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AGING AND THE CARDIOVASCULAR SYSTEM: STRUCTURAL AND FUNCTIONAL ADAPTATIONS

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Abstract:
Background-With increasing age, there is a higher prevalence of cardiovascular diseases such as hypertension, atherosclerosis, myocardial infarction, and heart failure. Aging induces several significant structural and functional changes in the heart and blood vessels, impacting cardiovascular performance and increasing the risk of cardiovascular diseases (CVD). This article has explored the structural and functional adaptations in the cardiovascular system due to aging and its implications for health and disease. Materials and Methods- This cross sectional observational study was conducted from May 2021 to Jan 2024 in tertiary care hospital, Agra. In this study considering the measurements made from autopsies subjects and data was collected and compared the findings with the standard age and gender. Results: The study included 20 subjects, comprising 11 (55%) male and 9 (45%) female. Among these, 14 (70%) were age more than 60 years. There was significant increase in myocardial thickness with spheroid shape among 16(80%) subjects and more common in male. There was atherosclerosis and vascular stiffness was noted among 14(70%) subjects and more common in female. A significantly higher prevalence of vascular stiffness that indicated increased workload and decrease its reserve capacity and significant differences observed when compared with standard age and gender. Conclusion- Aging induces significant structural and functional changes in the cardiovascular system, increasing the risk of cardiovascular disease. It is hoped that improved understanding of the aged heart will enable the development of therapies which prevent the genesis of HF or at a minimum help clinicians to treat the unique properties of the failing, senescent heart.

Keywords- Aging, Heart, Cardiovascular system, Structural Adaptation, Functional adaptation

INTRODUCTION

Cardiovascular aging refers to the natural alterations in the structure and function of the heart and vasculature that occur with age. With increasing age, there is a higher prevalence of cardiovascular diseases such as hypertension, atherosclerosis, myocardial infarction, and heart failure. This article explores the biological mechanisms that underlie these changes and the resultant cardiovascular outcomes.The incidence of heart failure doubles with each decade of life and the prevalence rises to almost 10% of those older than 80 years.CHF is a highly lethal condition, with significant mortality, morbidity, and associated costs in the older population. More than 90% of CHF deaths occur in

adults older than 65 years.[1] In the United States alone, it is estimated that there will be 70 million people over the age of 65 by the year 2030, representing almost 25% of the population [2]
Aging induces several significant structural and functional changes in the heart and blood vessels, impacting cardiovascular performance and increasing the risk of cardiovascular diseases (CVD). There are a number of factors that link aging to HF5 and gradually reduce the amount of cardiac reserve until finally the heart is "more likely to fail" [Figure 1]

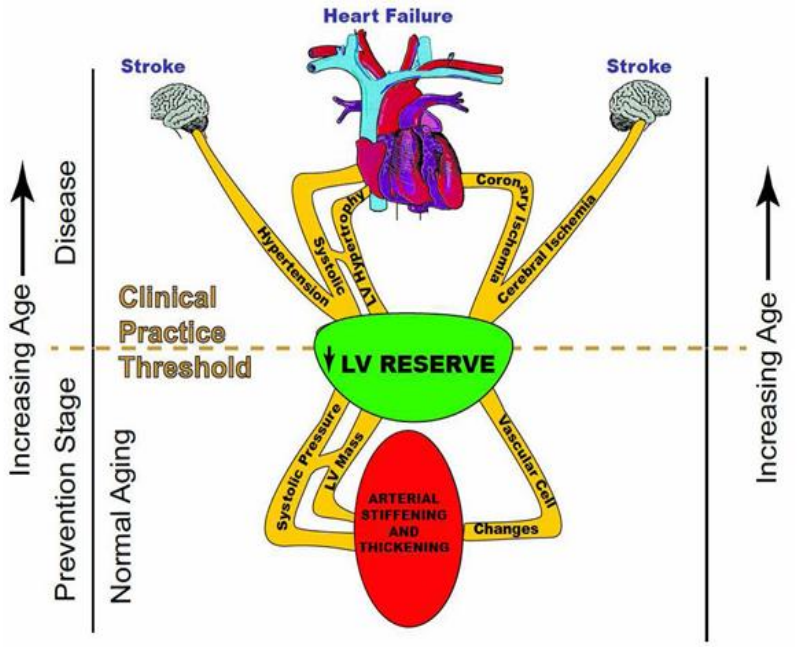

Figure 1 Pathway linking aging to heart failure[3]

