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THE IMPACT OF PHYSICAL ACTIVITY ON FUNCTIONING OF THE CARDIO-RENAL-PULMONARY AXIS IN INDIVIDUALS WITH VISCERAL OBESITY - THE SIGNIFICANCE OF EXERCISE AS A PREVENTIVE AND THERAPEUTIC STRATEGY

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ABSTRACT

Introduction: Visceral obesity contributes to dysfunction of the integrated cardio-renal-pulmonary (CORP) axis, promoting insulin resistance, chronic low-grade inflammation, hypertension, and glomerular hyperfiltration. Physical activity (PA) is recognized as an effective therapeutic and preventive strategy; however, its specific impact on all components of the CORP axis requires a comprehensive analysis.
Objective: To evaluate the effects of various forms of physical activity on: cardiovascular fitness and aerobic capacity (VO_2 max, cardiorespiratory fitness - CRF), renal function (glomerular filtration rate - GFR, albuminuria), pulmonary structure and function (lung volumes, tissue compliance), in adults with visceral obesity.
Methods: A systematic review of the literature and selected meta-analyses of randomized controlled trials and cohort studies was conducted using PubMed, PMC, and Embase databases up to June 2025. Interventions included aerobic training, high-intensity interval training (HIIT), resistance training, and combined exercise programs. Changes in CRF, visceral adipose tissue (VAT), GFR, blood pressure, and lung function indicators were analyzed.
Conclusions: Physical activity- particularly aerobic, interval, and combined training- has a beneficial effect on the function of the cardio-renal-pulmonary axis in individuals with visceral obesity. Key mechanisms include enhanced aerobic fitness, VAT reduction, improved metabolic profile, attenuation of inflammation, and nephroprotection. Regular exercise should be an essential component of therapeutic and preventive strategies in this population. Further research is warranted to clarify the dose-response relationship between exercise type/intensity and improvements in each CORP axis system.

KEYWORDS

Physical Activity, Visceral Obesity, Cardio-Renal-Pulmonary Axis, Cardiorespiratory Fitness, Chronic Kidney Disease, HIIT, Cardiovascular Prevention, Low-Grade Inflammation, Insulin Resistance, Non-Pharmacological Interventions

CITATION

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1. Introduction

Visceral obesity, defined as excessive accumulation of fat within the abdominal cavity and around internal organs, is one of the most significant risk factors for chronic diseases in the 21st century. Epidemiological data confirm the increasing prevalence of this form of obesity in both developed and developing countries, correlating with the rising incidence of metabolic syndrome, type 2 diabetes, hypertension, and chronic kidney disease (CKD)[1].

Visceral adipose tissue (VAT) functions as a metabolically and hormonally active gland, secreting adipokines and pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which induce chronic inflammation, insulin resistance, oxidative stress, and activation of the sympathetic nervous system. These processes lead to endothelial dysfunction, vascular remodeling, hypertension, microangiopathy, and nephropathy [2]. VAT also adversely affects the respiratory system by reducing chest wall compliance and lung volumes, resulting in impaired ventilatory capacity and decreased exercise tolerance [3].

Although studies consistently demonstrate the benefits of physical activity for metabolic health, cardiac, and renal function, exercise interventions remain insufficiently integrated into standard treatment of multi-organ dysfunction related to obesity. Clinical practice is dominated by pharmacological approaches and weight reduction strategies, often overlooking the direct effects of exercise on the cardio-renal-pulmonary axis function, independent of weight loss [4][5].

The aim of this paper is to review current scientific evidence on the impact of physical activity on the functioning of the integrated cardio-renal-pulmonary axis in individuals with visceral obesity, with particular emphasis on physiological mechanisms and types of training as therapeutic and preventive strategies.

2. Visceral obesity as a contributor to multi-organ dysfunction

Visceral obesity extends beyond passive energy storage, functioning as an active endocrine and immunologic organ. Excess accumulation of visceral adipocytes promotes hypertrophy and hypoxia within the tissue, leading to endoplasmic reticulum stress and triggering a cascade of molecular alterations. VAT is characterized by increased secretion of pro-inflammatory adipokines (leptin, resistin, TNF-α, IL-6, MCP-1) and decreased production of protective adiponectin, an adipokine with insulin-sensitizing and anti-inflammatory effects [6][7].

