group 1; EXG 2, Experimental Group 2; C G, Control Group; 1RM, One Repetitions Maximum. All values are presented as Mean ± Standard deviation.

Table 5.7. Descriptive Statistics, ANOVA between-within design 1RM (Leg Press)

Groups	1RM (Kg)		
	Pre-test	**Mid-test**	**Post-test**
EXG 1	78.8±2.04	83±2.53*¥	88.6±3.92*¥
EXG 2	78.2±2.89	78.7±2.89	79.2±2.82
C G	78±3.97	78.5±3.53	78.9±3.72

Note: * significant differences compared to pre-test; ¥ Significant difference compared to the control group; Abbreviations: EXG 1, Experimental Group 1; EXG 2, Experimental Group 2; C G, Control Group; 1RM, One Repetitions Maximum. All values are presented as Mean ± Standard deviation.

5.3.2. Endurance

Null hypothesis; VO2max in obese men isn't significantly affected by L-carnitine along with concurrent training.

Research hypothesis; VO2max in obese men is significantly affected by L-carnitine along with concurrent training.

The analysis of data for VO2max in the groups in three stages after the training protocol showed that there was a significant effect (developed) in the Experimental group1 than the Experimental group 2 and control group (Table 5.8). ($F(2, 54) = 45.55$, $p = .000$, $\eta p^2 = .62$).

For this reason, the Null hypothesis rejected and the research hypothesis is accepted. So, we can conclude: Eight weeks L-Carnitine supplementation during Concurrent training in EXG 1 improved Vo_2max more than EXG 2 and CG at midtest and posttest for obese men.

Table 5.8. Descriptive Statistics, ANOVA between-within design VO2max

Groups	VO2max (ml×kg-1×min-1)		
	Pre-test	Mid-test	Post-test
EXG 1	32.24±3.54	33.88±2.45*¥	34.21±3.65*¥
EXG 2	32.84±2.86	32.33±4.12	32.46±2.79
C G	32.01±3.66	32.78±2.40	32.37±4.95

Note: * significant differences compared to pre-test; ¥ Significant difference compared to the control group; Abbreviations: EXG 1, Experimental Group 1; EXG 2, Experimental Group 2; C G, Control Group; Vo_2Max, Maximal Oxygen Consumption; All values are presented as Mean ± Standard deviation.

5.3.3. Other functional capacity variables

Null hypothesis; RHR in obese men isn't significantly affected by L-carnitine along with concurrent training.

Research hypothesis; RHR in obese men is significantly affected by L-carnitine along with concurrent training.

The analysis of data for RHR in the groups in three stages after the training protocol showed that there was no significant effect (developed) in the Experimental group1 than the Experimental group 2 and control group (Table 5.9). ($F(2, 54) = 0.46$, $p = .62$, $\eta p^2 = .017$).

For this reason, the Null hypothesis is accepted and the research hypothesis is rejected. So, we can conclude: Eight weeks L-Carnitine supplementation during Concurrent training in EXG 1 has decreased RHR more than EXG 2 and CG at only in posttest for obese men.

Table 5.9. Descriptive Statistics, ANOVA between-within design RHR

Groups	RHR (bpm)		
	Pre-test	**Mid-test**	**Post-test**
EXG 1	76.60±24.15	75.20±4.46	71.70±4.37*¥
EXG 2	75.95±4.74	75.60±4.47	75.30±3.91
C G	77.10±4.29	77.00±4.29	76.90±4.12

Note: * significant differences compared to pre-test; ¥ Significant difference compared to the control group; Abbreviations: EXG 1, Experimental Group 1; EXG 2, Experimental Group 2; C G, Control Group; RHR, Resting Heart Rate; All values are presented as Mean ± Standard deviation.

Null hypothesis; SBP in obese men isn't significantly affected by L-carnitine along with concurrent training.

Research hypothesis; SBP in obese men is significantly affected by L-carnitine along with concurrent training.

The analysis of data for SBP in the groups in three stages after the training protocol showed that there was a significant effect (developed) in the Experimental group1 than the Experimental group 2 and control group (Table 5.10). ($F(2, 54) = 71.93$, $p = .000$, $\eta p^2 = .72$).

For this reason, the Null hypothesis rejected and the research hypothesis is accepted. So, we can conclude: Eight weeks L-Carnitine supplementation during Concurrent training in EXG 1 decresed SBP more than EXG 2 and CG at midtest and posttest for obese men.

Table 5.10. Descriptive Statistics, ANOVA between-within design SBP

Groups	SBP (mmHg)		
	Pre-test	**Mid-test**	**Post-test**
EXG 1	121.30±3.19	117.20±2.61*¥	114.70±2.21*¥
EXG 2	120±7.46	119±7.02	118.60±6.68
C G	122±4.24	121.80±4.31	121.80±4.31

Note: * significant differences compared to pre-test; ¥ Significant difference compared to the control group; Abbreviations: EXG 1, Experimental Group 1; EXG 2, Experimental Group 2; C G, Control Group; SBP, Systolic Blood Pressure;. All values are presented as Mean ± Standard deviation.

Null hypothesis; DBP in obese men isn't significantly affected by L-carnitine along with concurrent training.

Research hypothesis; DBP in obese men is significantly affected by L-carnitine along with concurrent training.

The analysis of data for DBP in the groups in three stages after the training protocol showed that there was a significant effect (developed) in the Experimental group1 than the Experimental group 2 and control group (Table 5.11). ($F(2, 54) = 97.32$, $p = .000$, $\eta p^2 = .78$).

