Journal of Social Research
P-ISSN: 2827-9832
E-ISSN: 2828-335x
Vol. 5, No. 2, January 2026
http://ijsr.internationaljournallabs.com/index.php/ijsr

The Effect of Physical Activity on Oxidative Stress in Inhibiting Systemic Aging

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ABSTRACT

Systemic aging accelerated by oxidative stress is a global health challenge that demands evidence-based intervention strategies. Physical activity offers a promising non-pharmacological approach, but its molecular mechanisms require a review of the relevant literature. This article aims to analyze the molecular mechanisms underlying the effectiveness of physical activity in suppressing oxidative stress and inhibiting the systemic aging process. This literature review employs a systematic search of the PubMed, Scopus, Web of Science, and ScienceDirect databases to identify studies published between 2021 and 2025. Inclusion criteria encompassed studies analyzing the interaction between physical activity, oxidative stress, and biomarkers of aging. Synthesis of the results showed that physical exercise consistently increased expression of endogenous antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase) through activation of redox-sensitive transcription factors. Combination therapy with aerobic and resistance exercise effectively lowered lipid peroxidation biomarkers (malondialdehyde) and increased total antioxidant capacity. Significant clinical adaptations were achieved at an optimal intensity of 70-85% VO_2max for 8-12 weeks, although individual responses showed heterogeneity influenced by genetic factors and baseline health status. The therapeutic effectiveness of physical exercise in combating aging—mediated by regulation of oxidative stress—has been consistently demonstrated in numerous studies. However, its application in clinical practice requires personalized interventions, with exercise programs individually tailored to ensure optimal therapeutic responses.

Keywords: *Physical Activity; Oxidative Stress; Systemic Aging; Antioxidants; Precision Exercise.*

INTRODUCTION

Aging is a biological mechanism characterized by a decrease in physiological function and increased susceptibility to degenerative diseases. Molecularly, oxidative stress is one of the main triggers of cellular and tissue damage. Free radical theory emphasizes how the imbalance between production Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) with endogenous antioxidant defense results in the accumulation of damage to essential biomolecules (proteins, lipids, nucleic acids). This accumulation of oxidative damage is believed to accelerate the aging process and exacerbate the decline in biological, physiological, and cognitive function (Ziada et al., 2020).

The pathophysiological manifestations of cellular redox imbalances involve complex molecular cascades in biological systems. Progressive damage to the mechanism of oxidative homeostasis not only results in structural damage to biomolecules, but also induces epigenetic modifications underlying the acceleration of cellular aging (Ziada et al., 2020). Previous studies have shown that the accumulation of protein and lipid oxidation products interferes with proteostasis which plays a role in the cell aging mechanism (Galli et al., 2024).

Oxidative stress is defined as a pathological condition that occurs when the production of free radicals exceeds the capacity of the body's antioxidant defense system resulting in oxidative damage to important cellular components (Chandimali et al., 2025). Manifestations of oxidative stress in the context of systemic aging include various pathophysiological changes ranging from mitochondrial dysfunction, chronic inflammation, to disruption of cellular homeostasis which then plays a role in the development of cardiovascular, neurodegenerative, and metabolic diseases (Dash et al., 2025). During the aging process, there is a chronic increase in oxidative and inflammatory stress that serves as the main pathophysiology. Both of these conditions also trigger a decline in function in the musculoskeletal and cardiovascular systems, resulting in a significant decline in the functional status and quality of life of elderly individuals (El Assar et al., 2020).

Inhibition of the acceleration of cellular aging processes through decreased oxidative stress is a major focus in modern gerontology research. A diverse range of intervention approaches have been explored to achieve these goals, but structured physical activity occupies a fundamental position as a nonpharmacological therapeutic approach with a significant efficacy and safety profile. Physical activity has been shown to increase the activity of the endogenous antioxidant defense system, which plays an important role in neutralizing ROS. This increased capacity not only strengthens the cellular ability to fight oxidative damage, but also supports the optimization of metabolic homeostasis and overall vascular function (Meng & Su, 2024).

