Healthcare: Jurnal Ilmiah Kesehatan
e-ISSN: xxxx-xxxx | Vol. 1. No. 1. Tahun 2026
https://doi.org/10.59923/healthcare.v1i1.804

ROS Signaling and Exercise Adaptation: The Physiological Basis of HIIT and MICT Responses

Shellya Puti Sudesty[1),*], Rifda El Mahroos[2)], Khorina Fatin Bilqis[1)], Sri Octa Handayani[1)]

[1)]Program Studi Kedokteran, Universitas Lampung, Indonesia
[2)]Program Studi Kedokteran, Universitas Pembangunan Nasional Veteran, Indonesia

*Correspondence: shellyaputisudesty@fk.unila.ac.id

ABSTRACT

Reactive oxygen species (ROS) are reactive molecules that play an important role in the physiological response to physical exercise. Although ROS are commonly associated with oxidative stress and cellular damage, recent scientific evidence suggests that ROS also function as signaling molecules that mediate metabolic, mitochondrial, and cardiometabolic adaptations during exercise. This literature review aimed to analyze the role of ROS signaling in exercise adaptation, particularly in high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT), from the perspective of exercise physiology and redox biology. The review employed a narrative literature review approach through article searches in Scopus, PubMed, ScienceDirect, and Google Scholar databases published between 2018 and 2026. A total of 24 eligible articles were qualitatively analyzed based on their focus on redox signaling, mitochondrial adaptation, molecular pathways, and cardiometabolic responses to exercise. The findings demonstrated that physiological levels of ROS activate signaling pathways including AMPK, PGC-1α, Nrf2, MAPK, and NF-κB, which contribute to mitochondrial biogenesis, endogenous antioxidant enhancement, insulin sensitivity, and metabolic efficiency. HIIT generally induces a greater and more rapid oxidative stimulus that promotes stronger molecular adaptation, whereas MICT produces a more stable and sustained redox response. Both exercise modalities provide beneficial effects on cardiometabolic health through distinct adaptive mechanisms. Therefore, ROS signaling represents an essential physiological component linking exercise stimuli to metabolic and mitochondrial adaptation.

Kata Kunci: Cardiometabolic Health; HIIT; MICT; Mitochondrial Adaptation; ROS Signaling

INTRODUCTION

Regular exercise is widely recognized as a potent physiological stimulus that improves health, yet its acute metabolic burden includes a transient rise in reactive oxygen species (ROS) production in active skeletal muscle (Powers et al., 2020; Bouviere et al., 2021). Contemporary evidence no longer positions ROS solely as harmful by-products of exercise; instead, ROS are understood as signaling molecules that can trigger adaptive responses, including antioxidant upregulation, metabolic remodeling, and muscle adaptation (Powers et al., 2020; Zhou et al., 2024). This dual role is central to the exercise redox paradigm, in which oxidative stress becomes beneficial when the stimulus remains within a physiologically tolerable range and when repeated exposure promotes adaptation rather than injury (Powers & Schrager, 2022; Martinez-Canton et al., 2024).

The redox response to exercise is closely linked to signal transduction pathways that govern cellular adaptation (Bouviere et al., 2021; Powers & Schrager, 2022). ROS-sensitive pathways such as Nrf2/Keap1, AMPK, and PGC-1α are repeatedly implicated in exercise-induced antioxidant defense, mitochondrial biogenesis, and skeletal muscle remodeling (Bouviere et al., 2021; Martinez-Canton et al., 2024). Recent reviews also show that exercise prescription variables, especially type, dose, frequency, and duration, shape mitochondrial responses in a highly specific manner, supporting the idea that the same exercise modality may produce different adaptations depending on its physiological context (Bishop et al., 2025; Torma et al., 2019).

Comparative evidence suggests that high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT) produce distinct ROS profiles and downstream adaptations (Reljic, 2025; Wang et al., 2021). High-intensity interval training (HIIT) tends to create a stronger, more transient oxidative stimulus, whereas MICT generally produces a more stable and sustained redox load (Torma et al., 2019; Powers & Schrager, 2022). In experimental and review-based studies, both modalities have been associated with improvements in oxidative balance and metabolic health, but HIIT is often reported as more time-efficient and, in some contexts, more effective in reducing skeletal muscle ROS or promoting mitochondrial signaling

e-ISSN: xxxx-xxxx | Vol. 1. No. 1. Tahun 2026
https://doi.org/10.59923/healthcare.v1i1.804

(Reljic, 2025; Yin et al., 2024). At the same time, the magnitude of benefit remains dependent on population, training dose, and outcome measure (Poon et al., 2024; Yang et al., 2024).

