International Journal of Progressive Sciences and Technologies (IJPSAT)
ISSN: 2509-0119.

https://ijpsat.org/

Vol. 50 No. 2 May 2025, pp. 278-287

Age-Dependent Myocardial Adaptation To Endurance Training: A Multimodal Assessment In A Rodent Model

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Abstract: Aging significantly impacts myocardial function and its adaptability to endurance training, yet the extent and mechanisms of these changes remain incompletely understood. This study investigates the myocardial adaptations to an eight-week progressive endurance training program in a controlled rodent model, stratified into four age groups: young (2–3 months), early-middle age (6–8 months), late-middle age (12–14 months), and elderly (>18 months). Echocardiographic assessments, heart rate variability (HRV) analysis, and metabolic biomarkers (serum lactate and troponin-I) were measured at baseline, mid-experiment, and post-experiment to evaluate cardiovascular function and stress responses. A sedentary control group was included to distinguish between exercise-induced and age-related myocardial changes. The results revealed significant improvements in left ventricular ejection fraction (LVEF) and stroke volume in younger and early-middle-aged rats, while older groups exhibited attenuated responses. HRV progressively declined with age, indicating reduced autonomic regulation, and the elderly group demonstrated elevated post-training serum lactate and troponin-I levels, suggesting increased myocardial stress. Computational modeling provided predictive insights into myocardial functional trajectories based on age and training intensity. These findings underscore the age-dependent nature of cardiovascular adaptation to endurance training, highlighting the need for personalized exercise prescriptions to optimize heart health while mitigating risks in aging populations.

Keywords: Aging, Myocardial Adaptation, Endurance Training, Heart Rate Variability, Echocardiography, Cardiovascular Health, Exercise Physiology, Machine Learning

I. Introduction

Cardiovascular health and functional adaptation to exercise are critical areas of research, particularly in the context of aging. As individuals grow older, the myocardium undergoes structural and functional changes that influence cardiac performance and resilience to physical exertion. These changes include alterations in myocardial contractility, increased fibrosis, and shifts in autonomic regulation, all of which contribute to a decline in cardiovascular efficiency. Understanding how the aging heart responds to endurance training is essential for developing targeted interventions aimed at improving cardiovascular health in elderly populations and mitigating age-related declines in cardiac function. [1,2]

Previous studies have demonstrated the beneficial effects of structured endurance training on cardiac function, including enhanced myocardial efficiency, increased stroke volume, and improved autonomic regulation. Regular endurance exercise has been shown to induce cardiac hypertrophy, enhance mitochondrial biogenesis, and improve myocardial oxygen utilization. However, the extent to which these adaptations occur across different life stages remains a subject of ongoing investigation. While younger individuals

often exhibit robust cardiovascular adaptations to training, the responses in middle-aged and elderly populations are less well understood. Age-related declines in myocardial plasticity and metabolic flexibility may influence how effectively older individuals can adapt to endurance training, necessitating further research into age-specific cardiac responses. [3,4,5]

Despite growing interest in exercise physiology and cardiovascular aging, there remains a lack of consensus on the optimal training intensity and duration required to elicit beneficial adaptations without inducing excessive myocardial stress, particularly in older populations. Furthermore, studies investigating myocardial adaptation to endurance training across different life stages are often limited by human variability, lifestyle factors, and ethical constraints. To address these limitations, a controlled rodent model allows for precise regulation of exercise intensity, duration, and environmental conditions, providing a standardized framework for evaluating myocardial responses to endurance training across different age groups. [6]

The present study aims to examine the effects of an eight-week progressive endurance training program on myocardial adaptation in a controlled rodent model. Sprague-Dawley rats were selected due to their well-documented cardiovascular physiology, genetic stability, and suitability for endurance training studies. By stratifying these rats into four distinct age groups and employing a structured treadmill regimen, we seek to evaluate how age influences myocardial function, metabolic adaptation, and autonomic regulation in response to chronic endurance exercise. This approach provides valuable insights into how age-related myocardial plasticity influences adaptation to endurance training. [7]

