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Physical Training in Metabolic Syndrome: Clinical and Physiological Evidence

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Abstract

Metabolic syndrome (MS) is characterized by the coexistence of metabolic disturbances such as insulin resistance, central obesity, dyslipidemia, and hypertension, which significantly increase the risk of cardiovascular diseases and type 2 diabetes. Physical training plays a central role in the prevention and treatment of MS by promoting physiological adaptations and widely documented clinical benefits. Evidence shows that aerobic exercise improves insulin sensitivity, endothelial function, and lipid profile, while resistance training contributes to increased lean mass, higher basal energy expenditure, and reduced visceral adiposity. Combined protocols (aerobic + resistance) produce superior synergistic effects on body composition and systemic inflammatory markers. Physiological mechanisms include increased mitochondrial biogenesis, reduced oxidative stress, regulation of adipokines, and improved peripheral glucose uptake mediated by GLUT-4. Clinically, structured exercise programs performed at least three times per week, at moderate to vigorous intensity, are effective in reversing syndrome components and reducing overall cardiovascular risk. Thus, physical training represents a highly relevant non-pharmacological intervention in the integrated management of metabolic syndrome, with a positive impact on metabolic physiology and patients' quality of life.

Keywords

Metabolic Syndrome, Physical Exercise, Insulin Resistance, Aerobic Training, Resistance Training

1. Introduction

The prevalence of metabolic syndrome (MS) has been rapidly increasing in both developed and developing countries and is commonly associated with obesity [1].

MS is a multifactorial clinical condition characterized by a cluster of metabolic disturbances that include central obesity, insulin resistance, dyslipidemia, and arterial hypertension. This grouping of risk factors is associated with a significant increase in cardiovascular morbidity and mortality, as well as a higher risk of developing type 2 diabetes mellitus [2]. The global rise in MS parallels the growth of sedentary behavior and obesity, reflecting behavioral and environmental changes related to modern lifestyle [3].

It is estimated that approximately one-quarter of the world's adult population meets the diagnostic criteria for MS, representing a major public health challenge [4]. Lifestyle-based interventions, particularly regular physical training, have been shown to be key strategies in preventing and treating this syndrome [5].

Considering the characteristics of this condition, one of the main treatments to reduce body weight and fat mass involves combining physical exercise with dietary re-education, as this strategy facilitates the establishment of a negative energy balance [6].

Physical exercise promotes several beneficial physiological and metabolic adaptations, among which the improvement of insulin sensitivity, increased energy expenditure and fatty acid oxidation, reduction of visceral adiposity, and positive modulation of inflammatory markers stand out [7]. Additionally, exercise training acts on molecular pathways such as AMPK, PI3K/Akt, and PGC-1α, stimulating mitochondrial biogenesis and reducing oxidative stress—central mechanisms in restoring metabolic homeostasis [8] [9].

From a clinical perspective, evidence shows that structured exercise programs—whether aerobic, resistance, or combined—can significantly reduce abdominal circumference, blood pressure, fasting glucose, and triglyceride levels in individuals with MS [10] [11]. These effects reinforce the role of physical training as a first-line intervention—safe, low-cost, and with a substantial impact on quality of life and cardiovascular prognosis [12].

Although the role of exercise in improving the components of metabolic syndrome is widely recognized, there are still gaps in the integrated understanding of the physiological and molecular mechanisms involved, as well as uncertainties regarding the most effective dose, intensity, and type of training for different patient profiles. Analyzing available clinical evidence, combined with elucidating the underlying mechanisms, is essential to guide personalized strategies for prevention and treatment.

2. Objective

To review the main clinical evidence and the physiological and molecular mechanisms associated with the effects of physical training on metabolic syndrome, highlighting the impacts on energy metabolism, insulin sensitivity, inflammatory profile, and cardiometabolic risk factors.

3. Methodology

This is a narrative literature review aimed at synthesizing the main scientific evi-

dence available on the effects of physical training on the clinical, physiological, and molecular aspects of MS. The literature search was conducted in the PubMed/MEDLINE, Scopus, ScienceDirect, and SciELO databases, including publications from 2010 to 2025.

The following English descriptors were used: *metabolic syndrome*, *exercise training*, *physical activity*, *aerobic exercise*, *resistance training*, *insulin sensitivity*, *inflammation*, and *mitochondrial function*. In Portuguese: *síndrome metabólica*, *treinamento físico*, *atividade física*, *exercício aeróbico*, *exercício resistido*, and *inflamação sistêmica*.