These conditions promote recruitment and activation of M1-type macrophages and the establishment of a chronic low-grade inflammatory state (meta-inflammation), which underlies metabolic and organ-specific complications [8].

This inflammatory activity drives the release of free fatty acids into the circulation and hepatic portal system, contributing to insulin resistance, lipotoxicity, activation of the renin-angiotensin-aldosterone system (RAAS), and sympathetic nervous system stimulation [9]. VAT also produces angiogenic and profibrotic factors, including those mediated via hypoxia-inducible factor 1 (HIF-1), exacerbating structural changes in blood vessels, cardiac tissue, the kidneys, and lungs [6].

3. Pathophysiological impact of visceral adipose tissue on the heart, kidneys, and lungs

Visceral adipose tissue, particularly epicardial and perirenal fat depots, exerts both local paracrine and systemic endocrine effects. In the cardiovascular system, epicardial fat acts as a pro-inflammatory signaling hub, releasing cytokines and adipokines that promote myocardial fibrosis, adverse cardiac remodeling, and coronary artery disease [7][8]. Clinical studies have demonstrated a positive correlation between visceral adiposity and coronary artery calcification scores (CACS), independent of traditional cardiovascular risk factors [8].

Furthermore, VAT increases hemodynamic load through sodium retention, expanded plasma volume, increased cardiac preload and afterload, and elevated systemic vascular resistance. This contributes to the development of hypertension, left ventricular hypertrophy, and ultimately heart failure [8].

With regard to the kidneys, visceral obesity is associated with obesity-related glomerulopathy, characterized by glomerular hyperfiltration, proteinuria, and a progressive decline in estimated glomerular filtration rate (eGFR) [9]. VAT-derived pro-inflammatory cytokines, notably TNF-α and IL-6, initiate tubulointerstitial inflammation, oxidative stress, and fibrosis, facilitating both acute kidney injury (AKI) and chronic kidney disease progression [10].

The respiratory system is adversely affected by increased VAT through mechanical restriction of diaphragmatic excursion, reduced lung volumes (functional residual capacity, total lung capacity), and increased thoracic stiffness. These changes impair gas exchange and predispose to hypoventilation and obstructive sleep apnea (OSA) [11]. Additionally, VAT-derived inflammatory mediators contribute to bronchial hyperresponsiveness and structural airway remodeling, aggravating pulmonary diseases such as asthma, chronic obstructive pulmonary disease, and obesity hypoventilation syndrome (OHS) [11].

VAT creates a convergence of four interrelated pathophysiological burdens: volume overload, pressure overload, chronic systemic inflammation, and hypoxemia. Hypertension and expanded intravascular volume jointly burden the heart and kidneys, while renal sodium retention further amplifies fluid accumulation and hemodynamic stress [9]. Simultaneously, hypoxemia secondary to obesity-related ventilatory disorders activates the sympathetic nervous system and RAAS, which in turn exacerbates hypertension and cardio-renal dysfunction [6][11].

Inflammation serves as a central mechanistic link between organ systems. Mediators originating from visceral adipose tissue, including TNF-α, IL-6, and resistin, contribute to endothelial dysfunction, myocardial remodeling, pulmonary fibrosis, and nephron damage. These inflammatory cascades are sustained by the organ injury itself; chronic kidney disease, for instance, amplifies systemic inflammation, thereby accelerating cardiovascular and pulmonary decline [12][13].

4. Physical Activity and Renal Function in People with Visceral Obesity

Visceral obesity is a substantial risk factor for the onset of chronic kidney disease (CKD). Visceral adipose tissue (VAT) demonstrates endocrine and pro-inflammatory functions, which contribute to metabolic disorders, insulin resistance, hypertension, and chronic inflammation- fundamental pathomechanisms of renal impairment [14].