The therapeutic paradigm in preventive gerontology is undergoing a fundamental change as the understanding of lifestyle modification-based interventions as a key strategy in modulating the mechanisms of biological aging (Mohd. Tohit & Haque, 2024). Emerging scientific evidence consistently suggests that nonpharmacological approaches, especially sports interventions, have the capacity to induce cellular rejuvenation through the activation of several protective pathways in biological systems. The concept of hormesis, in which exposure to mild stress induces favorable adaptation, is a theoretical framework that explains how paradoxically controlled physical stress can increase systemic resistance to oxidative damage. The application of scientifically evidence-based strategic exercise recipes not only provides immediate health benefits, but also has the potential to modify epigenetic regulation associated with longevity and healthy aging mechanisms (Zalukhu et al., 2016).

Physiological adaptation mechanisms to regular physical activity involve complex biochemical pathways, including activation of transcription factors sensitive to redox status and increased expression of endogenous antioxidant enzymes. Some studies show that exercise is an activity that can help increase natural antioxidants in the body, as well as minimize damage caused by oxidative stress. Long-term adaptations to physical exercise include an increase in the defense system of endogenous antioxidants such as superoxide dismutase, catalase, and glutathione peroxidase, which play an important role in neutralizing free radicals produced during aerobic metabolism (Simioni et al., 2018).

The process of adaptation to physical exercise involves multisystem integration, with complex coordination between neurological, hormonal, and molecular signaling pathways that increase cellular resistance to environmental stresses. In exercise physiology, cross-adaptation shows that physical exercise not only increases performance capacity, but also strengthens stress tolerance and recovery mechanisms in the face of a wide range of physiological challenges. The process of molecular adaptation due to exercise is characterized by the sequential activation of transcription programs that play a role in regulating the synthesis of antioxidant enzymes, stimulating mitochondrial biogenesis, and facilitating cell repair mechanisms. A comprehensive understanding of the dynamics and kinetics of exercise adaptation is an important foundation in designing appropriate intervention protocols to maximize therapeutic benefits while minimizing the risk of side effects due to inappropriate exercise prescriptions (Heza et al., 2020).

A targeted medical approach in modern gerontology emphasizes the importance of an exercise program based on individual profiles. The strategy is based on the stratification of genomic and metabolomics profiles to optimize adaptive responses and reduce the heterogeneity of clinical responses to oxidative stress. The validity of this approach is supported by empirical evidence demonstrating the superiority of multimodal interventions in modulating systemic redox homeostasis, which is demonstrated through changes in key biomarkers such as 8-OHdG. This is also confirmed by a significant positive correlation between objective fitness parameters with various biomarkers that serve as strong predictors of cellular health and life expectancy (Simioni et al., 2018).

Light to moderate intensity physical activity that is consistently clinically proven to facilitate endogenous repair and regeneration mechanisms (Militello et al., 2024). Structured physical exercise intervention is an essential nonpharmacological therapeutic modality with the main function of regulating redox balance and suppressing the progression of systemic senesenic processes. The clinical efficacy of these interventions depends on appropriate adjustment of exercise doses, including measured adjustments to intensity, duration, and frequency.

Therefore, an exercise program based on individual profiles through stratification based on the functional capacity and physiological status of the individual is an essential clinical need. This individual-profile-based exercise program approach is a key requirement for reducing response heterogeneity, optimizing adaptive responses, and maximizing the therapeutic potential of interventions in the context of preventive gerontology. In addition, the implementation of well-structured physical activity not only increases endogenous antioxidant capacity, but also stimulates beneficial hormonal adaptations, including a decrease in cortisol production known to play a role in accelerating collagen degradation and premature aging (Rebelo-Marques et al., 2021).

Determination of optimal exercise parameters to prevent age-related oxidative damage requires consideration of individual heterogeneity in physiological responses as well as genetic variations that affect adaptive capacity to physical activity. The appropriate therapeutic approach in the exercise program integrates biomarker analysis, genetic profiling, and functional assessment to develop intervention strategies that are appropriate to the biological characteristics and health status of each individual.

