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AN OBSERVATIONAL STUDY OF CARDIAC ATRIOVENTRICULAR VALVE CHANGES IN THE SENILE CADAVERIC HEARTS

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ABSTRACT

A layer of endothelial cells surrounds the highly organised extracellular matrix (ECM) and valve interstitial cells (VIC) that make up adult heart valves. The ECM of the valves is stratified into elastin, proteoglycan-, and collagen-rich layers that provide the leaflets and supporting structures unique biomechanical capabilities. They are each uniquely created to guarantee optimum performance in relation to their function during the cardiac cycle. In this article, we outline the key structural characteristics that, in our opinion, are crucial for comprehending heart valve function. These characteristics will also have a significant impact on how heart valve disease is treated. They may help to advance reconstructive methods while also expanding their expertise of the design of partial or alternative valves. Understanding the macro- and microstructure of the heart valve may also be useful for heart valve engineering procedures.

Keywords: Tricuspid valve, Mitral valve, Cardiovascular diseases

INTRODUCTION:

In the cardiovascular system, the heart, blood vessels, and cardiac valves can change with advancing age. Cardiovascular diseases are associated with dysfunction in the heart and vessels. These diseases are a major cause of death worldwide in the majority of populations. Heart valve disease is related to a high rate of mortality that can be affected by the structural or functional abnormality of the valve. Some pathological diseases of

the valves often induce changes in the heart and blood vessels that can lead to heart failure. Heart valve diseases can occur in all age groups especially in older age, the incidence of disease increasing progressively after 65 years. This indicates that heart valve disease has a high prevalence and is life threatening. Therefore, to better understand the pathological process of the valves, a detailed knowledge of how the structures change with age in comparison to the normal condition is needed to inform intervention **[1]**.

During the cardiac cycle, the purpose of the heart valves is to provide coordinated forward blood flow. valves are dynamic cell populations inside highly organised connective tissue structures. As a result of the creation of the endocardial cushion and significant remodelling of the extracellular matrix (ECM), valvulogenesis happens following the earliest phases of cardiogenesis. The biomechanical characteristics of the mature valve are supported by the stratified elastin, collagen, and proteoglycan distribution that is localised within the valve ECM. Stenosis or regurgitation of the valves is a serious public health issue. There are several forms of valve diseases and malformations, each of which is characterised by dysregulation of the ECM, cellular disarray, and frequently calcification. Each of the four heart valves is susceptible to damage **[2]**.

In this review, we present basic aspects of anatomy and structure of the normal and any abnormal valve and we focus on valve microstructure as a possible contributor to disease progression and future therapeutic target.

MATERIALS AND METHODS:

Ten human hearts were extracted from donor cadavers at the JSS Medical College in Mysuru's Department of Anatomy. Age of the donated cadavers was around 80 years. The Research Ethics Committee, JSS Medical College, authorised research involving human cadaver tissues. All pericardium extracts were extracted from the hearts after they had been removed from the cadavers, and we next dissected out every type of heart valve. The interchordal space at the free edge of the valve attachment was used to choose the tricuspid and mitral valve leaflets. Each valve leaflet was sliced in a radial path from the centre, perpendicular to the leaflet attachment base. Sectional width was 2 mm. We used Verhoff's staining and the Masson's Trichome dye to look at the valves' histological elements. Collagen fibres were stained using Masson's Trichome dye, and elastic fibres were stained using Verhoff's stain. The valves' further alterations were observed.

Photographs:

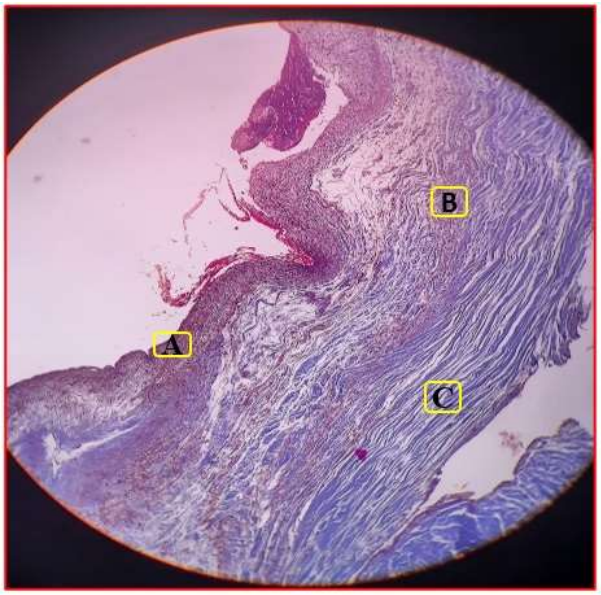

Photo: 1 Masson's trichrome stain: layers of atrioventricular valve leaflet, A- Internal layer, B- Middle layer, C- External layer

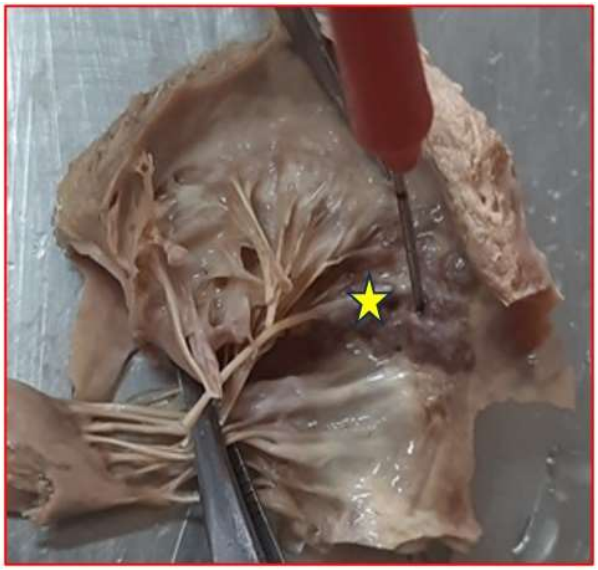

Photo: 2 Ventricular surface of mitral valve: star showing calcification mass embedding the chordae tendineae insertion

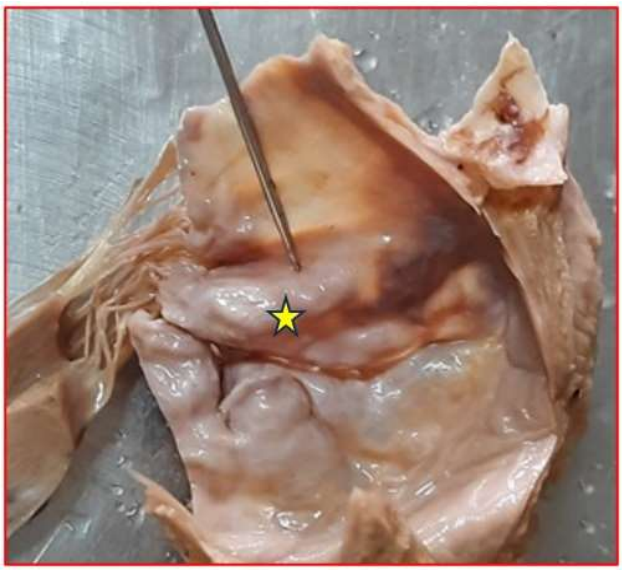

Photo:3 Star indicating leaflet bulging on the ventricular surface of tricuspid valve