For this reason, the Null hypothesis is rejected and the research hypothesis is accepted. So, we can conclude: Eight weeks L-Carnitine supplementation during Concurrent training in EXG 1 decresed DBP more than EXG 2 and CG at only posttest for obese men.

Table 5.11. Descriptive Statistics, ANOVA between-within design DBP

Groups	DBP (mmHg)		
	Pre-test	**Mid-test**	**Post-test**
EXG 1	76.5±3.47	72.30±3.49	69±3.62*¥
EXG 2	76.5±5.24	75.80±5.49	75.5±5.19
C G	78±5.77	77.70±5.69	74.06±6.05

Note: * significant differences compared to pre-test; ¥ Significant difference compared to the control group; Abbreviations: EXG 1, Experimental Group 1; EXG 2, Experimental Group 2; C G, Control Group; DBP, Diastolic Blood Pressure; All values are presented as Mean ± Standard deviation.

Null hypothesis; SpO2 in obese men isn't significantly affected by L-carnitine along with concurrent training.

Research hypothesis; SpO2 in obese men is significantly affected by L-carnitine along with concurrent training.

The analysis of data for SpO2 in the groups in three stages after the training protocol showed that there was no significant effect (developed) in the Experimental group1 than the Experimental group 2 and control group (Table 5.12). ($F(2, 54) = 43.8$, $p = .27$, $\eta p^2 = .61$).For this reason, the Null hypothesis is accepted and the research hypothesis is rejected. So, we

can conclude: Eight weeks of L-Carnitine supplementation during concurrent training doesn't has significant effect on functional capacities (SpO_2) in obese men.

Table 5.12. Descriptive Statistics, ANOVA between-within design SpO2

Groups	SpO2(%)		
	Pre-test	**Mid-test**	**Post-test**
EXG 1	95.10±1.10	96.6±0.84	97.80±0.78
EXG 2	95.10±0.87	95.30±1.05	95.50±1.17
C G	95.10±1.28	95.10±1.28	95.20±1.22

Note: * significant differences compared to pre-test; ¥ Significant difference compared to the control group; Abbreviations: EXG 1, Experimental Group 1; EXG 2, Experimental Group 2; C G, Control Group; SpO2, Oxygen Saturation; All values are presented as Mean ± Standard deviation.

6. DISCUSSION

6.1. Interpretation of results and comparison with previous studies

This is important that obesity is a growing health concern globally and is considered a substantial risk factor for several chronic diseases (Dixon, 2010). Several approaches have been suggested to treat obesity, among which lifestyle modification and administration of dietary supplements along with physical activity could be considered as safe approaches to promote weight loss (Askarpour et al., 2020). The current study sought to add to the existing research by investigating the effects of L-carnitine supplementation on the functional capacities and body composition in the general adult population following a concurrent training challenge. The main finding of our study showed consumption of L-Carnitine supplement combined with concurrent training for eight weeks significantly affects functional capacities (RHR, SBP, DBP, VO2max) and significant changes in body composition and strength (reduction in Weight, BMI, BF%, FFM and an increase in 1RM) for only experimental group 1 more than the experimental group 2 and control group in obese men. L-Carnitine as a nutritional supplement, since the 1960s, has been promoted as beneficial in a number of disorders of human carnitine deficiency of impaired fatty acid oxidation, suggesting that nutritional or pharmacologic supplements of carnitine might be beneficial in some disorders (Stanley, 2004) and as a protective via anti-inflammatory and antioxidant mechanisms and have a positive impact on body functions (Khodir et al., 2020).

This research explored the impact of L-Carnitine supplementation in combination with concurrent training on functional capacities and body composition among obese males. The primary outcome of this investigation revealed that an eight-week regimen of L-Carnitine supplementation paired with concurrent training led to substantial improvements in both functional capacities and body composition. Contrastingly, in the experimental group that consumed L-Carnitine supplements without engaging in physical exercise, no significant alterations were observed across the measured variables. These results highlight the critical role of physical exercise in eliciting beneficial changes in functional capacities and body composition, reinforcing the synergy between dietary supplementation and physical training.

$H_{1\text{-}1,2}$ – Weight and BMI in obese men was significantly affected by L-carnitine along with concurrent training.

In our results, LCR supplementation significantly reduced body weight and BMI, in experimental group1 after four and eight weeks but the reducing effect was not identified for other groups. This kind of training could help to reduce body weight and fat mass by increasing lean mass and basal metabolic rate.

This is supported by research by Talenezhad and Pooyandjoo et al., which demonstrated a significant drop in weight and body mass index for participants who received L-carnitine when compared to the control group (Pooyandjoo et al., 2016, Talenezhad et al., 2020). If people take supplements with the right quantity of L-carnitine and exercise regularly, they may be able to alter their body composition and address acquired L-carnitine shortage, which is indicated by increased body fat deposition. (Kruszewski, 2011).

Physical activity seems to be an important component of lifestyle interventions for weight loss and maintenance. There appears to be a dose response association between physical activity and weight reduction, despite the seemingly small effects of physical activity on weight loss. Engaging in physical activity appears to be a crucial behavior for supporting sustained weight loss and preventing weight gain. Those with extreme obesity have also been shown to benefit from physical activity in terms of weight loss (BMI≥30kg/m^2) (Jakicic and Davis, 2011).