The current research paradigm emphasizes the importance of longitudinal monitoring as well as adjustment of exercise programs according to the body's response based on physiological feedback real-time and biomarker profiles that reflect the effectiveness of the intervention. The integration of advanced technology and analytics in training programs has the potential to revolutionize antiaging interventions through continuous optimization tailored to individual responses. In addition, the use of predictive analysis allows the determination of the ideal exercise dosage to suppress oxidative stress and promote longevity (Li et al., 2025).

The complexity of the relationship between physical activity, oxidative stress, and systemic aging requires a thorough research approach to understand the molecular mechanisms underlying the protective effects of physical exercise. Identify specific biochemical pathways involved in antioxidant adaptation as physical activity is necessary for the development of more effective and personalized intervention strategies. Multidisciplinary research that integrates aspects of exercise physiology, molecular biochemistry, and gerontology is needed to optimize exercise protocols that can maximize antioxidant benefits while minimizing the risk of injury or excessive stress.

In that context, the process of systemic aging is understood as a complex phenomenon involving the interaction of various biological mechanisms, in which oxidative stress plays an important role in triggering cellular damage and deterioration of physiological function. In line with the development of the preventive gerontology paradigm, structured physical activity was identified as an effective nonpharmacological intervention to modulate the molecular pathways of aging through the enhancement of the endogenous antioxidant defense system. However, the relationship between intensity, duration, and type of exercise with antioxidant adaptation and systemic aging prevention still needs more in-depth study.

Based on this, this study aims to analyze in depth the mechanisms of physical activity in inhibiting oxidative stress and slowing down the biological aging process at the molecular and cellular levels. Specifically, this study focuses on the identification of biochemical pathways of antioxidant adaptation, characterization of exercise-responsive oxidative stress biomarkers, as well as the evaluation of various physical activity modalities to determine optimal exercise protocols. In addition, the study also examined individual factors such as age, gender, health status, and genetic polymorphisms that affect response to exercise. The results of this study are expected to provide a scientific basis for the formulation of evidence-based systemic aging prevention strategies that can be applied in the context of clinical and community practice.

METHOD

This study uses a literature review approach with a narrative method to comprehensively analyze the role of physical activity in preventing systemic aging through oxidative stress inhibition mechanisms. The narrative method was chosen for its ability to integrate findings from various disciplines (exercise physiology, molecular biochemistry, gerontology) to provide a holistic understanding. Literature searches are conducted systematically using major electronic databases (PubMed, Scopus, Web of Science, Science Direct) for publications with a time range of 2021-2025. The search strategy used a combination of Boolean keywords (AND, OR, NOT) in English and Indonesian, including: "physical activity", "exercise", "oxidative stress", "aging", "antioxidants", "free radicals", and "exercise-induced adaptation".

The search was extended through cross-referencing and the Cochrane Library. The search also includes theses, dissertations, research reports through university repositories, national portals (Garuda, Neliti), ProQuest, Google Scholar, and OpenGrey to ensure the completeness and relevance of the data.

The selection process is carried out with strict criteria to ensure the relevance and quality of the study.

Kriteria Inclusive: Article type: Original research, systematic review, meta-analysis, and clinical trials. 2) Topic: Investigating the relationship between physical activity and oxidative stress in the context of aging. 3) Period & Language: Published in 2021-2025 in English or Indonesian. 4) Subject: Involves an adult human subject or relevant animal model. 5) Output: Focus on biomarkers of oxidative stress and endogenous antioxidant parameters.

Exclusion Criteria: 1) Article type: Editorial, letter to editor, and case report. 2) Methodology: Studies with inadequate or unclear methodology. 3) Subject Conditions: Studies focusing on acute pathological conditions. 4) Interventions: Studies involving exogenous antioxidant supplementation (to focus analysis on the intrinsic effects of physical activity).

Methodological validation was carried out to ensure the consistency of the findings. Each article that passed the selection was evaluated for quality using standardized instruments: the Newcastle-Ottawa Scale (observational study), the Cochrane Bias Risk Tool (clinical trial), and AMSTAR-2 (systematic review). Studies with quality scores below the specified threshold were excluded from the final synthesis. Data extraction is done using standard forms. Data analysis uses a thematic (inductive) approach to identify patterns and themes through open coding, axial coding, and selective coding. Narrative synthesis was conducted to integrate the findings of the 29 included articles and identify knowledge gaps in the literature.