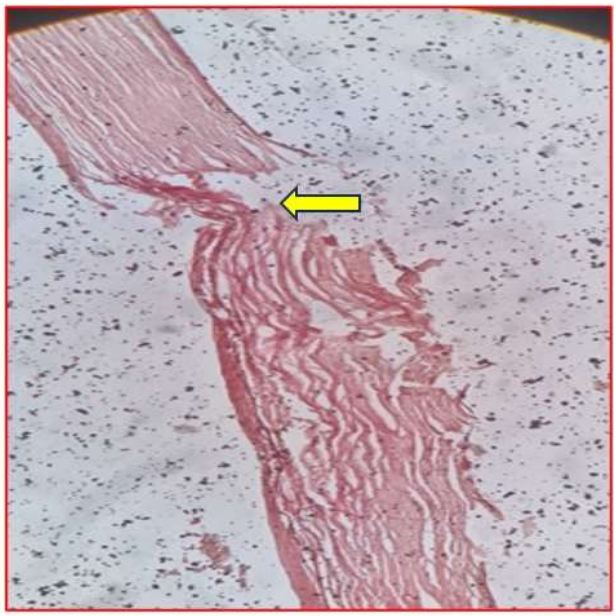

Photo:4 Verhoef's stain: Disrupted wall

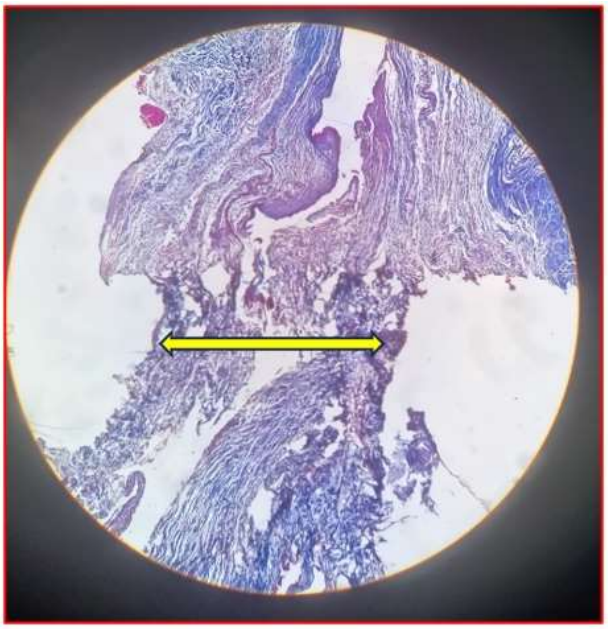

Photo:5 Masson's trichrome stain: Disrupted Ulcer

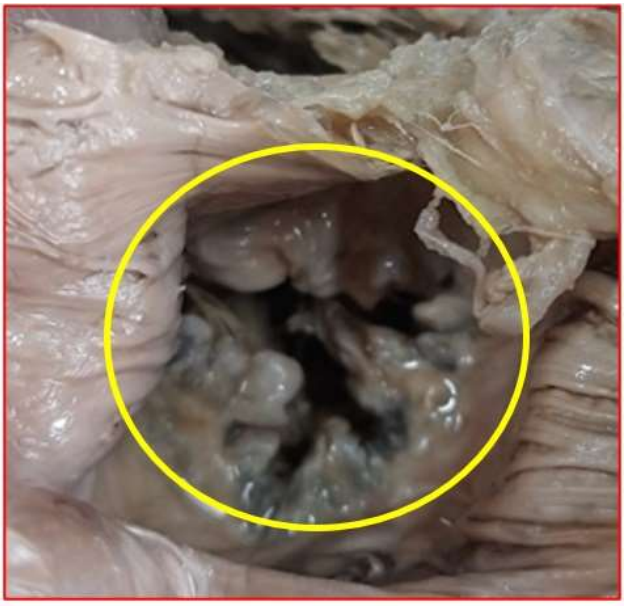

Photo:6 Tricuspid valve: showing retracted serrated margins of leaflets giving " Fish Mouth" Appearance"