Previous studies have demonstrated the importance of exercise in the treatment of obesity and its potential to prevent obesity-related comorbidities when done regularly and at a sufficient intensity. These results were also seen in a study by Willis et al., which showed that overweight persons who engaged in concurrent training three times a week at an intensity of 65–80% VO2peak reduced their weight, body fat percentage, and waist circumference. Nonetheless, two more groups in the same study that engaged in strength or aerobic training only saw a drop in their waist circumference, demonstrating the importance of the type of exercise (Medeiros et al., 2015).

$H_{1-3,4}$ –BF% and FFM in obese men was significantly decreased by L-carnitine along with concurrent training.

After just eight weeks of concurrent training with LCR, there were notable reductions in body composition (BF% and FFM) in the current study. Our findings were consistent with Gimenes' research about the impact of L-carnitine on exercise performance. (Gimenes et al., 2015) and concurred with Bellicha et al. regarding how exercise training affects changes in body composition. According to their findings, exercise training has a positive impact on weight loss and changes in body composition in persons who are overweight or obese (Bellicha et al., 2021). Eight weeks of resistance training led to a considerable reduction in the fat mass of males who were not trained, according to Ghahramanloo et al. However, inconsistent findings have been reported by a number of research. Mohammad-Rahimi and Attarzadeh-Hosseini, for instance, did not observe a discernible change following aerobic exercise. Variations in the respondents' characteristics, including their sex and training history, could be the cause of the disparities in the results. In actuality, consistent carnitine use would raise intracellular and plasma carnitine concentrations, encourage fat burning, and eventually reduce body fat reserves (Mohammadi et al., 2019).

H_{2-1} – Strength (1RM) in obese men was significantly increased by L-carnitine along with concurrent training.

After the midtest and posttest, our analysis revealed that L-carnitine combined with concurrent training significantly increased (1RM) strength in both the bench press and leg press exercises, but this effect was observed exclusively in Experimental Group 1. This outcome indicated a unique impact on upper and lower body strength gains within this group. This finding suggested that L-carnitine enhance muscular strength gains when paired with both resistance and aerobic exercises, potentially due to its role in fatty acid oxidation and energy production within muscle cells. The observed increase in 1RM strength also highlights the potential for L-carnitine supplementation to support strength adaptations in populations with higher body mass. This finding is consistent with other authors' studies and likely relates to the synthesis of myofibrillar proteins and the recruitment of fast twitch motor units (Koozehchian et al., 2018). Sawicka et al. shown, in contrast to earlier research, that eight weeks of LCR, exercise, L-leucine, and vitamin D dramatically increased muscle mass and strength because of increased mTOR pathway activation. But when LCR was examined on its own for a longer amount of time—24 weeks—and at the same dosage, no discernible impact

was discovered (Sawicka et al., 2018). This might be related to the moderate-intensity training regimen's nature, where the main energy source is the oxidation of long-chain fatty acids, and where LCR may speed up the pace at which fat is burned, protecting muscle glycogen stores (Berzosa et al., 2011).

$H_{2\text{-}2}$ – Endurance (VO2max) in obese men was significantly affected by L-carnitine along with concurrent training.

Our analysis demonstrated that L-carnitine supplementation, when paired with concurrent training, led to a significant improvement in VO_2max (a key measure of endurance) in Experimental Group 1. Specifically, after both four and eight weeks of intervention, VO_2max levels showed notable increases within this group. This improvement suggested that the combination of L-carnitine supplementation and concurrent training supported aerobic performance adaptations in obese men by increasing oxygen utilization efficiency during exercise. Since oxidation of fat requires more oxygen compared to carbohydrates, the cardiovascular system should receive more oxygen for muscles. In this regard, L-carnitine increases oxygen consumption and lipid oxidation by stimulating the pyruvate dehydrogenase complex and the entry of pyruvate into the beta-oxidation pathway (Kashef and Shabani, 2017). L-Carnitine protects the cell from acyl-CoA accretion through the generation of acylcarnitine. Mitochondrial fatty acid oxidation represents an important energy source for muscle metabolism, particularly during physical exercise. Considering the important role of fatty acids in muscle bioenergetics, and the limiting effect of free carnitine on fatty acid oxidation during endurance exercise, L-carnitine supplementation has been hypothesized to improve exercise performance. Differences in exercise intensity, training or conditioning of the subjects, amount of L-carnitine administered, route and timing of administration relative to the exercise led to different experimental results (Gnoni et al., 2020). Vecchiet et al. showed that 2 gr of L-carnitine given to athletes one hour prior to the exercise increases the maximal oxygen intake and the energy they spend. Marconi et al showed that 4 gr/day L-Carnitine given for two weeks improved VO2max (Vecchiet et al., 1990). Probably, the un-similarities of duration and period of LCR supplement consumption, gender, type of sports field, characteristics and physical qualifications of obesity/overweight people, type of exercises or training in studies could cause the differences.

H_{2-3} – RHR in obese men was significantly affected by L-carnitine along with concurrent training.

