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2. **Aging and Cardiovascular Diseases**
3. [***Suggestions: No more than 20 words. No abbreviations except for standardized ones e.g., DNA, RNA, gene or***
4. ***protein names, etc.***]

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12. According to the World Health Organization, the term elderly; It is meant for people over the age of 65. With aging, decreases in heart rate, heart function, oxygen consumption and stroke rate occur. With aging, physiological changes occur in senses such as gastrointestinal system, respiratory system, neurological system, cardiovascular system, excretory system, immune system, endocrine system, musculoskeletal system, vision, skin, taste, smell and hearing. The cardiovascular system is the most important system that affects mortality and morbidity due to cell loss in the conduction and muscle system in old age. Depending on the genetic background and age, the heart's ability to pump blood decreases, the myocardium loses its flexibility, and the heart valves thicken and increase in diameter. Due to arteriosclerosis, the thickness of blood vessels increases while their elasticity decreases. Functional and structural changes in the cardiovascular system in old age increase the risk of coronary artery disease, heart diseases, heart failure, venous thrombosis and hypertension. With aging, some changes occur in the cardiovascular system without the presence of morbidity. With aging, cardiac output and stroke volume decrease and the risk of postural hypotension increases. With advancing age, a continuous rise in systolic blood pressure occurs as a result of the hardening of the vessels and the decrease in their elasticity. At the age of 60 and beyond, there is either a slight decrease or no change in diastolic blood pressure.
13. **Keywords:** Aging, cardiovascular diseases, chronic diseases
14. **[*Please suggest 3-6 keywords which can be used for describing the content of the manuscript and will enable the***
15. ***full text of the manuscript to be searchable online.*]**

# INTRODUCTION

# Age is an important risk factor for cardiovascular diseases. Studies conducted indicate that the risk of cardiovascular disease increases in older individuals compared to younger individuals [1]. Cardiovascular disease will continue to be the leading cause of death in older individuals and the cost associated with treatment will continue to increase. Aging is an inevitable part of life and unfortunately constitutes the biggest risk factor for cardiovascular disease [2]. Aging is associated with a progressive decline in various physiological processes, resulting in an increased risk of health complications and disease. By delivering oxygenated blood to all tissues in the body, it is vital to the health of the cardiovascular system, the health of every tissue, and the longevity of the organism as a whole. Aging has a remarkable effect on the heart and arterial system, leading to an increase in cardiovascular diseases, including atherosclerosis, hypertension, myocardial infarction and stroke. Aging cardiovascular tissues may be associated with pathological changes, including hypertrophy, altered left ventricular diastolic function and decreased left ventricular systolic capacity, increased arterial stiffness, and impaired endothelial function [3] (Figure 1).

# According to the World Health Organization (WHO), old age; It was expressed as increasing disability and being more dependent on others, and the old age limit was determined as 65 years. WHO defined old age as the loss of the ability of the individual to adapt to the environment and her health, and becoming economically dependent, and reported that old age is a period in terms of physiological, social and economic criteria [4]. According to WHO, the scientific classification of old age is:

# • Early (Young) Age: 65-74 years

# • Middle Age: 75-84 years old

# • Advanced Age: 85 years and over [5].

# According to WHO data, while people live longer today, every country in the world is experiencing a growth in the proportion of the elderly in the population. The population aging rate is much faster than in the past. From 1960 to 2020, the number of people aged 65 and over was expected to increase gradually all over the world. This number increased from 150 million in 1960 to 722 million worldwide in 2020. European countries are currently experiencing an increase in aging population due to increasing life expectancy and falling fertility rates. The share of the population over 65 years old is increasing more than all other age groups [6]. The number of individuals aged 80 and over is expected to triple between 2020 and 2050, reaching 426 million. This increase is occurring at an unprecedented rate and will accelerate in the coming decades, especially in developing countries [7].

# 

1. Figure 1. Age-related changes in cardiovascular tissues [8].

# Also globally, the population aged 65 and over in 2019 was 703 million, with the East and Southeast Asia region hosting the largest number of seniors (261 million). It is predicted that 80% of the elderly will live in middle- and low-income countries by 2050 [7]. The aim of this review article is; to examine the physiological relationship between aging and cardiovascular diseases.

