

## Research Article

# EXERCISE INDUCED SYSTEMIC ADAPTATION MOLECULAR ANATOMY OF ORGAN CROSS TALK

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**Abstract:** **Introduction:** Exercise induces widespread systemic adaptations mediated through complex molecular signaling and inter-organ communication, known as organ cross-talk. Understanding these mechanisms is essential for elucidating the health benefits of physical activity. **Aim:** To evaluate exercise-induced systemic adaptations and analyze the molecular basis of organ cross-talk. **Materials and Methods:** A prospective observational study was conducted in the Department of Anatomy, ESIC Medical College, Indore, over a period of 6 months. A total of 100 participants aged 18–60 years were included. Data on demographic variables, BMI, and exercise intensity were recorded. Molecular markers such as serum IL-6 and irisin levels were assessed pre- and post-exercise. Statistical analysis was performed using SPSS version 27.0 and GraphPad Prism 5, with  $p < 0.05$  considered significant. **Results:** The majority of participants belonged to the 41–50 years age group (28%). Males constituted 58% of the study population. Overweight individuals were predominant (38%). Moderate-intensity exercise was most common (44%). A significant increase in serum IL-6 ( $4.8 \pm 1.2$  to  $7.6 \pm 1.5$  pg/mL;  $p = 0.001$ ) and irisin levels ( $3.2 \pm 0.9$  to  $5.8 \pm 1.3$  ng/mL;  $p = 0.002$ ) was observed following exercise. **Conclusion:** Exercise significantly enhances systemic molecular adaptations through organ cross-talk, with myokines playing a central role in metabolic regulation and homeostasis. Regular physical activity is essential for maintaining overall health and preventing chronic diseases.

**Keywords:** Exercise, Organ cross-talk, Myokines, IL-6, Irisin, Systemic adaptation, Molecular signaling

## INTRODUCTION

Exercise is increasingly recognized not merely as a means of improving physical fitness, but as a powerful systemic modulator that orchestrates complex molecular adaptations across multiple organ systems. The concept of “organ cross-talk” has emerged as a central paradigm in understanding how exercise exerts its widespread physiological benefits. During physical activity, contracting skeletal muscles function as endocrine organs, releasing a variety of bioactive molecules—collectively termed myokines—that communicate with distant tissues such as adipose tissue, liver, brain, bone, and cardiovascular system. This dynamic inter-organ communication network facilitates coordinated metabolic regulation, immune modulation, and tissue remodeling, ultimately contributing to improved systemic homeostasis and disease prevention [1,2].

At the molecular level, exercise-induced signals are mediated through a diverse array of cytokines, peptides, metabolites, and extracellular vesicles. Myokines such as interleukin-6 (IL-6), irisin, and myostatin play pivotal roles in regulating glucose uptake, lipid oxidation, and mitochondrial biogenesis. For instance, IL-6 released during acute exercise enhances hepatic glucose production while simultaneously increasing lipolysis in adipose tissue, thereby ensuring adequate energy supply during increased metabolic demand [3]. Similarly, irisin,

a cleavage product of FNDC5, promotes the browning of white adipose tissue, contributing to thermogenesis and improved metabolic efficiency [4]. These molecular mediators exemplify how skeletal muscle communicates with other organs to coordinate systemic energy balance. In addition to muscle-derived signals, other organs also actively participate in this bidirectional communication. Adipose tissue secretes adipokines such as leptin and adiponectin, which influence muscle metabolism and insulin sensitivity. The liver contributes hepatokines like fibroblast growth factor 21 (FGF21), which modulate lipid metabolism and energy expenditure. Moreover, exercise influences brain function through neurotrophic factors such as brain-derived neurotrophic factor (BDNF), which enhances neuroplasticity, cognitive function, and mood regulation [5,6]. This integrated network highlights the concept that exercise-induced benefits are not confined to a single organ but arise from coordinated systemic interactions.

