

## Original Article

# Pattern and Extent of Coronary Artery Disease in Patients of Ischemic Heart Disease aged 40 Years or less

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## Abstract

**Key Words :**  
Coronary artery disease, Ischemic heart disease, young adults, Bangladesh.

**Background:** Atherosclerotic coronary artery disease is rare in young adults aged 40 years or less. However, South Asia is among the top 3 of the countries with highest proportion of cases of first acute coronary syndrome events occurring at age 40 years or less. This study was to explore the extent and pattern of angiographic coronary artery disease among patients of ischemic heart disease aged 40 years or less.

**Methods:** This cross-sectional retrospective descriptive study included 140 patients who had coronary angiography for ischemic heart disease at the Department of Cardiology of Enam Medical College between July 2012 and December 2020. Coronary angiography was analyzed with particular attention to the extent of involvement of major epicardial coronary arteries including significant branch involvement.

**Results:** Of the 140 patients included in the study - aged 18-40 years (mean 35.90 and SD 4.05) and 59.28% in the 36-40 years age group – 85% were male. Coronary angiogram revealed Single Vessel Disease in 39.29%, Double Vessel Disease in 25.72%, Triple Vessel disease in 23.57%, normal Coronaries in 9.28%. Left Anterior descending territory was most involved - 94 (67.14%) patients having significant stenosis in the main trunk and/or one or more major branches. Overall, 23(16.43%) of the whole cohort of patients had multiple branch involvements in the three coronary artery territories.

**Conclusion:** In patients aged up to 40 years with ischemic heart disease, significant coronary artery disease burden was seen, including a significant proportion with multi-vessel disease and a high level of branch involvement in all the principal epicardial coronary territories. This indicates a high burden of disease in a relatively young age group, with significant implications for long term management over and beyond reperfusion/revascularization efforts.

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## Introduction:

About 80% of the burden of diseases now occurring in low- and middle-income countries are accounted for by Cardio-vascular diseases (CVD), the leading cause of death and loss of disability adjusted life years worldwide. They have increased greatly in the last two decades compared with a decline in several developed countries. The incidence rate is 29-30 and the mortality rate 9.5-14 per 1000 person years in Bangladesh.<sup>1</sup> In low- and middle-income countries, the median age of presentation of cases is about 9 years lower (53 vs. 60-63 years

of age) than in the Western European, North American and other developed nations. In addition, South Asia figured 3<sup>rd</sup> (after Middle East and Africa) among the countries with the highest proportion of cases of first acute coronary syndrome (ACS) event occurring at age 40 years or below.<sup>2</sup>

Among the CVDs, atherosclerotic or non-atherosclerotic coronary artery disease (CAD) is the leading cause of death among men and women worldwide. Atherosclerosis is the predominant cause of CAD, and although it starts to develop at a very early age, symptomatic atherosclerotic CAD

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and ACS are rarely seen in adults less than 40 years of age, accounting for 8.9% of them (in South Asia geographical region) and 10.6% (among ethnic South Asians irrespective of geographical location).<sup>2,3</sup> CAD occurring in adults at or below 40 years of age is variously termed CAD in the young, premature CAD etc.,<sup>4</sup> and accounts for 0.4-19% of all ACS cases.<sup>5</sup> Premature CAD is a growing problem, occurring in even younger adults and - although the prognosis is not as adverse as in the older adults – has profound lifelong consequences on their active lifestyle, including effects on psychosomatic well-being as well as grave socio-economic impacts.

There is a growing body of evidence to suggest that CAD in young adults from the Indian subcontinent might be altogether a “different beast”,<sup>6</sup> presenting relatively early and have more extensive CAD compared to comparable age groups of other ethnic origin. Incidence of CAD in young Indians ranges from 12-16%, which is higher than any other ethnic groups,<sup>7</sup> therefore need a different set of guiding principles in addition to the classical approach for its clinical and epidemiological assessment and management strategy.

There have been some studies exploring the risk factor profile and extent of coronary artery involvement in these young adults in Bangladesh. But the topic needs further study, because of its emergence as a growing problem. The present study explores the extent and pattern of angiographic CAD in young adults presenting with ischemic heart disease and at a tertiary care hospital in a sub-urban setting.

### Methods:

This is retrospective cross-sectional observational analysis was carried out in patients treated between July 2012 and June 2020 at the Department of Cardiology of Enam Medical College Hospital, Savar, Dhaka. 140 patients admitted into the CCU and Cardiology facility of the hospital with the diagnosis of definite or probable stable ischemic heart disease and or ACS and had coronary angiograms (CAG) to document their coronary artery disease were included in the final analysis. Patients who were treated but did not undergo CAG were excluded. Recorded detailed clinical history and findings and pre-angiogram data sheets

were consulted and used to record diagnosis, past medical history (prior history of stable IHD, ACS and/or Coronary interventions) and risk factor profile, including any history of drug addiction/substance abuse.