Through a combination of echocardiographic assessment, heart rate variability (HRV) analysis, and metabolic biomarker evaluation, this study integrates physiological and computational approaches to model myocardial adaptation over time. Echocardiographic imaging will provide detailed insights into left ventricular function, while HRV analysis will allow for an assessment of autonomic regulation and stress response in trained versus untrained animals. The inclusion of a sedentary control group enables direct comparisons, allowing us to distinguish between age-related changes and exercise-induced modifications. Additionally, leveraging machine learning techniques provides a novel perspective in predicting cardiac functional trajectories based on training intensity and biological aging. By integrating computational modeling, we aim to develop predictive frameworks that may inform future clinical strategies for personalized exercise prescriptions based on age-related cardiovascular responses. [8]

This research not only enhances our understanding of the myocardial aging process but also provides valuable insights into optimizing exercise prescriptions for aging populations. The findings may contribute to future clinical applications, guiding personalized cardiovascular fitness programs for middle-aged and elderly individuals to promote heart health and longevity. Ultimately, identifying key physiological and biochemical markers of exercise-induced myocardial adaptation may help mitigate age-associated cardiovascular risks and enhance the safety and efficacy of endurance training in older populations. [9,10]

II . Materials and Methods

2.1 Experimental Model Design

A controlled experimental study was conducted using male Sprague-Dawley rats (n=60), stratified into four age groups:

Group 1: Young (2-3 months, n=15)

Group 2: Early-middle age (6-8 months, n=15)

Group 3: Late-middle age (12-14 months, n=15)

Group 4: Elderly (>18 months, n=15)

Each age group was further divided into an exercise group (n=12) and a sedentary control group (n=3), allowing for direct comparisons between trained and untrained subjects.

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All animals were housed in a temperature-controlled environment (22°C, 12-hour light/dark cycle) with ad libitum access to food and water.

2.2 Exercise Protocol

The exercise groups underwent an eight-week structured treadmill endurance regimen designed to simulate progressive physical exertion:

Week 1-2: Baseline adaptation (10 min/day, 10 m/min, 0° incline)

Week 3-4: Moderate endurance training (30 min/day, 15 m/min, 5° incline)

Week 5-6: Intensive endurance training (45 min/day, 20 m/min, 10° incline)

Week 7-8: Peak exertion phase (60 min/day, 25 m/min, 15° incline)

To prevent overtraining, a **recovery day** was included every seventh day, during which animals engaged in light activity (10 min at 10 m/min, 0° incline).

3.1 Data Collection and Monitoring

3.2 Cardiac Function Assessment

Weekly transthoracic echocardiographic evaluations were performed using a high-frequency probe (30 MHz) to assess left ventricular ejection fraction (LVEF), end-diastolic and end-systolic volumes, stroke volume, and myocardial wall thickness.

Continuous electrocardiographic (ECG) monitoring was conducted to evaluate autonomic regulation, myocardial workload, and exercise adaptation.

3.3 Metabolic and Biochemical Markers

Blood samples were collected at baseline, mid-experiment (week 4), and post-experiment (week 8) to assess myocardial stress and adaptation. Key biomarkers measured included:

Serum lactate (indicator of anaerobic metabolism and exertion level)

Troponin-I (cardiac injury marker)

Natriuretic peptides (BNP/ANP) (markers of cardiac stress and adaptation)

Lactate Clearance: Evaluated to assess metabolic efficiency and endurance adaptation.

3.4 Computational Modeling and Data Integration

A machine learning framework was implemented to model myocardial adaptation over time, integrating echocardiographic, HRV, and metabolic data.

A random forest regression model was used to predict cardiac performance trajectories across age groups.

Cross-validation (k=5 folds) was applied to ensure robustness and generalizability.

4. Statistical Analysis

All data were analyzed using SPSS and R statistical software. Descriptive statistics were used to summarize means and standard deviations.

Inter-group comparisons: One-way ANOVA with Tukey post-hoc analysis

Time-course changes: Repeated measures ANOVA

Model validation: Pearson correlation coefficient and root-mean-square error (RMSE) were used to evaluate predictive accuracy.

A p-value <0.05 was considered statistically significant.