RESULTS AND DISCUSSION

In this study, a systematic literature search was conducted on major databases such as PubMed, Scopus, Web of Science, and Science Direct with a publication time range of 2021 to 2025. From the initial search, a total of 125 articles were successfully identified after the removal of duplication and screening of titles and abstracts.

After further selection based on strict inclusion and exclusion criteria, as well as methodological quality assessment using standard instruments such as the Newcastle-Ottawa Scale, the Cochrane Bias Risk Tool, and AMSTAR-2, a total of 29 studies were eligible for narrative analysis and synthesis in this study. These studies include a variety of research designs, including original research articles, systematic reviews, meta-analyses, and clinical trials that specifically investigate the relationship between physical activity and modulation of oxidative stress in the context of systemic aging.

Molecular Mechanisms of Physical Activity in Modulation of Oxidative Stress

A comprehensive analysis of various scientific publications shows that physical activity plays a key modulator in cellular redox balance through a series of highly complex and coordinated molecular adaptations. The findings of the study suggest that the application of physical exercise consistently triggers a significant increase in the synthesis of endogenous antioxidant enzymes, including superoxide dismutase, catalase, and glutathione peroxidase, which serve as an early protective mechanism in neutralizing free radicals formed during oxidative metabolic processes.

El Assar et al. (2022) provides strong evidence that interventions in the form of physical activity are able to significantly increase endogenous antioxidant capacity, accompanied by a significant decrease in oxidative stress and staged proinflammatory signals that play a role in age-related degenerative processes. In addition, physical activity is also known to trigger the activation of anabolic pathways as well as promote mitochondrial biogenesis in skeletal muscle. This fundamental adaptation mechanism is controlled by the selective activation of transcription factors sensitive to changes in cellular redox status, particularly Nuclear factor erythroid 2–related factor 2 (Nrf2), which is responsible for the genomic regulation of antioxidant protein-encoding complexes. In exercise-induced oxidative stress, physical activity of a certain intensity can temporarily increase ROS production, but this increase also acts as a trigger to strengthen and maintain the activation of the antioxidant defense system.

Follow-up research shows that acute oxidative stress triggered by high-intensity exercise is transient and can be recovered with a tendency to return to physiological levels within 24 hours through activation of endogenous antioxidant systems. This activation has a delayed onset, but it provides a long-lasting protective effect. This complex molecular adaptation process is mediated by the activation of various signaling pathways, including the mitogen-activated protein kinase (MAPK) and the phosphoinositide 3-kinase (PI3K) which interacts with protein kinase B (Akt) and synergistically regulates cellular responses to oxidative stress. In addition to regulation at the transcription level, increased expression of antioxidant enzymes also involves complex posttranslational modifications that significantly amplify the catalytic activity of these enzymes. Thus, the cell develops a series of complementary protective mechanisms to minimize the impact of oxidative damage (Lu et al., 2021).

The epigenetic aspect of redox regulation triggered by physical activity suggests the presence of an important additional regulation in the cell's adaptive response to oxidative stress. Recent genomic findings indicate that physical exercise can alter DNA methylation patterns as well as histone modifications, which further affect chromatin accessibility to transcription factors that regulate the expression of antioxidant genes. These changes form a persistent epigenetic memory that allows the cell's defense system to be reactivated more quickly when repeated oxidative stress exposure occurs.

In addition, findings regarding the transgenerational inheritance of epigenetic markers influenced by physical activity suggest that such protective adaptations have the potential to be passed on to offspring, so the impact of lifestyle interventions could provide long-term benefits to population health. This entire process reflects a coordinated interaction between metabolic signals, redox status, and epigenetic mechanisms, which together regulate the expression of protective proteins through a stratified regulatory mechanism to optimize cellular function and resistance to stress.