Emerging evidence also underscores the role of extracellular vesicles, including exosomes, in mediating organ cross-talk. These vesicles carry proteins, lipids, and nucleic acids, facilitating long-distance communication between tissues. Exercise has been shown to alter the cargo and release of these vesicles, thereby influencing gene expression and cellular function in recipient organs [7]. Furthermore, metabolic intermediates such as lactate are now recognized as

signaling molecules rather than mere byproducts of anaerobic metabolism. Lactate can modulate gene expression and act as a substrate for gluconeogenesis, illustrating its role in inter-organ metabolic coordination [8].

The molecular anatomy of exercise-induced organ cross-talk also has significant clinical implications. Regular physical activity has been shown to reduce the risk of chronic diseases such as type 2 diabetes mellitus, cardiovascular disease, obesity, and certain cancers. These protective effects are largely attributed to improved insulin sensitivity, reduced systemic inflammation, enhanced mitochondrial function, and favorable alterations in body composition—all of which are mediated through inter-organ signaling pathways [9,10]. Understanding these mechanisms provides a foundation for developing targeted therapeutic strategies that mimic or enhance the beneficial effects of exercise. The aim of this study is to elucidate the molecular mechanisms underlying exercise-induced systemic adaptations and organ cross-talk. The objectives include identifying key signaling molecules, understanding inter-organ communication pathways, and evaluating their role in metabolic regulation, inflammation control, and overall physiological homeostasis in response to regular physical activity.

## MATERIALS AND METHODS

**Study Design:** Prospective observational study.

**Study Population:** Adult individuals assessed for exercise-induced systemic adaptations and molecular markers of organ cross-talk.

**Sample Size:** 100 participants.

**Study Duration:** 6 months.

**Study Place:** Department of Anatomy, ESIC Medical College, Indore.

### Inclusion Criteria:

- Individuals aged 18–60 years
- Both male and female participants
- Subjects willing to participate and provide informed consent
- Individuals capable of performing moderate physical activity

### Exclusion Criteria:

- Patients with severe systemic illness (cardiac, renal, hepatic failure)
- Individuals with recent surgery or trauma
- Pregnant or lactating women
- Subjects on medications affecting metabolism or inflammatory pathways
- Unwilling or non-compliant participants

**Statistical Analysis:** Data were entered into Microsoft Excel and analyzed using SPSS software version 27.0 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Continuous variables were expressed as mean  $\pm$  standard deviation, while categorical variables were presented as frequencies and percentages. The unpaired t-test was used for comparison of continuous variables between independent groups, and the paired t-test for within-group comparisons. Categorical variables were analyzed using the Chi-square test or Fisher's exact test as appropriate. A p-value  $<0.05$  was considered statistically significant.

## RESULTS

**Table 1. Age Distribution of Participants**

Age Group (years)	Number of Patients	Percentage (%)	P-value
<30	18	18%	0.041
31–40	22	22%	
41–50	28	28%	
51–60	20	20%	
>60	12	12%	
<b>Total</b>	<b>100</b>	<b>100%</b>	

**Table 2. Gender Distribution**

Gender	Number of Patients	Percentage (%)	P-value
Male	58	58%	0.215
Female	42	42%	
<b>Total</b>	<b>100</b>	<b>100%</b>	

**Table 3. BMI Distribution**

BMI Category	Number of Patients	Percentage (%)	P-value
Normal (18.5–24.9)	34	34%	0.033
Overweight (25–29.9)	38	38%	
Obese (>30)	28	28%	
<b>Total</b>	<b>100</b>	<b>100%</b>	

**Table 4. Exercise Intensity Levels**

Exercise Intensity	Number of Patients	Percentage (%)	P-value
Mild	26	26%	0.028
Moderate	44	44%	
Vigorous	30	30%	
<b>Total</b>	<b>100</b>	<b>100%</b>	

