

An Autopsy Based Study of Coronary Atherosclerosis Using Modified American Heart Association Classification: Cross-Sectional Study in a Tertiary Care Hospital

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ABSTRACT

Background: Atherosclerosis is characterized by lipid rich intimal lesions which protrude into and obstruct vascular lumen, thus weaken the underlying media. Ischemic heart disease (IHD) following atherosclerosis is the most common cause of cardiac deaths and single largest non communicable disease accounting for nearly one-third of all deaths. This study was designed to assess age and sex related prevalence of coronary atherosclerosis by applying Modified American Heart Association classification in autopsy cases.

Material & Methods: A cross sectional study was conducted for duration of one year on 140 post-mortem heart specimens received in the Department of Pathology at Bhagat Phool Singh Government Medical College for Women, Khanpur Kalan, Sonapat. Grossing of heart was performed by inflow outflow method. Sections from various parts of heart and from three main coronary arteries were processed and examined.

Result: Intimal xanthoma was most common non-atherosclerotic lesion followed by advanced atherosclerotic lesions mainly fibrous cap atheroma (FCA) and fibrocalcific plaque. The overall prevalence of coronary atherosclerosis was 60.71% with maximum cases of atherosclerosis belong to 35-55 years of age group (64.70%). Non-atherosclerotic lesions were more commonly observed in <35 years subjects (55.32%) whereas in age group >55 years, advanced lesions were commonly observed (70%). Atherosclerosis was observed in 48.57% of LCA followed by 38.57% in RCA and 37.86% in LAD.

MAHA classification for atherosclerosis is useful in subdividing the intermediate lesions of atherosclerosis which are precursor lesions of advanced atherosclerosis and thus clinically important. The awareness regarding atherosclerosis and various preventive measures in form of healthy dietary habits, routine exercise and screening of cardiovascular risk factors should be initiated in young population as early as second decade.

Keywords: Coronary Atherosclerosis, Fibrous Cap Atheroma, Intimal Thickening, Modified American Heart Association Classification

INTRODUCTION

Coronary Artery Disease (CAD) is a major cause of disability and premature death worldwide with atherosclerosis being the main etiology.^{1,2} Atherosclerosis is characterized by atheromatous plaques or fibrofatty plaques medium sized arteries of many organs in body. It can lead to myocardial infarction due to reduced blood flow due across to

obstructive lesions in the coronary arteries.⁴ According to "response to injury" hypothesis, atherosclerosis is characterized by chronic inflammation and healing response of the arterial wall to endothelial injury in which lesion progression occurs through interaction of modified lipoproteins,

monocyte-derived macrophages, and T lymphocytes with endothelial cells of the arterial wall.⁵

Globally, morbidity related to cardiovascular diseases accounted for 17.3 million per year in 2013, which increased to about 17.9 million (44%) in 2016.⁶ This indicates a rising trend in death due to cardiovascular diseases over the past years and is expected to rise sharply by 2030, which is related to population growth, increased longevity and higher vulnerability related to life style changes like lack of exercises.³ In India, the cardiovascular disease accounted for 161,865 deaths (27%) out of the total number of 599,500 deaths due to non-communicable disease in 2015.⁶

American Heart Association (AHA) classified atherosclerosis in year 1994 in which definition of initial lesion, fatty streak and intermediate lesion was given. Later on, advanced type atherosclerotic lesion was added in 1995 and finally eight categories of histological classification of atherosclerosis were given.⁷ To overcome these limitations of AHA classification it is replaced in 2000 by MAHA classification for atherosclerosis. AHA implied a single sequence of events in progression of all the lesions and also because of long list of roman numerals modified by letter codes which are difficult to remember.⁸ MAHA describes intermediate lesions which are comparable to the raised fatty streaks in AHA classification. It also categorizes thick and thin fibrous cap atheroma separately, out of which thin fibrous cap atheroma carries higher chances of rupture and thrombosis.⁹ The present study is intended to assess the atherosclerotic lesions in coronary arteries in cases subjected to autopsy by applying MAHA classification and its correlation of atherosclerosis with ischemic heart disease in population of Sonapat district of Haryana.