In this situation, physical activity can serve a significant preventive function. An expanding corpus of research demonstrates that consistent physical activity, particularly aerobic and moderate-intensity activities, might diminish visceral fat and enhance kidney function metrics [15][16][17].

Visceral adipose tissue is distinguished by heightened metabolic activity, secreting several adipokines and proinflammatory cytokines, including interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α), and C-reactive protein (CRP). These compounds provoke a condition of chronic inflammation that leads to the impairment of the glomerular filtration barrier and the aggravation of albuminuria. Furthermore, VAT induces insulin resistance, which exacerbates problems of glucose and lipid metabolism, and stimulates the renin-angiotensin-aldosterone system (RAAS), resulting in elevated blood pressure — a critical element in the advancement of CKD. An investigation of 35,000 adults from NHANES (2005–2018) indicated that a greater visceral fat accumulation index (VAI) correlates with a 30% elevated risk of microalbuminuria and a 27% heightened risk of chronic kidney disease (CKD) [18].

Visceral obesity is more strongly correlated with renal dysfunction than general obesity, as measured by BMI. Numerous studies show that indicators such as waist circumference, waist-to-hip ratio (WHR), or visceral adipose tissue volume assessed by imaging methods (e.g. MRI, CT) better predict the risk of CKD than BMI [19][20]. The lowering of VAT is thus a therapeutic objective with potential nephroprotective implications.

Physical activity markedly diminishes VAT independent of alterations in body weight. A meta-analysis conducted by Rao et al. (2019) encompassing 17 long-term randomized controlled trials exceeding six months, evaluated the impact of exercise and pharmacotherapy on the reduction of VAT as measured by CT or MRI [21]. The findings indicated that exercise enhanced the profile of VAT reduction, even in the absence of significant alterations in body weight. Physical therapies decreased VAT with a modest impact, while medication shown a comparatively lesser effect.

An increasing number of studies validate that the reduction of visceral adipose tissue positively impacts renal function via multiple processes. Initially, diminished VAT correlates with enhanced hypertension management, resulting in decreased renal strain and a deceleration of nephron deterioration [22].

Epidemiological statistics indicate that regular physical exercise correlates with a reduced risk of albuminuria. A substantial 2024 cohort study with 12,961 adults with hypertension demonstrated that physically active individuals exhibited a markedly reduced risk of albuminuria in comparison to their inactive counterparts [23]. These effects were noted irrespective of the existence of diabetes or other concomitant conditions. Comparable findings were observed in the Maastricht Study, which examined accelerometer data from 2,258 people [24]. It was determined that each additional hour of moderate or intense physical activity daily correlated with an elevation in eGFR and a diminished risk of albuminuria. A sedentary lifestyle, quantified by duration of inactivity, correlated with diminished kidney function scores and a heightened probability of albuminuria. Randomized controlled trials offer robust data supporting the advantages of physical activity in diminishing albuminuria. The 2019 RENEXC trial of individuals with CKD stages 3–5 shown that a 12-month regimen of daily physical activity (30 minutes, five times per week) resulted in a 33% decrease in albuminuria within the strength training cohort, with no significant alterations in eGFR [25]. Meta-analyses demonstrate that aerobic training (minimum of 30 minutes per session, 3–5 times weekly) correlates with a substantial decrease in albuminuria or total proteinuria, independent of body weight loss [26][27].

Moreover, consistent physical activity and decreased VAT are associated with enhanced insulin sensitivity, which diminishes glycation and oxidative stress, so safeguarding glomeruli from additional harm [28].

The reduction of VAT results in a substantial decline in blood concentrations of inflammatory markers. Interventions that incorporate lifestyle modifications, including dietary adjustments and consistent physical exercise, resulting in the reduction of visceral adipose tissue (VAT), led to reduced levels of TNF-α, IL-6, and CRP [29]. The meta-analysis of randomized controlled trials by Rao et al. [21] demonstrates that merely 12–16 weeks of aerobic exercise and/or resistance training results in a substantial reduction in VAT and a corresponding decline in inflammatory markers, irrespective of total weight loss. A reduction in VAT is associated with enhanced metabolic parameters and a diminished risk of renal problems.