From a physiological perspective, this topic is important because ROS signaling may serve as the bridge between acute exercise stress and chronic adaptation across multiple systems, including skeletal muscle, mitochondria, vascular function, and cardiometabolic regulation (Powers et al., 2020; Zhou et al., 2024). The literature from 2022 to 2025 increasingly supports the view that exercise-induced redox signaling contributes not only to mitochondrial remodeling, but also to broader metabolic outcomes such as glucose regulation, lipid homeostasis, and cardiometabolic risk reduction (Bishop et al., 2025; Reljic, 2025). However, the evidence remains fragmented across experimental models, human populations, and biomarker panels, making it difficult to formulate a unified mechanistic model of HIIT and MICT adaptation (Poon et al., 2024; Powers & Schrager, 2022). For this reason, a focused review on ROS signaling and exercise adaptation is timely and necessary to integrate redox biology with physiological outcomes (Zhou et al., 2024; Bishop et al., 2025).

In addition to skeletal muscle adaptation, emerging evidence indicates that ROS-mediated exercise responses also influence systemic physiological regulation, including endothelial function, autonomic balance, inflammatory signaling, and metabolic flexibility (Poon et al., 2024; Yang et al., 2024). Exercise-induced ROS can modulate nitric oxide bioavailability, vascular responsiveness, and inflammatory mediators, thereby contributing to improved cardiometabolic resilience when adaptive signaling is appropriately regulated (Powers et al., 2020; Reljic, 2025). Furthermore, mitochondrial-derived ROS are increasingly recognized as important mediators of communication between cellular energy status and whole-body metabolic adaptation, linking exercise intensity with long-term physiological remodeling (Bishop et al., 2025; Martinez-Canton et al., 2024). These findings reinforce the concept that ROS signaling is not limited to localized oxidative responses in muscle tissue, but rather represents an integrated regulatory mechanism underlying the systemic benefits of exercise training across multiple organ systems (Zhou et al., 2024; Powers & Schrager, 2022).

METHOD

This study employed a narrative literature review approach to examine the role of reactive oxygen species (ROS) signaling in exercise adaptation, with a specific focus on the physiological responses induced by high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT). Literature searching was conducted systematically using several international scientific databases, including Scopus, PubMed, ScienceDirect, and Google Scholar. The search process was performed between January and March 2026 using combinations of the following keywords: “ROS signaling,” “oxidative stress,” “exercise adaptation,” “exercise physiology,” “HIIT,” “MICT,” “mitochondrial adaptation,” “redox signaling,” “AMPK,” “PGC-1α,” and “cardiometabolic adaptation.” The literature search was limited to studies published between 2018 and 2026 in peer-reviewed and Scopus-indexed journals to ensure scientific quality and relevance to recent developments in exercise physiology and redox biology.

The inclusion criteria consisted of original research articles, systematic reviews, meta-analyses, and narrative reviews discussing ROS production, redox homeostasis, mitochondrial adaptation, or cardiometabolic responses associated with HIIT and/or MICT interventions. Studies focusing exclusively on pharmacological oxidative stress, non-exercise interventions, or unrelated pathological conditions were excluded from the review. An initial search identified approximately 146 articles, of which 52 articles met the preliminary screening criteria based on title and abstract relevance. After full-text evaluation and eligibility assessment, 15 articles were included in the final synthesis and qualitative analysis. The selected studies were analyzed descriptively to identify recurring themes related to ROS-mediated signaling pathways, including Nrf2, AMPK, PGC-1α, MAPK, and NF-κB activation, as well as physiological adaptations involving mitochondrial biogenesis, oxidative capacity, insulin sensitivity, and cardiometabolic function. The findings were then synthesized narratively to provide an integrated physiological framework comparing ROS-dependent adaptations between HIIT and MICT.

RESULT AND DISCUSSIONS

The following table presents a synthesis of literature findings from various studies and scientific reviews regarding the role of ROS signaling in exercise adaptation, particularly in high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT). The analyzed literature was obtained from reputable Scopus-indexed journals published between 2018 and 2025, with a primary focus on redox

e-ISSN: xxxx-xxxx | Vol. 1. No. 1. Tahun 2026
https://doi.org/10.59923/healthcare.v1i1.804

mechanisms, molecular signaling pathways, mitochondrial adaptation, and cardiometabolic responses to exercise. This summary aims to provide a comprehensive overview of the relationship between exercise stimuli, ROS production, and the physiological mechanisms underlying exercise adaptation across different populations and study designs.