1. **PHYSIOLOGICAL CHANGES DUE TO AGING**
2. During the aging period, some changes occur in elderly individuals. These generally consist of psychological, physical, social and economic changes and affect the life of the elderly person [9].
3. In this context, when we look at the physiological changes, after the age of 60, there is an increase in fat ratio and a decrease in muscle weight, different in men and women. The decrease in joint flexibility, calcium level in bones and muscle mass in the human body makes it difficult for the person to perform daily life activities. For this reason, the level of physical activity of people decreases. Losses in muscles and bones cause an increase in the risk of fractures in bones, shortening of the neck, tooth loss, thinning of the subcutaneous fat layer, humpbacks and curvatures in the legs. With aging, decreases occur in heart stroke volume, heart function, oxygen consumption and stroke rate [9]. Hardening of the chest wall, loss of flexibility of the lung tissues and decrease in respiratory muscle strength cause changes in respiratory functions. The decrease in the effectiveness of insulin, which is important in the regulation of blood glucose, leads to "type 2" diabetes. Insulin resistance occurs as a result of an increase in adipose tissue and a decrease in physical activity. There is also a decrease in the metabolic rate of the brain. As a result of the decrease in basal metabolic rate, calorie requirement and total energy expenditure decrease. As a result of the decrease in the flexibility of the lenses, loss of close focusing, decrease in depth perception, color discrimination and visual acuity occur in the eyes. Falls occur in unsafe environments, such as slippery floors, due to problems related to the nervous system, balance and vision in the elderly. In the elderly, injuries such as bone fractures, painful soft tissue damage and cerebral hemorrhage come to the fore as a result of falling. In old age, the proliferation of immune cells decreases and the body's resistance to micro-organisms decreases. As a result of the decrease in hormone levels in older women, the ovaries and uterus become smaller in terms of their function and structure. Dryness and thinning of the vaginal tissue are noticeable. Nipple sensitivity decreases and breasts are hard. These changes experienced by women do not have a negative effect on sexual act. Although men's reproductive system changes also occur, they have the opportunity to have children until they die. In addition, as a result of the decrease in hormone production, changes in the quality and number of sperm, decrease in seminal fluid, reduction in testicles, penis and enlargement in the prostate occur [9].
4. Some age-related changes include a gradual decline in physiological aging-related function. With aging, physiological changes occur in senses such as gastrointestinal system, respiratory system, neurological system, cardiovascular system, excretory system, immune system, endocrine system, musculoskeletal system, vision, skin, taste, smell and hearing. Common conditions in old age include hearing loss, cataracts and refractive errors, back and neck pain and osteoarthritis, chronic obstructive pulmonary disease, diabetes, depression and dementia. As people age, they are more likely to experience several conditions at the same time. Old age is also characterized by the emergence of several complex health conditions, commonly referred to as geriatric syndromes. It is usually the result of more than one underlying factor and includes frailty, urinary incontinence, falls, delirium, and pressure ulcers [7].
5. There is no typical old person. Some 80-year-olds have similar physical and mental capacities to many 30-year-olds. Other people experience significant declines in capacity at a much younger age. A comprehensive public health response must address these broad experiences and needs of older people. The variation seen in older ages is not random. Much is due to people's physical and social environments and the impact these environments have on their opportunities and health behaviors. All or some of these changes may not be due to hormonal changes. While some variation in older people's health is genetic, most stem from people's personal characteristics such as gender, ethnicity or socioeconomic status, as well as their physical and social environment, including their home, neighborhood and community. The environments in which people live as children – even as developing fetuses – combined with their personal characteristics have long-term effects on how they age [7].
6. Physical and social environments can affect health directly or through barriers or incentives that affect opportunities, decisions and health behaviors. Maintaining healthy behaviors throughout life, especially a balanced diet, regular physical activity, and avoiding tobacco use contribute to reducing the risk of noncommunicable diseases, improving physical and mental capacity, and delaying dependency on care. Supportive physical and social environments enable people to do what matters to them despite their loss of capacity. The availability of safe and accessible public buildings and transportation, and easy-to-walk places are examples of supportive environments. In developing a public health response to aging, it is important to consider not only individual and environmental approaches that ameliorate loss associated with advanced age, but also approaches that can enhance recovery, adjustment and psychosocial growth [7].
7. Elderly people often have multiple chronic systemic diseases and are taking multiple medications. With age, psychomotor decline, loss of function in organs and tissues, and therefore limitation in daily activities and increase in accident rates, more serious and frequent infections are expected conditions. These changes due to aging affect the daily life activity, addiction status, communication with the environment and working life of the individual [10].
8. Physical and physiological changes that occur with aging cause failure in social relations due to depressive mood, deterioration in cognitive functions, and limitation in daily living activities [11]. Physiological changes occur in many body systems during the aging process. These changes affect the individual's addiction status, communication with the environment, daily life and working life [12]. Brain structures, environmental and personal factors, genetic characteristics play a role in the development of addiction. While the substances used cause addiction, they cause changes in the brain structures related to the reward system, decision making and memory. The mesocorticolimbic system is an important part of the reward system. Dopamine is the main neurotransmitter in this system. Behaviors such as gambling, internet use, eating and shopping also increase dopamine release by activating the reward pathway, just like addictive substances. Disorders in the mesocorticolimbic pathway and related brain structures play a role in addiction. Apart from the dopaminergic mesocorticolimbic system, other systems and neurotransmitters are also thought to be effective in the development of addiction [13].
9. **AGING AND CARDIOVASCULAR DISEASES**

