

Grade 0: Sections showing normal histology or adaptive thickening without macrophages or foam cells.
 Grade 1: Presence of isolated macrophage foam cells.
 Grade 2: Intracellular lipid accumulation with formation of multiple foam cell layers.
 Grade 3: Grade 2 lesions along with small extracellular lipid pools.
 Grade 4: Grade 2 changes along with a core of extracellular lipid.
 Grade 5: Lipid core and fibrotic layer or multiple lipid cores and fibrotic lipid layers.
 Grade 6: Complicated plaques with surface defects, and/or hematoma-hemorrhage, and/or thrombosis.

2.2 Morphometric Analysis

The histomorphometric analysis was performed using the ProgResC3 CapturePro (Jenoptik AG, GmbH; Jena, Germany) imaging software. Morphometric measurements were performed after calibration of the system. Direct analysis of the arterial lumen was achieved by magnification of 40x, while analysis of the intimal layer thickness/changes and tunica media was attained at a magnification of 200x.

Morphometric measurements and calculated measurements [5] mentioned below were done on all three major coronary arteries (LAD, LCX and RCA).

Morphometric measurements done included:

- width of intima (distance between intima and IEL),
 - width of media (area between IEL and EEL)
 - diameter internal to the media (Diameter of lumen plus intima; DLI).
- (IEL = internal elastic lamina; EEL = external elastic lamina)

Calculated measurements done included:

- Lumen area (in mm²) = πr^2 (where r = diameter of lumen/2).
- IEL area (in mm²) = πR^2 (where R = DLI/2).
- Intimal area (in mm²) = IEL area – Lumen area.

Based on the above measurements, following two morphometric parameters were derived to evaluate the degree of coronary atherosclerosis. Also termed as severity indices of atherosclerosis [5]:

- (a) Percentage of luminal narrowing,
- (b) Intima-to-Media Ratio (IMR)

These parameters were derived using the following formulas:

- Percentage of luminal narrowing = 100 X intimal area / IEL area;
- IMR = width of intima at maximal intimal thickness / width of media at maximal intimal thickness.

Percentage of luminal narrowing in all the atherosclerotic coronary arteries was calculated and grouped as under those with <25%, 25-50%, 50-75% and >75% luminal narrowing.

However, for the assessment of correlation between the morphometric parameters and morphological grades, mean Percentage of luminal narrowing and mean IMR was calculated for each AHA grade of atherosclerosis in all the

three atherosclerotic coronaries. Values thus obtained were tabulated and comparison of results was carried out.

3. Results

The present study included 114 males and 36 females between the age group of 30-60 years. Majority were in the age group of 30-40 years followed by 41-50 years and 51-60 years respectively (Table 1).

Table 1: Showing Age-wise Sex Distribution of cases (n=150)

Sl. No.	Age (years)	Males		Females		Total
		No. of cases	Percentage	No. of cases	Percentage	
1	30-40	58	38.6 %	23	15.3 %	81
2	41-50	38	25.3 %	10	6.6 %	48
3	51-60	18	12.1 %	03	2.1 %	21
	Total	114	76 %	36	24 %	150

3.1 Prevalence of coronary atherosclerosis

Out of 150 cases studied, 28 cases including 16 males and 12 females showed normal histology in all three major coronaries. Coronary atherosclerosis was present in 122 cases (81.3%) with mean age of 43 years. 85.9% (98/114) males and 66.6% (24/36) females had coronary atherosclerosis.

3.2 Distribution of atherosclerotic lesions

LAD was the most commonly involved coronary artery (74%) followed by LCX (68%) and RCA (60%) respectively. 63% (77/122) cases showed atherosclerotic lesions in all three major coronaries (triple-vessel disease), while 22% (27/122) in any two coronaries (double- vessel disease) and only 15% (18/122) showed involvement of any one coronary artery (single-vessel disease). Thus majority of the cases in our study had triple vessel disease. Among the cases of single artery involvement, LAD was involved in 9 cases, LCX in 6 cases and RCA in 3 cases.

3.3 Morphological Assessment (AHA Grading)

AHA Grade 2 (Figure 1) atherosclerotic change was the most common type of atherosclerotic lesion seen in both LAD and LCX while in RCA; AHA Grade 1 atherosclerotic change was most common. AHA Grade 4 (Figure 2) and 5 atherosclerotic changes were highest in LAD followed by LCX and RCA (Table 2). None of the coronaries showed AHA Grade 6 changes.