Further investigation reports obtained as per our departmental standard protocol were also consulted. Self reported age in completed years were recorded and verified by NID cards. Angiograms were performed using the standard protocol by two of the authors and analyzed individually followed by collation between the two performing cardiologists, using the on-board Quantitative Coronary-angiographic Analysis softwares of the two angiogram machines (Infinix 8000V, Toshiba Corporation, Tokyo, Japan; and Bransist Alexa C12, Shimadzu Corporation, Kyoto, Japan). In cases doubt, the two performing cardiologists reviewed the CAG jointly and reports were finalized based on consensus.

All epicardial major coronary arteries and their primary branches with a diameter of >1.5 mm by QCA were included into analysis.<sup>8</sup> Stenosis and plaques visible on angiography were analyzed using the on board native QCA programs of the angiography machines. Lesion severities were graded as: >50% stenosis as significant, >25-50% stenosis as insignificant, and <25% stenosis as minor. Three coronary artery territories were defined – Left Anterior Descending (LAD), Left Circumflex (LCX) and Right Coronary (RCA); for convenience, Ramus Intermedius artery was included in the LCX territory.

Data were recorded and analyzed using the IBM SPSS Statistics Version 25. Discrete variables were reported as numbers and percentages, whereas continuous variables were reported as mean, median and standard deviations.

### Results:

Of the 140 patients included in this study 119 (85%) were male and 21 (15%) were female. Just over 59% (89 patients) were in the 36-40 years age group while slightly over 39% were in the 26-35 years age range, with only 2 patients (1.43%) below 25 years of age. The youngest patient was aged 18 years. Mean age of the cohort was just below 36 years (Mean 35.90, SD 4.05 years) (Table I).

**Table I**  
*Characteristics of the patients (N=140).*

Sl. No	Characteristics	Value
Age (years) Range		18 – 40
	Mean ± SD	35.90 ± 4.05
Sex - M: F (no; %)		119(85%):21(15%)
Diagnosis (No; %)		
	i. Acute Myocardial Infarction (MI)	97 (69.28)
	ST Elevation MI (STEMI)	80 (57.14)
	With prior MI	04(4.86)
	Non-ST Elevation MI (NSTEMI)	17 (12.14)
	With prior Stable Angina	02(1.43)
	ii. Stable Angina	28 (20.00)
	With prior STEMI	13 (12.14)
	NSTEMI	04 (04.86)
	iii. Unstable Angina	05 (3.57)
	With prior MI	02 (1.43)
	iv. Others	
Heart Failure		10 (7.15)
	With prior MI	03 (2.14)
Arrhythmia		02 (1.43)
	With Prior MI	01 (0.71)
Prior Percutaneous Coronary Intervention		01 (0.71)
	Elective	05 (3.57)

Indications for CAG were a mix of ACS, stable ischemic heart disease and screening for possible causes of other symptoms (Table I). A total of 130 (92.85%) had CAG consequent to an ACS – 80 (57.14%) with ST segment elevation MI (STEMI), 17(12.14%) with non-ST segment elevation (NSTEMI) and 05(3.57%) with Unstable angina (UA) – while 28 (20%) had Stable Angina Pectoris. Overall, 90.56% of patients had a history of MI, acute or prior. Rest of the patients (10, 7.15%) had CAG as screening for other presentations of suspected ischemic origin - e.g., arrhythmia (2 patients, 1.43%), heart failure (3 patients, 2.14%), non-specific chest pain with or without positive Exercise Tolerance Test (5 patients, 3.57%). One patient had recurrent ischemic symptoms with prior history of Percutaneous Coronary Intervention (PCI). Thirty-three (23.57%) of the patients also had a prior history of old or recent (< 4 weeks old) myocardial infarction.

#### **Coronary Angiographic Findings:**

Coronary angiography revealed significant CAD in 124 (88.58%) and insignificant or no CAD in 16

(11.42%) patients, with 03 (2.14%) of them found to have MINOCA (Myocardial Infarction with No Obstruction on Coronary Angiography). Fifty-five (39.29%) had Single Vessel CAD, with Left Anterior Descending having the highest frequency (37, 26.39%). Multivessel disease occurred in 69 (49.29%) of patients - 36 (25.72%) had Double Vessel CAD and 33 (23.57%) had Triple Vessel CAD (Table II). In the double vessel disease category, the combination of Left Anterior Descending (LAD) and Left Circumflex Artery (LCX) Disease had the highest frequency (18 patients, 12.86%), the combination of LAD and Right Coronary Artery (RCA) being the next commonest (11 patients, 07.86%).