MATERIAL AND METHODS

A descriptive cross-sectional study was conducted on autopsy specimens of heart received in the Department of Pathology at Bhagat Phool Singh Government Medical College for Women Khanpur Kalan, Sonapat. The study was approved by Institutional Ethical Committee. A total of 140 autopsy cases were studied from July 2019 to June 2020. Post-mortem specimens of heart were received in our department along with forwarding letter and postmortem examination report. Autolytic

specimens, heart of children <10 years as well as fetal heart are excluded from the study. Specimens fixed in 10% formalin were grossed by inflow-outflow method. Grossly, heart was examined for any areas of mottling, fibrosis or scar. All three major coronary arteries were traced by inserting a probe from their ostias and dissected longitudinally thereafter sectioned at 3 mm interval to examine grossly for presence of atherosclerotic plaque, calcification or thrombus (Figure 1). Sections from various portions of heart including any grossly pathologic areas and coronary arteries were taken and processed. Hematoxylin and Eosin stain sections were examined by two pathologists and microscopic assessment of atherosclerosis was done using MAHA classification (Table 1).

RESULT

In this study, demographic data and histopathological findings of 140 autopsy specimens of heart were studied. Maximum cases seen in the age group of 40-49 years 40 (28.58%) followed by 35 cases (25%) in 30-39 years of age group (Figure 2). Youngest case found in this study was 13 years old and eldest case seen was 80 years old. Mean age is 40.6 ± 13.56 years with M: F ratio observed to be 8.3:1 (Table 2).

In our study, a total of 95 arteries were found to be unremarkable with maximum cases in LAD. Intimal xanthoma was most common non-atherosclerotic lesion observed in 26.15%, most frequently reported in LAD. Among advanced atherosclerotic lesions, fibrous cap atheroma was the most common lesion observed in 78 arteries (24%) with highest number of cases reported in LCA (Table 3, Figure 3). The prevalence of coronary atherosclerosis reported in our study was 60.71% with maximum percentage observed in 35-55 years of age group (Table 2). The percentage of age wise involvement by coronary atherosclerosis showed gradual increase from second decade onwards (Figure 4). Correlation between prevalence of coronary atherosclerosis with age found to be statistically significant with $p < 0.05$ ($p = 0.001$). Coronary atherosclerosis was observed in 65.6% of males and 20% of females in our study. Statistical correlation between both gender and atherosclerosis revealed highly significant correlation with male gender as $p < 0.05$ ($p = 0.001$).

Out of three major coronary arteries, LCA is most frequently involved by atherosclerotic lesions

48.47% followed by 38.57% in RCA and 37.86% in LAD (Table 2). Non-atherosclerotic lesions were reported higher in females (66.67%) than males (25.60%). Advanced atherosclerotic lesions in males constitute 52.80% cases with maximum cases reported in LCA whereas in females only 20.00% cases show PIT with none of the case reported as advanced atherosclerotic lesion. Non- atherosclerotic lesions were more commonly observed in subjects <35 years of age (17.02%) and percentage decreased with increasing age (Table 4).

On evaluating 85 cases of coronary atherosclerosis, triple vessel involvement was most frequently observed in 38.82% cases followed by single vessel involvement in 32.94%. Subjects of 35-55 years age group and male gender showed predilection for triple vessel involvement.

Among females, all 3 cases showed atherosclerosis involving single vessel only. It was observed that in all seven cases of MI (100%) and 21 cases of CIHD (95.46%) revealed atherosclerosis in their coronary arteries, while only one case of CIHD revealed non-atherosclerotic lesion. A highly significant statistical correlation was observed between ischemic heart disease and atherosclerosis with p value <0.05 (p=0.001). However, no significant statistical correlation was observed between myocardial infarction and chronic ischemic heart disease with type of coronary artery lesion p>0.05 (p=0.341 and p=0.104 respectively).

