PHYSICAL ACTIVITY AND CARDIOVASCULAR AGING: THE MECHANISM AND RECENT EVIDENCES

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ABSTRACT

Lower the health burden and maintain the wellbeing is a definition of successful aging in population. There are some factors that influence the successful aging, such as physiological, mental, social, and lifestyle variables. The one of most significant lifestyle factors that can reducing the chronic diseases, improving health and survival, and enhancing cognitive and physical functions in elderly is physical activity. Recent systematic review showed the benefit of exercise for overall health and cardiovascular system. In the younger population, physical activity promotes successful aging. To explain the correlation between exercise and successful aging was the main aim of this narrative review.

Keywords: exercise; healthy life style; cardiac aging

INTRODUCTION

Aging is a neither simple nor very complex process. The definition of aging is a gradual physiological integrity loss that occurs depending on time. This process ultimately leads to decreased physical function¹, molecular and cellular damage over the life cycle of the organism frequently contributes to pathological conditions associated with age².

These days, aging becomes a global health problem. The data from World Health Organization showed that the elderly population (aged 65 years or older) will rise to 1.6 billion in 2050 and constitute up 16 % of the global residents³. The increase of aging population is linked with many health condition problems and large medical cost. Non-communicable diseases and chronic including diabetes, cardiovascular disease, dementia, blood pressure disease and cancer are common disease that we found in elderly⁴.

There is a need for senior citizen to experience morbidity and disability to protect their roles successfully⁵. Being able to preserve the quality of life and reduce the burden of wellbeing is considered as successful aging⁶. Many factors, including physiological, psychological, social, and lifestyle factors, affect successful aging⁷. One of the most important lifestyle factor that can prevent chronic diseases, boosting durability as well as sustainability, and also develop physical functions and cognitive in elderly is physical activity⁶,⁷. Therefore, to explain the correlation between exercise and successful aging is the main aim of this narrative review.

DISCUSSION

Mechanism of physical activity and aging prevention

Genomic instability, mitochondrial dysfunction, telomere protection, and low grade inflammation plays very important role in aging⁸. One of the important process that caused aging is genetic injury accumulation during the person’s lifespan⁹. The two main factors in the process of genomic instability are exogenous & endogenous which cause translocations, mutations, losses and gains in chromosomes, destruction of gene and shortening of telomeres. Exogen factors were made
from physical, chemical, and biological, while endogenous factors consisted of deoxyribonucleic acid (DNA) replication defects, uncontrolled hydrolytic responses, and reactive oxygen species (ROS)\textsuperscript{10}.

Exercise and good physical activity plays important role in preserving genomic integrity. A result shows that aerobic physical activity enhances the repairing mechanism of DNA and the signaling of nuclear factor kappa B (NF-κB) and peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α) in a study using animal models\textsuperscript{11}. The increased number of DNA repairs combined with the lowered amount of DNA damages (up to 77\%) are able to overcome aging process and make the disease that related to cardiovascular risk reduce, which can be done through physical exercises\textsuperscript{12}.

Mitochondrial dysfunction plays important part in aging\textsuperscript{10}. Some mechanisms are linked to mitochondrial integrity and biogenesis, including mitochondrial deficiencies that enhance their predisposition in the presence of stress, thus triggering inflammatory reactions mediated by ROS (Reactive Oxygen Species) and permeabilization-facilitated, which also speed up the aging process\textsuperscript{13}.

One of positive effect of daily physical activity is on mitochondrial function. The previous study showed people that train their endurance has expression of mitochondrial proteins, mtDNA, and TFAMs in higher levels\textsuperscript{14}. An animal-based study found that mtDNA systemic mitochondrial biogenesis was induced by a 5-month aerobic physical activity program and enhanced multi-organ oxidative capacity, offering phenotypic protection and minimizing the risk of premature mortality and multisystem pathology\textsuperscript{15}.

Low grade inflammation plays important role in aging. Regular physical activity reduces inflammatory markers in older adults. Furthermore, inflammation of the low-grade, including chronic illness, has been related to most of the elements of good aging and can speed down the aging process\textsuperscript{16,17}. A recent study in population showed that the chance of life free of chronic conditions, cognitive decline and physical disability for an additional 10 years increases with higher level of physical activity\textsuperscript{18}.

Recent studies have shown that the activation of telomerase will reverse aging, to be specific, in premature aging mice which lacked in telomerase when the reactivation of the enzyme occurs\textsuperscript{19}. Aging promotes the accumulation of DNA damage, particularly in very sensitive chromosome areas like the telomeres. Latest research shows that there would be a protective function for physical activity against stress-related telomere loss. Physical activity gives a massive effect on telomere length, es in chronic design and moreover in older people in contrary to age-induced decline in telomere reduction. A few possible pathways have been reported to correlate workout and reduced telomere longevity with altered activity of telomerase, inflammation, oxidative stress, and lowered composition of skeletal muscle satellite cells\textsuperscript{20}.