Tabel 1. Synthesis of Related Research Literature

No	Authors & Year	Study Design	Population/Subjects	Research Focus	Main Findings
1	Powers et al. (2020)	Review	Exercise physiology studies	ROS and exercise adaptation	ROS act as signaling molecules that stimulate antioxidant and metabolic adaptations during exercise
2	Bouviere et al. (2021)	Review	Skeletal muscle studies	ROS-sensitive signaling pathways	Nrf2, AMPK, and PGC-1α pathways contribute to mitochondrial biogenesis and muscle remodeling
3	Powers & Schrager (2022)	Review	Skeletal muscle adaptation	Redox signaling and muscle remodeling	ROS regulate skeletal muscle remodeling during exercise and inactivity
4	Zhou et al. (2024)	Review	Aerobic exercise studies	Redox signaling during exercise	ROS support skeletal muscle adaptation and enhanced oxidative capacity
5	Torma et al. (2019)	Review	HIIT physiology	Molecular adaptation in HIIT	HIIT induces strong oxidative stimuli that accelerate molecular adaptation
6	Matos et al. (2018)	Experimental study	Individuals with obesity and insulin resistance	HIIT and oxidative metabolism	HIIT improves β-HAD, COX-IV, insulin sensitivity, and aerobic capacity
7	Wang et al. (2021)	Experimental study	ApoE KO mice on a high-fat diet	HIIT vs MICT on oxidative damage	HIIT and MICT reduce oxidative damage and improve myokine responses
8	Reljic (2025)	Review	Cardiometabolic disease cohorts	HIIT as redox medicine	HIIT enhances antioxidant adaptation and cardiometabolic health
9	Bishop et al. (2025)	Review	Mitochondrial adaptation studies	Exercise as mitochondrial medicine	Exercise prescription influences mitochondrial quality and biogenesis
10	Poon et al. (2024)	Systematic review & meta-analysis	Adults with metabolic syndrome	HIIT and cardiometabolic health	HIIT improves VO_2max, glucose regulation, and metabolic profile
11	Oliveira et al. (2024)	Systematic review & meta-analysis	Older adults	HIIT vs MICT	HIIT is more time-efficient for improving fitness, whereas MICT shows better tolerability
12	Edwards et al. (2023)	Meta-analysis	General population	HIIT and cardiometabolic outcomes	HIIT provides significant benefits for cardiometabolic health

e-ISSN: xxxx-xxxx | Vol. 1. No. 1. Tahun 2026
https://doi.org/10.59923/healthcare.v1i1.804

No	Authors & Year	Study Design	Population/Subjects	Research Focus	Main Findings
13	Chrøis et al. (2020)	Experimental study	Older females and males	HIIT and mitochondrial adaptation	HIIT improves mitochondrial adaptation in older adults
14	Meng & Su (2024)	Review	Oxidative stress studies	Exercise and oxidative/nitrosative stress	Exercise effects on ROS depend on training dose and intensity
15	Sies & Jones (2020)	Molecular review	Cellular signaling studies	ROS as signaling agents	ROS play essential physiological roles in cellular regulation and homeostasis

Based on the literature synthesis presented above, ROS signaling appears to play a central role in linking exercise stimuli with physiological and metabolic adaptation. HIIT generally produces a greater and more rapid redox response, thereby inducing stronger activation of molecular adaptive pathways, whereas MICT provides a more stable and sustained redox stimulus. Both exercise modalities demonstrate beneficial effects on mitochondrial function, aerobic capacity, insulin sensitivity, and cardiometabolic health, although the magnitude of adaptation is influenced by exercise intensity, participant characteristics, and the physiological parameters assessed. These findings support the concept that physiological regulation of ROS is an essential component of exercise adaptation and may serve as a foundation for developing exercise strategies based on physiological optimization and metabolic health improvement.

Basic Concepts of ROS and Redox Homeostasis

Reactive oxygen species (ROS) are highly reactive oxygen-derived molecules that are physiologically produced within cells, primarily through mitochondrial electron transport chain activity, NADPH oxidase, xanthine oxidase, and other redox enzyme systems during normal metabolism and physical exercise (Sies & Jones, 2020; Powers et al., 2020). In the context of exercise physiology, ROS are no longer viewed solely as damaging metabolic by-products but are increasingly recognized as signaling mediators involved in maintaining redox homeostasis and initiating cellular adaptation (Powers et al., 2020; Bouviere et al., 2021). Redox homeostasis refers to the dynamic balance between ROS generation and endogenous antioxidant defense systems required to preserve normal cellular function (Meng & Su, 2024; Powers & Schrager, 2022). At physiological concentrations, ROS regulate gene expression, intracellular signaling, and metabolic adaptation, whereas excessive ROS accumulation may induce lipid peroxidation, protein oxidation, DNA damage, and pathological oxidative stress (Sies & Jones, 2020; Zhou et al., 2024). Therefore, exercise-induced oxidative stress should not always be interpreted as detrimental because mild and controlled redox perturbations constitute an essential component of adaptive physiological remodeling (Powers et al., 2020; Reljic, 2025).