DISCUSSION

Coronary artery disease has been expanding at alarming pace and causing significant morbidity and mortality globally.¹⁰ Coronary atherosclerosis and myocardial infarction are the most common fatal cardiac diseases discovered in autopsies. The study of human atherosclerotic lesion is difficult task in a living subject and an autopsy study is the best possible and cost- effective procedure. Premature atherosclerosis is characterized by formation of atherosclerotic plaques in individuals below 40 years of age.¹¹

In our study, Intimal xanthoma was most common non-atherosclerotic lesion followed by advanced atherosclerotic lesions mainly fibrous cap atheroma (FCA). Similar findings were reported by Thej et al⁹ and Bhanvadia et al¹². However, Bhandari et al¹¹

reported intimal xanthoma as the most frequent reported lesion with PIT as the most common lesion in atherosclerotic category with a significantly lower prevalence of FCA. In contrast, Gupta et al¹³ conducted a study on coronary artery samples received from living population who underwent coronary artery bypass grafting for coronary artery stenosis due to atherosclerosis, reported a higher percentage of fibrocalcific plaque followed by FCA as the second most common.

Prevalence of coronary atherosclerosis in our study was comparable with findings reported by Thej et al⁹, Bhanvadia et al¹² and Bhandari et al¹¹ by using MAHA classification. However, Singh et al¹⁴ and Puri et al¹⁵ reported a higher prevalence of atherosclerosis in studies conducted on Indian population by using AHA classification. The non-atherosclerotic lesions of MAHA intimal thickening and intimal xanthoma were considered as atherosclerotic lesions in AHA classification, thus leading to higher prevalence reported by these studies.

In most previous studies, highest frequency of atherosclerosis was observed in LAD, while in our study LCA is the most frequently involved artery; however, the difference of percentage was small from few other studies. As we have included all autopsy heart specimens received during study period irrespective of cause of death, further studies with higher number of cases with cardiac and non-cardiac causes of death should be performed to analyze the difference in findings.

The prevalence of coronary atherosclerosis reported in our study was 60.71%. Percentage of coronary atherosclerotic lesions, the number of coronary vessels involved and the severity of atherosclerosis increased significantly from 3rd decade onwards. Thus, concluded that 3rd decade of life appeared to be a turning point in the pathogenesis of coronary atherosclerosis. In concordance to our study, Wu et al¹⁶ also reported high prevalence of coronary atherosclerotic heart disease in 35-55 years and >55 years of age group 53% and 81% respectively. Similarly, Thej et al⁹ and Bhanvadia et al¹² also reported substantially higher prevalence of coronary atherosclerosis in younger individuals. Bhandari et al¹¹ conducted a study on individuals with age group 15-34 years it was observed that in age group 15- 20

years, non-atherosclerotic lesions were more frequent whereas in 31-34 years, atherosclerotic lesions were more commonly observed.

In concordance to our study, most studies reported more prevalence of atherosclerosis in male as compared to female. The higher autopsy rate of males of all age group worldwide contributed to higher frequency of atherosclerosis reported in them but hormonal factors such as estrogen may be responsible for low prevalence of atherosclerotic lesions among young women.

Similar to our study, Marwah *et al*17, Garg *et al*18 and Dantkale *et al*19 reported triple vessel in 52%, 44.4% and 54.8% respectively but few studies like Bansal *et al*20 and Wu *et al*16 observed most frequent pattern as single vessel involvement in 83% and 47% cases respectively. Garg *et al*18, Udhreja *et al*4 and Rani *et al*21 reported prevalence of myocardial infarction comparable with our study, however, none of them correlated IHD with atherosclerosis

CONCLUSION

This study highlighted the advantage of MAHA classification in categorizing non atherosclerotic lesions as separate entity which was earlier considered to be atherosclerotic in AHA classification, thus helping in estimating the exact disease burden in the population. Our study will help in providing valuable data to the literature regarding the morphology of atherosclerotic lesion and its relation to the significant cardiac lesion.

This small autopsy study conducted in district Sonapat, Haryana showed relatively high prevalence of atherosclerosis and even subjects in second decade are reported with advanced atherosclerotic lesions. Thus, this study indicates need of substantial efforts both at individual and community levels to reduce the dreaded effects of this disease. Incorporation of healthy practices including dietary care and physical exercises, reduction of risk factors and availability of diagnostic and treatment facilities need to be augmented. Future researches targeting development of novel medical and surgical modalities for treating atherosclerosis should be promoted.