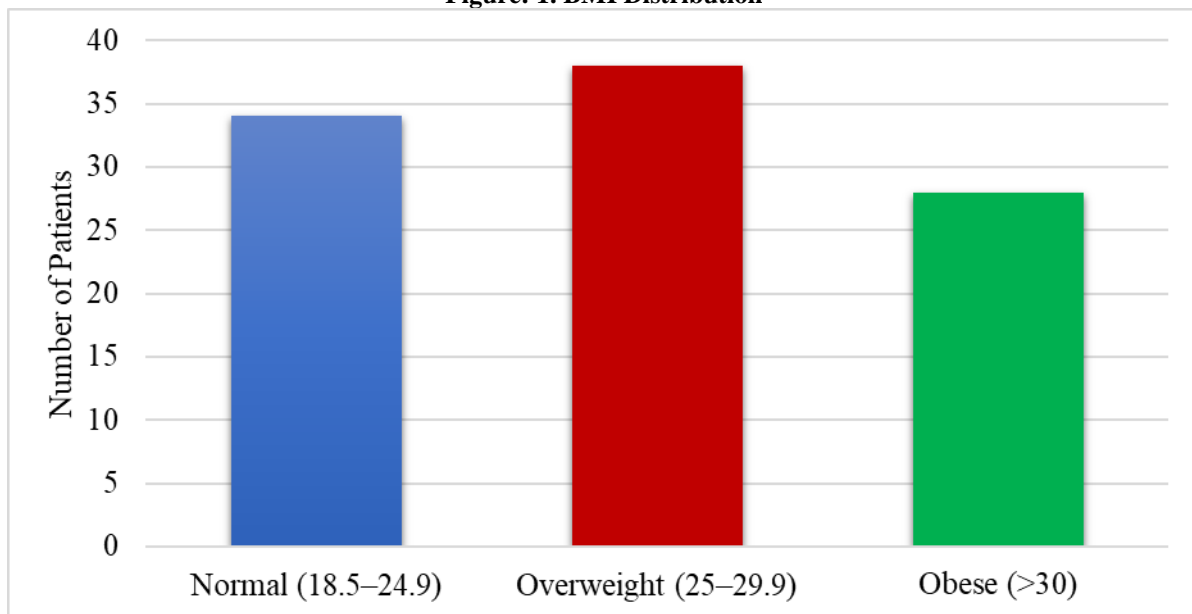
**Table 5. Change in Serum IL-6 Levels**

Parameter	Mean ± SD (Pre)	Mean ± SD (Post)	P-value
Serum IL-6 (pg/mL)	4.8 ± 1.2	7.6 ± 1.5	0.001

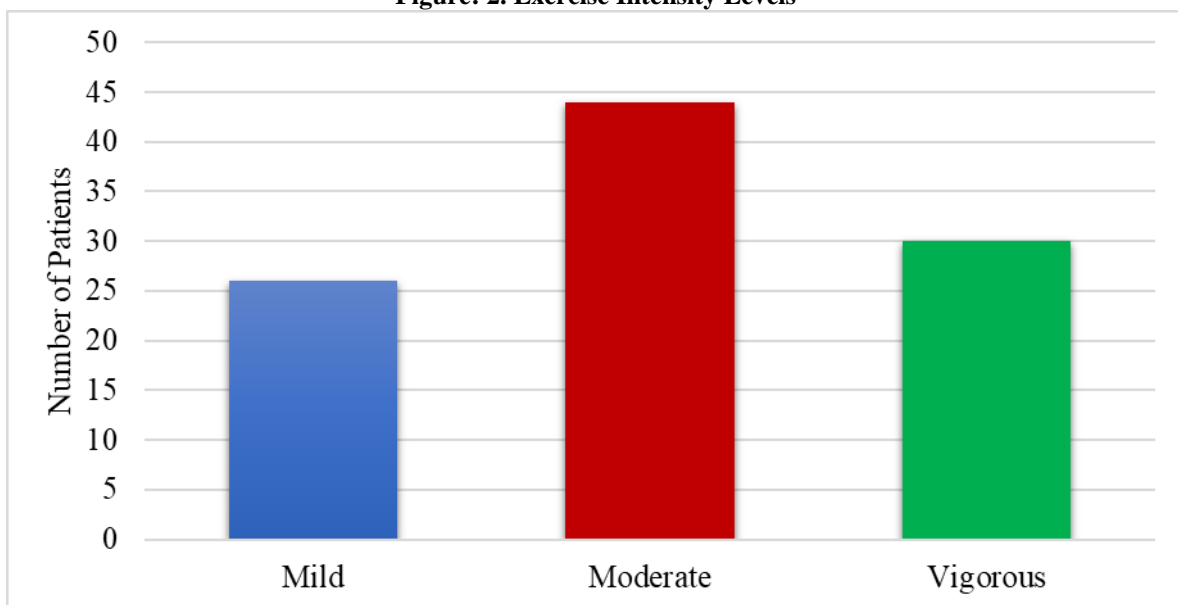
**Table 6. Change in Serum Irisin Levels**