Visceral adipose tissue demonstrates specific metabolic activity, generating surplus free fatty acids (FFA) that, through hepatorenal circulation, contribute to atherogenic dyslipidemia. It is marked by elevated triglyceride levels, reduced HDL concentration, and a heightened proportion of tiny, dense LDL particles. This lipid profile fosters lipotoxicity, characterized by lipid buildup in non-storage cells, such as renal and tubular cells. This results in mitochondrial abnormalities, oxidative stress, inflammation, and death of renal cells. Research indicates that diminishing visceral fat enhances the lipid profile, characterized by a reduction in triglyceride levels, an elevation in HDL concentrations, and a decrease in small LDL particle fractions, thereby mitigating kidney lipotoxicity and indirectly lowering the risk of renal structural damage [21]. Significantly, these alterations are noted even with a modest overall decrease in body weight, underscoring the importance of qualitative modifications in body composition—particularly the reduction of visceral adipose tissue—as a crucial therapeutic element. These data substantiate the notion that VAT lowering not only alters cardiovascular risk variables but also actively fosters regeneration and structural safeguarding of the kidneys in persons with chronic renal disease or elevated metabolic risk.

Recent years have seen an increasing interest in the efficacy of combining flozin medications (SGLT2 inhibitors) with behavioral therapies, like as regular physical activity, to enhance kidney function in individuals with visceral obesity. Sodium-glucose cotransporter 2 inhibitors (SGLT2 inhibitors), including dapagliflozin and empagliflozin, exhibit multifaceted nephroprotective benefits that extend beyond glycemic regulation [30]. They have demonstrated the ability to diminish glycotoxicity and lipotoxicity, lower intraglomerular pressure, and mitigate hyperfiltration, especially evident in cases of obesity. Moreover, the weight reduction resulting from flozin medication, averaging 2–3 kg, is primarily associated with VAT. Research indicates that the combination of flozin and regular physical activity may produce a synergistic impact. Both therapies diminish visceral adipose tissue, and their synergistic application may enhance the reduction of inflammation and indicators of renal impairment [31][32]. Physical activity enhances insulin sensitivity and augments glucose efficiency, so complementing the mechanism of action of flozins, which entails increased glucosuria. Decreasing the activation of the RAA system and oxidative stress subsequently results in a reduction of interstitial fibrosis and the progression of CKD. Randomized clinical trials are necessary to evaluate the synergistic effect of these therapies in individuals with visceral obesity and CKD.

Interventions that result in VAT reduction, including consistent physical activity, a suitably chosen diet, and, in specific instances, medication, must be essential components of the management for individuals with visceral obesity and CKD risk. By modifying many pathophysiological pathways, the lowering of VAT may decelerate kidney damage progression and diminish the risk of cardiovascular consequences. The reduction of visceral fat is crucial for safeguarding renal function, influencing several pathways that contribute to kidney

injury. Implementing treatment measures to diminish VAT can yield substantial clinical advantages, such as decreased albuminuria, enhanced metabolic indices, and regulated blood pressure, ultimately resulting in improved prognosis for patients with chronic renal disease.

5. Physical activity and the respiratory system

During physical exertion, the body requires additional oxygen, resulting in heightened airflow within the lungs. After many minutes, it became apparent that ventilation stabilizes at a level commensurate with the intensity of the exertion. Lung capacity correlates directly with exercise intensity until the workload surpasses 70% of the maximum oxygen uptake per minute. Upon reaching this value, hyperventilation may ensue. As lung oxygen stores diminish and deeper breaths prove inadequate, the respiratory rate alters. This results in a substantial rise in energy demand and an escalation of weariness. Regular exercisers exhibit advantageous alterations, notably enhanced lung capacity. This phenomena correlates with enhanced respiratory muscle strength and increased chest flexibility. In such instances, there is a decrease in dead space volume, despite total lung ventilation remaining constant.