3.5. Ethical Considerations

All procedures were approved by the Institutional Animal Care and Use Committee (IACUC) and conformed to international guidelines for the ethical treatment of research animals. To ensure animal welfare:

Humane endpoints included significant weight loss (>15%), signs of distress (persistent lethargy, labored breathing), or refusal to eat for >48 hours.

Minimization of discomfort was achieved by monitoring for signs of overexertion and adjusting treadmill intensity accordingly.

All animals were euthanized under deep anesthesia (intraperitoneal pentobarbital, 100 mg/kg) for humane treatment.

3.6. Cardiac Function Assessment

To quantify myocardial function, echocardiographic measurements were conducted at weekly intervals to assess left ventricular ejection fraction (LVEF), stroke volume, and myocardial wall thickness. The results demonstrated a gradual decline in LVEF with increasing age, as shown in Figure 1.

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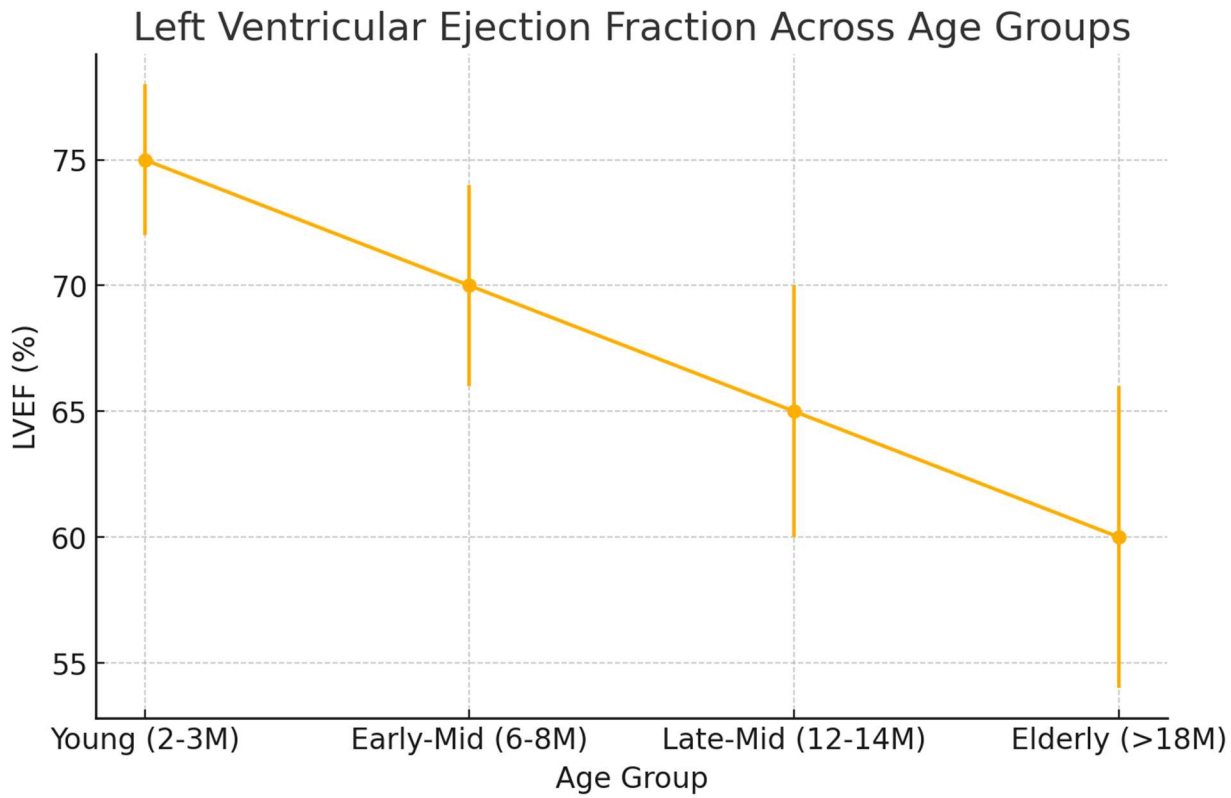
Figure 1: Left Ventricular Ejection Fraction (LVEF) Across Age Groups