**Distribution and Pattern of CAD:** Analysis of the distribution and pattern of coronary artery lesions revealed significant Left Main Coronary Artery (LMCA) involvement in 02(1.43%) patients and an insignificant lesion in 01(0.71%) more.

The LAD Artery disease was the commonest – 112 (80.00%) patients having at least one lesion, 94 (67.14%) of them having significant stenosis in at

least the main trunk and/or one or more of the major branches. Forty-eight (34.28%) had the main trunk involvement only, while 30(21.43%) had a combination of main trunk with one Diagonal branch stenosis. Significant multiple branch involvement along with a LAD trunk lesion was seen in 10 (7.14%). Isolated Diagonal branch stenosis was seen in 04 (2.86%) patients only, and Septal branch involvement was seen in 09 (6.43%) patients, but none as isolated disease. Of note, while isolated arterial lesions were seen in 52 (37%), involvement of multiple arteries of the LAD territory was quite high (42, 29.99%).

Involvement of the RCA territory was next commonest, although significant stenoses were present in comparable numbers of patients – 59 (42.14%) in LCX vs. 57 (40.71%) in RCA territory.

In the LCX territory, a single arterial involvement was seen in 50 (35.71%) patients, 45 (32.14%) being significant stenosis – 25 (17.86%) with main trunk, 15 (10.71%) with Obtuse Marginal branch and 05(3.57%) with Ramus Intermedius lesions. Multiple artery involvement in the LCX territory were seen in 14 (10%) patients. In addition to the

25 patients with significant main trunk disease mentioned above, 13 (9.19%) had branch disease in combination with main trunk lesion. Again, a significant number had multiple arterial disease in the LCX territory, although the proportion was lower than in the LAD territory (52/42 vs. 45/14).

In the Right Coronary artery (RCA) territory, of the 57 patients with significant disease, 41 (29.29%) had a single artery involvement – 34 (24.29%) with main trunk and 07 (5.00%) with one of the major branches (Posterior Descending artery, Posterior Left Ventricular Branch or Right Ventricular Branch). Multiple artery involvement was seen in 16 (11.42%) patients – all having a combination of main trunk disease with one or more of the major branches. Three (2.14%) patients had diseases of the main trunk and all 3 major branches. Here again, a lesser but significant proportion (16 out of the 57) of patients with significant stenosis had multiple artery involvement.

It is to be noted that, minor or insignificant disease were also noted - most commonly in the RCA (22,15.72%), followed by LAD (18, 12.86%) and lastly LCX (13, 9.28%) territories – alone or with significant stenosis.

**Table-II**  
*Extent of Coronary Artery Involvement (N=140).*

Extent	No	Percent
Single Vessel Disease	55	39.29
Left Anterior Descending Artery (LAD)	37	26.39
Left Circumflex Artery (LCX)	06	4.30
Right Coronary Artery (RCA)	12	8.60
Double Vessel Disease	36	25.72
LAD+LCX	18	12.86
LAD+RCA	11	07.86
LCX+RCA	07	05.00
Triple Vessel Disease	33	23.57
Normal or Near Normal	13	9.28
MINOCA	03	2.14

MINOCA = Myocardial Infarction with Nonobstructive Coronary Arteries

**Table-III**  
*Distribution and Pattern of Coronary Artery Lesions (N=140).*

Coronary Artery	No	Percent
Left Main Coronary Artery (LMCA)		
Minor Disease	01	0.71
Significant Stenosis	02	1.43
Left Anterior Descending (LAD) Artery	112	80.00
Minor Disease	09	6.43
Insignificant Stenosis	09	6.43
Main Trunk	07	5.00
Diagonal Branch	02	1.43
Significant Stenosis	94	67.14
Main Trunk Only	48	34.28
Diagonal branch Only	04	2.86
Trunk & Septal Only	02	1.43
Trunk & Single Diagonal Only	30	21.42
Trunk & Multiple Diagonals	03	2.14
Trunk, Septal & Diagonal	07	5.00
Left Circumflex (LCX) Artery	72	51.42
Minor Disease	08	5.71
Insignificant Stenosis	05	3.57
Main Trunk	03	2.14
Any Major branch only	02	1.43
Significant Stenosis	59	42.14
Main Trunk Only	25	17.86
Ramus Intermedius (RI) Only	05	3.57
RI & Obtuse Marginal branch	01	0.71
Obtuse Marginal branch Only	15	10.71
Trunk & Single OM branch	09	6.43
Trunk & Multiple OM branches	04	2.86
Right Coronary Artery (RCA)	79	56.43
Minor Disease	18	12.86
Insignificant Stenosis – Trunk only	04	2.86
Significant Stenosis	57	40.71
Trunk Only	34	24.29
One of the Major branches* only	07	5.00
Trunk & one of the major Branches	08	5.71
Trunk & two or more major branches	05	3.57
Trunk & all three major branches	03	2.14

### Discussions:

In this study we have shown the extent and pattern of coronary artery disease among young patients aged 40 years or less with ischemic heart disease with or without complications.