The changes in the cardiovascular system increase the susceptibility to heart disease, stroke, and other CVDs in elderly populations. Various epidemiological studies explained the fact that there is a progressive increase in the prevalence of cardiovascular disease (CVD); e.g. coronary artery disease (CAD), hypertension, and diabetes leading to the development of ischemic, hypertensive, or diabetic cardiomyopathy.

Structural Adaptations in the Cardiovascular System with Aging
Structural changes: There is significant structural change in the heart and vasculature per se. There are a number of structural and functional changes in the heart with aging and each of these can have significant implications for cardiovascular disease. Structurally, there is a significant increase in myocardial thickness [4] a result of increased cardiomyocyte size.[5] In addition, the heart changes its overall shape from elliptical to spheroid with an asymmetric increase in the interventricular septum more than the free wall. [6] The understanding of the changes in LV mass with aging has developed over time as researchers have made improvements in exclusion criteria, statistical correction, and technological approach.

The Heart:
Myocardial Changes:
Age-related fibrosis leads to an increase in collagen deposition, causing stiffness of the myocardium. There is a reduction in the number of cardiomyocytes due to apoptosis and necrosis, contributing to reduced cardiac efficiency. Left ventricular hypertrophy is common due to increased pressure from vascular resistance.
Valvular Changes:
Calcification and thickening of the aortic and mitral valves increase the risk of stenosis or insufficiency.

Electrical Conductance:
SA node degeneration contributes to arrhythmias such as atrial fibrillation and heart block.

Blood Vessels:
Vascular Stiffness:
Elastin degradation and increased collagen deposition result in loss of arterial elasticity. Increased arterial stiffness elevates systolic blood pressure, leading to isolated systolic hypertension.
Atherosclerosis:
Progressive development of atherosclerotic plaques due to endothelial dysfunction, lipid deposition, and chronic inflammation is a hallmark of aging arteries.

Functional Adaptations in the Cardiovascular System with Aging
There are a number of functional changes and compensatory responses that the aged heart undergoes that diminish its ability to respond to increased workload and decrease its reserve capacity.

Cardiac Function:
Reduced Maximal Cardiac Output: Decreased contractility and heart rate response reduce maximal cardiac output during exertion.
Diastolic Dysfunction: Impaired ventricular relaxation leads to diastolic heart failure, more common in elderly patients.
Cardiac Reserve:
Decreased beta-adrenergic receptor sensitivity and reduced autonomic modulation impair the heart's ability to respond to physiological stress.

Vascular Function:
Endothelial Dysfunction: Aging is associated with reduced nitric oxide (NO) production, leading to impaired vasodilation and increased vascular tone.
Impaired Baroreceptor Sensitivity: Declining sensitivity of the baroreceptors results in less effective blood pressure regulation, contributing to postural hypotension and syncope.
Increased Pulse Wave Velocity (PWV): Due to vascular stiffness, the increased PWV is linked with greater cardiovascular risk, as it reflects the hardening of arteries. In addition, Aging-associated changes in other organ systems may also affect cardiac structure-function and thereby contribute to HF development.

On reviewing the autopsy-based studies it concludes that cardiac mass increased significantly with aging.[7] Initial echocardiographic studies that calculated LV mass by wall thickness measurements corroborated these findings. However, measurements made from autopsies on subjects free from hypertension and CAD then corrected for body surface area, suggested that there is no actually no change in the cardiac mass of men with aging.[8]
Similarly, autopsies of hospitalized patients free of CVD did not show an increase in cardiac mass with aging. In fact, they found a decrease in the cardiac mass of men and no change in cardiac mass for women. This finding has received support from an MRI-based study of healthy participants in the BLSA [9] as well as multiple echocardiographic studies [10, 11] Based on these and other studies, it now appears that there is no change in LV mass in women and an actual decrease in LV mass in men with aging. It appears that the increased wall thickness represents an asymmetric increase in the interventricular septum more than the free wall redistributing cardiac muscle but not increasing total cardiac mass.
With above background it is important for researchers to understand the anatomical and physiologic changes that occur with aging if new approaches to disease identification and treatment and health maintenance are to be devised that not only increase longevity but also improve the quality of life at advanced ages. While knowledge gained from autopsy-based studies has formed an indispensible