The results showed that L-carnitine combined with exercise training led to a significant reduction in resting heart rate (RHR) in experimental group 1. It is well known that RHR after exercise could be modified by weight loss and RHR after exercise has been shown to be an independent risk factor for cardiovascular disease and mortality in healthy adults (Nagashima et al., 2010). Brinkworth et al. reported an improvement in RHR after a weight loss program that only involved dieting without any change in physical activity (Richard et al., 2021). They found a good correlation of the change in RHR with the reduction of metabolic parameters (weight, BMI, waist circumference, TG, glucose, and the TG/HDL-Chol ratio) (Brinkworth et al., 2006). Previous studies by Belayneh et al. on healthy individuals among students at Haramaya University were compatible with our studies and indicated that L-carnitine ingestion probably improved the heart's ability to pump blood efficiently and that human muscle contains large amounts of carnitine, but this depends on the uptake of this compound from the bloodstream (Belayneh, 2013). Engaging in regular physical activity improves autonomic regulation of the heart in adults by lowering resting heart rate and lowering the risk of obesity-related cardiovascular disease via improving autonomic function (Sinha et al., 2023).

$H_{2-4,5}$ – SBP and DBP in obese men were significantly affected by L-carnitine along with concurrent training.

It was hypothesized that L-carnitine supplementation would result in a significant reduction in systolic blood pressure after four and eight weeks and diastolic blood pressure only after eight weeks of concurrent training in experimental group 1. Obesity-related mortality has increased significantly, leading to a greater focus on illness prevention and improved management strategies. Making changes to one's diet and exercise routine is one of the most popular adjunct therapies. Several studies have shown that increasing physical exercise helps lower and regulate systemic blood pressure. constant with the findings of this study, Jean Tamayo Acosta's research also discovered that constant training lowers blood pressure (Acosta et al., 2022).

$H_{2\text{-}6}$ – SpO2 in obese men wasn't significantly affected by L-carnitine along with concurrent training.

However, our results did not show any significant change in oxygen saturation between the groups. This may be due to the low lactate tolerance in the blood and potential changes in intracellular biochemical processes, as our subjects were healthy but inactive. L-carnitine has been shown to help in fatty acid metabolism, but its effects on oxygen saturation may not be as pronounced as other physiological markers, especially in populations with obesity. The subjects may not have been able to reach a level of metabolic efficiency where L-carnitine could significantly influence SpO2. Our results were inconsistent with other research, such as that by Kashef et al., who observed a positive relationship between lactate clearance rate (LCR) and oxygen saturation, likely because their subjects were active athletes (Kashef and Shabani, 2017).

6.2. Mechanisms of L-Carnitine and concurrent training effects

The most important mechanism of L-carnitine is to act as a carrier for transporting fatty acyl-CoA to themitochondrial matrix on the inner membrane of mitochondria, allowing β-oxidation of fatty acids toprovide energy for the body.

L-Carnitine, as an essential coenzyme in fat metabolism, can promote the metabolism of human fat, accelerate the burning of fat, and may achieve the desired fat burning slimming effect. It is essential for the transport of long-chain fatty acids into the mitochondria where they are oxidized for energy. Enhanced fatty acid oxidation can reduce fat stores, contributing to weight loss. This process enhances fat metabolism, potentially leading to reduced fat stores (Liu, X, 2023).

By increasing the availability of fatty acids for oxidation, L-carnitine supports ATP production, which can improve physical factors and endurance during exercise. Increased energy availability can enhance exercise performance, leading to higher caloric expenditure and weight loss.

Concurrent training, combining aerobic and resistance exercises, can lead to reductions in fat mass while preserving or increasing lean muscle mass. The increased availability of fatty acids for oxidation due to L-carnitine, combined with the elevated energy demands of concurrent training, can enhance overall fat metabolism and energy expenditure.

The combination of increased fat oxidation, higher energy expenditure, and improved muscle mass and metabolic rate can result in greater weight loss and a more favorable body composition compared to concurrent training alone. Also, Higher caloric burn contributes to a negative energy balance, leading to weight loss and improved cardiovascular health supports sustained physical activity and weight management. By understanding these mechanisms, the combined approach of L-carnitine supplementation and concurrent training can be effectively utilized to combat obesity and improve overall health outcomes in obese individuals.

7. CONCLUSION

7.1. Summary of findings

L-carnitine supplementation, in conjunction with concurrent training, emerges as a highly effective approach for enhancing body composition and boosting functional capacities in obese adult men. This synergistic approach is thus recommended for overweight male individuals, advocating for the integration of concurrent training into their fitness routines alongside L-carnitine supplementation.

This kind of research could be beneficial for prevention of cardiovascular disease in obese men and reduced costs and effects of non-pharmacological in related to exercise. Future studies should investigate the potential incremental benefits of this combined protocol L-carnitine supplementation with concurrent training over the sole application of concurrent training. Such investigations will be crucial in further delineating the specific advantages and optimizing intervention strategies for this demographic.

L-carnitine is a compound with well-established functions in cellular metabolism, in particular for energetics purposes, as it supports fatty acid transport into mitochondria for β-oxidation and consequent ATP production (Gnoni et al., 2020). In fact, of the experimental result of the study, the following conclusion was made; the combination of L-carnitine during concurrent training could have more efficacy than any single method. Training can have a positive effect on the functional capacities and body composition, but for further improvement of variables, losing weight, weight management and reducing risk factors in obesity men, a therapeutic approach and long-term consumption of L-carnitine is recommended.

A greater understanding of these pathways and consequences of L-carnitine supplementation in men might certainly boost their performance and could be used as a dietary supplement to optimize and enhance health outcome. Therefore, the results of the current study will highlight the beneficiary effects of L-carnitine on the functional capacities and body composition as a potential supplementation for the muscle regeneration and repair of them.

This kind of research could be beneficial for prevention of cardiovascular disease in obese men and also a combination of strength and endurance training could induce enhancement in the total antioxidant system and this study showed reduced costs and effects of non-pharmacological in related to exercise.