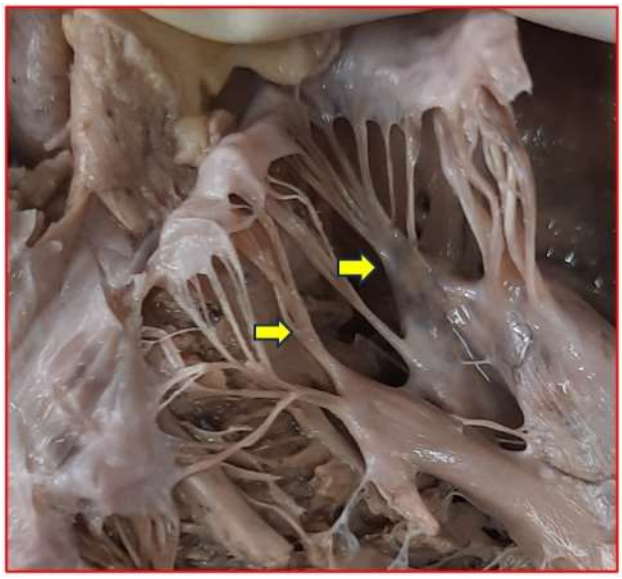

Photo: 7 Tricuspid Valve: arrows showing chordae tendineae thickening

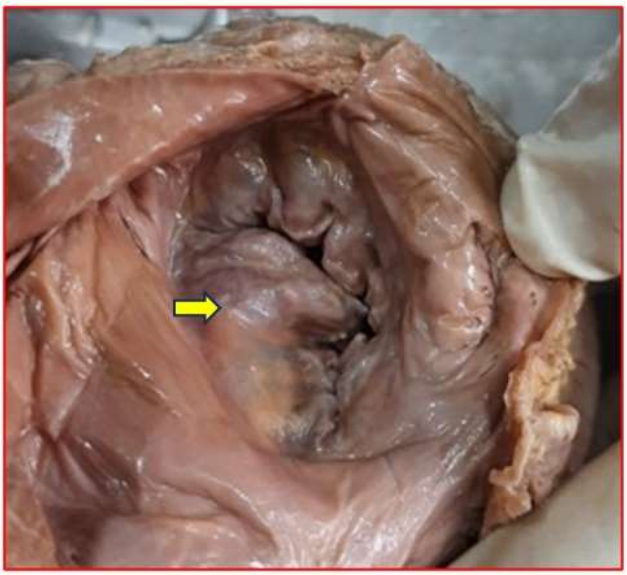

Photo:8 Tricuspid valve: star showing prolapse of leaflet surface raising above the margin of fibrous rim

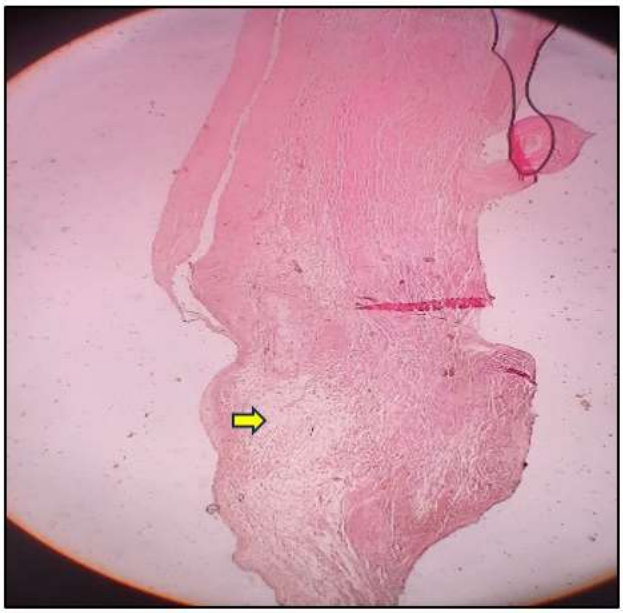

Photo: 9 Verhoef's stain
Showing atheromatous plaques

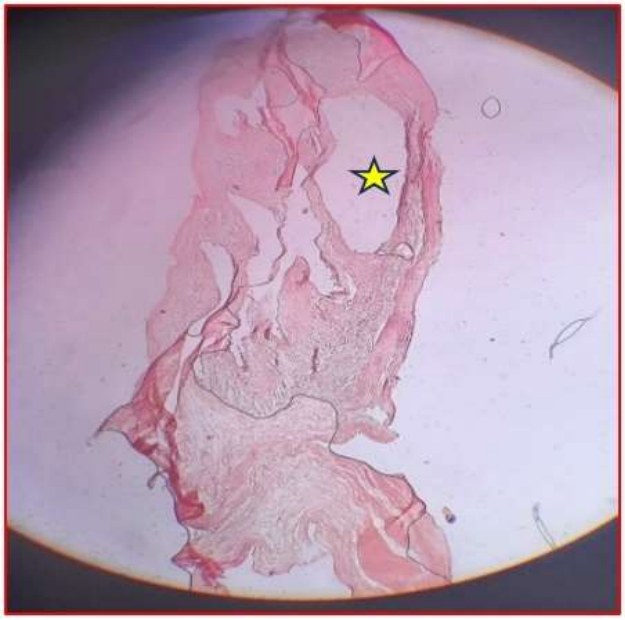

Photo: 10 Verhoef's stain: Cystic degeneration

RESULTS:

Specimen no	Discription
H1	Smooth internal layer, with collagen and elastic fibres ++ on both sides, middle layer is thick and external layer is thin
H2	Disrupted ulcer seen in internal layer, thick prominent blood vessel with thrombi seen in middle layer and smooth external layer with collagen fibres ++ in right side and + on left side and elastic fibres+ on both sides
H3	Smooth internal layer, thick disrupted collagen bundles in middle layer and smooth internal layer with ++ collagen fibres on both sides and ++ elastic fibres on both sides
H4	Disrupted vegetations seen in internal layer, normal middle layer and smooth external layer with ++ collagen fibres on both sides and ++ elastic fibres on right side and + on left side
H5	All the three layers are normal with + collagen fibres on both sides and + elastic fibres on both sides
H6	Normal internal and external layer and thickened collagen bundles in middle layer with + collagen fibres on both sides and + elastic fibres on both sides
H7	Normal internal and external layer and cystic degeneration rupture seen in middle layer with + collagen fibres on both side and + elastic fibre on both side
H8	Atheromatous plaque seen in internal layer and normal middle and external layer with ++ collagen fibres on right side and + on left side, ++ elastic fibres on right side and + on left side (with disruption)
H9	++ collagen fibres on right side and + on left side, + elastic fibres on both sides, disruption in all three layers seen on right side and normal on left side
H10	Collagen + on right side and ++ on left side, elastic fibres + on both sides with disruption on left side, and normal internal and external layer with thickened and disrupted middle layer

DISCUSSION

Cardiac valve biology and pathology are important from the view of preclinical and clinical standpoint. Heart valve diseases mark the common cause to a large extent for morbidity and mortality worldwide. There is a large spectrum of cardiac valvular diseases which may affect the structure and functional dynamics of the heart valve complex at variable points in time in an individual's life span. Abnormality in the cardiac valve could be due to factors like congenital defects, aging, infections, systemic diseases, autoimmune diseases, inherited genetic diseases **[3]**, etc. Donnelly KB Increasing cardiovascular diseases are adding to the long list that poses a considerable risk leading to death among the geriatric population. The atrioventricular valve and semilunar valvular apparatus play an important role in the cardiac cycle, which are positioned in the plane of the base of the heart. The existing literature reiterates relatively less attention towards the histomorphology (**Photo:1**) of the mitral and tricuspid valves in the advanced age, often gross or microscopic adverse changes in the cardiac valvular complex are seen as benign transformations which may remain uneventful for a considerable duration of life-span **[4]**. Misfeld M, Sievers HH In the present study, the gross observations made on the existing bicuspid and tricuspid valvular complexes on each side have shown a considerable change in their outlook when compared between other cadavers in the cohort. They were showing shrinkage-like changes in the leaflets. Atypical blackish-brown nodular changes with rough consistency were appreciated in the inferior

surface (ventricular surface) of leaflets which are likely suggestive of calcification changes as reported in other studies **[5]**. Rosa H. A. M. Henriques (**Photo**:2)

The atrial surface of the valve leaflet showed an unusual pattern of unevenness' with wall ballooning intermittently throughout the surface along with retraction of leaflet wedges were seen. (**Photo:3**). These findings were found consistent with previous reports. Such redundant disintegrated changes may indicate a myxomatous condition due to noninflammatory reactions affecting the structural integrity in leaflet connective tissues, probably attributing to advanced aging. (**Photo:4 and 5**) Because most of the donated cadavers are eighty and above years of age. Studies underscore the occurrences of myxomatous valvular changes more frequently with the tricuspid valve than with the mitral valve **[6]**. Lazar Neto F. These noted changes in the valves may likely cause failure in an apt approximation of leaflets leading to improper closure, hence showing a large gap. The AV leaflets are showing a typical "Fish Mouth" appearance showing the non-coaptation, and commissural fusion when viewed from the atrial side. (**Photo:6**) Probably this appearance could be due to was shortening and thickening in the chordae tendineae **(Photo:7)**. These changes are suggestive of the consequence of infectious diseases like rheumatic heart disease-induced changes We have noticed a rise in the leaflet atrial wall protrusion 2mm above the margin of the annular ring, which is considered as valve prolapse (**Photo: 8**). Despite the sporadicity in the event of mitral valve prolapse variety of congenital systemic diseases like Marfan's syndrome, osteogenesis imperfecta, etc. showing disarray in the morphology of cardiac valves **[7]**. Dietz, H.C.

