THE STUDY OF AGE RELATED CHANGES IN CORONARY ARTERIES AND ITS RELEVANCE TO THE ATHEROSCLEROSIS.

Rashmi Deopujari, Asha Dixit*

Assistant Professor, Peoples College of medical sciences and research centre, Bhopal.
*Professor and head, Gandhi Medical College, Bhopal.

ABSTRACT

The study of coronary artery disease has always been a topic of special interest to the physicians. Several studies have been focused on coronary arteries but limited have been addressed to the histological changes in coronary arteries with increase in age leading to the development of atherosclerosis. The histomorphometric study was carried on coronaries of autopsied heart specimens from 50 males and 30 females between the age group of 10-60 years. The thickness of tunica intima, tunica media and tunica adventia and diameter of coronary arteries were measured using ocular micrometer.

Verhoeffs stained sections were used to study changes in internal elastic lamina. With increase in age there was increase in thickness of tunica intima up to 4th decade through the growth of sub endothelial tissue from the undifferentiated smooth muscle cells of the media. The thickness of tunica media was observed to increase up to 4th decade due to medial fibrosis. After 4th decade thickness of both tunica intima and tunica media registered a gradual fall. The increase in tunica intima was found to be the basic pathological change which ultimately progress to atherosclerosis. Intimal thickness was found to be more in males as compared to females. Internal elastic lamina showed splitting, fraying, fragmentation and reduplication in various age groups.

Key words: Coronary arteries, Atherosclerosis, Tunica intima, Tunica media, Internal elastic lamina, Coronary artery disease.

INTRODUCTION

Cardiovascular system is the first major system to function in embryo (3-4 week). Since inception, the arteries undergo a continuous change. The final differentiation of the structure of the vessel wall cannot be sharply demarcated from regressive changes. The changes that develop with aging lead to atherosclerosis[1]. There is a long period of silent, slowly progressive coronary atherosclerosis before coronary artery disease (CAD) manifests. With this idea, the present study was designed to study histomorphometeric changes in different age groups leading to atherosclerosis.

MATERIAL & METHOD

The present study was conducted on 80 human hearts including 50 males and 30 females, obtained from medico legal autopsies done within 6 hours of death. The study was carried out in the department of Anatomy, Gandhi medical college, Bhopal. Hearts showing no obvious pathological changes of atherosclerosis and without any apparent lesion in the segment of vessel were selected from the age group 10 - 60 years in males and 20 - 40 years in females. Study material was divided into five age groups with a range of ten years.

Tissue samples were obtained from both right & left coronaries up to 2cm away from the coronary ostium. These tissue samples were processed for paraffin embedding & 8-10 micron thick sections were obtained. These slides were stained with H&E stain and Verhoeff's haematoxylin elastic tissue stain.

Thickness of tunica intima (TI), tunica media (TM), and tunica adventitia (TA) were measured with the help of ocular micrometer in all the samples[2]. Mean thickness of TI, TM, TA and total arterial thickness and diameter were calculated in various age groups. Sections were stained with Verhoeff's stain to delineate internal elastic lamina (IEL) & elastic tissue.

OBSERVATIONS

Total thickness, Thickness of TI, TM, TA and diameter were measured (Table no. 1).

It was observed that the thickness of TI was increased up to the age group of 41-50 years and falls thereafter

Correspondence
DR. RASHMI DEOPUJARI
Asst. Prof.
Peoples College of Medical Sciences & Research Center, Bhopal - 462037
Tel : 9826027433, 0755 - 4005113
Email : rashmideopujari@rediffmail.com

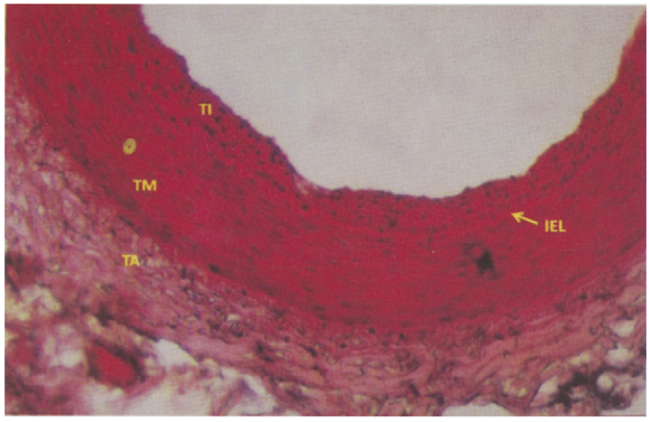

Figure 1: Photomicrograph of human coronary artery from 21-30 years age group showing all the three layers of arterial wall. (H&E×10)
TI- Tunica Intima; TM - Tunica Media; TA: Tunica Adventitia; IEL - Internal Elastic Lamina