Inclusion criteria comprised original articles, systematic reviews, meta-analyses, and controlled clinical trials that investigated the effects of physical exercise on clinical parameters (blood pressure, body composition, glycemia, lipid profile) and physiological parameters (mitochondrial biogenesis, insulin sensitivity, inflammatory markers) in individuals with MS. Exclusion criteria were: studies exclusively with animal models, narrative reviews without a critical approach, articles without full-text access, and publications in languages other than Portuguese or English.

Study selection was conducted in three stages: title screening, abstract analysis, and full-text reading of eligible articles. Extracted information included: author and year, sample characteristics, type and duration of training, main clinical outcomes, and physiological mechanisms. Data were organized descriptively and interpretatively, allowing for an integrated discussion between clinical evidence and underlying physiological mechanisms.

4. Literature Review

4.1. Clinical Effects

Evidence indicates that an adequate lifestyle helps in the management and prevention of metabolic syndrome (MS) and its associated factors. Modification of eating habits and structured exercise prescription should be considered first-line, non-pharmacological and non-invasive treatments to improve MS, providing cardioprotective benefits associated with increased cardiorespiratory fitness [13]. These benefits result largely from improvements in endothelial function and peripheral blood flow, favored by greater nitric oxide (NO) bioavailability and reduced vascular oxidative stress [14].

Resistance (strength) training complements these effects by promoting increases in skeletal muscle mass, higher basal metabolic rate, and enhanced insulin-dependent and insulin-independent glucose uptake, partly mediated by activation of the AMPK pathway [15]. Activation of this pathway clinically contributes to reducing triglycerides, improving lipid profile, and enhancing glycemic control through increased fatty acid oxidation and intramuscular glucose uptake, in addition to inhibiting hepatic lipogenesis—fundamental processes in controlling MS components [16] [17]. This modality also aids in preserving lean mass and attenuating metabolic sarcopenia, which is frequently observed in individuals with MS

and central obesity [18].

The literature shows that combining aerobic and resistance training potentiates visceral fat reduction, optimizes lipid profile, and increases cardiorespiratory fitness (VO_2max), considered one of the strongest predictors of cardiovascular mortality [19] [20]. Thus, integrating different training modalities represents an effective and clinically relevant strategy for comprehensive management of metabolic syndrome.

4.2. Molecular and Metabolic Adaptations

From a molecular and bioenergetic perspective, exercise activates the AMPK–PGC-1α pathway, which is essential for mitochondrial biogenesis and increased oxidative capacity of skeletal muscle [21] [22].

AMPK activation plays a central role in improving the lipid profile by stimulating metabolic pathways that increase fatty acid oxidation and reduce hepatic lipid synthesis. Once activated, AMPK inhibits acetyl-CoA carboxylase (ACC), decreasing malonyl-CoA production and consequently releasing carnitine palmitoyltransferase-1 (CPT-1) to enhance fatty acid transport into mitochondria for oxidation. Simultaneously, AMPK reduces the activity of HMG-CoA reductase and the transcription factor SREBP-1c, leading to decreased hepatic lipogenesis and cholesterol synthesis. These combined effects result in lower plasma triglyceride and LDL-cholesterol levels, favoring a more efficient and cardioprotective metabolic environment [23] [24].

4.3. Immunometabolic Modulation

Physical exercise also directly impacts the immunometabolic system by promoting a shift in adipose tissue macrophages from a pro-inflammatory (M1) to an anti-inflammatory (M2) phenotype [25]. This shift is accompanied by increased secretion of myokines with beneficial metabolic effects, such as irisin, IL-6, IL-10, and SPARC, which promote thermogenesis, lipolysis, and improved energy metabolism [26] [27].

The myokine IL-6, when acutely released during exercise, exerts systemic anti-inflammatory effects by inhibiting TNF-α production and stimulating IL-10 secretion [28].

4.4. Endocrine Axis

The effect of physical exercise on insulin sensitivity may last 12 to 48 hours after a training session but returns to baseline within three to five days after the last session, reinforcing the need for regular and frequent physical activity [29].

4.5. Epigenetic Effect

In addition to metabolic and inflammatory adaptations, recent evidence indicates that exercise influences epigenetic mechanisms such as DNA methylation and histone modification, modulating the expression of genes involved in en-

ergy metabolism and inflammation [30]. These epigenetic changes appear to mediate part of the sustained benefits of exercise, even after temporary interruptions in training.