foundation for our understanding of the aging process, there has been an inherent difficulty in separating the effect of aging per se from those of the co-morbid illnesses that caused a subject's death. Keeping aim to explore the structural and functional adaptations in the cardiovascular system due to aging and its implications for health and disease this study was planned with following research questions.

1. What are the key structural adaptations in aging cardiovascular system?
2. Can functional changes be predicted by structural modifications?

MATERIALS AND METHODS

This cross sectional observational study was conducted from May 2021 to Jan 2024 in tertiary care hospital, Agra. During this study period, total 20 subjects cadavers specimens were considered and embalmed to preserve tissue integrity. The record of medical history, age, and cause of death were collected from the available records in the department.

Dissection and Examination- Dissection was done for exposing heart, great vessels, and peripheral arteries and documented all findings of structural changes (e.g., atherosclerosis, calcification observed.

Measurement of vessel diameters and wall thickness was done and changes in heart chamber size, valve morphology were recorded.

For Structural Analysis histology section were prepared and examined microscopically (e.g., H&E staining). Immunohistochemistry was done for Detection of specific proteins (e.g., collagen, elastin).

For Functional Analysis- Pressure myography was conducted to measure vascular stiffness and for assessment of blood flow and velocity.

For Aging related parameters also considered following;

1. Atherosclerosis: Plaque formation, vessel narrowing.
2. Arterial stiffness: Increased pulse wave velocity.
3. Cardiac hypertrophy: Increased heart weight, chamber size.

Data Analysis- All specimens data were collected and compared with the findings of standard age and gender and correlated with structural and functional measurements.

RESULTS:

The study included 20 subjects, comprising 11 (55%) male and 9 (45%) female. Among these, 14 (70%) were age more than 60 years with mean age 69.71+/- 7.769.