CONFLICT OF INTEREST: None

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TABLES AND FIGURES

Table 1: Modified American Heart Association classification

Non-Atherosclerotic Lesions		
Lesions	Description	Thrombosis
Intimal thickening	Normal accumulation of smooth muscle cells in the intima in absence of lipid or macrophage foam cells.	Absent
Intimal xanthoma or fatty streak	Luminal accumulation of foam cells without a necrotic core or fibrous cap	Absent
Progressive Atherosclerotic Lesions		
Pathological intimal thickening	SMCs in a proteoglycan-rich matrix with areas of extracellular lipid accumulation without necrosis.	Absent
Erosion	Luminal thrombosis; plaque same as above	Thrombus mural and infrequently occlusive
Fibrous cap atheroma	Well formed necrotic core with an overlying fibrous cap	Absent
Erosion	Luminal thrombosis plaque same as above; no communication of thrombus with necrotic core	Thrombus mural and infrequently occlusive
Thin Fibrous cap atheroma	A thin fibrous cap infiltrated by macrophage and lymphocytes with rare SMCs and an underlying necrotic core.	Absent
Plaque rupture	Fibroatheroma with cap disruption; luminal thrombus communicates with the underlying necrotic core	Absent
Calcified nodule	Eruptive nodular calcification with underlying fibrocalcific plaque	Thrombus usually non-occlusive

Fibrocalcific plaque	Collagen- rich plaque with significant stenosis usually contains large areas of calcifications with few inflammatory cells; a necrotic core may be present.	Absent
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Table 2: Distribution of coronary atherosclerosis

	Category	Total Cases	Coronary atherosclerosis	
			n	%
GENDER	Male	125	82	65.60
	Female	15	03	20.00
AGE WISE DISTRIBUTION	<35 Years	47	13	27.66
	35-55 Years	73	55	75.34
	>55 Years	20	17	85.00
CORONARY ARTERY	RCA	140	54	38.57
	LCA	140	68	48.57
	LAD	140	53	37.86
OVERALL PREVALENCE	Total	140	85	60.71

Table 3: Distribution of coronary artery lesions based on morphological description according Modified American Heart Association (MAHA) classification

Coronary artery lesions	RCA		LCA		LAD		Total	
	n	%	n	%	n	%	n	%

Non Atherosclerotic lesion	Intimal Thickening	27	25	21	17.95	17	17	65	20.00
	Intimal Xanthoma	27	25	28	23.93	30	30	85	26.15
PIT	PIT	15	13.89	18	15.38	23	23	56	17.23
	PIT with Erosion	00	00	00	00	00	00	00	00
Advanced lesions	Fibrous Cap Atheroma	25	23.15	34	29.1	19	19	78	24
	FCA with Erosion	01	0.93	03	2.57	01	1.0	05	1.55
	Thin Fibrous Cap Atheroma	00	00	00	00	00	00	00	00
	Plaque Rupture	00	00	00	00	00	00	00	00
	Calcific Nodule	05	4.63	06	5.13	05	5	16	4.92
	Fibrocalcific Plaque	08	7.40	07	5.98	05	5	20	6.15

Table 4: Age and gender wise distribution of coronary atherosclerosis

CATEGORIZATION		Unremarkable		Non Atherosclerotic lesions		PIT		Advanced lesions	
		n	%	n	%	n	%	n	%
AGE	<35 Years (n=47)	08	17.02	26	55.32	07	14.90	06	12.76
	35-55 Years (n=73)	03	4.11	14	19.17	10	13.69	46	63.01
	>55 Years	01	5.00	03	15.00	02	10.00	14	70.00

	(n=20)								
GENDER	Male (n=125)	11	8.00	32	25.60	16	12.80	66	52.80
	Female (n=15)	02	13.33	10	66.67	03	20.00	00	00