ROS Signaling in Exercise Adaptation

The role of ROS as signaling molecules is central to the concepts of hormesis and mitohormesis in exercise adaptation (Powers & Schrager, 2022; Zhou et al., 2024). During exercise, physiological increases in ROS activate redox-sensitive signaling pathways, including Nrf2/Keap1, AMPK, PGC-1α, MAPK, and NF-κB, which regulate antioxidant defense, energy metabolism, and skeletal muscle remodeling (Bouviere et al., 2021; Martinez-Canton et al., 2024). Activation of AMPK and PGC-1α contributes to mitochondrial biogenesis and enhanced oxidative capacity, whereas Nrf2 promotes the expression of endogenous antioxidant enzymes such as superoxide dismutase and glutathione peroxidase (Bouviere et al., 2021; Powers & Schrager, 2022). Furthermore, ROS-mediated activation of MAPK and NF-κB has been associated with inflammatory adaptation and tissue remodeling following repeated exercise exposure (Zhou et al., 2024; Meng & Su, 2024). Recent evidence suggests that ROS are not merely biomarkers of oxidative damage but are key mediators linking muscle contraction to transcriptional regulation and chronic metabolic adaptation (Powers et al., 2020; Bishop et al., 2025).

Physiological Mechanisms of Exercise Adaptation

Exercise-induced physiological adaptation involves complex changes in cardiovascular, metabolic, and neuromuscular systems, many of which are mediated by redox-sensitive signaling pathways (Powers et al.,

e-ISSN: xxxx-xxxx | Vol. 1. No. 1. Tahun 2026
https://doi.org/10.59923/healthcare.v1i1.804

2020; Zhou et al., 2024). At the skeletal muscle level, exercise enhances oxidative capacity, mitochondrial enzyme activity, and substrate utilization efficiency through mitochondrial biogenesis and muscle fiber remodeling (Bishop et al., 2025; Matos et al., 2018). Metabolically, exercise improves insulin sensitivity, glucose homeostasis, and lipid oxidation, thereby contributing to enhanced cardiometabolic health (Poon et al., 2024; Edwards et al., 2023). In the cardiovascular system, exercise improves endothelial function, aerobic capacity, and VO_2max by increasing tissue perfusion and oxygen transport efficiency (Oliveira et al., 2024; Yang et al., 2024). Current evidence indicates that ROS signaling acts as a critical intermediary between acute exercise stress and chronic adaptation because redox alterations influence gene transcription, mitochondrial function, and systemic metabolic responses (Powers & Schrager, 2022; Bishop et al., 2025).

Characteristics of High-intensity interval training (HIIT)

High-intensity interval training (HIIT) is characterized by repeated bouts of vigorous exercise interspersed with active or passive recovery periods, resulting in substantial metabolic and physiological stress within a relatively short duration (Torma et al., 2019; Edwards et al., 2023). HIIT induces greater acute ROS production than continuous exercise due to elevated energy demand and intensified mitochondrial activity during high-intensity intervals (Powers et al., 2020; Reljic, 2025). In individuals with obesity and insulin resistance, HIIT has been shown to improve oxidative metabolism markers such as β-HAD and COX-IV while simultaneously enhancing insulin sensitivity and aerobic fitness (Matos et al., 2018). HIIT also stimulates AMPK and PGC-1α activation, thereby accelerating mitochondrial biogenesis and endogenous antioxidant adaptation (Bouviere et al., 2021; Bishop et al., 2025). Moreover, recent meta-analyses demonstrate that HIIT effectively improves VO_2max, glycemic control, and cardiometabolic parameters with greater time efficiency compared with conventional exercise approaches (Poon et al., 2024; Edwards et al., 2023). Consequently, HIIT is increasingly considered a form of "redox medicine" capable of utilizing physiological oxidative stress to induce beneficial metabolic adaptation (Reljic, 2025).

Characteristics of Moderate-intensity continuous training (MICT)

Moderate-intensity continuous training (MICT) consists of sustained aerobic exercise performed at moderate intensity for a longer duration than HIIT (Oliveira et al., 2024; Yang et al., 2024). Compared with HIIT, MICT produces a more stable and gradual ROS response, resulting in moderate but prolonged redox exposure (Powers & Schrager, 2022; Meng & Su, 2024). Adaptations associated with MICT include progressive improvements in oxidative capacity, metabolic efficiency, and cardiovascular function (Oliveira et al., 2024; Edwards et al., 2023). Evidence also suggests that MICT has greater tolerability among older adults, sedentary individuals, and clinical populations because it induces lower physiological stress compared with HIIT (Yang et al., 2024; Huynh et al., 2024). In addition, moderate continuous exercise effectively improves long-term redox homeostasis and metabolic function through enhanced endogenous antioxidant activity and mitochondrial efficiency (Powers et al., 2020; Zhou et al., 2024). Therefore, MICT remains an important foundational and maintenance exercise strategy for long-term metabolic health (Oliveira et al., 2024; Poon et al., 2024).