Regarding the results, our analysis suggested that L-carnitine could be an effective factor to improve body composition and develop functional capacities among obese men along with exercise. Therefore, overweight individuals, especially men, are recommended to take L-carnitine accompanied by concurrent training to achieve significant changes in systolic blood pressure, maximal oxygen consumption, and maximal one repetition, and significantly decrease the rate of weight loss and body mass index. The result of this study also suggests that carnitine supplementation combined with exercise is more efficient at improving resting heart rate, diastolic blood pressure, body fat percentage and fat free mass.

7.2. Final remarks

The investigation into the effects of L-carnitine supplementation on functional capacity and body composition in obese men during concurrent training holds considerable promise. This research area bridges the gap between nutritional science and exercise physiology, offering potential benefits for health, performance, and quality of life in individuals struggling with obesity. L-carnitine supplementation can enhance fat metabolism, which may lead to improved in obesity management during exercise.

These changes not only support weight management but also improve metabolic health, reducing the risk of chronic diseases associated with obesity. The current study for obese men is a valuable contribution to the fields of nutrition and exercise science.

By enhancing our understanding of how this supplement can improve functional capacity and body composition, we can develop more effective strategies to combat obesity and promote overall health. Continued research and application of these findings hold the potential to significantly impact public health and individual well-being.

7.3. Contributions to knowledge

Several noteworthy advances in understanding can be derived from the current study: In order to manage obesity, provide a greater understanding of how L-carnitine supplements impact metabolism, specifically fat oxidation and energy production during exercise. This knowledge will help develop individualized training and supplementation regimens that will optimize the health benefits of exercise for obese people.

This study gives evidence-based recommendations for the use of L-carnitine supplements in conjunction with exercise programs for obese clients and public health initiatives that aim to reduce obesity and improve physical health through combined exercise and nutrition interventions to healthcare providers, nutritionists, and fitness professionals.

Another piece of information has been the potential for L-carnitine supplementation to prevent obesity-related chronic diseases like diabetes, metabolic syndrome, and cardiovascular disease.

By advancing these fields, research on L-carnitine supplementation can significantly advance our knowledge of obesity and its treatment, which will ultimately result in more comprehensive and successful health initiatives. Research on L-carnitine supplementation can make a substantial contribution to these fields, which will ultimately improve our understanding of obesity and its treatment, resulting in more comprehensive and successful health interventions.

Finally, Lastly, the possible advantages of nutrition supplementation for adult men are frequently investigated, especially with regard to energy metabolism, exercise capacity, and general health. In adult men, supplementing with L-carnitine is mostly linked to better energy metabolism, increased exercise capacity, and possibly even positive impacts on metabolic and cardiovascular health. This is especially crucial while engaging in continuous exercise, as fat starts to play a big role as an energy source.

7.4. Practical implications

Regarding applications, the primary role of carnitine in the body is to facilitate lipid oxidation by moving long-chain fatty acids into the inner mitochondrial area, where they are processed by β-oxidation. Because of this, the majority of dietary lipids cannot be used by our body as an energy source without carnitine, and as a result, fatty acid accumulation leads to obesity.

L-carnitine is a well-liked supplement that is frequently used to improve body composition and exercise performance, especially when combined with concurrent training (a mix of resistance and aerobic exercise) and obesity. Here are some practical implications based on current research:

- Enhanced aerobic performance: L-carnitine supplementation may enhance aerobic performance by increasing the transport of fatty acids into the mitochondria, where they are burned for energy. This can lead to improved endurance and reduced fatigue during prolonged exercise. Regular supplementation and consistent training are key. The benefits of L-carnitine are most pronounced when combined with a structured exercise program and healthy diet.
- Increased exercise Tolerance: Improved energy metabolism and reduced accumulation of metabolic by-products (such as lactic acid) can increase overall exercise tolerance, enabling obese individuals to sustain higher intensities or longer durations of exercise.
- Fat loss: By enhancing fat metabolism, L-carnitine may contribute to greater fat loss when combined with regular exercise. This can be particularly beneficial for obese men looking to reduce body fat percentage. Concurrent training itself is effective at promoting lean muscle mass while reducing fat mass. L-carnitine might amplify these effects by improving exercise performance and recovery, thus supporting more effective training sessions.
- Weight management: While L-carnitine supplementation alone may not lead to significant weight loss, its potential to improve exercise performance and recovery can support a more active lifestyle, which is critical for long-term weight management.

- Individual response: The effectiveness of L-carnitine can vary among individuals. Factors such as baseline L-carnitine levels, diet, and overall health can influence outcomes.

Finally, L-carnitine supplementation can be a useful adjunct to concurrent training for obese men, potentially enhancing functional capacity and supporting favorable changes in body composition. However, it should be integrated thoughtfully into a broader program of exercise and nutrition.

7.5. Limitations of the study

There are various potential limitations to take into account when analyzing the effects of L-carnitine supplementation on body composition and functional ability in obese men during concurrent training: Because of the small sample size, the findings of this study cannot be broadly applied. The tiny sample size of this study was its primary limitation.

The present study focused on obese males with BMIs over 30 kg/m2, hence it is vital to exercise caution when extrapolating the findings to other populations. Another drawback of our research was the absence of a placebo group, which would have made it difficult to determine the actual impact of L-carnitine supplementation. Participants' reported results and perceptions may be impacted by the placebo effect.