Physical activity has been connected to increased regulation of protective proteins (like telomeric repeat-binding factor 2) and proteins of DNA repair pathway (like Ku protein) and also the decreased control of negative regulatory proteins of cell cycle growth (like p16) in middle-aged athletes that hold up such association\textsuperscript{21}. Antioxidant activity and decreasing ROS levels, holding up the REDOX balance, defending against DNA destruction and consequently diminishes telomere alleviation are affiliated with regularly physical activity\textsuperscript{20,21}.

Recent evidences

An epidemiological studies showed that the risk of all-caused deaths and the risk of developing conditions such as type 2 diabetes and cardiovascular disease is lower for older adults who regularly exercise at a moderate level\textsuperscript{22}. Physical activity, health and all – causes mortality were reported to have a strong inverse relationship, as shown in epidemiological studies\textsuperscript{23}. A prospective cohort study showed a 40 – 50\% reduction in certain cause, cardiovascular disease and cancer mortality rates and were associated with a higher physical activity level compared to the lower activity levels\textsuperscript{24}.

Mortality is strongly attributed to objectively measured cardiovascular fitness\textsuperscript{25}. Functional independence has been strongly linked to muscle strength and aerobic fitness. Enhancements in muscle strength and aerobic fitness also show in functional independence in older adults without disabilities\textsuperscript{26}. A reduced risk of approximately 30-50\% of functional limitations and disability was shown in older adults who performed physical activity of adequate amount and duration has been carried out as reported in a systemic review recently\textsuperscript{26}.
A recent review showed a positive association among high levels of cardiovascular fitness and great health. There may be advantages of some kind of physical activity that increases cardiovascular fitness. Improving cardiovascular fitness in older adults means improving their health. The same benefit is also offered by starting from a low level of cardiovascular fitness\textsuperscript{27}.

**Physical exercise and cardiac aging**

Aging makes changes in the heart on structural and functional changes that are associated with a levitating risk of cardiovascular disease and weakened functional capacity in the elderly. Advanced age is considered a major independent risk factor for HF (heart failure). The accumulating effect of repetitive insults and injuries to the heart during its lifespan, such as myocardial infarctions and hypertension, is irrefutably a major cause of maladaptive myocardial remodeling in the elderly. Cardiac aging also developed from intrinsic aging that occurs at a cellular and molecular level that the role of the heart can influence\textsuperscript{28}. Stress response, metabolism of fatty acids, hypertrophy, contractility, inflammation of mitochondrial function, and development of extracellular matrix have been identified as key molecular phenotypes of cardiac aging associated with transcriptional pathway alterations\textsuperscript{29}.

Desensitization of β-adrenergic receptor (β-AR) is a mechanism of sympathetic dysregulation in the aged core. During normal aging, circulating levels of norepinephrine rise by 10-15 percent per decade\textsuperscript{29}. Post-synaptic machinery desensitization is triggered by higher β-AR catecholamine occupancy, which activates a compensatory mechanism in aged cardiomyocytes\textsuperscript{28,29}.

Prolonged Ca\textsuperscript{2+} transients that occurred in aging myocardium is caused by the decreasing amount of sarcoplasmic reticulum Ca\textsuperscript{2+}-ATPase (SERCA2a), and changes that is related to aging in the proteins involved on EC coupling can prevent the restoration of the Ca\textsuperscript{2+} intracellular impairments\textsuperscript{30}.

A study using animal model showed result that training in aerobic physical activity causes a faster increase and decay of Ca\textsuperscript{2+} + transients in cardiomyocytes and subsequent improvement in systolic and diastolic activity. Via more efficient coupling of L-type Ca2 + channels and RyR receptors, increased SERCA2a and NCX expression, enhanced SERCA2a function through transient CaMKII activation or PLB inhibition, and enhanced Ca2 + myofilament sensitivity, the mechanisms for such modification induced by physical activity in Ca2 + cycling in young hearts are potentially mediated\textsuperscript{30}.

Recent systematic review showed the benefit of exercise for overall health and cardiovascular system. Physically active middle-aged and older adults were more likely than sedentary adults to age successfully (OR=1.64, 95 % CI: 1.40–1.94). In the younger group (OR=1.71, 95 percent CI: 1.41–2.08), the impact of physical activity was greater than in the older group (OR=1.54, 95 percent CI: 1.13–2.08)\textsuperscript{31}.

**CONCLUSION**

Our review showed that there was good evidence of physical inactivity in older adults for chronic health problems. They must increase regularly exercise to minimize mortality and morbidity. The research shows that daily exercise is good for healthy and vulnerable elderly people. If physical exercises are regularly done, the probability of acquiring serious cardiovascular and metabolic diseases, osteoporosis, obesity, falls, cognitive problems, and weak muscle will be reduced. Regular physical activity is effective to prevent aging for middle-aged and older adults, particularly among the younger population.

**REFERENCES**

23. Iijima K, limuro S, Shinozaki T et al. Lower physical activity is a strong predictor of cardiovascular events in elderly patients with type2 diabetes mellitus beyond traditional