Systematic effort enhances respiratory depth and decreases the respiratory rate, hence optimizing the performance of the muscles involved in respiration. Consistent workout elevates oxygen levels by 25% and diminishes oxygen debt. Individuals in optimal physical condition exhibit enhanced blood circulation in the superior regions of their lungs. This impact enhances gas exchange in the lungs, positively influencing the ratio of alveolar ventilation to capillary blood flow. In well-conditioned individuals, hyperventilation manifests at elevated exertion levels compared to those with a sedentary lifestyle. This effect alleviates the sensation of dyspnea during vigorous activity.

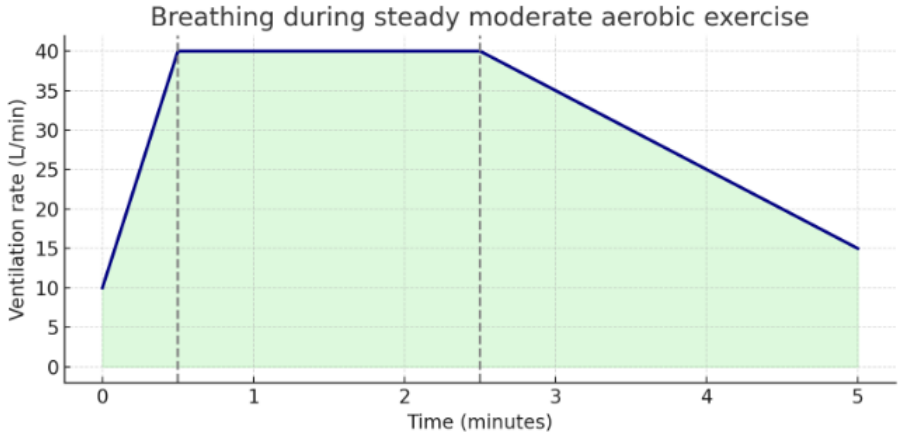

Fig. 1. *Breathing during steady moderate aerobic exercise*

During physical exertion, there is an elevation in both oxygen demand and carbon dioxide output. Notwithstanding this, the concentrations of gases dissolved in arterial blood remain remarkably steady. The complete process behind this phenomena is inadequately researched. The tidal volume (VT) and respiratory rate both increase, influenced by various factors such as the intensity of central nervous system impulses, alterations in arterial blood pH, potential changes in potassium concentration, and adjustments in the carotid body's sensitivity to CO2 levels.

Providing respiratory support for obese individuals might be difficult due to alterations in the structure and function of their respiratory system. This condition is characterized by diminished respiratory compliance, expiratory reserve volume, functional residual capacity, and total lung capacity. A 5% to 15% decrease in FRC is expected for each 5 kg/m² rise in BMI [33]. Overweight individuals exhibit diminished spirometry outcomes, including forced vital capacity, forced expiratory volume in one second, and peak expiratory flow, which are inversely linked with BMI [34]. As body weight rises due to an increase in adipose tissue, respiratory performance declines, presenting as a restrictive pattern [35].

Shortness of breath affects 10 to 25 percent of the general population, however among obese individuals, this prevalence may reach up to 80 percent. The diaphragm in obese persons endures increased mechanical stress compared to healthy individuals of normal weight; this muscle must exert additional energy to generate

chest pressure during inhalation, despite its restricted range of motion. Individuals with excess weight exhibit a more rapid yet shallower respiratory pattern in comparison to those who are healthy [36].

6. Types of Physical Activity and Therapeutic Effects

The diversity of physical activity forms plays a crucial role in modulating visceral adipose tissue metabolism and the functioning of the cardio-renal-pulmonary (CORP) axis. The selection of appropriate training types should be based on scientific evidence regarding the specific mechanisms of action of different forms of exercise on the human organism.

Aerobic Training

Aerobic training demonstrates high effectiveness in reducing visceral adipose tissue through multiple physiological mechanisms. Continuous moderate-intensity exercise (50-70% HRmax) for 30-60 minutes stimulates lipolysis and enhances fat oxidation capacity [37]. Studies indicate that aerobic training reduces visceral fat by 12-20% over 12-16 weeks, with concurrent improvements in insulin sensitivity and cortisol regulation [38]. The anti-inflammatory effects of aerobic exercise contribute to breaking the vicious cycle of chronic low-grade inflammation associated with visceral obesity.