Table 2: Showing AHA grade distribution for all three coronaries

Coronary Artery	AHA Grade					Total (%)
	1	2	3	4	5	
LAD	18	34	22	14	23	111 (74%)
LCX	26	35	19	10	12	102 (68%)
RCA	40	25	12	6	7	90 (60%)

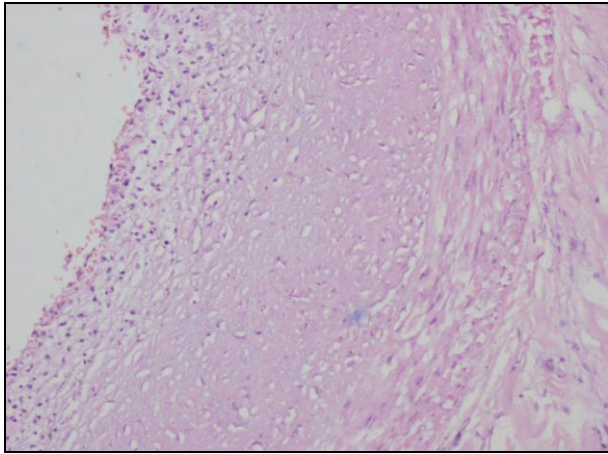


Figure 1: Photomicrograph of Coronary artery showing Intimal thickening with foam cell aggregates and underlying medial thinning: AHA Grade 2 atherosclerosis (H & E, 200x)

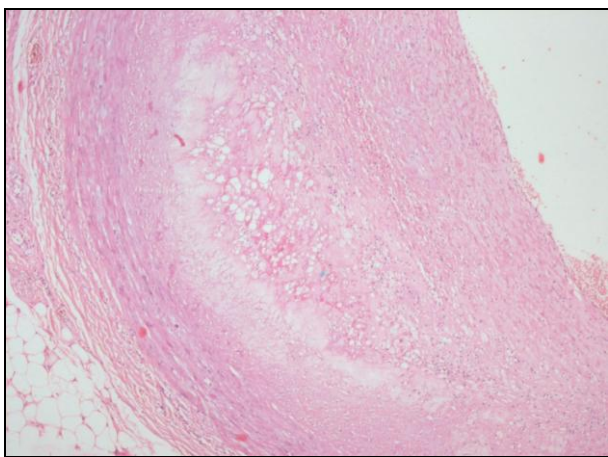


Figure 2: Photomicrograph of Coronary artery showing Atheroma composed of lipid core, foam cells, fibrous cap composed of SMCs and collagen with thinned out underlying media: AHA Grade 4 atherosclerosis (H & E, 100x)

3.4 Morphometric Analysis

Majority of atherosclerotic LADs and LCXs showed 25-50 % lumen narrowing while most atherosclerotic RCAs showed <25 % lumen narrowing. Critical narrowing (>75%) was seen in 7 LADs, 4 LCXs and 2 RCAs respectively (Table 3).

Table 3: Showing Percentage of luminal narrowing for all three coronaries

Coronary Artery	Percentage of Luminal Narrowing				Total
	<25%	25-50%	50-75%	>75%	
LAD	33	59	12	7	111
LCX	37	49	12	4	102
RCA	54	30	4	2	90

3.5 Correlation between morphometric parameters and morphological grades

Comparison result of both mean Percentage of luminal narrowing and mean IMR value for each AHA grade of atherosclerosis showed a linear increase in the values of both these parameters with each higher grade of atherosclerosis in all three coronaries. Thus, the morphometric parameters correlated well with the grade of atherosclerosis (Table 4, 5).

Table 4: Showing values of Mean Percentage of luminal narrowing for each AHA Grade in all three coronaries

Coronary Artery	Atherosclerosis Grade				
	1	2	3	4	5
LAD	25%	27%	31%	46%	55%
LCX	24%	26%	27%	55%	59%
RCA	22%	22%	26%	39%	61%

Table 5: Showing values of Mean IMR for each AHA Grade in all three coronaries

Coronary Artery	Atherosclerosis Grade				
	1	2	3	4	5
LAD	2.2	2.9	3.8	6.9	13.2
LCX	2.5	2.2	3.2	9.5	12.6
RCA	2.2	2.4	3.2	5.6	11.6

4. Discussion

Atherosclerosis of coronaries is the most common cardiac pathology found in autopsies [9]. Atherosclerosis is a chronic immunoinflammatory, fibroproliferative disease of large and medium-sized arteries fuelled by lipid [10]. Autopsy is a tool of real value for assessment of pathologies that are difficult to assess in the living [11].