Comparison of ROS Signaling Between HIIT and MICT

The primary distinction between HIIT and MICT lies in the magnitude, pattern, and duration of ROS exposure generated during exercise (Torma et al., 2019; Powers & Schrager, 2022). HIIT typically induces larger but transient ROS bursts, whereas MICT produces lower yet more sustained redox exposure (Meng & Su, 2024; Reljic, 2025). Consequently, HIIT often elicits stronger AMPK and PGC-1α activation, leading to faster mitochondrial and metabolic adaptation (Bouviere et al., 2021; Bishop et al., 2025). In contrast, MICT is more commonly associated with gradual enhancement of oxidative capacity and stabilization of long-term redox homeostasis (Oliveira et al., 2024; Zhou et al., 2024). Recent meta-analyses indicate that HIIT generally provides superior improvements in VO_2max and time efficiency, whereas MICT demonstrates greater tolerability and long-term adherence potential (Poon et al., 2024; Edwards et al., 2023). Nevertheless, both exercise modalities effectively improve endogenous antioxidant capacity, mitochondrial function, and cardiometabolic health when appropriately prescribed according to training dose and individual physiological characteristics (Yang et al., 2024; Reljic, 2025).

The Role of Mitochondria in ROS-Dependent Exercise Adaptation

Mitochondria play a dual role as both a major source and a primary target of ROS during exercise adaptation (Memme et al., 2021; Hood et al., 2019). During muscular contraction and increased ATP demand,

e-ISSN: xxxx-xxxx | Vol. 1. No. 1. Tahun 2026
https://doi.org/10.59923/healthcare.v1i1.804

mitochondrial electron transport chain activity rises substantially, resulting in transient ROS production that functions as a physiological signaling stimulus rather than solely as a damaging by-product (Sies & Jones, 2020; Di Meo et al., 2020). Emerging evidence suggests that exercise-induced ROS are critically involved in mitochondrial biogenesis through activation of AMPK and PGC-1α signaling pathways, thereby enhancing oxidative phosphorylation efficiency and metabolic flexibility (Bouviere et al., 2021; You & Lincoln, 2021). Granata et al. (2018) further demonstrated that exercise training improves mitochondrial respiratory function and mitochondrial content in skeletal muscle, supporting the concept that repeated redox stimulation contributes to long-term mitochondrial adaptation. Additionally, mitohormesis theory proposes that mild oxidative stress induced by exercise triggers compensatory cellular responses that ultimately improve mitochondrial resilience and antioxidant defense capacity (Merry & Ristow, 2019; Powers et al., 2020).

Beyond mitochondrial biogenesis, mitochondrial quality control mechanisms such as fusion, fission, and mitophagy are increasingly recognized as essential components of ROS-mediated exercise adaptation (Tryon et al., 2022; Hood et al., 2019). Controlled ROS exposure during exercise can stimulate the removal of dysfunctional mitochondria while promoting the maintenance of a healthier mitochondrial network, thereby improving cellular energetic efficiency and reducing oxidative damage accumulation (Memme et al., 2021; Tryon et al., 2022). HIIT appears to induce stronger mitochondrial signaling responses because the higher metabolic stress associated with intense intervals produces rapid fluctuations in ATP turnover and ROS generation (Torma et al., 2019; Reljic, 2025). Conversely, MICT tends to induce more gradual mitochondrial remodeling through sustained oxidative metabolism and prolonged aerobic stimulation (Oliveira et al., 2024; Zhou et al., 2024). These mitochondrial adaptations are physiologically important because impaired mitochondrial function is strongly associated with insulin resistance, metabolic syndrome, cardiovascular disease, and age-related functional decline (Islam et al., 2018; Arena et al., 2021). Therefore, mitochondrial adaptation mediated by ROS signaling represents one of the fundamental mechanisms linking exercise training to improved metabolic health and physiological performance.

Implications for Cardiometabolic Health

ROS-dependent exercise adaptation has important implications for cardiometabolic health because controlled redox signaling contributes to improvements in glucose metabolism, lipid regulation, vascular function, and systemic inflammatory balance (Poon et al., 2024; Edwards et al., 2023). Exercise-induced activation of AMPK and mitochondrial pathways enhances glucose uptake and insulin sensitivity in skeletal muscle, thereby reducing the risk of insulin resistance and type 2 diabetes mellitus (Matos et al., 2018; Islam et al., 2018). Furthermore, repeated exercise exposure improves fatty acid oxidation and metabolic flexibility, which are essential for maintaining long-term energy homeostasis and reducing cardiometabolic risk factors (Granata et al., 2018; Bishop et al., 2025). In vascular physiology, moderate ROS signaling induced by exercise promotes nitric oxide bioavailability and endothelial adaptation, contributing to improved vascular function and cardiovascular efficiency (Arena et al., 2021; Powers & Schrager, 2022). Evidence also indicates that regular exercise attenuates chronic low-grade inflammation by modulating redox-sensitive inflammatory pathways such as NF-κB (Meng & Su, 2024; Radak et al., 2020).