Resistance Training

Resistance training offers unique benefits through muscle mass preservation and metabolic enhancement. High-intensity resistance exercise (70-85% 1RM) stimulates growth hormone and testosterone secretion, which counteracts cortisol-induced protein catabolism. Meta-analyses demonstrate that resistance training reduces visceral fat by 6-10% while maintaining or increasing lean body mass, resulting in improved metabolic profile [39]. The post-exercise oxygen consumption (EPOC) effect following resistance training enhances metabolic rate for up to 48 hours post-exercise [40].

High-Intensity Interval Training (HIIT)

HIIT protocols demonstrate superior time-efficiency in visceral fat reduction compared to continuous moderate exercise. Short bursts of high-intensity exercise (85-95% HRmax) alternated with recovery periods induce significant metabolic adaptations [41]. Research shows that HIIT reduces visceral adiposity by 17% over 12 weeks with only 45 minutes of weekly training [42]. The mechanism involves enhanced fat oxidation, improved insulin sensitivity, and favorable hormonal responses including reduced cortisol reactivity to stress [43].

Combined Training Protocols

Concurrent training combining aerobic and resistance components demonstrates synergistic effects on body composition and metabolic health. Studies indicate that combined protocols result in greater visceral fat reduction (15-25%) compared to single-modality training approaches [44]. The integration of different training stimuli optimizes hormonal responses, particularly growth hormone and IGF-1 secretion, while maintaining elevated post-exercise metabolic rate [45].

7. Practical Aspects and Recommendations

7.1. Volume and Intensity Requirements for Visceral Fat and CORP Axis Modulation

The minimal effective dose for visceral fat reduction requires 150-300 minutes of moderate-intensity aerobic activity or 75-150 minutes of vigorous-intensity exercise weekly, as recommended by international guidelines [46]. However, for significant visceral adiposity reduction, higher volumes may be necessary. Studies demonstrate that 225-420 minutes of moderate-intensity exercise weekly results in clinically meaningful visceral fat loss [47].

For resistance training, the American College of Sports Medicine recommends 2-3 sessions weekly targeting major muscle groups with 2-4 sets of 8-15 repetitions at 70-85% 1RM. HIIT protocols require only 75-100 minutes weekly but should be performed 2-3 times per week with adequate recovery periods.

Regarding CORP axis modulation, regular exercise of moderate intensity (40-60% VO_2max) for 30-45 minutes daily effectively reduces cortisol reactivity and improves stress resilience [48]. Higher intensities may transiently increase cortisol but result in improved long-term regulation [49].

7.2. Reversibility of Early Organ Changes

Early metabolic dysfunction and organ changes associated with visceral obesity demonstrate significant reversibility through structured exercise interventions. Hepatic steatosis, a common comorbidity, shows improvement within 4-8 weeks of aerobic training initiation, with 25-40% reduction in liver fat content [50]. Insulin resistance markers improve within 2-4 weeks of training commencement, with continued enhancement over 12-16 weeks [51].

Cardiovascular adaptations, including endothelial function improvement and arterial stiffness reduction, manifest within 6-12 weeks of regular exercise [52]. However, the window for complete reversibility may be limited, emphasizing the importance of early intervention before irreversible structural changes occur.

7.3. Individualization of Training Programs

Age-Specific Considerations

Training prescription must account for age-related physiological changes. Older adults (>65 years) benefit from combined aerobic and resistance training with emphasis on functional movements and fall prevention. Progressive volume increases should be more gradual, with initial intensities at 40-50% HR max, advancing to 60-70% as adaptation occurs [53]. Middle-aged adults (40-65 years) can tolerate higher intensities but require careful monitoring for cardiovascular risk factors. HIIT protocols may be particularly effective in this population for time-efficient visceral fat reduction.