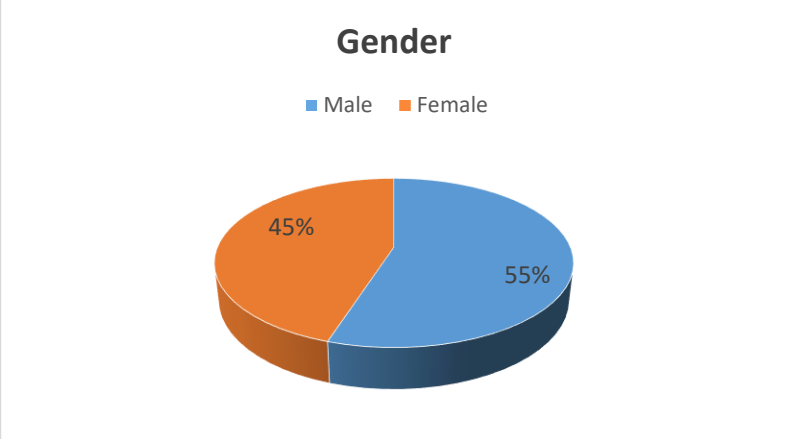

Figure 1 Gender wise distribution

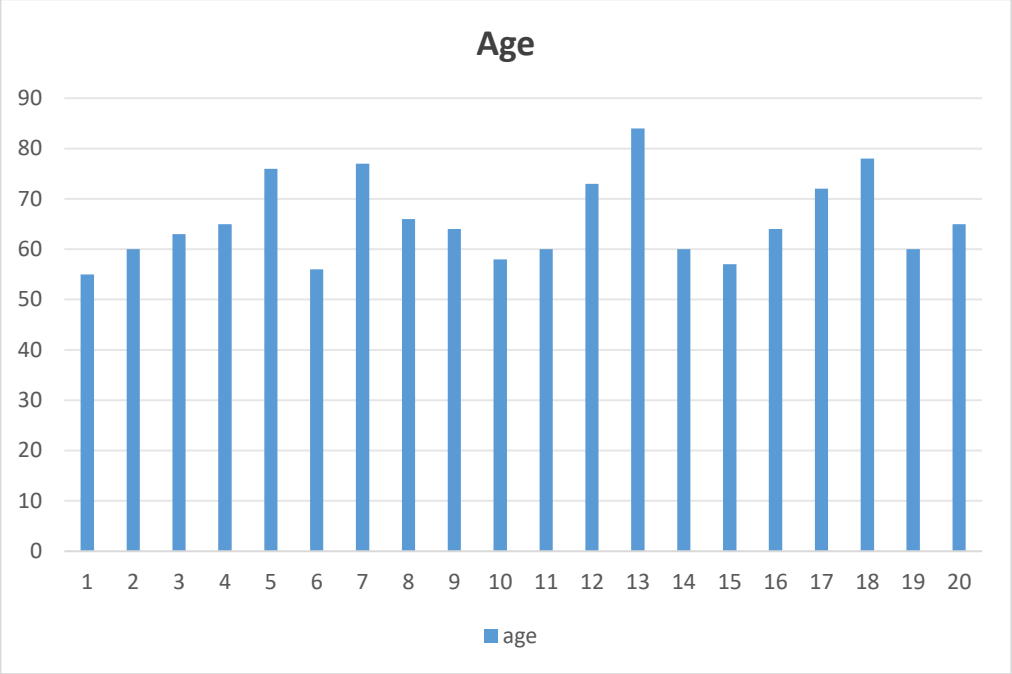

Figure 2- Age wise distribution

There was significant increase in myocardial thickness with spheroid shape among 16(80%) subjects and more common in male. There were significant differences observed when compared with standard age and gender. (p=0.001).

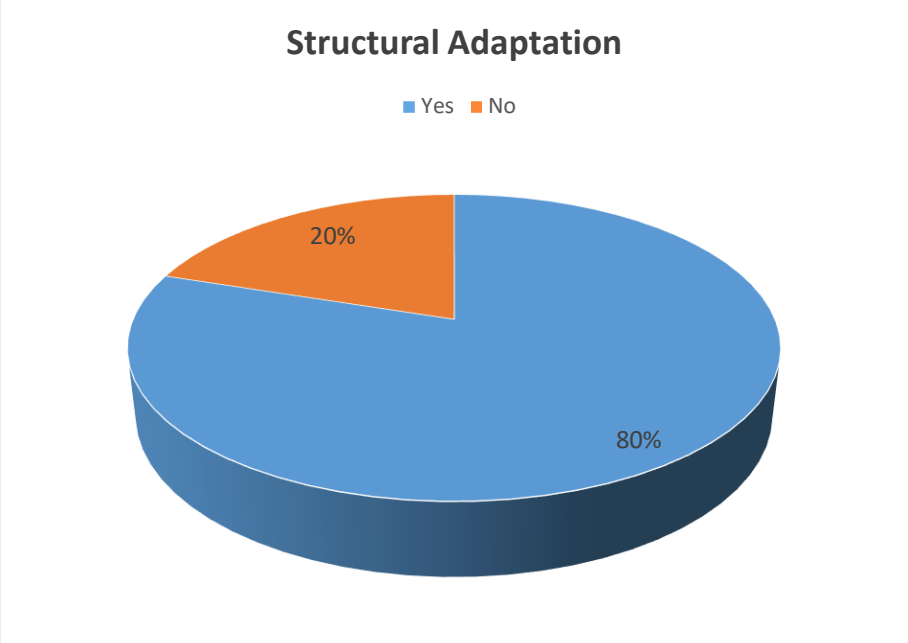

Figure 3- Distribution of Structural Adaptation

There was atherosclerosis and vascular stiffness was noted among 14(70%) subjects and more common in female. A significantly higher prevalence of vascular stiffness that indicated increased workload and decrease its reserve capacity. There were significant differences observed when compared with standard age and gender. (p=0.0001).