The absence of monitoring stress variables linked to the hypothalamus-pituitary-adrenal axis, such as corticosterone, may have shed light on the possible neurophysiological effects of LCR supplementation. The outcomes may also be impacted by other variables like stress, sleep, and extra physical activity done outside of the study procedure. Although frequently difficult, accounting for these factors is crucial.

7.6. Suggestions for future research

Future research should investigate the variables that affect physical performance values in greater detail, particularly by looking at how fat affects body weight. More research is needed to comprehend how exercise affects the cardiovascular system and investigate how various exercise programs can help prevent related comorbidities. Studying how L-carnitine supplements affect fat men's concurrent training is an intriguing topic that can help advance the study of exercise physiology, nutrition, and obesity management. The following are potential research directions and suggestions for further investigation.

- Investigate the dose-response relationship of L-carnitine supplementation on body composition and functional capacities in obese men and compare different doses of L-carnitine to determine the optimal supplementation level.
- Examine the impact of short-term and long-term L-carnitine supplementation on different training protocols (e.g., varying intensity, duration, and frequency) to identify the most effective combination with L-carnitine other training outcomes and evaluate changes over weeks or months to understand the sustainability of effects.
- Explore the potential synergistic effects of combining L-carnitine with other nutrients supplements or pharmacological agents to assess potential synergistic effects commonly used in obesity management. For example, combining L-carnitine with omega-3 fatty acids or antioxidants.
- Assess the impact of L-carnitine supplementation on metabolic markers such as insulin sensitivity, lipid profiles, and inflammatory markers.
- Conduct randomized controlled trials with a placebo group to establish a clearer understanding of the specific effects attributed to L-carnitine supplementation.
- Explore the role of genetic factors in determining individual responses to L-carnitine supplementation with differnt subjects for women or children.

By addressing these areas, future research can provide a more comprehensive understanding of how L-carnitine supplementation can optimize functional capacity and body composition in obese men during concurrent training. This can lead to more effective, personalized, and evidence-based interventions for obesity management.

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9. APPENDICES
9.1 Participant Consent Form

Participant Consent Form

Study Title: The effects of L-carnitine supplementation during concurrent training on body composition and functional capacities in obese men

Principal Investigator:

[Ghadir Zahabi] [Faculty of Sport and Physical Education, University of Belgrade, Serbia] [Contact: +381628340379, +98911257192] [Gh.zahabi@yahoo.com]

Study Purpose:

You are invited to participate in a research study in related to doctorate dissertation. The goal of this study is to better understand how L-carnitine affects exercise performance and body composition changes during a structured training program.

Participation:

I have received, read and kept a copy of the information letter statement. I understand the general purposes, risks and methods of this research. I consent to participate in the research project and the following has been explained to me:

- the research may not be of direct benefit to me
- my participation is completely voluntary
- my right to withdraw from the study at any time without any implications to me
- whom I should contact for any complaints with the research or the conduct of the research
- I am able to request a copy of the research findings and reports
- security and confidentiality of my personal information

Study Procedures:

If you agree to participate, you will be asked to:

1. Complete a health screening and baseline assessment, including measurements of variables.
2. Consume an L-carnitine supplement for the duration of the study (8 weeks).
3. Follow a concurrent training program that includes both resistance and aerobic exercises, as instructed by the research team.
4. Attend regular follow-up sessions for re-assessment of body composition, functional capacity in 3 times.

Risks and Discomforts:

Potential risks and discomforts associated with this study include:

- Mild gastrointestinal discomfort from L-carnitine supplementation.
- Muscle soreness or fatigue from exercise.
- Minor discomfort from blood sample collection.

Confidentiality:

All information collected during the study will be kept confidential. Your identity will not be revealed in any publication or presentation of the study results. Data will be stored securely and only accessible to the research team.

Consent:

By signing below, you indicate that you have read and understood the information provided above, that you have had the opportunity to ask questions, and that you agree to participate in this study.

Participant's Name: _____
Participant's Signature: _____
Date: _____

Contact details: _____
Age: _____
Education: _____

Investigator's Name: _____
Date: _____

Investigator's Signature: _____

9.2. Ethic committee approval

Islamic Azad University-Marvdasht Branch

Research Ethics Certificate

Approval ID:	IR.IAU.M.REC.1401.037	**Approval Date:**	2022-09-13
Evaluated by:	Islamic Azad University-Marvdasht Branch		
Status:	**Approved**		
Approval Statement:	The project was found to be in accordance to the ethical principles and the national norms and standards for conducting Health Research Iran. Notice: 1. Although the proposal has been approved by the research ethics committee, meeting the professional and legal requirements is the sole responsibility of the PI and other project collaborators. 2. This certificate is reliant on the proposal/documents received by this committee on 2022-09-13. The committee must be notified by the PI as soon as the proposal/documents are modified.		
Thesis Title:	The effects of L-carnitine supplementation during concurrent training on body composition and functional capacities in obese men		
Supervisor:	Name: Ghadir Zahabi Email: Gh.zahabi@yahoo.com		

Dr. Javad Cerami
Director of Institutional Research Ethics Committee
Islamic Azad University-Marvdasht Branch

Dr. Masoud Jabbari
Secretary of Institutional Research Ethics Committee
Islamic Azad University-Marvdasht Branch

9.3. Published Paper

Article published online: 2024-03-26

Original Article

The Effects of L-Carnitine Supplementation During Concurrent Training on the Functional Capacities and Body Composition in Obese Men

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J Health Allied Sci[NU]

Abstract

Background Despite extensive research, the effects of L-carnitine supplementation in treating obesity are still unclear and equivocal. L-carnitine transports fatty acids into mitochondria for oxidation and is marketed as a weight loss supplement. The purpose of the present research is to investigate the efficacy of L-carnitine during concurrent training on the functional capacities and body composition in obese men.