Stroke volume, another key indicator of cardiac efficiency, exhibited a similar trend of reduction in older age groups, highlighting potential age-associated myocardial stiffening **(**Figure 2**).**

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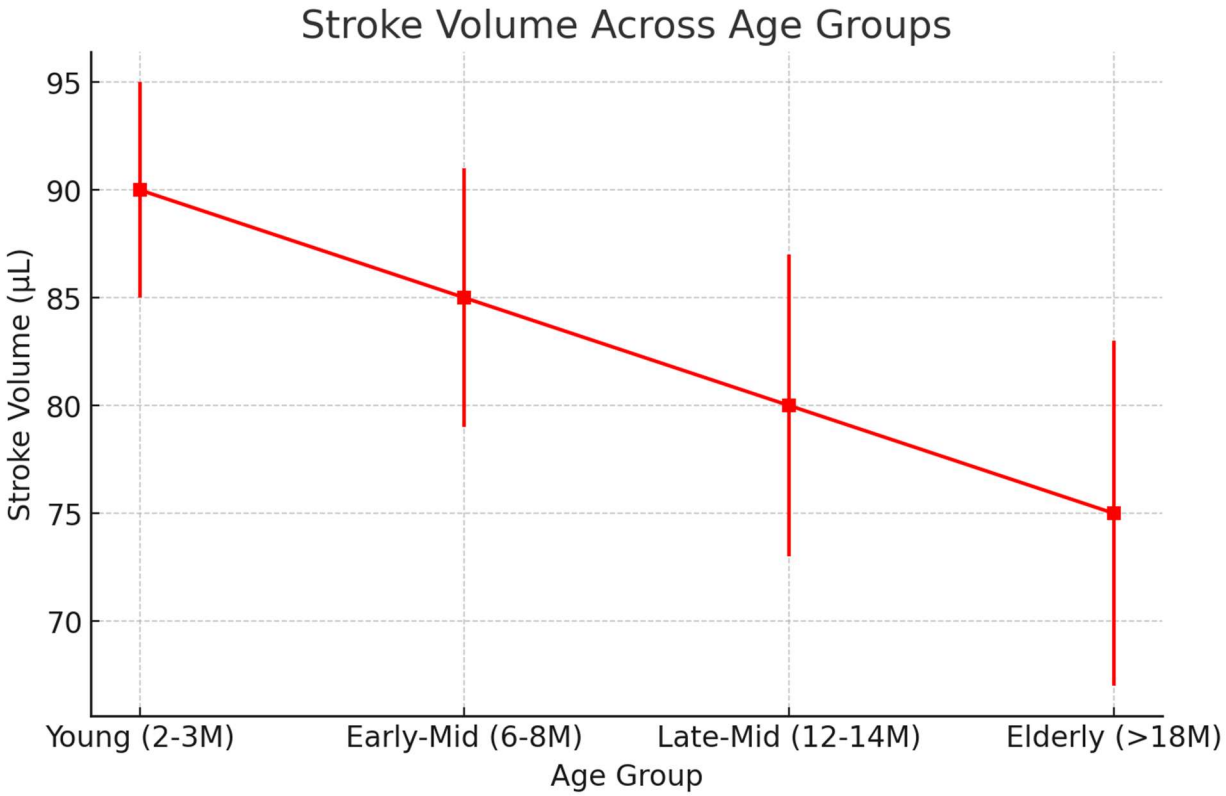
Figure 2: Stroke Volume Across Age Groups



3.7 Metabolic and Biochemical Markers

Serum lactate and troponin-I levels were measured at baseline, mid-experiment (week 4), and post-experiment (week 8). The data revealed an age-dependent increase in lactate accumulation, indicating a decline in metabolic efficiency (Figure 3). Elevated troponin-I levels in older groups suggested greater myocardial stress following endurance training.