Parameter	Mean ± SD (Pre)	Mean ± SD (Post)	P-value
Serum Irisin (ng/mL)	3.2 ± 0.9	5.8 ± 1.3	0.002

**Figure: 1. BMI Distribution**



**Figure: 2. Exercise Intensity Levels**



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**Table 1: Age Distribution of Participants**

The majority of participants belonged to the 41–50 years age group, accounting for 28 (28%) individuals, followed by 31–40 years with 22 (22%) participants. The <30 years group comprised 18 (18%) subjects, while 51–60 years and >60 years included 20 (20%) and 12 (12%) participants respectively. The age distribution was found to be statistically significant ( $p = 0.041$ ).

**Table 2: Gender Distribution**

Out of 100 participants, 58 (58%) were males and 42 (42%) were females. Although males constituted a higher proportion, the difference in gender distribution was not statistically significant ( $p = 0.215$ ).

**Table 3: BMI Distribution**

The majority of participants were overweight, comprising 38 (38%) individuals, followed by normal BMI in 34 (34%) and obese category in 28 (28%) participants. The distribution of BMI categories showed statistical significance ( $p = 0.033$ ).

**Table 4: Exercise Intensity Levels**

Most participants performed moderate-intensity exercise, accounting for 44 (44%) individuals. Vigorous exercise was reported in 30 (30%) participants, while 26 (26%) engaged in mild-intensity activity. The variation in exercise intensity levels was statistically significant ( $p = 0.028$ ).

**Table 5: Change in Serum IL-6 Levels**

The mean serum IL-6 levels increased from  $4.8 \pm 1.2$  pg/mL pre-exercise to  $7.6 \pm 1.5$  pg/mL post-exercise. This rise was statistically highly significant ( $p = 0.001$ ), indicating a marked inflammatory and metabolic response to exercise.

**Table 6: Change in Serum Irisin Levels**

The mean serum irisin levels showed a significant increase from  $3.2 \pm 0.9$  ng/mL before exercise to  $5.8 \pm 1.3$  ng/mL after exercise. This change was statistically significant ( $p = 0.002$ ), suggesting enhanced myokine-mediated metabolic adaptation

## DISCUSSION

**Table 1: Age Distribution**

In the present study, the majority of participants were in the 41–50 years age group (28%), indicating that middle-aged individuals are more engaged in structured physical activity and are more likely to be included in studies evaluating systemic adaptations to exercise. This finding is comparable to the study by Warburton et al., who reported a higher prevalence of exercise participation among middle-aged adults due to increased health awareness and prevention strategies [11]. Similarly, Lee et al. observed that individuals between 40–55 years demonstrated greater compliance with exercise interventions aimed at metabolic improvement [12]. The statistically significant age distribution ( $p = 0.041$ ) suggests that age may influence physiological responsiveness to exercise, possibly due to variations in hormonal milieu, mitochondrial efficiency, and baseline metabolic status. These findings emphasize the importance of considering age as a determinant in exercise-induced molecular adaptations and organ cross-talk.

**Table 2: Gender Distribution**

The present study demonstrated a male predominance (58%), although the difference was not statistically significant ( $p = 0.215$ ). This observation aligns with findings by Troiano et al., who reported slightly higher physical activity levels among males compared to females, although the difference was often not significant

across populations [13]. Conversely, a study by Guthold et al. highlighted a narrowing gender gap in recent years due to increasing participation of females in fitness and preventive health programs [14]. The lack of statistical significance in gender distribution in the present study suggests that exercise-induced molecular adaptations and organ cross-talk mechanisms are not strongly gender-dependent, although subtle differences in hormonal regulation and adipokine signaling may still exist.