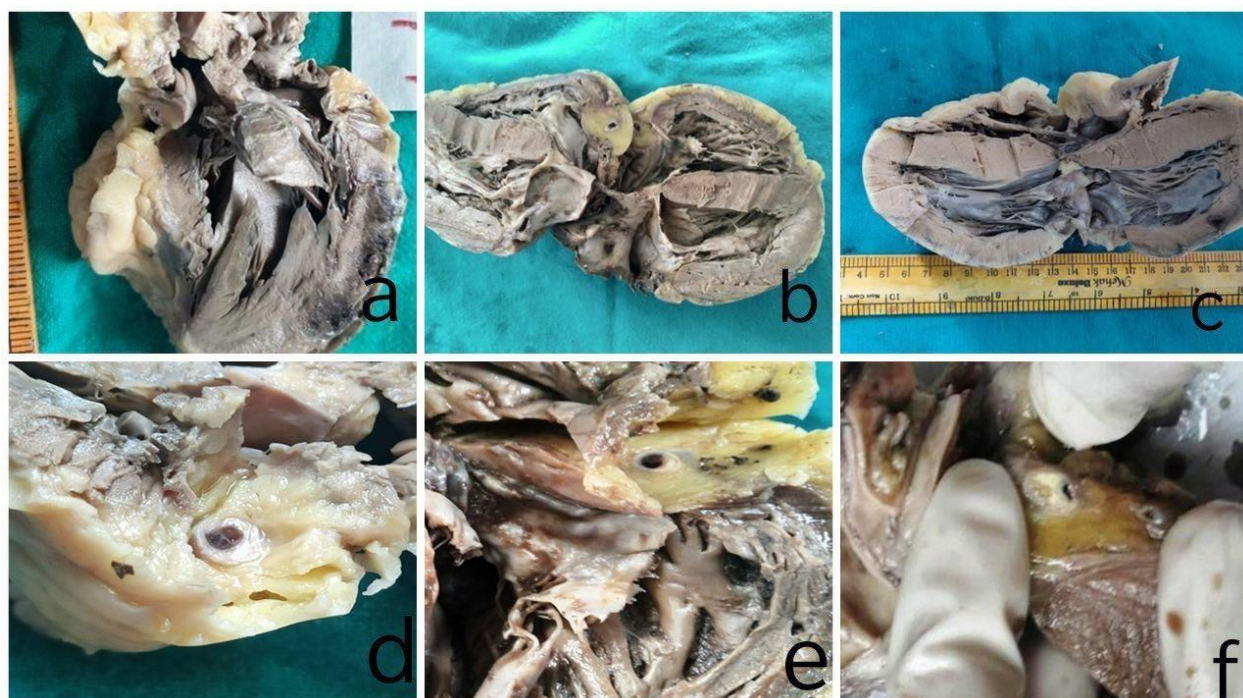


Figure 1: a) Gross specimen of heart showing areas of mottling in LVW, b) Gross specimen of heart showing gray white areas of fibrosis in apex, c) Gross specimen of heart showing areas of mottling in LVW, d) Gross specimen of heart showing atherosclerosis with thrombus in right coronary artery e) Gross specimen of heart showing atherosclerosis in right coronary artery, f) Gross specimen of heart showing atherosclerosis in left circumflex artery.