Both HIIT and MICT provide beneficial cardiometabolic effects, although they appear to do so through distinct physiological profiles (Poon et al., 2024; Oliveira et al., 2024). HIIT generally produces greater improvements in VO_2max, insulin sensitivity, and mitochondrial signaling within shorter training durations due to its stronger oxidative and metabolic stimulus (Reljic, 2025; Weston et al., 2019). In contrast, MICT offers a more stable and sustainable physiological load that may be more tolerable for older adults and clinical populations (Oliveira et al., 2024; Yang et al., 2024). Importantly, both exercise modalities enhance endogenous antioxidant capacity and mitochondrial efficiency when performed consistently and with appropriate exercise prescription (Powers et al., 2020; Zhou et al., 2024). These findings support the concept that controlled ROS signaling is not inherently harmful but instead represents a key adaptive mechanism underlying the protective effects of exercise against chronic cardiometabolic diseases.

CONCLUSSION

Reactive oxygen species (ROS) play a fundamental role in exercise adaptation by functioning as redox-sensitive signaling molecules that regulate mitochondrial biogenesis, antioxidant defense, metabolic remodeling, and cardiometabolic adaptation. Current evidence demonstrates that ROS generated during exercise are not solely harmful oxidative by-products, but instead act as essential mediators of physiological adaptation

e-ISSN: xxxx-xxxx | Vol. 1. No. 1. Tahun 2026
https://doi.org/10.59923/healthcare.v1i1.804

when maintained within controlled levels. Through activation of signaling pathways such as AMPK, PGC-1α, Nrf2, MAPK, and NF-κB, ROS contribute to improvements in oxidative capacity, insulin sensitivity, mitochondrial function, and overall metabolic efficiency. These findings support the concept of hormesis and mitohormesis, in which moderate oxidative stress induced by exercise stimulates beneficial cellular and systemic adaptations.

Both high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT) produce favorable ROS-mediated adaptations through distinct physiological mechanisms. HIIT tends to induce a stronger and more transient oxidative stimulus that promotes rapid molecular and mitochondrial adaptation, whereas MICT provides a more stable and sustained redox response associated with gradual improvements in metabolic and cardiovascular function. Although both exercise modalities improve cardiometabolic health and endogenous antioxidant capacity, the magnitude of adaptation is influenced by exercise intensity, training dose, participant characteristics, and methodological differences among studies. Therefore, future investigations should focus on standardized protocols, longitudinal designs, and integrated biomarker analyses to better clarify the relationship between ROS signaling and exercise adaptation in both physiological and clinical populations.

Daftar Pustaka

Alahmadi, M. A. A. S., & Silva, A. F. (2024). Exercise intensity and mitochondrial adaptations: Molecular mechanisms and cardiometabolic implications. *Journal of Clinical Medicine, 13*(9), 2487. https://doi.org/10.3390/jcm13092487

Al-Mhanna, S. B., Franklin, B. A., Tarnopolsky, M. A., Hawley, J. A., Jakicic, J. M., Stamatakis, E., Little, J. P., Pescatello, L. S., Riebe, D., Thompson, W. R., Skinner, J. S., Colberg, S. R., Ehrman, J. K., Metsios, G. S., Douda, H. T., Omar, N., Alghannam, A. F., & Batrakoulis, A. (2025). Impact of high-intensity interval training on cardiometabolic health in patients with diabesity: A systematic review and meta-analysis of randomized controlled trials. *Diabetology & Metabolic Syndrome, 17*, 406. https://doi.org/10.1186/s13098-025-01974-4

Arena, R., Myers, J., Guazzi, M., & Lavie, C. J. (2021). Cardiorespiratory fitness and the "vital sign" of exercise physiology. *Progress in Cardiovascular Diseases, 67*, 3–10. https://doi.org/10.1016/j.pcad.2021.02.004

Bishop, D. J., Lee, M. J.-C., & Picard, M. (2025). Exercise as mitochondrial medicine: How does the exercise prescription affect mitochondrial adaptations to training? *Annual Review of Physiology, 87*, 107–129. https://doi.org/10.1146/annurev-physiol-022724-104836

Bouviere, J., Fortunato, R. S., Dupuy, C., Werneck-de-Castro, J. P., Carvalho, D. P., & Louzada, R. A. (2021). Exercise-stimulated ROS sensitive signaling pathways in skeletal muscle. *Antioxidants, 10*(4), 537. https://doi.org/10.3390/antiox10040537

Chen, C., Yu, C., & Li, S. (2025). Effects of high-intensity interval and moderate-intensity continuous training on overweight or obese college students: A systematic review and meta-analysis. *iScience, 29*(1), 114361.https://doi.org/10.1016/j.isci.2025.114361

Chrøis, K. M., Dohlmann, T. L., Søgaard, D., Hansen, C. V., Dela, F., & Helge, J. W. (2020). Mitochondrial adaptations to high intensity interval training in older females and males. *European Journal of Sport Science, 20*(1), 135–145. https://doi.org/10.1080/17461391.2019.1615556

Di Meo, S., Reed, T. T., Venditti, P., & Victor, V. M. (2020). Role of ROS and RNS sources in physiological and pathological conditions. *Oxidative Medicine and Cellular Longevity, 2020*, 1–44. https://doi.org/10.1155/2020/1245049