Different Exercise Effectiveness on Biomarkers of Oxidative Stress

Analysis of different forms of physical activity showed that each modality had different levels of effectiveness in lowering biomarkers of oxidative stress and improving indicators of systemic antioxidant status. The combination of aerobic exercise and resistance training produces a strong synergistic effect, which is reflected in the marked decrease in the rate of lipid peroxidation of cells as well as an increase in the total antioxidant capacity in the biological system. Studies conducted by That is why et al. (2023) Through a network metaanalysis methodology, it revealed the revolutionary finding that an integrated program combining aerobic exercise with low-intensity resistance training showed high potential in reducing cellular lipid peroxidation. The results of the analysis showed that the modality had a probability of 0.31 to occupy the most effective position and 0.20 to be in the second place.

Research results by That is why et al. (2023) emphasizing that a coordinated multimodal approach has advantages over the application of one type of exercise in optimizing the systemic antioxidant response. Resistance training protocols showed a moderate effect on increased concentrations of circulating 8-OHdG, a specific biomarker of oxidative DNA damage that is also associated with accelerated tissue regeneration processes. Research conducted by Yes et al. (2021) definitively proving that endurance training produced a standard mean difference of 0.66 at increased circulating 8-OHdG concentrations, with consistent effects evident in both trained status and untrained population of participants.

In different studies, aerobic exercise modalities showed a heterogeneous response pattern and were highly dependent on the status of individual exercise conditions, where participants with trained status experienced an improvement with a small category effect on 8-OHdG concentrations (standard mean difference = 0.42), while untrained participants showed a decrease with a large category effect (standard mean difference = -1.16) especially after an extended duration aerobic exercise protocol. Thirupathi et al. (2021) reports that each form of exercise has the potential to increase oxidative damage depending on the type as well as the intensity parameters of the exercise.

Individual physical condition factors and the specificity of biomarkers of oxidative damage play an important role in predicting the occurrence of damage due to sports training loads. The complexity of this variation of responses underscores the importance of personalizing the design of exercise programs tailored to the individual characteristics and specific goals of the targeted antioxidant intervention.

Each individual's oxidative response to physical activity varies greatly because it is influenced by differences in their respective metabolic phenotypes. To maximize therapeutic benefits, a personalized approach to exercise is required. Advanced metabolomics analysis can help identify specific metabolic profiles in each individual.

This mass spectrometry-based metabolomics analysis is carried out through the process of extracting metabolites from biological samples, separation using chromatography techniques, and molecular detection through mass spectrometry to produce a comprehensive metabolite profile. The raw data is then analyzed by bioinformatics methods to identify and quantify the relevant metabolites. Through these measures, individual metabolic patterns can be precisely mapped allowing grouping based on predicted exercise responses and supporting the development of more targeted interventions with optimal effectiveness (Hajnajafi & Iqbal, 2025).

The Impact of Exercise Duration and Intensity on Antioxidant Adaptation

Exercise programs designed for the long term show significant efficacy advantages in inducing sustained and self-sustaining antioxidant adaptation compared to acute exercise intervention protocols that are episodic in nature. Longitudinal studies proved that the application of a structured physical exercise program for 12 weeks resulted in a significant improvement in the performance parameters of functional tests and induced a decrease in the risk of falls in the elderly female population, with the manifestation of an increase in the concentration of sulfhydryl groups from a baseline value of 0.53 ± 0.06 to a level of 0.58 ± 0.08 in the group with insufficient vitamin D status and from 0.54 ± 0.03 to 0.59 ± 0.04 in the group with vitamin D that was Sufficient (Rodziewicz-Flis et al., 2022).

The results of this study show that that improvements in functional performance and reduced risk of falls in elderly women after undergoing a related training program by strengthening the antioxidant defense system. This is shown by the increased concentration of sulfhydryl groups as a marker of antioxidant capacity. In addition, the results indicated that the effectiveness of exercise in increasing antioxidant defenses was not affected by vitamin D status, as a comparable increase in sulfhydryl groups was observed in participants with vitamin D deficiency and adequacy.