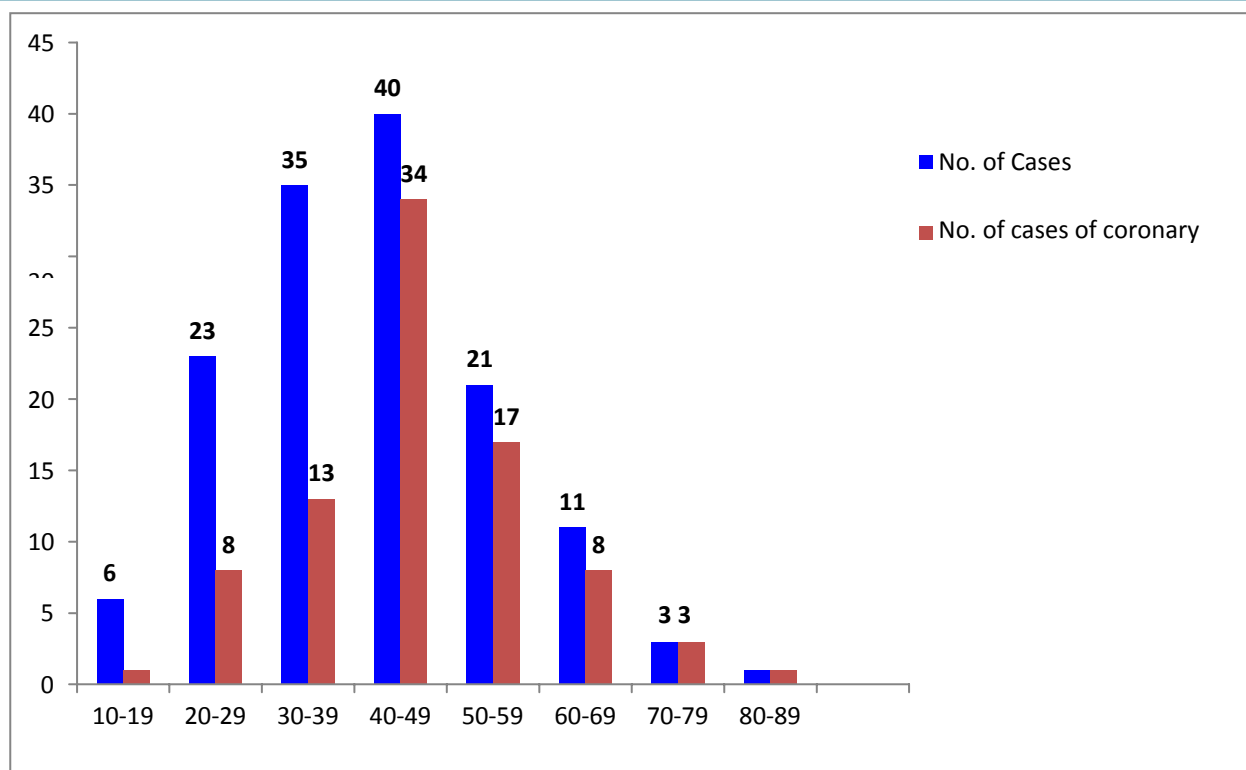


Figure 2: Distribution of coronary atherosclerotic cases according to age

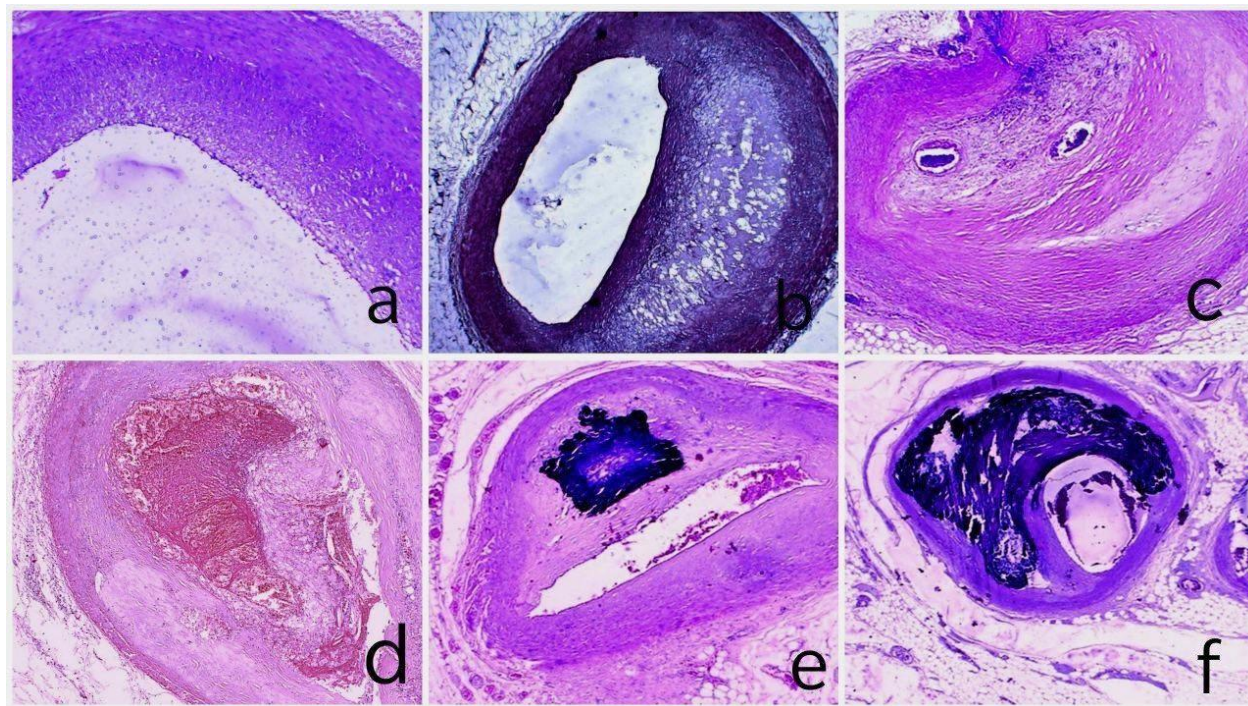


Figure 3: a) Microphotograph of intimal xanthoma showing luminal accumulation of foam cells (H&E, 100X), b) Microphotograph showing fibrous cap atheroma in coronary artery (H&E, X40), c) Microphotograph showing fibrous cap atheroma with complete occlusion