Methods Thirty nonactive, obese males (age = 37.2 ± 1.5 years; body mass index = 33.8 ± 2.5 kg/m^2) participated in this research. The participants were randomly divided into three groups: experimental group 1 (EXP1)—concurrent training with L-carnitine supplementation; experimental group 2 (EXP2)—L-carnitine supplementation without training; and control group—without training or L-carnitine supplementation. Concurrent training was performed for 8 weeks, three sessions per week, with a training intensity ranging from 60 to 75% of the maximum heart rate reserve and one-repetition maximum. Both experimental groups were supplemented with 35 mg L-carnitine supplement per kilogram body weight. Various functional and body composition variables were collected at three time points (pre-test, mid-test, and post-test).

Results A number of variables were significantly improved in EXP1 after 4 and 8 weeks (systolic blood pressure, maximal oxygen consumption, weight, body mass index, and one-repetition maximum) and only after 8-weeks (diastolic blood pressure, resting heart rate, percentage of body fat, and fat-free mass). No significant changes were observed for EXP2 and the control group.

Conclusion L-carnitine supplementation, in conjunction with concurrent training, emerges as a highly effective approach for enhancing body composition and boosting functional capacities in obese adult men. Therefore, it is recommended that overweight male individuals integrate concurrent training into their regimen while taking L-carnitine.

Keywords
- L-carnitine
- Exercise Training
- Body Composition
- one-repetition maximum

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9.4. Biography

- ✓ I was born on January 8, 1985. in Behshahr (Iran). I finished high school in 2002, and graduated at pre-university studies in 2003. In basic academic studies at Payame Noor University, in Gorgan (Iran), in 2009, I graduated in Bachelor's degrees, while in 2013 graduated with a Master of science in exercise physiology at the Faculty of Sports and Physical Education in University of Sari (Iran). I has been actively engaged in wrestling since 1995, as a professional wrestler and head coach.
- ✓ Native language: Persian
- ✓ Other: English language

Work Experience

- Head coach of freestyle wrestling (Wrestling Federation of Serbia and KK "Crvena zvezda", Belgrade - 2021 – Present; Wrestling Federation of Serbia, 2022 - Present
- Trainer and fitness instructor (Ministry of Sports and Youth, Iran; 2013 – 2021);
- Sports Nursing (Federation of Sports Medicine, Iran; 2013 – 2021);
- Director of Medical Committee (Wrestling Association Board, Iran; 2019 – 2020);
- University lecturer (Public and Private University, Iran; 2014 – 2018).
- Teacher of physical education (High School and Elementary School; 2010 – 2013, 2019 – 2020).

9.5. Personal bibliography

JOURNAL ARTICLES:

1. **Zahabi, G.,** Ilic, V., García-Ramos, A., & Cokorilo, N. (2024). The Effects of L-Carnitine Supplementation During Concurrent Training on the Functional Capacities and Body Composition in Obese Men. Journal of Health and Allied Sciences NU. https://doi.org/10.1055/s-0044-1779724
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4. Abbassi-Daloii, A., Barari, A., Michaelpour, N., Emami, F., **Zahabi, G,** et al**.** (2024). High – Intensity Interval Training and Aloe vera Supplementation Improve METRNL Levels, Reduce Oxidative Stress, and Enhance Antioxidant Status in Men with T2DM. **Accepted from GAZZETTA MEDICA ITALIANA ARCHIVIO PER LE SCIENZE MEDICHE.**
5. **Zahabi, G.,** Ilic, V., Radaković, M., Pekas, D., & Zabihzadeh, F. (2023). THE EFFECTS OF LONG-TERM L-CARNITINE SUPPLEMENTATION DURING CONCURRENT TRAINING ON PHYSIOLOGICAL INDICATORS AND ANTHROPOMETRIC CHARACTERISTICS IN OBESE YOUNG WOMEN. (2023). Journal of Research Administration, 5(2), 14271-14284. https://journlra.org/index.php/jra/article/view/1873.
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9. **Zahabi,** G, Barari, A., Farzanegi, P., Ahmadi, M., (2014). Effect of concurrent training on the serum paraoxonase-1 (PON-1) activity and lipid profile in obese men. Intl Res J Appl Basic Sci, 8(9), 1434-7.

Participation at Conferences and Seminars:

1. The effects of long-term L-Carnitine supplementation during concurrent training on physiological indicators and anthropometric characteristics in obese young women, International Conference on Sport Medicine and Sport Science (ICSMSS-2024). Hamburg, **Germany, 2024].**
2. The effects of L-Carnitine supplementation during Concurrent training on body composition and functional capacities in obese men. International scientific conference „International Conference of Sport Science, Physical Education and Health ", Book of abstracts, 88, Belgrade. [Faculty of sport and physical education, University of Belgrade, **Serbia, 2022**].
3. The effect of creatine supplementation during strength training on the development of physical performance and hypertrophy in wrestlers. International scientific conference neuromuscular and strength training in of Sport, [Faculty of sport and physical education, University of Granada, **Spain, 2022**].
4. Effect of Concurrent Training on Paraoxonase Activity Levels and Some of the Lipid Plasma Markers in the Blood of obese women. International congress about health and women. [University of Medical Sciences, Shiraz, **Iran, 2014**].
5. Effect of Concurrent Training on Paraoxonase Activity Levels and Some of the Lipid Plasma Markers in the Blood of obese men and women. National conferences about sport sciences. [University of Shahid Beheshti, **Iran, 2013**].
6. Effect of sports exercise on PON1 activity levels and some lipid indices for cancer prevention in obese men [Tehran Center for International Audio-Visual Conference, **Iran, 2013**].
7. The effect of concurrent training on the level of the enzyme paraoxonase 1 and some lipid indices in the blood of obese non-athlete men. National conferences about exercise physiology. [Faculty of Sports Sciences, University of Tehran, **Iran, 2013**].