Fitness Level Adaptations

Sedentary individuals require extended adaptation periods with gradual progression. Initial programs should emphasize movement quality and enjoyment rather than intensity. Trained individuals may require higher volumes and intensities to achieve continued adaptations, with periodized approaches preventing plateaus.

Comorbidity Management

Diabetes mellitus requires careful glucose monitoring and potential medication adjustments during exercise progression. Combined aerobic and resistance training provides optimal glycemic control. Hypertensive individuals benefit from moderate-intensity continuous training with gradual progression, avoiding excessive isometric contractions.

Individuals with metabolic syndrome require comprehensive lifestyle interventions combining structured exercise with dietary modifications. Multi-component programs addressing all metabolic syndrome components demonstrate superior outcomes compared to single-intervention approaches [54].

7.4. Integration with Pharmacotherapy

GLP-1 Receptor Agonists

The combination of GLP-1 receptor agonists with structured exercise demonstrates synergistic effects on weight loss and metabolic improvement. Exercise enhances GLP-1 secretion naturally, potentially augmenting pharmaceutical effects. Studies indicate that combined interventions result in 8-15% body weight reduction compared to 5-10% with medication alone [55].

Timing considerations suggest exercising 2-4 hours post-injection to minimize gastrointestinal side effects while maximizing metabolic benefits. The combination appears particularly effective for visceral fat reduction, with studies showing 20-30% greater loss compared to monotherapy approaches [56].

Metformin and Exercise

Metformin's effects on exercise adaptation require careful consideration. While the medication enhances insulin sensitivity independently, it may blunt some exercise-induced mitochondrial adaptations. However, the combined effects on visceral fat reduction and glycemic control generally outweigh potential interference with training adaptations [57].

Monitoring and Safety

Combined pharmacotherapy and exercise require enhanced monitoring protocols. Regular assessment of blood glucose, blood pressure, and body composition ensures optimal outcomes while minimizing adverse events. Healthcare provider collaboration is essential for medication adjustments as fitness improves and body composition changes.

8. Perspectives and Future Research

8.1. Lack of Randomized Controlled Trials (RCTs) with Physical Activity as the Primary Intervention for the Cardio-Renal-Pulmonary Axis

Although several randomized trials have demonstrated that physical activity can reduce visceral adipose tissue (VAT) in obese individuals, there is a lack of studies directly targeting the cardio-renal-pulmonary (CORP) axis as a unified system. A meta-analysis confirmed that aerobic and resistance training interventions longer than six months significantly reduce VAT measured via CT or MRI imaging [58]. However, these studies rarely assess downstream effects on integrated cardiac, renal, and pulmonary function.

Moreover, few trials stratify patients by visceral obesity or use physical activity as the sole therapeutic intervention, isolated from confounding factors such as pharmacological treatment or caloric restriction. The heterogeneity of protocols and lack of harmonized outcome measures further limits generalizability. There is an urgent need for multi-center RCTs with well-characterized populations and outcomes, including VO_2 peak, eGFR, pulmonary function tests, and advanced echocardiographic or MRI-based parameters assessing cardiac remodeling and vascular compliance.

8.2. The Need to Validate Biomarkers of Exercise Response

Inflammatory and metabolic biomarkers such as C-reactive protein (CRP), leptin, and galectin-3 are promising as mediators and indicators of cardio-metabolic stress, yet their role in monitoring response to exercise in patients with visceral obesity remains underexplored.

One study demonstrated that 12 weeks of aerobic training in obese men significantly reduced CRP, IL-6, and leptin while increasing adiponectin [59]. In patients with heart failure with preserved ejection fraction (HFpEF), elevated CRP and leptin levels correlated with impaired exercise tolerance and adverse hemodynamic responses [60]. Galectin-3, a fibrosis-associated biomarker, has shown positive correlations with BMI, CRP, IL-6, and TNF-α in obese individuals [61]. Yet, standardized thresholds for interpreting exercise-induced changes in galectin-3 have not been established.

Future studies should assess serial biomarker changes alongside objective CORP functional outcomes. Trials should evaluate CRP, leptin, galectin-3, and IL-6 before and after intervention and correlate these with VAT reduction, VO_2 max, renal function, and pulmonary parameters.