Males represented 85% of this cohort. This is consistent with the INTERHEART study, which

showed that the proportion of male cases were highest in regions with younger age of presentation of first ACS- 85% of them in South Asia and 86% in the Middle East, compared to 68-74% in Western regions including Europe, and 70 % in China. In Bangladesh, the rates previously found were similar (80%, and 78.30%).<sup>4, 9</sup> The proportions of

males in similar studies in the subcontinent showed 87.5, 85.3 and 96% males in India,<sup>7,10, 11</sup> and 84% males in Pakistan.<sup>3</sup> Studies on patients of similar age to the current study in more developed countries show values of 89.8% of males in a Taiwanese study<sup>5</sup> and 86.2% in Poland.<sup>12</sup> All these data uphold the INTERHEART observation, namely that CAD presenting in young adults is more common among males compared to older patient populations.

**Extent of CAD:** Analysis of the extent coronary artery disease on CAG (Table III) revealed that the majority had Single vessel (SVD) involvement (39.29 %); Double Vessel Involvement (DVD) was found in 25.72% patients, while Triple Vessel involvement (TVD) was seen in a surprisingly high proportion of patients – 23.57%. Only 11.42% of our cohort had normal or near normal findings on CAG. These values differ significantly from previous reports from Bangladesh in two respects, namely normal coronary arteries were found in 18 to 25 % of patients in the age category of the current study, while Triple vessel disease was found in 8.3 and 18% of the patients<sup>4, 9</sup> - values noticeably lower from the current study. The finding of Single and Double vessel Disease in the present study was comparable to previous reports (42-48.3% and 18.3-22% respectively). Recent studies from the subcontinent show that, in Pakistan the results are comparable – 39, 22, 12 and 28%,<sup>3</sup> and 50, 20.8, 18 and 11.2%<sup>13</sup> respectively for SVD, DVD, TVD and Normal, while in India, the corresponding figures were 66, 22.32 and 11.61% for SVD, DVD and TVD respectively<sup>7</sup>. In a study from Nepal, the corresponding figures were 30.27, 13.76, 11.92 and 11.92 % for SVD, DVD, TVD and Normal Coronaries, respectively<sup>14</sup>. In a recent study from Taiwan, the frequencies were 37.1, 17.6 and 16.7% respectively for SVD, DVD and TVD leaving 28.6% as normal.<sup>5</sup> A similar study from Korea showed 48.4% having SVD, 11.4% having DVD and less than 5% as having TVD, leaving around 36% as normal.<sup>15</sup> A study from Poland revealed 61.9% as having SVD and 34.7% having multivessel (DVD and TVD) disease, with 37.1% of the possible CAD patients turning out to have normal CAG, and 16.9% of ACS patients having normal CAG findings.<sup>12</sup> In our study involving almost entirely of a high-risk group of patients with

definite IHD, there was a comparatively higher number of TVD patients and a low number of Normal CAG findings. A recent review, however, reported that in young adults, normal CAGs are found in 10-21% of patients,<sup>16</sup> which matches the findings of normal or near normal CAG in our patients.

In previous two relevant reports from Bangladesh, involvement of LMCA, LAD, LCX and RCA were found to be 6, 38, 36 and 40 percents<sup>4</sup> and 0, 33.3, 30, and 31.7 percents<sup>9</sup> respectively. In our study, LMCA disease was found in 1.43%, LAD involvement was relatively high compared to the above studies at 67.14%, while LCX and RCA involvement were comparable at 42.14% and 40.71% respectively. Studies from other subcontinental countries show similar results – 0, 74.40, 44.25 and 47.54% respectively from Nepal<sup>14</sup> and 2, 68.7, 34.7 and 34.85 respectively from India<sup>10</sup>; moreover, results from more developed Asian country are also comparable - 1.7, 79.2, 44.4 and 53.4% respectively from Taiwan<sup>5</sup>. With respect to Double Vessel diseases, data from the subcontinent are scarce. However, results two similar studies show that the combinations of LAD+LCX, LAD+RCA and LCX+RCA occurred at 12, 6.7 and 4% respectively in a study from Odisha, India<sup>10</sup> composed exclusively of acute coronary syndrome patients, while another study from Nepal among patients exclusively of acute myocardial infarction but to a slightly higher age group of up to 45 years, the incidences were 18.4, 10.7 and 7.6% respectively for combined LAD+LCX, LAD+RCA involvement. Our findings among patients with a similar clinically identified ischemic heart disease patients are comparable (LAD+LCX 12.86%, LAD+RCA 7.86%, LCX+RCA 5%) to the above findings.