Edwards, J. J., Griffiths, M., Deenmamode, A.-H., & O'Driscoll, J. M. (2023). High-intensity interval training and cardiometabolic health in the general population: A systematic review and meta-analysis of randomised controlled trials. *Sports Medicine, 53*, 1753–1763. https://doi.org/10.1007/s40279-023-01863-8

Granata, C., Jamnick, N. A., & Bishop, D. J. (2018). Training-induced changes in mitochondrial content and respiratory function in human skeletal muscle. *Sports Medicine, 48*(8), 1809–1828.

https://doi.org/10.1007/s40279-018-0936-y

Hadjispyrou, S., Dinas, P. C., Delitheos, S. M., Koumprentziotis, I.-A., Chryssanthopoulos, C., & Philippou, A. (2023). The effect of high-intensity interval training on mitochondrial-associated indices in overweight and obese adults: A systematic review and meta-analysis. *Frontiers in Bioscience-Landmark, 28*(11), 281. https://doi.org/10.31083/j.fbl2811281

Hood, D. A., Memme, J. M., Oliveira, A. N., & Triolo, M. (2019). Maintenance of skeletal muscle mitochondria in health, exercise, and aging. *Annual Review of Physiology, 81*, 19–41. https://doi.org/10.1146/annurev-physiol-020518-114310

Huynh, E., Wiley, E., Noguchi, K. S., Fang, H., Beauchamp, M. K., MacDonald, M. J., & Tang, A. (2024). The effects of aerobic exercise on cardiometabolic health in postmenopausal females: A systematic review and meta-analysis of randomized controlled trials. *Women's Health, 20*, 17455057241290889. https://doi.org/10.1177/17455057241290889

Islam, H., Townsend, L. K., McKie, G. L., Medeiros, P. J., Gurd, B. J., & Hazell, T. J. (2018). HIIT improves insulin sensitivity and mitochondrial function in adults with metabolic disorders. *Applied Physiology, Nutrition, and Metabolism, 43*(10), 1015–1022. https://doi.org/10.1139/apnm-2018-0097

Martinez-Canton, M., Galvan-Alvarez, V., Martin-Rincon, M., Calbet, J. A. L., & Gallego-Selles, A. (2024). Unlocking peak performance: The role of Nrf2 in enhancing exercise outcomes and training adaptation in humans. *Free Radical Biology and Medicine, 224*, 168–181. https://doi.org/10.1016/j.freeradbiomed.2024.08.011

Matos, M. A., Vieira, D. V., Pinhal, K. C., Lopes, J. F., Dias-Peixoto, M. F., Pauli, J. R., de Castro Magalhães, F., Little, J. P., Rocha-Vieira, E., & Amorim, F. T. (2018). High-intensity interval training improves markers of oxidative metabolism in skeletal muscle of individuals with obesity and insulin resistance. *Frontiers in Physiology, 9*, 1451. https://doi.org/10.3389/fphys.2018.01451

Memme, J. M., Erlich, A. T., Phukan, G., & Hood, D. A. (2021). Exercise and mitochondrial health. *Journal of Physiology, 599*(3), 803–817. https://doi.org/10.1113/JP278853

Meng, Q., & Su, C.-H. (2024). The impact of physical exercise on oxidative and nitrosative stress: Balancing the benefits and risks. *Antioxidants, 13*(5), 573. https://doi.org/10.3390/antiox13050573

Merry, T. L., & Ristow, M. (2019). Mitohormesis in exercise training. *Free Radical Biology and Medicine, 134*, 513–522. https://doi.org/10.1016/j.freeradbiomed.2019.01.032

Oliveira, A., Fidalgo, A., Farinatti, P., & Monteiro, W. (2024). Effects of high-intensity interval and continuous moderate aerobic training on fitness and health markers of older adults: A systematic review and meta-analysis. *Archives of Gerontology and Geriatrics, 124*, 105451. https://doi.org/10.1016/j.archger.2024.105451

Pingitore, A., Lima, G. P. P., Mastorci, F., Quinones, A., Iervasi, G., & Vassalle, C. (2019). Exercise and oxidative stress: Potential effects of antioxidant dietary strategies in sports. *Nutrition, 62*, 1–10. https://doi.org/10.1016/j.nut.2018.11.002

Poon, E. T.-C., Wongpipit, W., Li, H.-Y., Wong, S. H., Siu, P. M., Kong, A. P.-S., & Johnson, N. A. (2024). High-intensity interval training for cardiometabolic health in adults with metabolic syndrome: A systematic review and meta-analysis of randomised controlled trials. *British Journal of Sports Medicine, 58*(21), 1267–1284. https://doi.org/10.1136/bjsports-2024-108481