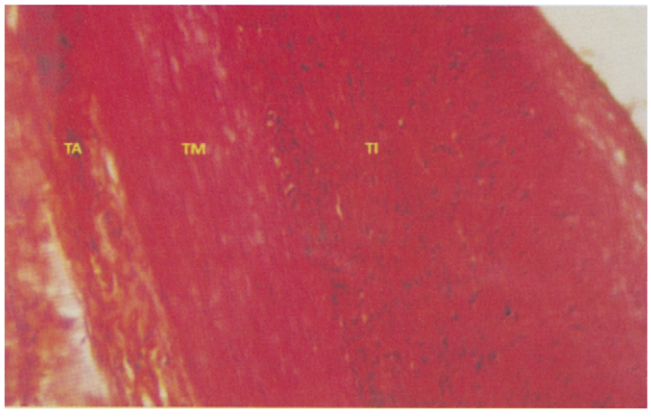

Figure 2: Photomicrograph of human coronary artery from 41-50 years age group showing increased thickness of TI. (H&E×10)
TI- Tunica Intima; TM Tunica Media; TA: Tunica Adventitia.

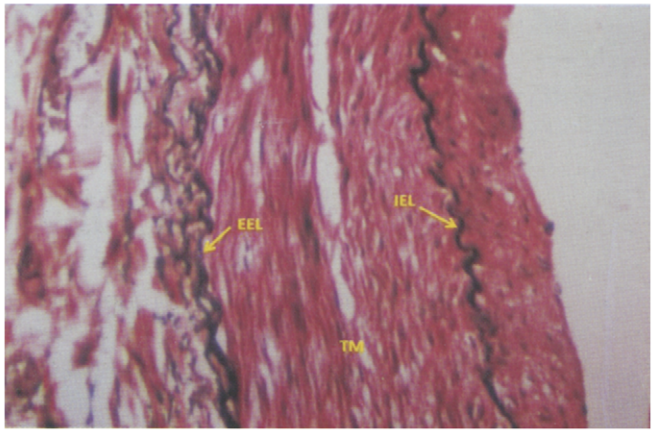

Figure 3: Photomicrograph of human coronary artery from 21-30 years age group showing increased thickness of tunica media. (Verhoeff's stain×10)
TI- Tunica Intima; TM Tunica Media; TA: Tunica Adventitia.

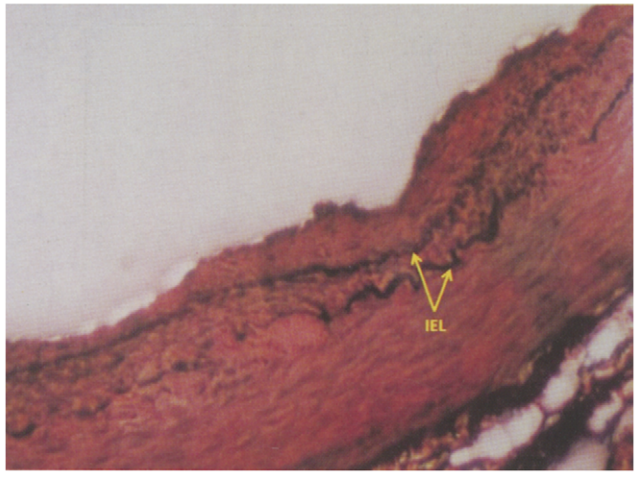

Figure 4: Photomicrograph of human coronary artery showing reduplication of IEL. (Verhoeff's stain×10)
IEL Internal Elastic Lamina.