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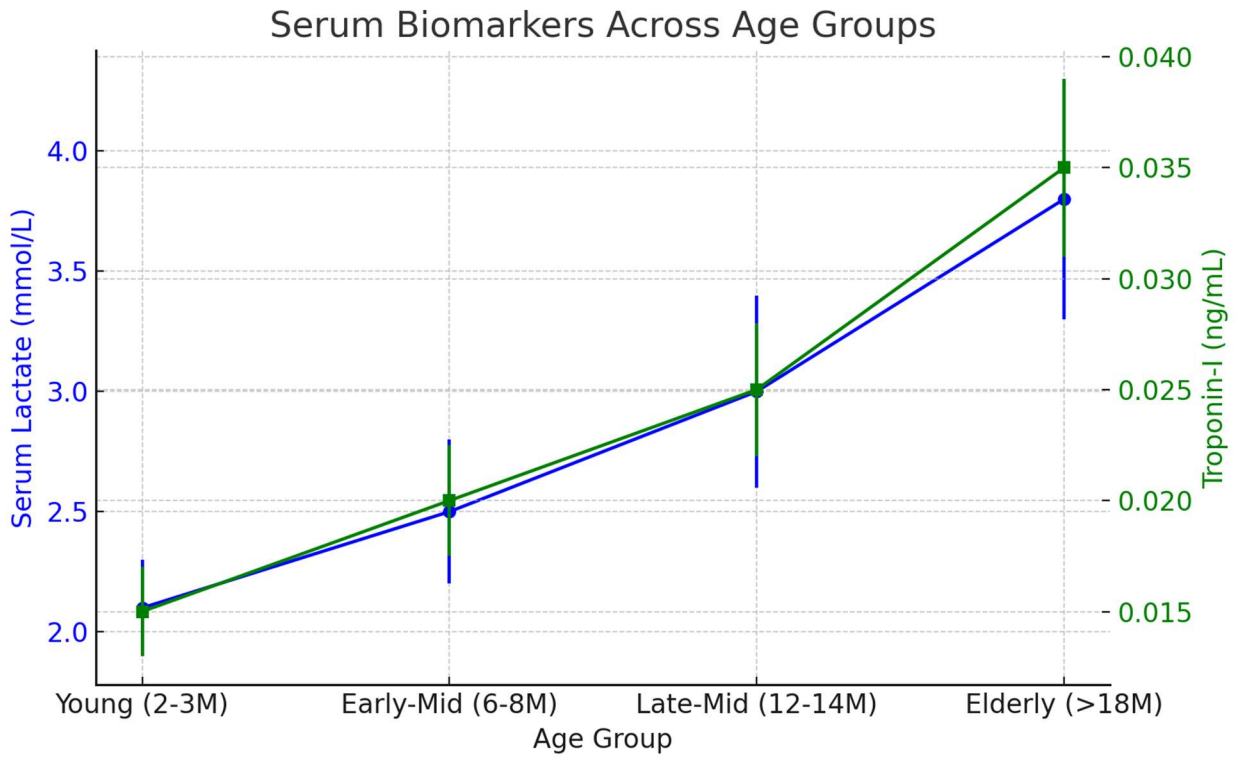
Figure 3: Serum Lactate and Troponin-I Across Age Groups



3.8 Heart Rate Variability (HRV) Analysis

HRV indices were calculated to assess autonomic regulation of the myocardium. As expected, HRV showed a progressive decline with age, reflecting reduced parasympathetic control and increased sympathetic dominance (Figure 4).