The present study included 76% males and 24% females. This is in concordance with the data of other similar autopsy studies by Dhruva et al, [12] (73.6% males and 26.4% females), Puri et al, [13] (80% males and 20% females), Garg et al, [14] (81% males and 19% females), Thej et al, [15] (69% males and 31% females) and Singh H et al, [16] (84% males and 16% females). Higher number of autopsied males was the feature in our study and also other similar studies as well. This is because most autopsied cases include the victims of events such as road traffic accidents which commonly involve the males rather than females.

Prevalence of coronary atherosclerosis in the present study was found to be 81.3%, which matches with the data given by Kumar et al, [17] Puri et al, [13] and Singh H et al, [16] as 80%, 86% and 78 % respectively. But Thej et al, [15] have reported a prevalence rate of 66.3% which is due to the fact that they have used the Modified AHA classification where early lesions like intimal thickening and intimal xanthoma are not considered as atherosclerotic lesions.

Among all three major coronaries, LAD had the highest incidence of atherosclerotic involvement (74%), which is in concordance with data given in studies by Kumar et al, [17] and Yazdi et al, [18] as 68% and 60% respectively. LAD is the most commonly involved coronary vessel in atherosclerosis, possibly due to the hemodynamic stress that it undergoes through.

In the present study, AHA Grade 2 atherosclerotic change was the most common type of atherosclerotic lesion seen in both LAD and LCX while in RCA, AHA Grade 1 atherosclerotic change was most common. But in studies by Dhruva et al, [12] and Garg et al, [14] the commonest type of atherosclerotic change was AHA Grade 4 and Grade 3 respectively. This variation possibly, could be due to the fact that most autopsy cases in our study were in the 30-40 years

age group.

Degree of lumen narrowing in majority of the atherosclerotic LADs and LCXs was between 25-50 %, while most atherosclerotic RCAs showed <25 % lumen narrowing. But in study by Kumar et al, [17] majority showed lumen narrowing in the range of 50-75%. In the present study, the intimal area, rather than the thickness of the intima was measured in order to allow an accurate evaluation of eccentric or irregular atherosclerotic lesion.

In the present study, the values of both morphometric parameters derived from morphometry of atherosclerotic lesions showed a linear increase with each higher AHA grade of atherosclerosis reflecting the severity of atherosclerotic involvement. The mean percentage of luminal narrowing was highest for grade 5 lesions. The fibromuscular caps in AHA Grade 5 lesion contain a greater proportion of collagen fibers which oppose outward expansion of the vessel wall and thus narrowing of the lumen is a prominent feature of Grade 5 lesions [19]. The increase in mean IMR value with each higher grade of atherosclerosis reinforces the fact that medial thickness underlying the diseased intima (atherosclerotic plaque) is considerably thinner [20]. However, in the case of living subjects, measurement of Intima-Media thickness (IMT) by B-mode ultrasonography is used for determining the extent of atherosclerosis and for assessing the cardiovascular risk [21]. The major limitation of our study is absence of correlation of the study findings with the cardiovascular risk factors such as smoking and lifestyle habits, as there was no information available on these at autopsy.

5. Conclusion

The values of both mean percentage of luminal narrowing and mean IMR show linear increase with each higher AHA grade of atherosclerosis consistently in all the three coronaries. Hence, both these morphometric parameters correlate well with the morphological grades of atherosclerosis. These parameters, thus can serve as reliable indices for assessing the severity of atherosclerotic lesions supplementing the histomorphological analysis. Our study has attempted a comprehensive analysis of both morphological and morphometrical data on coronary atherosclerotic lesions. Future research on larger samples is suggested to confirm the findings of our study. It is also proposed to study the clinical correlates and associated risk factors of coronary atherosclerosis.

References

[1] Schoen FJ, Mitchel RN. The Heart in Robbin and Cotran Pathologic Basis of Disease. Kumar V, Abbas AK, Fausto N, Aster JC (Eds). 8th ed. Philadelphia. Elsevier, 2010:545-559.
[2] Morrow AD, Gersh JB. Chronic Coronary Artery Disease in Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, 8th edition. Libby, ed. Elsevier Saunders; 2007:1353.