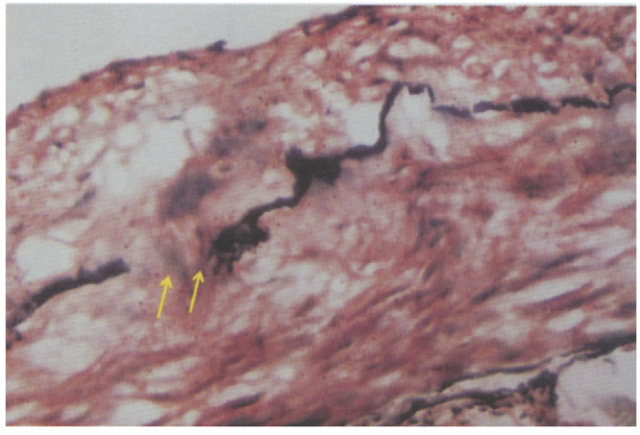

Figure 5: Photomicrograph of human coronary artery showing fraying of IEL (Arrows) (Verhoeff's stain×10)

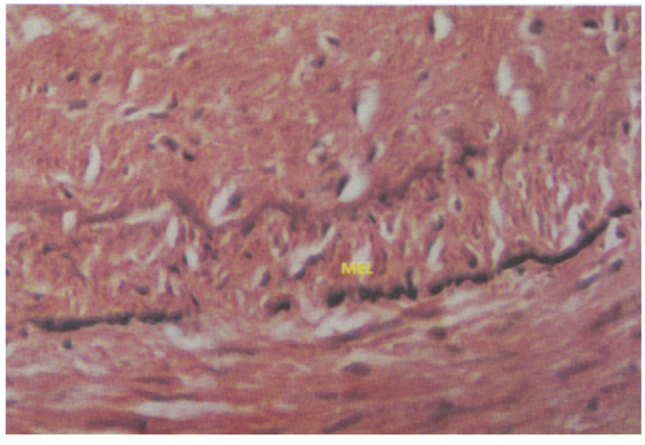

Figure 6: Photomicrograph of human coronary artery showing musculoelastic layer. (Verhoeff's stain×10)
MEL Musculoelastic layer.

Age in years	TI		TM		TA		Total thickness		Diameter	
	M	F	M	F	M	F	M	F	M	F
10-20	0.45	--	0.47	--	1.18	--	2.05	--	08.20	--
21-30	1.00	0.42	0.74	0.53	0.68	1.87	2.79	2.83	11.16	09.94
31-40	1.47	1.16	0.91	0.81	2.10	1.25	2.97	3.06	12.72	11.40
41-50	1.77	--	1.17	--	1.10	--	4.03	--	15.00	--
51-60	1.60	--	0.92	--	1.00	--	3.50	--	16.12	--
Mean	1.25	0.79	0.84	0.67	1.01	1.56	3.06	2.94	12.64	10.67

Table I: Table showing mean values of thickness & diameter of coronary arteries in males (M) and females (F). [All measurements in micrometer (μm)]
TI- Tunica Intima; TM Tunica Media; TA: Tunica Adventitia

in males (figure 1 & 2). Similarly the thickness of TM was increased up to the 4th decade and decreases thereafter in males (figure 3). In TA no specific trend was observed but the thickness of adventitia was found to be much increased in the age group of 31 - 40 years.

In males the mean thickness of TI & TM was found to be more in age group from 21 40 years as compared to females.

The diameter was found to have direct correlation with the advancing age. The diameter of coronary arteries was more in males as compared to females.

Sections stained with Veroeff's stain were critically analyzed for the changes in internal elastic lamina (IEL). It showed that there was reduplication (figure 4), fraying (figure 5) and fragmentation of IEL in all the age groups. So these findings were inconclusive with respect to age. Also musculo-elastic layer was observed in certain cases of age group 31-40 years in males and females (figure 6). Elastic fibers were observed to be increased up to 4th decade and decrease thereafter.

DISCUSSION

Changes in coronaries are bound to occur with the advancing age. There is no sharp demarcation point between normal age changes in arteries & pathological atherosclerosis. It is difficult to distinguish between physiological and pathological process. There is no point at which artery can be said to have stopped growing or developing and started to degenerate or become diseased [3, 4, 5, 6]. Hence the knowledge of changes in arterial anatomy with age is vital for understanding of atherosclerosis.