A well-documented example is the epigenetic modulation of the PGC-1*α* gene, considered a central regulator of mitochondrial biogenesis and oxidative metabolism. Studies show that acute exercise sessions reduce methylation in promoter regions of PGC-1*α*, increasing its expression and promoting metabolic adaptations such as greater oxidative capacity and improved insulin sensitivity [31] [32]. These findings reinforce that epigenetic alterations may contribute to maintaining metabolic benefits of exercise even after training interruptions.

4.6. Individualization of Exercise Prescription

Another relevant aspect concerns the individualization of exercise prescription. Metabolic response varies according to sex, age, body composition, and presence of comorbidities. Women with MS, for example, tend to show greater resistance to lipid oxidation and more pronounced inflammatory responses, often requiring combined and progressive protocols [33].

Individualization is essential to optimize therapeutic outcomes and ensure safety, especially in patients with MS or other cardiometabolic comorbidities. Factors such as baseline fitness level, functional limitations, and specific clinical conditions guide the choice between aerobic, resistance, or combined programs. Individuals with low cardiorespiratory fitness or advanced obesity may initially benefit from moderate-intensity aerobic exercise with gradual progression as tolerated [34]. Patients with sarcopenia, frailty, or age-related muscle loss tend to respond better when resistance training is prioritized, given its effectiveness in improving strength, increasing lean mass, and reducing inflammatory markers [35] [36].

In situations where multiple risk factors coexist—such as insulin resistance, hypertension, and increased waist circumference—combined programs demonstrate superior benefits by simultaneously promoting cardiorespiratory, metabolic, and musculoskeletal adaptations [37] [38]. Thus, modality selection should always be guided by clinical and functional assessment and individual goals, ensuring a personalized approach that maximizes benefits and minimizes risks.

5. Conclusions

Physical training is a fundamental therapeutic tool for the prevention and treatment of metabolic syndrome (MS), with well-established clinical and molecular benefits. Exercise-induced adaptations—especially through combined aerobic and resistance training—improve insulin sensitivity, reduce systemic inflammation, stimulate mitochondrial biogenesis, and promote metabolic homeostasis. At the molecular level, exercise regulates central metabolic pathways, including AMPK activation, PGC-1*α* expression, and GLUT4 signaling, contributing to en-

ergy balance and preventing metabolic dysfunctions associated with obesity and insulin resistance. Furthermore, regular physical activity exerts cardioprotective effects by modulating plasma lipids, blood pressure, and inflammatory markers—key components in reducing the elevated cardiovascular risk characteristic of individuals with MS.

Beyond these physiological effects, exercise prescription should follow structured, evidence-based guidelines. Current recommendations indicate that adults with MS should perform aerobic exercise 3 to 5 times per week at moderate to vigorous intensity, accumulating 150 - 300 minutes per week of moderate activity or 75 - 150 minutes of vigorous activity [39]. Resistance training is recommended 2 - 3 times per week, involving major muscle groups, with 1 - 3 sets of 8 - 12 repetitions. Combined training (aerobic + resistance) provides the greatest impact on visceral fat reduction, improved insulin sensitivity, and modulation of inflammatory markers [40]. High-intensity interval training (HIIT) may be incorporated for clinically stable individuals, offering superior improvements in cardiorespiratory fitness and glycemic control [41]. Exercise prescription should also be individualized, considering baseline fitness level, comorbidities, and patient preferences to optimize adherence and clinical outcomes [42].

Therefore, physical exercise should be considered a first-line, low-cost, and highly effective intervention with substantial public health impact. Strategies that promote regular participation—particularly when individualized and combined with nutritional guidance—can significantly reduce the incidence, progression, and complications associated with metabolic syndrome.

6. Limitations

Despite their usefulness in synthesizing broad and heterogeneous evidence, narrative reviews present important limitations, particularly regarding the potential for selection bias. Because they do not follow strictly structured protocols—such as explicit inclusion and exclusion criteria, systematic assessment of methodological quality, or standardized search strategies—there is greater subjectivity in the choice of included studies [43] [44]. This flexibility may result in disproportionate emphasis on certain findings, inadvertent exclusion of relevant studies, or overlapping interpretations influenced by the authors' prior experience [45]. Additionally, the absence of quantitative methods to evaluate the consistency of results limits the strength of the conclusions and reduces reproducibility [46]. Thus, although useful for integrating knowledge and discussing physiological mechanisms, narrative reviews should have their conclusions interpreted with caution, acknowledging the inherent biases of this study design.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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