9.6. Obrazac 5
образац изјаве о ауторству

Изјава о ауторству

Име и презиме аутора: **Ghadir (Bashir) Zahabi**
Број индекса: **5013/2020**

Изјављујем

да је докторска дисертација под насловом

THE EFFECTS OF L-CARNITINE SUPPLEMENTATION DURING CONCURRENT TRAINING ON BODY COMPOSITION AND FUNCTIONAL CAPACITIES IN OBESE MEN.
ЕФЕКТИ СУПЛЕМЕНТАЦИЈЕ Л-КАРНИТИНА ТОКОМ ИСТОВРЕМЕНОГ ТРЕНИНГА НА САСТАВ ТЕЛА И ФУНКЦИОНАЛНЕ КАПАЦИТЕТЕ КОД ГОЈАЗНИХ МУШКАРАЦА

• резултат сопственог истраживачког рада;

• да дисертација у целини ни у деловима није била предложена за стицање друге дипломе

према студијским програмима других високошколских установа;

• да су резултати коректно наведени и

• да нисам кршио/ла ауторска права и користио/ла интелектуалну својину других лица.

Потпис аутора

Потпис аутора

У Београду,
10.10. 2024. године

9.7. Obrazac 6
образац изјаве о истоветности штампане и електронске верзије докторског рада

Изјава о истоветности штампане и електронске верзије докторског рада

Име и презиме аутора: **Ghadir (Bashir) Zahabi**
Број индекса: **5013/2020**

Студијски програм: **Experimental research methods of human locomotion**
Наслов рада: **THE EFFECTS OF L-CARNITINE SUPPLEMENTATION DURING CONCURRENT TRAINING ON BODY COMPOSITION AND FUNCTIONAL CAPACITIES IN OBESE MEN.**
ЕФЕКТИ СУПЛЕМЕНТАЦИЈЕ Л-КАРНИТИНА ТОКОМ ИСТОВРЕМЕНОГ ТРЕНИНГА НА САСТАВ ТЕЛА И ФУНКЦИОНАЛНЕ КАПАЦИТЕТЕ КОД ГОЈАЗНИХ МУШКАРАЦА

Ментор: **Dr Vladimir Ilic** , Full professor, Faculty of Sport and Physical Education, University of Belgrade; **Dr Amador García-Ramos,** Full professor, Department of Physical Education and Sport, Faculty of Sport Sciences, University of Granada, Cam. de Alfacar, 21, Norte, 18071 Granada, Spain

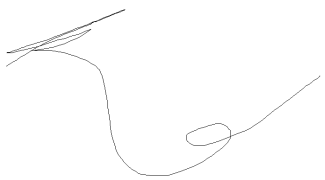
Изјављујем да је штампана верзија мог докторског рада истоветна електронској верзији коју сам предао/ла ради похрањивања у **Дигиталном репозиторијуму Универзитета у Београду.**

Дозвољавам да се објаве моји лични подаци везани за добијање академског назива доктора наука, као што су име и презиме, година и место рођења и датум одбране рада.

Ови лични подаци могу се објавити на мрежним страницама дигиталне библиотеке, у електронском каталогу и у публикацијама Универзитета у Београду.

Потпис аутора

У Београду,
10.10. 2024. године



9.8. Obrazac 7
образац изјаве о коришћењу

Изјава о коришћењу

Овлашћујем Универзитетску библиотеку „Светозар Марковић“ да у Дигитални репозиторијум Универзитета у Београду унесе моју докторску дисертацију под насловом:

THE EFFECTS OF L-CARNITINE SUPPLEMENTATION DURING CONCURRENT TRAINING ON BODY COMPOSITION AND FUNCTIONAL CAPACITIES IN OBESE MEN.
ЕФЕКТИ СУПЛЕМЕНТАЦИЈЕ Л-КАРНИТИНА ТОКОМ ИСТОВРЕМЕНОГ ТРЕНИНГА НА САСТАВ ТЕЛА И ФУНКЦИОНАЛНЕ КАПАЦИТЕТЕ КОД ГОЈАЗНИХ МУШКАРАЦА

која је моје ауторско дело.

Дисертацију са свим прилозима предао/ла сам у електронском формату погодном за трајно архивирање.

Моју докторску дисертацију похрањену у Дигиталном репозиторијуму Универзитета у Београду и доступну у отвореном приступу могу да користе сви који поштују одредбе садржане у одабраном типу лиценце Креативне заједнице (Creative Commons) за коју сам се одлучио/ла.

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(Молимо да заокружите само једну од шест понуђених лиценци. Кратак опис лиценци је саставни део ове изјаве).

Потпис аутора

У Београду,
10.10. 2024. године