In the present study, thickness of TI was observed to be gradually increased up to 4th decade & then there was a gradual fall. These findings were in conformity with the earlier observations made by Crawford[7] and Tyagi and Dadgar[8]. Elias reported that postnatal development of artery is accompanied by

remarkable increase in the thickness of TI through the growth of the sub endothelial element[9]. This hypothesis was supported by Crawford who reported that at birth endothelium lie almost directly on IEL and by childhood these layers become separated by sub endothelial tissue[7]. Ikari et al also reported that coronary arteries grow rapidly with age in perinatal and postnatal periods through intimal expansion[10].

Coronaries have a fixed starting point in aorta and subsequent to their subepicardial course, a point of fixation at which they penetrate the muscular wall. During the cardiac action these two points have a slightly varying distance as a result of which coronaries are alternately elongated and shortened. The subepicardial course of these arteries also lack outside myocardial support .These two factors with high lateral pressure to which the vascular wall is subjected increase the stress on the arterial wall. This increased lateral pressure and stress on coronaries give rise to intimal hyperplasia. This intimal thickening should be regarded as a normal phenomenon of adaptation [11, 12, 13]. But an abnormal increase in intimal thickness leads to atherosclerosis.

In the present study overall mean thickness of tunica intima and tunica media and diameter of coronary artery was found to be more in males as compared to females. The same was reported by Dhall et al [14]. Males have slower cardiac action and larger stroke volume. Therefore greater demands were made on coronaries in males than females. Thus intimal thickening was also more in case of males. This could be the reason behind the higher incidence of atherosclerosis in males than in females[11].

The tunica intima and greater part of the tunica media lack capillaries and receive nutrition by diffusion; hence oxygen and other nutrients including soluble blood lipids must diffuse from lumen through the intercellular substance of the intima and most of the media. With abnormal increase in intimal thickening this diffusion mechanism gets very much deranged resulting in insufficient oxygen tension in tissues of arterial wall. This puts metabolic stress on endothelium and induces endothelial dysfunction. The lipids fail to metabolize properly and will be taken by smooth muscle cells initiating the whole chain of events ultimately leading to atherosclerosis.[13].

In the present study thickness of TM was also seen to be increased up to 4th decade and then shows a decline. With the advancing age, there occurs medial fibrosis, characterized by increase in amount of collagen & ground substance in media of the artery. In earlier decades of life this increase in collagen was partly an addition to the bulk of the media but in later life it was partly at the expense of smooth muscle. Boucek et al also reported the atrophy of media after the age of 40 years [15].

In Verhoeff stained sections, elastic tissue in TM was seen as fine slightly wavy fibers or lamellae in younger subjects. In the present study these elastic fibers were seen to increase up to 4th decade and fall thereafter. Gross et al and M Mumtaz Uddin also recorded similar findings [16, 17]. The function of elastic fibers in the arterial wall is the maintenance of tension without constant expenditure of energy. According to Burton the arterial tension has a correlation to the amount of elastic tissue present in the vessel wall [18]). Since coronary arteries arise from the root of aorta, they are subjected to maximum pressure during each cardiac cycle and hence have abundant elastic fibers to maintain arterial tension. But after 40 years of age medial fibrosis causes a decrease in elastic fibers.

In present study the thickness of TA does not show any specific trend with the age and hence cannot be a marker for atherosclerosis.

In the present study various changes like reduplication, fraying or fragmentation and splitting of IEL were observed in all the age groups hence cannot be used as marker for atherosclerosis for specific age group. Similar observations were made by M-Mumtaz Uddin-Ahmed and Levene [17, 19]. These changes were attributed to the increase in strain or signify the wear and tear of the aging or a physiological remodeling of the arterial wall [20]. This finding does not show any specific trend related with the age group. Sims et al hypothesized that a substantial internal elastic membrane subjacent to the endothelial cells provides a secure attachment for the endothelial cells .It acts as a barrier to the entry of lipid macromolecules and cells to the intima. Hence its absence will be associated with progressive intimal thickening and atherosclerosis [21] .In present study IEL was observed to split in two layers enclosing the longitudinally arranged muscle fibers in the age group of 31-40 years. This layer was described as musculoelestic layer by Gross et al [16] but its role in atherosclerosis remains unclear.