of coronary artery (H&E, 40X), d) Microphotograph showing fibrous cap atheroma with occlusive thrombus in coronary artery (H&E, 40X), e) Microphotograph showing fibrocalcific plaque in coronary artery (H&E, 40 X), f) Microphotograph showing calcific nodule in coronary artery (H&E, 20 X)

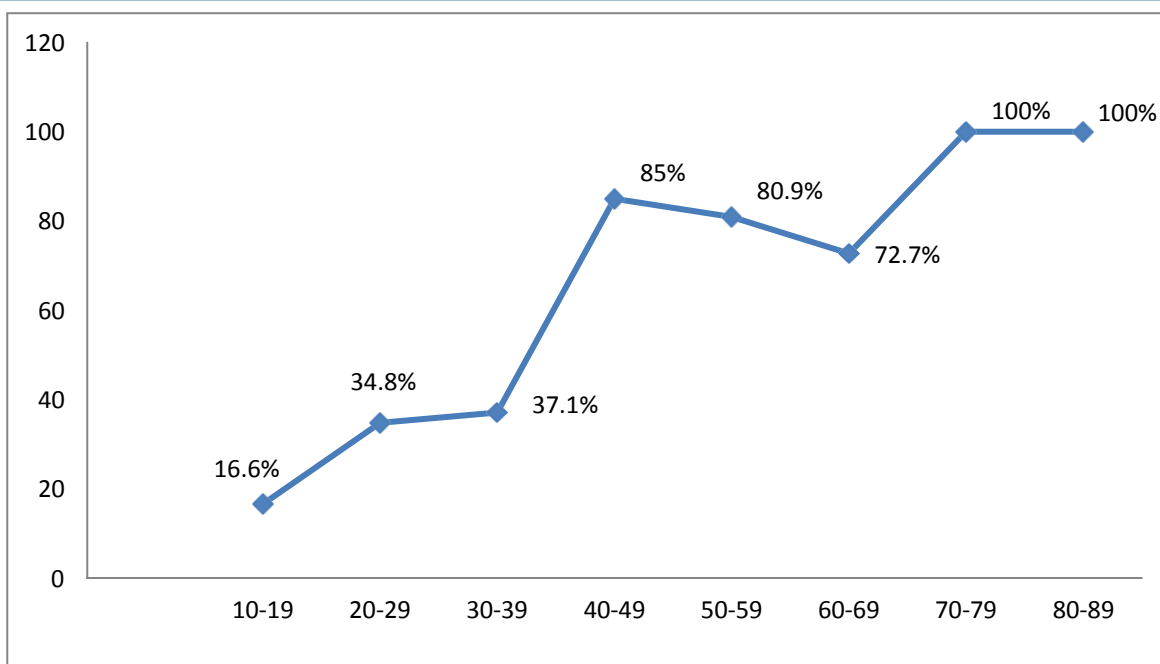


Figure 4: Age wise distribution of percentage of coronary atherosclerotic lesions