The antioxidant adaptations induced by physical exercise are robust and independent of initial nutritional status, as shown in the study by Rodziewicz-Flis et al. (2022) that protective benefits occur regardless of vitamin D levels. (2021) used the Standardized Mean Difference (SMD), a statistical measure for the magnitude of effects suggesting that aerobic exercise resulted in a large decrease in damage markers (e.g., malondialdehyde, SMD = -1.80) and a large increase in protective factors (e.g., total antioxidant capacity, SMD = 1.22; superoxide dismutase, SMD = 0.63). To achieve clinically significant adaptation, an optimal dose of moderate-high intensity exercise (70–85% VO_2max) performed 3–4 times per week for a minimum of 8–12 weeks is applied, to balance adaptive stimulation and recovery.

Increased antioxidant activity is characterized by an initial phase of acute oxidative stress which is then followed by a compensatory response in the form of an increase in defense capacity beyond baseline physiological levels for a longer period of time. The timing of exercise on circadian rhythm has a significant effect on the magnitude of induced oxidative stress and the speed of recovery, where morning exercise results in higher antioxidant activation than night exercise due to circadian fluctuations in cellular redox status.

A molecular strategy that applies systematic variation in the parameters of the exercise stimulus, supports the progressive improvement of the antioxidant system while preventing maladaptive responses due to monotonous exercise patterns. To maintain the long-term benefits of exercise-induced antioxidants, exercise stimuli must be administered at thresholds sufficient to trigger protective adaptations without inducing excessive oxidative stress that has the potential to impair cellular integrity and physiological function in both the elderly group and the general population.

Individual and Determinant Responses in Antioxidant Adaptation

Inter-individual variability in response to physical activity protocols reflects complex biological dynamics and is influenced by a variety of determinants including age parameters, sex characteristics, basic health status, and genetic predisposition. A comprehensive analysis of the literature suggests that adaptations in geriatric populations differ from those of young adult cohorts, but meaningful clinical improvements are still possible even if responses vary. The findings of the study stated that the elderly with increased oxidative stress and systemic inflammation experienced pathological changes in the musculoskeletal and cardiovascular systems that had an impact on decreased functional status. However, physical exercise protocols remain effective in modulating inflammatory parameters characterized by decreased interleukin-6 and increased interleukin-10 (Bacanoiu et al., 2023).

Sex differences have been shown to play an important role in determining the amount and pattern of antioxidant adaptation. Women showed a more pronounced response to a combination aerobic and resistance exercise program, particularly on parameters related to bone metabolism and reduced risk of falls. In addition, genetic polymorphisms in genes encoding important antioxidant enzymes, such as superoxide dismutase-2 and glutathione peroxidase-1, play a substantial role in interindividual variation in basal antioxidant capacity as well as responses to oxidative stress induced by physical exercise.

Early health status, including the presence of subclinical inflammation and manifestations of metabolic dysfunction, has a significant influence on adaptive capacity and plays a role in determining optimal individual exercise programs. Individuals who show inflammatory markers increase in the initial condition, showing more significant improvement potential, but simultaneously require a more conservative approach to avoid excessive oxidative load and potentially harmful effects.

Exercise history and level of physical fitness are very important determinants in determining the characteristics of the acute response to oxidative stress caused by sports activities. Individuals with trained status show superior tolerance and faster recovery ability compared to individuals with no prior exercise experience. Overall nutritional status, especially related to antioxidant vitamin intake and mineral availability, has a modulative role to exercise-induced adaptation. It can also determine whether exogenous antioxidant supplementation is necessary or has the potential to have negative effects that interfere with the body's natural adaptation mechanisms.

A multidimensional phenotype-based classification system that includes functional, molecular, and genetic parameters, allows the development of appropriate training programs taking into account the complex interactions between individual characteristics and environmental factors that affect adaptation capacity (Marotta et al., 2025). In addition, the computer modeling approach (in silico) that integrates molecular data and physiological measurements resulting in predictive algorithms that can project individual responses and identify optimal intervention parameters according to specific phenotype profiles (Watson et al., 2022).

The assessment of biological age uses an integrated biomarker panel, which is a combination of several biological indicators such as oxidative stress, telomere length, and inflammatory markers, thus providing a more accurate picture of physiological status than just chronological age (Vaiserman & Krasnienkov, 2021). This allows for the development of more appropriate exercise programs for individuals with different biological aging levels. A dynamic phenotype approach that monitors changes in biomarker profiles throughout the training intervention, allowing for the adaptation of the protocol *real-time* as well as early identification of individuals who may require alternative therapeutic strategies to achieve optimal anti-aging benefits.