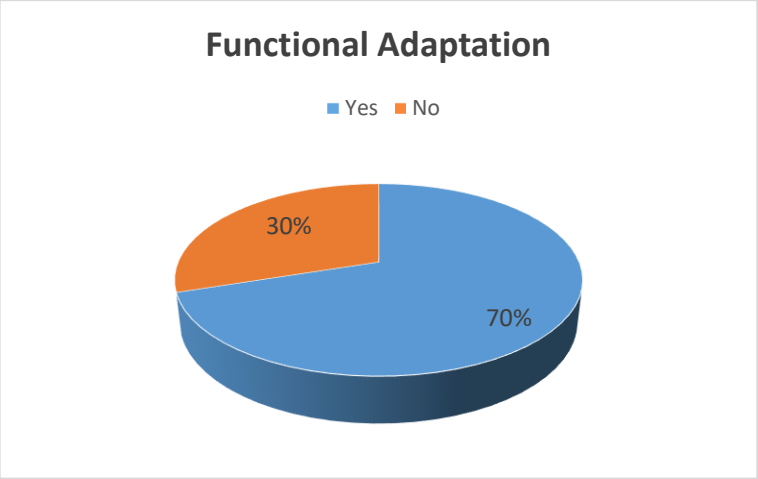

Figure 4- Distribution of Structural Adaptation

DISCUSSION

By 2030, approximately 20% of the population will be aged 65 or older. In this age group, cardiovascular diseases (CVD) will result in 40% of all deaths and rank as the leading cause. Furthermore, the cost to treat cardiovascular disease will triple in that time.[12] However, until recently, the fields of cardiovascular disease and molecular biology of aging have remained largely separate. Most rodent studies of atherosclerosis or cardiomyopathies were performed in young mice, whereas studies of genetic and pharmacological interventions that extend lifespan rarely assessed whether CVD or heart function are improved.

Age dominates risk factors for cardiovascular disease (CVD) [13] Although an enormous success from an individual perspective, the resultant demographic shift presents one of the greatest challenges for the social and health care systems worldwide. [14] Indeed,by 2020, the number of people 60 years of age and older will sur pass the number of children below 5 years of age. The pace of population aging around the world is increasing dramatically, particularly in low- and middle-income countries (e.g., Chile, China, Iran, and Russia).

More than 2 decades of dedicated research have firmly established the concept that increased oxidative stress and inflammation promote CV aging. However, generalized antioxidant supplementation, including vitamin E and b-carotene, failed to reduce CV events in asymptomatic individuals, as well as in patients at high CV risk. [15, 16]

Measuring the Impact of Aging on the Heart and Vasculature Aging is associated with a progressive decline in numerous physiological processes, leading to an increased risk of health complications and disease. By delivering oxygenated blood to all tissues in the body, the health of the cardiovascular system is vital for health of every tissue and longevity of the organism as a whole. Aging has a remarkable effect on the heart and arterial system, leading to an increase in CVD including atherosclerosis, hypertension, myocardial infarction, and stroke.[17] Aging cardiovascular tissues are exemplified by pathological alterations including hypertrophy, altered left ventricular (LV) diastolic function, and diminished LV systolic reverse capacity, increased arterial stiffness, and impaired endothelial function [18,19] [figure 5]

Vascular dysfunction associated with aging leads to a variety of age-related pathologies, including loss of adequate tissue perfusion (resulting in ischemia), insufficient vascular growth or regression (resulting in hypertension), or excessive growth and remodeling (resulting in age-related macular degeneration). The vasculature undergoes structure and function alter ations with age that are well documented, such as luminal enlargement with wall thickening and a decline in endothelial cell function negatively affecting endothelium-dependent di lation and promoting vascular stiffness. [20]