Meta-analysis of valve prolapse (MVP) cases are showing a consistent match with fatal consequences associated with the incidence of sudden cardiac death (SCD). Such correlation may be strongly suggestive of age-related cardiac valve changes pushing towards fatal consequences resulting in death, particularly in the elderly population. We have noticed such prolapse in 2 cadaveric valve leaflets with bulging upwards facing the atrial chamber **[8]**. Nalliah CJ.

Cardiovascular ailments involving the heart valvular complex tend to show a progressive risk of malfunctioning as age advances[9]. Schoen FJ. Anatomical knowledge of different parts of the heart valvular complex and its age-related changes are having great clinical importance. The study involving various age groups of cadavers ascertained possible change in the histomorphological pattern of valve apparatus. Where collagen and elastic fibers were seen in abundance,

the elastic fibre fragmentation was found more strikingly in the cadavers aged below fifty years. Some research findings showing inconsistent adverse histomorphological patterns in different age groups are elusive. Extracellular matrix components of the valvular complex are one of the important factors associated with the functional integrity of the whole heart valve system. Mucopolysaccharides are found in the spongiosa of the tricuspid atrioventricular valve; the former is a content seen in the connective tissues. Its adverse changes are exhibited by decreased integrity and calcification changes. In contrast, a relatively thin spongiosa component was seen with elastic fibre fragmentation among the cadavers belong to sixth- and seventh-decade age groups. In a similar age-match cadaveric groups, mitral valve complex elastic fibre fragmentation was seen predominantly in the atrial layer of its valve leaflet. A vague permutation and combination in the consistency of connective tissues are suggestive of progressive changes in the quality and quantity of ECM, collagen, and elastic fibers in various layers of valve leaflets belonging to 20 to 90 years aged cadaver groups. A similar pattern of disruption of connective tissue fibers has much resemblance with our study **[1]**. Gumpangseth, T. The endothelial lining of cardiac valves is having continuity with the endocardium. The subtle microanalysis of the leaflet proper shows the quantitate variation in the density of collagen fibers in the AV showing a large quantity of type I, a moderate quantity of type III, and a very small quantity of type V collagen fibers. Though the present study is having limitations in identifying a particular type of collagen fibers, our microscopic findings are showing consistency with respect to the existence of collagen fibers in the section **[10]**. McCarthy, K. P There are microscopic findings showing the atheromatous plaques formation and cystic degenerative signs. (**Photo:9 and Photo:10**) Because of streptococcal bacterial infection during early childhood, it is likely targeting the mitral (bicuspid) cardiac valves referred to as rheumatic heart valve diseases (RHVD). Such diseased valve leaflets were showing gross leaflet retraction, microscopic view is showing focal fibrotic changes **[11]**. A Passos, L. S., P. Nunes, Cardiac valve dysfunction affects hemodynamic function, which is indicated through the symptoms of regurgitation due to overlapping and non-synchronizing events of the cardiac cycle. As a result of its long-term consequence, it might result in ventricular hypertrophy which is followed by hypertension, ischemic heart disease, pulmonary oedema, etc. Out of 10 dissected hearts 2 of them have shown striking signs of “surface ballooning” indicating the “Floppy Valve Syndrome” which could be

due to adverse and progressive microarchitectural changes. In the absentia of long-term illness history of donated cadavers to the department of anatomy, the probability of cause of "Natural Death" prominently due to the above-mentioned factors involving the atrioventricular valves cannot be ruled out **[12, 13]**. (Cannistra 2005, Schoen 2001)

Heart being a highly modified form of a blood vessel, its valves are likely showing many adverse histomorphological changes aligning with age. Probably abnormal atherosclerotic changes seen in atrioventricular leaflets are showing many similarities with the coronary artery disease seen in the old age cohort **[14]**. Xu, X., Wang, B., Ren.