8.3. Can Exercise Delay or Halt the Progression of Multiorgan Dysfunction?

Preclinical data suggest that exercise can attenuate organ damage linked to obesity. In rodent models, endurance training improved renal histopathology, reduced fibrosis, and decreased oxidative stress, partly via AMPK activation and autophagy [62][63].

In humans, physical inactivity and elevated inflammatory markers (especially leptin and CRP) are associated with reduced cardiac reserve and exercise capacity in obese individuals and those with HFpEF [60]. However, there is a paucity of long-term data examining whether physical activity prevents or delays clinical deterioration across the CORP axis.

Future research should prioritize long-term (>12-month) RCTs tracking clinical outcomes (e.g., development of HFpEF, CKD progression, pulmonary dysfunction) and biomarker trajectories in stratified groups undergoing exercise interventions.

9. Conclusions

This review clearly demonstrates that physical activity plays a crucial role both as a therapeutic and preventive strategy in managing multi-organ dysfunction associated with visceral obesity, particularly concerning the cardio-renal-pulmonary axis. Regular exercise leads to significant reduction of visceral adipose tissue, which underlies improvements in cardiovascular, renal, and respiratory function.

Physical training positively affects endothelial function, reduces arterial stiffness, and improves heart rate variability (HRV), resulting in lower incidence of hypertension and heart failure with preserved ejection fraction (HFpEF). In the kidneys, exercise reduces microalbuminuria, enhances autoregulation and renal blood flow, and lowers inflammatory markers. In the respiratory system, physical activity alleviates symptoms of obstructive sleep apnea and obesity hypoventilation syndrome, improves lung vital capacity, and increases exercise tolerance, significantly reducing dyspnea.

Various exercise modalities- aerobic, resistance, interval, and combined training- show therapeutic benefits; however, combined programs appear most effective in addressing the complex pathophysiology of visceral obesity. Individualizing exercise plans based on age, fitness level, and comorbidities is key.

Incorporating physical activity into standard treatment protocols for visceral obesity and metabolic syndrome should be regarded as a fundamental and accessible strategy to improve health and quality of life. Combining exercise with pharmacotherapy, such as GLP-1 receptor agonists and SGLT2 inhibitors, may provide synergistic effects, though further research is needed.

There is a pressing need for large-scale clinical trials with physical activity as the primary intervention to determine optimal exercise dosages and to verify the potential for reversing early organ changes. Validating exercise response biomarkers (CRP, galectin-3, leptin) could advance personalized exercise prescriptions for treating visceral obesity.

In summary, physical activity is an effective and cost-efficient tool for preventing and managing multi-organ dysfunction in individuals with visceral obesity. Promoting awareness of the role of exercise and integrating it as a standard component of comprehensive medical and rehabilitation care is essential.

Disclosure

Author's contribution: Aleksandra Sowa, Kacper Trząsalski, Conceptualisation: Patrycja Jędrzejewska-Rzezak, Katarzyna Oświeczyńska; Methodology: Sebastian Kupisiak, Katarzyna Oświeczyńska; Software: Patrycja Jędrzejewska-Rzezak, Sebastian Kupisiak; Check: Katarzyna Oświeczyńska; Formal: Patrycja Jędrzejewska-Rzezak; Investigation: Aleksandra Sowa; Resources: Kacper Trząsalski, Patrycja Jędrzejewska-Rzezak; Data curation: Katarzyna Oświeczyńska, Patrycja Jędrzejewska-Rzezak; Writing-Rough Preparation: Aleksandra Sowa, Kacper Trząsalski; Writing-Review and Editing: Sebastian Kupisiak, Aleksandra Sowa; Visualisation: Kacper Trząsalski, Sebastian Kupisiak; Supervision: Sebastian Kupisiak, Aleksandra Sowa; Project Administration: Kacper Trząsalski, Katarzyna Oświeczyńska

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In preparing this work, the authors used ChatGPT (chatGPT.com) as a tool for translation, improving language and readability. After using the tool, the authors have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

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