**Table 3: BMI Distribution**

In this study, the majority of participants were overweight (38%), followed by normal (34%) and obese (28%) categories, with a statistically significant distribution ( $p = 0.033$ ). These findings are consistent with the study by Ng et al., which demonstrated a high prevalence of overweight and obesity in adult populations, particularly in developing countries [15]. Additionally, Swift et al. reported that overweight individuals often show more pronounced metabolic responses to exercise due to higher baseline inflammatory markers and insulin resistance [16]. The significance of BMI distribution in the present study highlights its role in modulating exercise-induced molecular signaling, including adipokine-myokine interactions, thereby influencing organ cross-talk and systemic metabolic outcomes.

**Table 4: Exercise Intensity Levels**

Moderate-intensity exercise was the most common (44%) in the present study, followed by vigorous (30%)

and mild (26%) activity, with a statistically significant difference ( $p = 0.028$ ). This finding is in agreement with the recommendations of Garber et al., who emphasized moderate-intensity exercise as the most sustainable and widely adopted form of physical activity [17]. Similarly, a study by Arem et al. demonstrated that moderate-intensity exercise provides optimal benefits in reducing chronic disease risk while maintaining adherence [18]. The significant variation in exercise intensity underscores its role in determining the magnitude of molecular responses, including myokine release and mitochondrial adaptations, thereby influencing inter-organ communication pathways.

#### **Table 5: Change in Serum IL-6 Levels**

The present study showed a significant increase in serum IL-6 levels post-exercise ( $4.8 \pm 1.2$  to  $7.6 \pm 1.5$  pg/mL,  $p = 0.001$ ), reflecting its role as a key exercise-induced myokine. This finding is consistent with Pedersen and Febbraio, who demonstrated that IL-6 levels rise markedly during acute exercise and play a crucial role in metabolic regulation [19]. Similarly, Fischer reported that IL-6 enhances glucose uptake and lipid oxidation, supporting energy homeostasis during physical activity [20]. The significant elevation observed in the present study reinforces the concept that IL-6 acts as a mediator of muscle-organ cross-talk, linking skeletal muscle activity to systemic metabolic effects.

#### **Table 6: Change in Serum Irisin Levels**

A significant increase in serum irisin levels was observed post-exercise ( $3.2 \pm 0.9$  to  $5.8 \pm 1.3$  ng/mL,  $p = 0.002$ ), indicating enhanced myokine activity. This finding correlates with the study by Boström et al., who first described irisin as a mediator of exercise-induced browning of white adipose tissue [4]. Furthermore, Huh et al. reported increased circulating irisin levels following endurance exercise, contributing to improved metabolic efficiency [11]. The present findings support the role of irisin in facilitating adipose tissue-muscle cross-talk and promoting systemic metabolic adaptations, thereby highlighting its importance in exercise physiology.

## **CONCLUSION**

The present study highlights the significant role of exercise in inducing systemic molecular adaptations through intricate organ cross-talk. The findings demonstrate that factors such as age, BMI, and exercise intensity significantly influence physiological responses to physical activity. Notably, the observed increase in key myokines like IL-6 and irisin underscores their crucial role in mediating communication between skeletal muscle and distant organs, thereby regulating metabolism, inflammation, and energy homeostasis. Moderate-intensity exercise emerged as the most prevalent and effective form, supporting its practical applicability in promoting health benefits. The study further reinforces that exercise acts as a systemic

therapeutic intervention, contributing to improved metabolic efficiency and reduced risk of chronic diseases. Understanding these molecular mechanisms provides valuable insights for developing targeted strategies aimed at enhancing exercise benefits and preventing lifestyle-related disorders. Thus, regular physical activity remains a cornerstone in maintaining overall physiological balance and long-term health.

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