[3] Park K. Epidemiology of Chronic Non-communicable Diseases and Conditions in Park's Textbook of Preventive and Social Medicine, 20th ed., Banarsidas Bhanot Publishers, 2009. Chapter 6:303-05.
[4] Malhotra R, Bedi HS, Bazaz S, Jain S, Trehan N. Morphometric analysis of the right gastroepiploic artery and the internal mammary artery. *Ann Thorac Surg.* 1996;61:124-127.
[5] Ruengsakulrach P, R Sinclair, M Komeda, J Raman, I Gordon and B Buxton. Comparative Histopathology of Radial Artery versus Internal Thoracic Artery and Risk Factors for Development of Intimal Hyperplasia and Atherosclerosis. *Circulation.* 1999, 100:II-139-144.
[6] Edwards WD. Cardiovascular system in Handbook of autopsy practice, Ludwig J (Editor). Totowa, NJ, Humana Press, 2002;21-43.
[7] Stary HC, Chandler AB, Glagov S, Guyton JR, Insull W Jr, Rosenfeld ME, Schaffer SA, Schwartz CJ, Wagner WD, Wissler RW. A definition of initial, fatty streak, and intermediate lesions of atherosclerosis: a report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. *Arterioscler Thromb.* 1994;14: 840-856.
[8] Stary HC, Chandler AB, Dinsmore RE, Fuster V, Glagov S, Insull W Jr, Rosenfeld ME, Schwartz CJ, Wagner WD, Wissler RW. A definition of advanced types of atherosclerotic lesions and a histological classification of atherosclerosis. A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis. American Heart Association. *Circulation.* 1995;92:1355-1374.
[9] Catellier MJ, Waller BF, Clark MA, et al. Cardiac pathology in 470 consecutive forensic autopsies. *J Forensic Sci.* 1990;35(5): 1042-1105.
[10] Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. *N Engl J Med* 2005;352:1685-95.
[11] Fausto N. Atherosclerosis in young people: The value of the autopsy for studies of the epidemiology and pathobiology of disease. *Am J Pathol* 1998;153:1021-2.
[12] Dhruva GA, Agrawal AH, Sanghvi HK. Atherosclerosis of Coronary Arteries as Predisposing Factor in Myocardial Infarction: An Autopsy Study. *Online J Health Allied Scs.* 2012;11(3):1.
[13] Puri N, Gupta PK, Sharma J, Puri D. Prevalence of atherosclerosis in coronary artery and internal thoracic artery and its correlation in North-West Indians. *Indian Journal of Thoracic & Cardiovascular Surgery.* 2010; 26:243-246.
[14] Garg M, Agarwal AD, Kataria SP. Coronary Atherosclerosis and Myocardial infarction: An Autopsy Study. *J Indian Acad Forensic Med.* 2011;33(1):39-42.
[15] Thej MJ, Kalyani R, Kiran J. Atherosclerosis in coronary artery and aorta in a semi-urban population by applying modified AHA classification of atherosclerosis: An autopsy study. *J Cardiovasc Dis Res* 2012;3:265-71.
[16] Singh H, Oberoi SS, Gorea RK, Bal MS. Atherosclerosis in Coronaries in Malwa Region of Punjab. *J Indian Acad Forensic Med* 2005;27(4):32-35.

- [17] Kumar S, Verma AK, Kumar N, Verma RK. Prevalence of Coronary Atherosclerosis in Different Age Groups-A Postmortem Study. Biomedical Research 2013; 24 (1): 139-141.
- [18] Yazdi SAT, Rezaei A, Azari JB, Hejazi A, Shakeri MT, Shahri MK. Prevalence of Atherosclerotic Plaques in Autopsy Cases with Noncardiac Death. Iranian Journal of Pathology (2009), 4 (3), 101- 104.
- [19] Stary HC. Natural History and Histological Classification of Atherosclerotic Lesions: An Update. Arterioscler Thromb Vasc Biol 2000;20;1177-1178.
- [20] Waller BF: The eccentric coronary atherosclerotic plaque: Morphologic observations and clinical relevance. Clin Cardiol 12,1989;14-20.
- [21] Pavel Poredos. Intima-media thickness: indicator of cardiovascular risk and measure of the extent of atherosclerosis. Vasc Med 2004; 9: 46-54.

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