The key is that population aging and slower population growth will almost certainly bring a slowdown in Gross Domestic Product and GDP growth. But the impact on per capita income and consumption can be quite different from experience at the individual level. The aging of the population means increasing dependency on old age, to the extent that the elderly are not self-sufficient with their wealth income or their own increased labor. But population aging can result in more capital per worker and increased productivity and wages, especially if rising government debt does not support capital investment. One analysis concludes that moderately low fertility, about 1.7 births per woman, is favorable to living standards [6]. Only very low fertility at levels found in East Asia, Germany and Eastern and Southern Europe will produce aging that lowers living standards. The increase in the elderly population presents significant financial, social and economic challenges, especially at the macroeconomic level. With an aging population comes concerns about increased public spending on long-term care, health and other age-related expenditures, particularly through the pension system. The European policy of "active aging", which has two complementary goals: raising the retirement age and increasing the employment rate of older workers, are strategies to resolve the aging population dilemma. The negative impact of the aging population on the economy is striking [6].

The cardiovascular system is the most important system that affects mortality and morbidity due to cell loss in the conduction and muscle system in old age. Depending on the genetic background [14] and age, the heart's ability to pump blood decreases, the myocardium loses its flexibility, and the heart valves thicken and increase in diameter. Due to arteriosclerosis, the thickness of blood vessels increases while their elasticity decreases. Functional and structural changes in the cardiovascular system in old age increase the risk of coronary artery disease, heart diseases, heart failure, venous thrombosis and hypertension. Healthcare professionals should be aware of these physiological changes that affect the quality of life of elderly people [15].

With aging, some changes occur in the cardiovascular system without the presence of morbidity. With aging, cardiac output and stroke volume decrease and the risk of postural hypotension increases. The vessel walls thicken and decrease in their elasticity. With advancing age, a continuous rise in systolic blood pressure occurs as a result of the hardening of the vessels and the decrease in their elasticity. At the age of 60 and beyond, there is either a slight decrease or no change in diastolic blood pressure. With the accumulation of calcium minerals in the heart, the valves in the heart thicken and murmurs appear. Cardiac output also decreases during exercise, as the response to beta-adrenergic stimuli in smooth muscles decreases [10]. Important problems that can be seen as a result of physiological changes that occur with aging; heart failure, arrhythmia, and cardiac hypertrophy. In this context; The risk of cardiovascular disease increases with the existence of other associations such as age-related diabetes, obesity and hypertension. With increasing age, heart failure, heart valve problems, arrhythmias and coronary artery diseases also increase. Therefore, there is a need to know the changes that occur with aging [16].