Clinical and Translational Implications for Preventive Practice

The process of translating findings from basic research into clinical practice is essential to develop evidence-based guidelines that are applicable and applicable to a wide range of populations with diverse health conditions and fitness levels. A comprehensive synthesis of the available evidence suggests that a precisely structured physical activity program has the potential to serve as an effective therapeutic intervention to prevent the acceleration of premature aging and reduce aging-related oxidative damage.

Clinical application allows for an individualized approach by taking into account factors such as chronological age, physiological age, comorbidities, and individual preferences to maximize adherence and minimize risk (El Assar et al., 2022) . The optimal exercise program for the geriatric population should combine 30–45 minutes of moderate-intensity aerobic exercise (50–70% of maximum heart rate reserve) with low- to moderate-intensity endurance training of 2–3 sessions per week, with an emphasis on gradual weight progression and strict control of safety parameters (Zhang et al., 2025).

Physical exercise protocols are able to improve endothelial function and reduce arterial stiffness through mechanisms that inhibit inflammatory and oxidative damage to vascular tissues, accompanied by increased antioxidant enzyme activity and optimization of nitric oxide availability. Overall, these effects support improved functional performance and promote a healthy aging process (Königstein et al., 2023) Monitoring using biomarkers such as malondialdehyde, 8-OHdG, and inflammatory cytokines can be an important tool for assessing the effectiveness of interventions as well as providing a basis for adjustments to exercise programs based on scientific evidence (El Assar et al., 2022).

The integration of health care systems from sports-based antiaging interventions requires the development of a comprehensive infrastructure that supports the implementation, monitoring, and effectiveness of systematic evaluations in a wide range of clinical regulations and population demographics. A scientifically evidence-based clinical approach that integrates standardized assessment protocols, individual exercise program design algorithms, and outcome evaluation frameworks is critical to ensure the consistent implementation of high-quality exercise interventions that have been proven effective in preventing aging-related oxidative damage (Izquierdo et al., 2021).

Health practitioners need to understand that an initial increase in oxidative stress markers after starting an exercise program is a normal and physiological adaptive response, which will be followed by a significant increase in antioxidant capacity if exercise consistency is maintained. The implementation of technology-based monitoring systems has the potential to improve compliance and provide feedback real-time for the optimization of training programs based on individual profiles. In addition, community-based programs that combine social support and motivation from the environment have been shown to be more effective in maintaining long-term compliance while achieving sustainable and significant health outcomes (Chimberengwa & Naidoo, 2020).

From a pharmacoeconomic perspective, the evaluation of the cost and effectiveness between exercise programs and pharmacological interventions for age-related conditions consistently shows that exercise programs offer higher value. Physical exercise provides broad health benefits, minimal side effects, and reduced long-term health care costs (Mo et al., 2023). Current research focuses on developing a combination therapy model to address complex aging processes more comprehensively. This approach is often called a multimodal intervention that combines exercises tailored to individual needs and supportive therapeutic strategies such as nutritional interventions. By targeting multiple physiological pathways at once, combination therapy aims to more effectively manage age-related biological changes, thereby helping to maintain functional health and prolong periods of healthy living (healthspan).

CONCLUSION

Physical activity serves as an effective anti-aging strategy with strong potential for programmatic clinical application, as it systematically stimulates the body's endogenous antioxidant defenses to combat cellular damage from oxidative stress. Optimal protection arises from combining moderate-to-high-intensity aerobic exercise with resistance training, which enhances enzyme expression and reduces biomarkers like malondialdehyde while boosting total antioxidant capacity. However, individual response variability underscores the need for personalized exercise programs tailored to genetic and metabolic profiles to promote healthy, functional aging. For future research, investigators should conduct randomized controlled trials exploring gene-exercise interactions using advanced biomarkers (e.g., telomere length, epigenomic clocks) to develop precision-based protocols that account for demographic factors like age, sex, and baseline fitness in diverse populations.

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