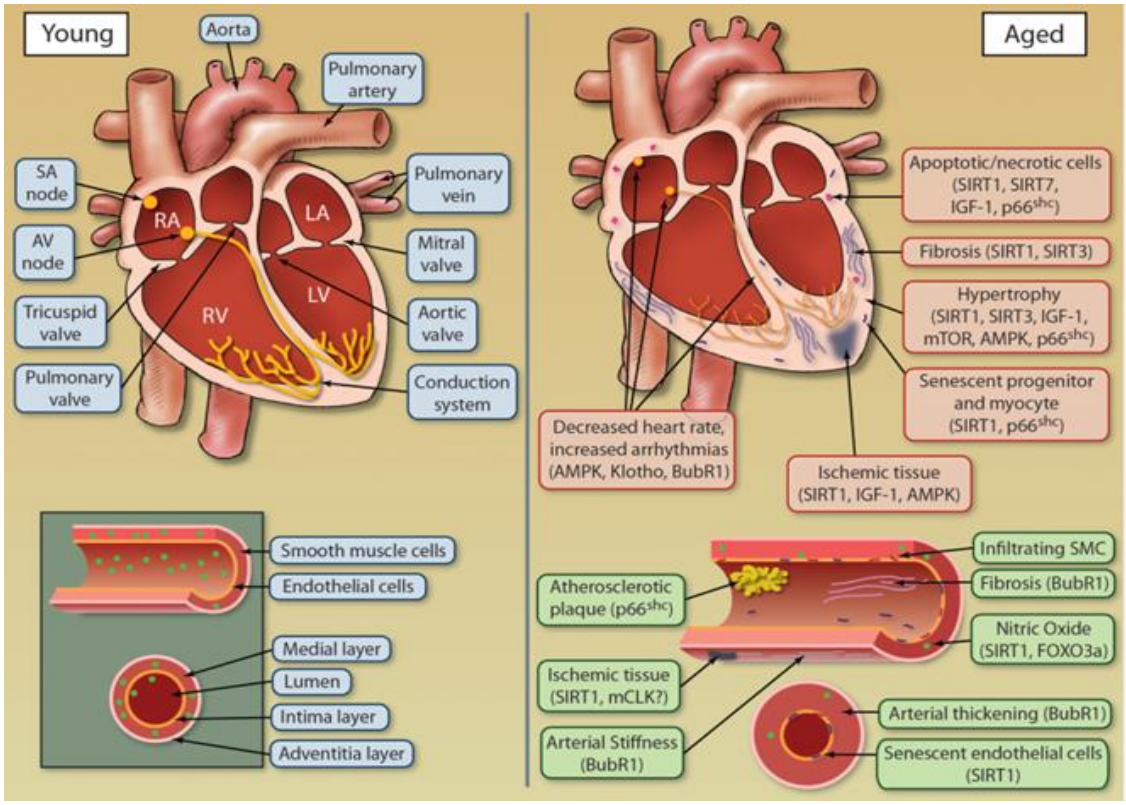

Figure 5. Age-dependent changes in cardiovascular tissues[18,19]

The most observed structural cardiac modification accompanying aging mainly affects the left ventricle (LV) wall. [21] Even without hypertension or another cause of augmented cardiac afterload, during the aging process is observed a moderate increase of the LV wall. [22, 23] that leads to concentric hypertrophy (defined by the rise of the LV wall with a reduction of the chamber size)
The aging process can also affect the intraventricular septum size, a cause of LV outflow obstruction resulting in further augmented LV afterload. Blood pressure has been described to increase with age, contributing to LV hypertrophy. However, neurohormonal and other molecular factors cannot be discarded in the genesis of LV hypertrophy. Indeed, women experience a greater age-related concentric hypertrophy and a fast increase of LV thickness than men [25] It is often helpful to investigate whether any reversible precipitants are present in older individuals who present with new-onset or worsening heart failure symptoms, including anemia, infection, thyroid disease, atrial fibrillation and dietary or medication non compliance. Investigation for common co-morbidities is also useful as they are frequent and associated with increased hospitalizations and adverse clinical outcomes. [24] Findings of this study in implication of above indicated that aging has impact on structural and functional changes in the cardiovascular system and impact their health and role in various diseases, Although study has some limitations as below
1. Small sample size and selection bias.
2. Confounding variables like hypertension, diabetes, co-morbid conditions
3. Interobserver variability

CONCLUSION

Aging induces significant structural and functional changes in the cardiovascular system, increasing the risk of cardiovascular disease. While these changes are inevitable, lifestyle modifications and medical interventions can mitigate their impact, promoting cardiovascular health into old age.
It is hoped that improved understanding of the aged heart will enable the development of therapies which prevent the genesis of HF or at a minimum help clinicians to treat the unique properties of the failing, senescent heart.

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