Cardiovascular diseases are the leading cause of death in people aged 65 and over, and 80% of deaths from cardiovascular diseases occur in this age range. For this reason, it is important for healthcare professionals to interpret and understand the physiological changes that will reduce the quality of life in later life [17]. The shadow of the heart is enlarged when looking at the chest X-ray. As a result of various calcifications in the heart, mitral and aortic valves are affected, causing sclerosis and murmurs are observed [18].

Systolic blood pressure generally increases with advanced age, whereas diastolic blood pressure either tends to decrease slightly or does not change after 60 years of age. The main reason for this is the hardening of the arteries due to the loss of flexibility of the great arteries. An increase in systolic blood pressure can cause hypotension and impair left ventricular filling. Arrhythmias and ectopic beats are common, and the activity of baroreceptors decreases, vasoconstriction occurs in the lower extremity veins, and the adipose tissue around the heart increases. The blood flow to all organs decreases, the superficial veins of the skin become prominent and the veins dilate. A serious decrease in physical activity capacity due to aging, hypertension, atrial fibrillation, atherosclerosis, valve diseases, heart attack, venous thrombosis and heart failure occur. Appropriate exercises should be recommended to elderly people according to their physical capacities, and the elderly should avoid excessive fatigue, stress and situations that cause tachycardia [10].

Hypertension is a fairly common condition with numerous health risks, and the incidence of hypertension is highest among older adults. Several key mechanisms, including inflammation, oxidative stress, and endothelial dysfunction, are common in the development of biological aging and hypertension and appear to have important mechanistic roles in the development of collateral risks of cardiovascular and late life hypertension. Older adults, in particular, are responsible for the majority of hypertension-related morbidity and mortality, with hypertension largely having a higher prevalence among the elderly [19]. No matter how diverse the etiologies of age-related diseases are, substantial evidence suggests two interconnected mechanisms among the most common biological causes of age-related disease: 1) chronic, low-grade inflammation [20] and 2) increased cellular oxidative stress. [21]. The inflammatory biomarkers most consistently associated with aging are high circulating concentrations of interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor alpha (TNF-α) [20]. In particular, these markers increase during aging even in the absence of acute infection and have been associated with the prevalence of advanced age. This leads to cardiovascular diseases [22].

Atherosclerosis is known as the disease of aging. Thus, increasing age is an independent risk factor for the development of atherosclerosis. Atherosclerosis is also associated with premature biological aging, as atherosclerotic plaques show evidence of cellular aging characterized by reduced cell proliferation, irreversible growth arrest and apoptosis, elevated DNA damage, epigenetic modifications, and telomere shortening and dysfunction. Not only is cellular aging associated with atherosclerosis, there is evidence that cellular aging increases the occurrence of atherosclerosis. Increasing evidence indicates that aging is also an important risk factor for atherosclerosis and persists as an independent contributor when all other known factors are controlled. Premature or accelerated vascular aging may be manifested by cardiovascular risk factors, and cellular aging is also observed in individuals with atherosclerosis [23]. Therefore, atherosclerosis is a disease of both organismal aging and cellular senescence [24].

The incidence of coronary heart disease increases with aging. The majority of deaths caused by coronary artery disease are people over the age of 65. With the treatment of coronary artery disease in the elderly, it is aimed to reduce both mortality and morbidity and to obtain a more qualified life. The treatment of coronary artery disease in advanced age includes some considerations compared to treatment in younger patients. The effects of age on the coronary arteries should be reviewed in order to examine the increase in the incidence rate of CAD and the worsening of its prognosis in the elderly [25]. With aging, the coronary arteries become more convoluted and the intima layer thickens. Calcium, phospholipid and cholesterol deposition are responsible for this thickening, independent of atherosclerosis. Changes in the morphology of endothelial cells are accompanied by functional changes such as decreased ability to produce nitric oxide (NO) and increased NO consumption. The most important change in the media layer is calcification and fragmentation of elastin fibers. In addition to the migration of activated smooth muscle cells to the intima layer, an increase in matrix metalloproteinases, angiotensin II, transforming growth factor-beta and adhesion molecules is seen in the elderly. This process, which results in intima/media thickening, is an indicator of arterial aging. It is important that these events, which are involved in the physiology of aging, also play a role in the pathophysiology of atherosclerosis. Along with these physiological conditions, coronary heart diseases come to the fore in old age [25].