CONCLUSION

Comprehensive knowledge about the histomorphology of all types of cardiac valves is essential; having vast implications from the point of inferring the subtle pathophysiological changes resulting in explicit manifestation of adverse clinical events. Consistency in our gross and microscopic findings are suggestive of proneness of cardiac valve involvement with advanced aging process. Therapeutic procedures involving heart valve prosthesis, or valve repair solely depend on apt anatomical knowledge of cardiac valves from the point of extent of damage causing malfunctioning heart valvular complex. Hence anatomical knowledge is vital from the point of surgical practice which is focusing on reconstructive technics to make appropriate geometrical designs to develop functionally competitive artificial valve substitutes. These gross and microscopic findings provide knowledge in age-related morphological changes of the heart valves and will increase understanding concerned to valvular heart diseases and treatment options

REFERENCES

[1] Gumpangseth, T., Lekawanvijit, S., & Mahakkanukrauh, P. Histological assessment of the human heart valves and its relationship with age. *Anatomy & Cell Biology*, 2020:*53*(3), 261-271.

[2] Robert B. Hinton and Katherine E. Yutzey*, Heart Valve Structure and Function in Development and Disease.

[3] Donnelly KB. Cardiac valvular pathology: comparative pathology and animal models of acquired cardiac valvular diseases. Toxicol Pathol. 2008; 36(2): 204-17.

[4] Misfeld M, Sievers HH. Heart valve macro- and microstructure. Philos Trans R Soc Lond B Biol Sci. 2007 Aug 29;362(1484): 1421-36.

[5] Rosa H. A. M. Henriques de Gouveia & Francisco M. A. Corte Real Gonçalves Sudden cardiac death and

valvular pathology, Forensic Sciences Research, 2019:4:3, 280-286, DOI: 10.1080/20961790.2019.1595351

[6] Lazar Neto F, Marques LC, Aiello VD. Myxomatous degeneration of the mitral valve. Autops Case Rep [Internet]. 2018;8(4): e2018058. https://doi.org/10.4322/acr.2018.058

[7] Dietz, H.C., *et al*. Marfan syndrome caused by a recurrent de novo missense mutation in the fibrillin gene. Nature. 1991: 352:337–339.

[8] Nalliah CJ, Mahajan R, Elliott AD*, et al* Mitral valve prolapse and sudden cardiac death: a systematic review and meta-analysis *Heart* 2019;**105:**144-151.

[9] Schoen FJ. Morphology, clinicopathologic correlations, and mechanisms in heart valve health and disease. Cardiovasc Eng Technol 2018; 9:126-40.

[10] McCarthy, K. P., Ring, L., & Rana, B. S. Anatomy of the mitral valve: Unders.tanding the mitral valve complex in mitral regurgitation. *European Journal of Echocardiography*, 2010;*11*(10), i3-i9.

[11] A. Passos, L. S., P. Nunes, M. C., & Aikawa, E. (2020). Rheumatic Heart Valve Disease Pathophysiology and Underlying Mechanisms. *Frontiers in Cardiovascular Medicine*, *7*. https://doi.org/10.3389/fcvm.2020.612716

[12] Cannistra, A. J. (2005). Adult valvular heart disease: A practical approach. Prim Care 2005: 32, 1109–14.

[13] Schoen, F. J., and Edwards, W.D. (2001). Valvular Heart Disease: General Principles and Stenosis. In Cardiovascular Pathology (M. D. Sliver, A. I. Gotlieb, and F. J. Schoen, ed.). Philadelphia: Churchill Livingstone, pp. 402–42.

[14] Xu, X., Wang, B., Ren, C., Hu, J., Greenberg, D. A., Chen, T., Xie, L., & Jin, K. (2017). Age-related Impairment of Vascular Structure and Functions. *Aging and Disease*, 2017;*8*(5), 590-610.