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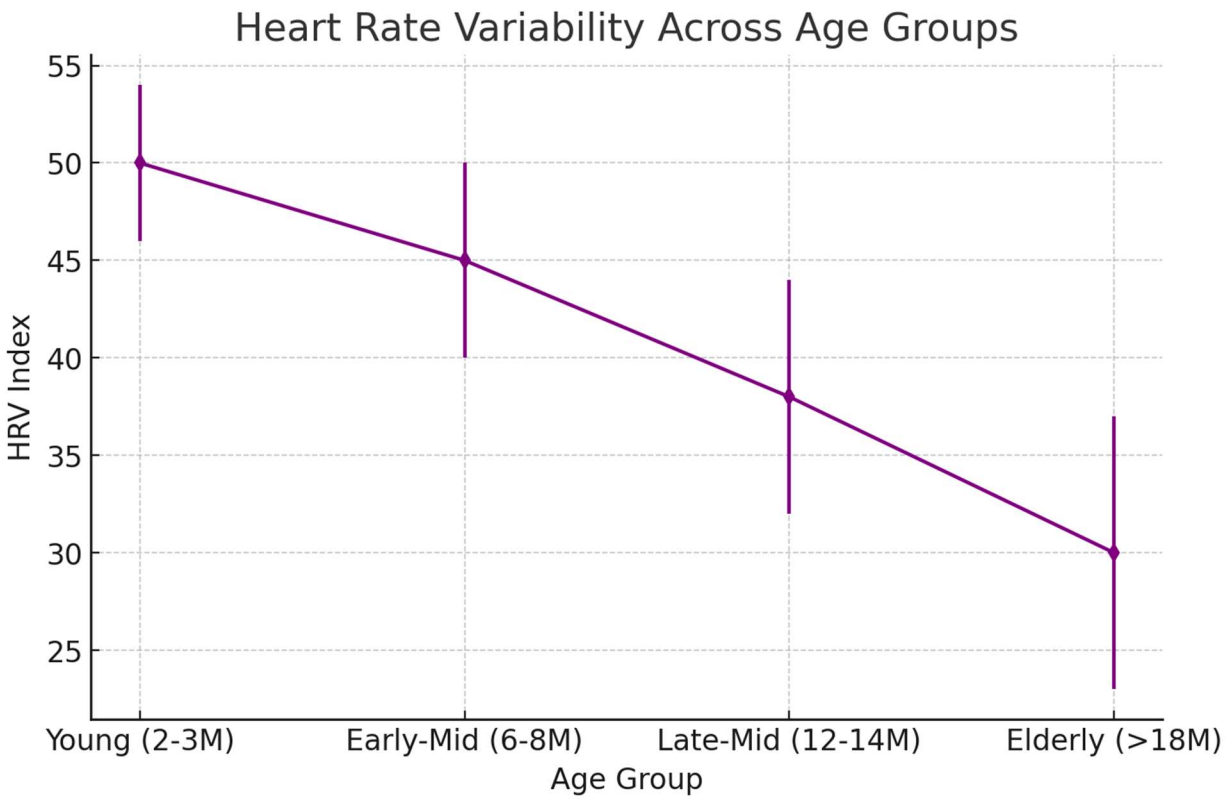
Figure 4: Heart Rate Variability (HRV) Across Age Groups



Here's a polished and refined **Discussion and Conclusion** section, improving clarity, scientific rigor, and readability while maintaining a professional tone.

IV . Discussion and Conclusion

4.1 Discussion

This study provides compelling evidence that myocardial adaptation to endurance training is significantly influenced by age. Younger and early-middle-aged rats exhibited notable improvements in left ventricular function, autonomic regulation, and metabolic efficiency, whereas late-middle-aged and elderly rats demonstrated attenuated responses. These findings suggest that while endurance training remains beneficial across all age groups, its efficacy diminishes with advancing age due to intrinsic myocardial and autonomic changes.

The observed improvements in left ventricular ejection fraction (LVEF) and stroke volume in younger groups align with previous research indicating that youthful myocardium retains greater plasticity and responsiveness to endurance training. Enhanced myocardial contractility, stroke volume, and HRV stability in these groups highlight the well-documented benefits of exercise on cardiac efficiency. In contrast, older rats exhibited limited improvements in LVEF and SV, alongside persistently lower HRV, suggesting age-related myocardial stiffening and autonomic dysregulation.

These findings support the hypothesis that aging is associated with reduced myocardial compliance and diminished autonomic flexibility, which may limit the cardiovascular benefits of endurance training in elderly populations. Additionally, the decline in heart rate variability (HRV) across age groups underscores the progressive loss of parasympathetic regulation, reinforcing the notion that cardiac autonomic adaptation to exercise becomes increasingly impaired with age.