CONCLUSION

Age is a non modifiable risk factor for atherosclerosis. Though the manifestations of atherosclerosis like, angina pectoris, myocardial infarction, chronic ischemic heart disease with

congestive heart failure and sudden cardiac death are seen in the later age groups, actual process for atherosclerosis begins much earlier during childhood. Major changes that occur with aging are intimal thickening and medial fibrosis. It is the intimal thickening that carries the seeds of modern epidemic, CAD. Atherosclerosis is pathological when its degree of development is beyond the norm for that age. TI & TM in this study was found to be increased up to the fourth decade and decrease thereafter. Therefore these findings can be used as baseline markers for risk assessment of atherosclerosis. This study can be used as reference to assess the effect of other risk factors like smoking, increased LDL etc.

REFERENCES

1. Bloom W, Fawcett D. A text book of histology. 9th edition. Philadelphia, London. W B Saunders and company. 1968; 372-373.
2. Singh DR. Principles and technique in histology, microscopy and photomicrography.1st edition. New Delhi and Bangalore. CBS publishers and distributors. 2003;152-156
3. Moschowitz WL.The coronary arteries of infants, American Journal of Medical Sciences .1947; 214: 623-9.
4. Wilens SL. The nature of diffuse intimal thickening of arteries. American Journal of Pathology .1951.27:825-840
5. Lober PH. Pathogenesis of coronary sclerosis, American Medical Association Archives of Pathology1953; 55: 357-383.
6. Kovanen, Petri T, Tabas, Ira. In search of a starting point .Current Opinion in Lipidology. 2001; 12(5). 475-476
7. Crawford T. Symmers systemic pathology chapter I and II A 2nd edition volume I. London .Churchill living stone 1976; 8:120-123
8. Tyagi SP, Dadgar SK. Histological changes in coronary arteries in relation to age .Indian Heart Journal .1978; 30(4):246-8.
9. Elias H. Histology and dynamics of capillaries and arteries. Dental Digest 1950; 56(10). 440-443.
10. Ikari Y, Bruce M. McManus; Kenyon J, Stephen M. Schwartz Neonatal Intima Formation in the Human Coronary Artery. Arteriosclerosis, Thrombosis, and Vascular Biology. 1999;19:2036-2040
11. Geringer E. Intimal vascularisation and atherosclerosis Journal of pathology and Bacteriology.1951; 63:201-211
12. Wolkoff K. ober die altersveranderungen den arterien bei Tieren. Archives of Pathological Anatomy. 1924; 252.208-228
13. Ham AW. Histology. The circulatory System; 7th edition; Philadelphia and Toronto. J B Lippin Cott Company; 1974: 561-565.
14. Dhall, U, Chaudhary S and Sirohiwal B. Histomorphometric Analysis Of Coronary Arteries : Sexual Dimorphism J Anat. Soc. India 52(2) 144-146 (2003)
15. Boucek RJ, Takeshita R, Brady AL H. Intimal hypertrophy in coronary arteries and consideration of the papillary muscle arteries (man). Anatomical record .1965; 153. 243-244.
16. Gross L, Epstein EZ, Kugel MA. Histology of coronary arteries and their branches in human hearts American Journal of pathology 1934; 10: 253-274.
17. M. Mumtaz Uddin Ahmed. Age and sex difference of tunica media of the coronary arteries in Chinese subjects. Acta anatomica.1969; 73: 431-441.
18. Burton A.C. Relation of structure to the function of the tissues of the wall of blood vessel. Physiology Rev.1954; 34:619-642.
19. Levene C I. The early lesion of atheroma in coronary arteries. Journal of Pathology and bacteriology.1956;72:79-83
20. Gillman T. Reduplication, remodeling, regeneration, repair and degeneration of arterial elastic membranes American Medical Association Archives of Pathology 1959; 67: 624-641.
21. Sims FH, Chen X , Gavin JB The importance of a substantial elastic lamina subjacent to the endothelium in limiting the progression of atherosclerotic changes Histopathology.2007 ;23(4)307-317