Aging is the strongest unmodifiable risk factor for stroke, which doubles every 10 years after age 55. About three-quarters of all strokes occur in people aged ≥65 years. As the number of people aged ≥65 years is predicted to increase, the number of stroke events in older adults is expected to increase, posing great challenges for clinicians and policy makers in the near future [26]. Stroke remains the second leading cause of death in the world and its prevalence is expected to increase in the United States and globally. The main driver of the increasing prevalence of stroke is the aging of the population [27]. A number of additional studies reveal other important risk factors and predisposing conditions for stroke development. The prevalence of certain stroke risk factors, such as diabetes, hypertension, atrial fibrillation, and coronary and peripheral artery disease, increases with age. Risk factors are not equivalent in estimating stroke risk in all age groups. Body mass index, high-density lipoprotein cholesterol, systolic blood pressure, blood sugar, or relative stroke risks associated with smoking decrease with age. However, risk factors often cluster among older adults and thus significantly alter stroke occurrence [26]. With aging, both the cerebral microcirculation and macrocirculation undergo structural and functional changes. Age-related microcirculatory changes are likely mediated by endothelial dysfunction and impaired cerebral autoregulation and neurovascular coupling. While endothelial dysfunction promotes neuro-inflammation, impaired cerebral autoregulation can lead to microvascular damage and impaired neurovascular coupling promotes a decline in cortical function, all of which are potential targets for future therapeutic interventions [26].

With aging, the number of cardiac output and cardiac output decreases, the wall thickness increases, and the vessels lose their flexibility. The fat layer surrounding the heart is increasing. These changes, which occur with advancing age, significantly affect the function of the heart and create an environment for the development of non-communicable diseases. Congestive heart failure, hypertension, ischemic heart disease, coronary artery disease are common cardiovascular diseases in the elderly. Due to these problems, circulation decreases, weakness, fatigue, edema, oxygen deficiency and adaptation to different states become difficult [28]. The physical capacities of individuals decrease with age, which limits the functional independence of the elderly [29]. It is stated that regular physical exercise reduces the risk of major cardiovascular and metabolic diseases, cognitive loss, falls and obesity in advanced age [30].

# CONCLUSION

# With aging, some changes occur in the cardiovascular system, and as a result of these changes, the risk of cardiovascular disease increases. Cardiovascular diseases are one of the leading causes of death in the elderly. Therefore, necessary precautions should be taken to reduce the risk of developing these diseases. Excess weight, a life without physical activity, unhealthy diet [31], etc. conditions that increase the risk of cardiovascular disease. Providing weight control, encouraging physical activity, gaining adequate fluid intake and healthy eating habits, preventing smoking and alcohol use, avoiding stress, ensuring the correct use of drugs, etc. These are important practices in preventing the risk of cardiovascular disease and the progression of the existing disease.

# Unhealthy nutrition and the resulting obesity cause the formation of nutrition-related non-communicable diseases (cancer, cardiovascular diseases, osteoporosis, diabetes, etc.). Studies have shown that physical exercise; revealed that it reduces the risk of developing type 2 diabetes and having a heart attack by 50 percent, and that this significant reduction may also be valid for some cancer diseases and high blood pressure.

# DECLARATIONS

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## Authors’ contributions

1. Single author:
2. The author contributed solely to the article.
3. Two or more authors: Topuz İ, Şişko E
4. Made substantial contributions to conception and design of the study and performed data analysis and
5. interpretation: Topuz İ, Şişko E;
6. Performed data acquisition, as well as provided administrative, technical, and material support: Topuz İ, Şişko E

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## Conflicts of interest

1. All authors declared that there are no conflicts of interest.

## Ethical approval and consent to participate

1. Not applicable.

## Consent for publication

1. Not applicable.

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# Supplementary Materials

1. None.