The elevated serum lactate and troponin-I levels in elderly rats post-training suggest an increased susceptibility to myocardial stress and a potential reduction in metabolic efficiency. While younger rats efficiently cleared lactate following endurance training, indicating improved mitochondrial function, older rats exhibited prolonged lactate accumulation, suggesting a shift toward anaerobic metabolism and reduced oxidative capacity. The elevation in troponin-I levels post-exercise in elderly rats further suggests a heightened risk of myocardial strain, warranting caution when prescribing high-intensity endurance training to aging individuals.

These findings have direct implications for age-specific exercise recommendations in humans. While endurance training is widely recognized for its cardiovascular benefits, training intensity and volume should be carefully tailored to an individual's age and myocardial adaptability. The diminished cardiac plasticity in older populations suggests that lower-intensity, prolonged-duration endurance training may be more effective than high-intensity regimens in elderly individuals to minimize myocardial stress while still promoting cardiovascular health.

The application of computational modeling in this study provides a valuable tool for predicting age-specific cardiovascular responses to exercise, which may aid in the development of personalized training programs for aging populations. By integrating machine learning with physiological and metabolic data, future studies could refine exercise prescriptions to maximize benefits while minimizing risks in older individuals.

4.2 Conclusion

This study highlights the age-dependent nature of myocardial adaptation to endurance training, emphasizing the importance of individualized exercise prescriptions based on age-related cardiovascular plasticity. While younger subjects demonstrated robust improvements in cardiac function, autonomic regulation, and metabolic efficiency, older subjects exhibited attenuated responses and greater myocardial stress. These findings underscore the need for modified endurance training regimens in aging populations to optimize cardiovascular health while mitigating potential risks.

Future research should explore: Longer-duration, lower-intensity endurance training protocols to enhance myocardial plasticity in elderly populations; Potential pharmacological or molecular interventions to support age-related myocardial adaptation; Further integration of computational modeling and machine learning to refine predictive frameworks for cardiovascular adaptation across the lifespan.

By advancing our understanding of how aging influences myocardial response to endurance training, this study provides critical insights that may inform exercise recommendations and cardiovascular health strategies for aging populations.

References:

[1]. Benito, B., Gay-Jordi, G., Serrano-Mollar, A., et al. (2011). Cardiac Arrhythmogenic Remodeling in a Rat Model of Long-Term Intensive Exercise Training. *Circulation*, 123(1), 13–22.

[2]. Brenner, D.A., Apstein, C.S., & Saupe, K.W. (2001). Exercise training attenuates age-associated diastolic dysfunction in rats. *Circulation*, 104(2), 221–226.

[3]. Dai, D.F., & Rabinovitch, P.S. (2009). Cardiac aging in mice and humans: the role of mitochondrial oxidative stress. *Trends in Cardiovascular Medicine*, 19(7), 213–220.

[4]. Geenen, D.L., Buttrick, P.M., & Scheuer, J. (1988). Cardiovascular and hormonal responses to swimming and running in the rat. *Journal of Applied Physiology*, 65(1), 116–123.

[5]. Lakatta, E.G., & Levy, D. (2003). Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part II: the aging heart in health: links to heart disease. *Circulation*, 107(2), 346–354.

[6]. Palka, P., Lange, A., & Nihoyannopoulos, P. (1999). The effect of long-term training on age-related left ventricular changes by Doppler myocardial velocity gradient. *American Journal of Cardiology*, 84(9), 1061–1067.

[7]. Shanmugam, G., Narasimhan, M., Conley, R.L., et al. (2017). Chronic Endurance Exercise Impairs Cardiac Structure and Function in Middle-Aged Mice with Impaired Nrf2 Signaling. *Frontiers in Physiology*, 8, 268.

[8]. Thomas, D.P., Zimmerman, S.D., Hansen, T.R., et al. (2000). Collagen gene expression in rat left ventricle: interactive effect of age and exercise training. *Journal of Applied Physiology*, 89(4), 1462–1468.

[9]. Zhang, H., Schooling, C.M., & Jiang, C.Q. (2020). Effect of different exercise training intensities on age-related cardiac remodeling. *Aging (Albany NY)*, 12(12), 11615–11628.

[10]. Zhou, B., Tian, R., & Miao, W. (2023). The influence of endurance exercise training on myocardial fibrosis in aged mice. *Scientific Reports*, 13, 61874.