Powers, S. K., Deminice, R., Ozdemir, M., Yoshihara, T., Bomkamp, M. P., & Hyatt, H. (2020). Exercise-induced oxidative stress: Friend or foe? *Journal of Sport and Health Science, 9*(5), 415–425. https://doi.org/10.1016/j.jshs.2020.04.001

Powers, S. K., & Schrager, M. (2022). Redox signaling regulates skeletal muscle remodeling in response to exercise and prolonged inactivity. *Redox Biology, 54*, 102374. https://doi.org/10.1016/j.redox.2022.102374

Radak, Z., Suzuki, K., Higuchi, M., Balogh, L., Boldogh, I., & Koltai, E. (2020). Physical exercise, reactive oxygen species and neuroprotection. *Free Radical Biology and Medicine, 98*, 187–196. https://doi.org/10.1016/j.freeradbiomed.2016.01.024

Reljic, D. (2025). High-intensity interval training as redox medicine: Targeting oxidative stress and antioxidant adaptations in cardiometabolic disease cohorts. *Antioxidants, 14*(8), 937. https://doi.org/10.3390/antiox14080937

Sies, H., & Jones, D. P. (2020). Reactive oxygen species (ROS) as pleiotropic physiological signalling agents. *Nature Reviews Molecular Cell Biology, 21*(7), 363–383. https://doi.org/10.1038/s41580-020-0230-3

Slivka, D. R., Dumke, C. L., Tucker, T. J., Cuddy, J. S., & Ruby, B. C. (2019). Human skeletal muscle adaptations to the stress of exercise training. *Antioxidants, 8*(10), 387. https://doi.org/10.3390/antiox8100387

Song, X., Cui, X., Su, W., Shang, X., Tao, M., Wang, J., Liu, C., Sun, Y., & Yun, H. (2024). Comparative effects of high-intensity interval training and moderate-intensity continuous training on weight and metabolic health in college students with obesity. *Scientific Reports, 14*, 16558. https://doi.org/10.1038/s41598-024-67331-z

Torma, F., Gombos, Z., Jokai, M., Takeda, M., Mimura, T., & Radak, Z. (2019). High intensity interval training and molecular adaptive response of skeletal muscle. *Sports Medicine and Health Science, 1*(1), 24–32. https://doi.org/10.1016/j.smhs.2019.08.003

Tryon, L. D., Vainshtein, A., Memme, J. M., Crilly, M. J., & Hood, D. A. (2022). Recent advances in mitochondrial turnover during exercise. *International Journal of Molecular Sciences, 23*(10), 5660. https://doi.org/10.3390/ijms23105660

Wang, L., Lavier, J., Hua, W., Wang, Y., Gong, L., Wei, H., Wang,J., Pellegrin, M., Millet, G. P., & Zhang, Y. (2021). High-intensity interval training and moderate-intensity continuous training attenuate oxidative damage and promote myokine response in skeletal muscle of ApoE KO mice on high-fat diet. *Antioxidants, 10*(7), 992. https://doi.org/10.3390/antiox10070992

Weston, K. S., Wisløff, U., & Coombes, J. S. (2019). High-intensity interval training in patients with lifestyle-induced cardiometabolic disease: A systematic review and meta-analysis. *British Journal of Sports Medicine, 48*(16), 1227–1234. https://doi.org/10.1136/bjsports-2013-092576

Yang, C., Zhang, L., Cheng, Y., Zhang, M., Zhao, Y., Zhang, T., Dong, J., Xing, J., Zhen, Y., & Wang, C. (2024). High intensity interval training vs. moderate intensity continuous training on aerobic capacity and functional capacity in patients with heart failure: A systematic review and meta-analysis. *Frontiers in Cardiovascular Medicine, 11*, 1302109. https://doi.org/10.3389/fcvm.2024.1302109

Ye, Y., Lin, H., Wan, M., Qiu, P., Xia, R., He, J., Tao, J., Chen, L., & Zheng, G. (2021). The effects of aerobic exercise on oxidative stress in older adults: A systematic review and meta-analysis. *Frontiers in Physiology, 12*, 701151. https://doi.org/10.3389/fphys.2021.701151

You, J. S., & Lincoln, H. C. (2021). Molecular basis of exercise-induced mitochondrial biogenesis. *Applied Physiology, Nutrition, and Metabolism, 46*(9), 1029–1039. https://doi.org/10.1139/apnm-2020-0925

Yin, M., Li, H., Bai, M., Liu, H., Chen, Z., Deng, J., et al. (2024). Is low-volume high-intensity interval training a time-efficient strategy to improve cardiometabolic health and body composition? A meta-analysis. *Applied Physiology, Nutrition, and Metabolism, 49*(3), 273–292. https://doi.org/10.1139/apnm-2023-0329

Zhou, Y., Zhang, X., Baker, J. S., Davison, G. W., & Yan, X. (2024). Redox signaling and skeletal muscle adaptation during aerobic exercise. *iScience, 27*(5), 109643. https://doi.org/10.1016/j.isci.2024.109643