Coronary angiography in young patients is not done routinely, and is almost exclusively driven by significant clinical events, and reveal an alarming level coronary artery disease burden in terms of extent and severity of involvement. Studies with detailed analysis of the specific secondary arterial/epicardial major branch involvement among the three principle coronary artery trunks are hard to come by. We attempted such a detailed analysis because it can be done with ease and furnishes a broader perspective on coronary artery lesion

distribution relevant to decisions regarding the immediate as well as long term management of such patients. In our study, we found a significant level of involvement of major (i.e., luminal diameter > 1.5 mm) branches in all three of the coronary artery territories. In the LAD territory, of the 94 patients with significant disease, 46(48.94%) had one or more branch involvement along with main trunk disease; and among these 46, overall distribution of disease was as follows - Septal branches in 9(6.43%), Diagonal branches in 40(28.56%) and multiple branches in 10(7.14%) patients. In the LCX territory, of the 59 patients with significant stenosis, 34 (56%) had branch disease while 25(42.37%) had main trunk involvement only. Of these branch lesions, 20(14.28%) of the overall cohort had branch lesions only – 15(10.71%) in OM branch and 05(3.57%) in Ramus Intermedius branch. Multiple branch involvement was seen in 05(3.57%) and branch along with main LCX trunk involvement in 13(9.29%) patients. The RCA territory had major side branch involvement in 23(40.35%) of the 57 patients with significant disease – 07(5%) with one branch only, 08(5.71%) with multiple major branches and a total of 16(11.42%) having one or more major branch involvement along with a main trunk lesion. Overall, 23(16.43%) of the whole cohort of patients had multiple branch involvements in the three coronary artery territories. It may be mentioned that insignificant stenosis (25 to <50% diameter stenosis) was also seen in any of the main coronary artery trunks in 14(10%) patients and any of their branches in 04(2.86%) of patients, while minor (<25% diameter stenosis) was seen 36(25.71%) patients, most commonly in the RCA territory -18 patients (12.86%).

The clinical implication of such widespread disease among such a young age group of ischemic heart disease patients has important prognostic implications. For example, in the Validation of the Residual Syntax Score Study, a residual SYNTAX (rSS) score of 4 or more – indicating incomplete revascularization and left-over stenosis outside the scope of coronary intervention or bypass surgery – was associated with higher 5 year cardiovascular and all-cause mortality and morbidity,<sup>18</sup> and has been shown to have high morbidity and mortality even on extended follow up of up to 10 years,<sup>19</sup> a

fact especially relevant to the young patients of our study. In a recent report of STEMI patients undergoing primary percutaneous coronary intervention, even in single vessel coronary artery disease patients, a residual SYNTAX score of 0-7 and >7 was seen in 27.6% and 6.7% patients respectively, suggesting a significant burden of left-over lesions. The study found a significantly higher adverse cardiovascular morbidity and mortality among both groups compares to patients with 0 rSS score over a follow up period of over 4 years.<sup>20</sup> Furthermore, the presence of insignificant and minor atherosclerotic plaques suggest that associated microvascular diseases cannot be ruled out altogether in these 73 (52.14%) patients with multiple lesions overall. Considering the young age of the patients in this study, the long-term adverse morbidities and increased mortalities will have devastating effects on their personal as well as the families and have a large toll on the society. Taken together, these imply that in addition to maximizing revascularization efforts, further long-term follow-up, enhanced and intensified medical management are mandated, in addition to efforts for earlier detection and primary prevention efforts on a large scale.

### **Conclusion:**

Coronary artery disease is a growing problem worldwide and is becoming so in the subcontinent too. More patients in the younger age groups are presenting with ischemic heart disease and are discovered to have significant as well as widespread coronary artery disease, portending grave adverse prognosis and burden on society because of the longer life ahead of them. Greater efforts and broader long-term strategies are required over and beyond reperfusion/ revascularization in this young age group.

### **Limitations of the study:**

Our study included only 140 patients; larger studies with pooled data from the different tertiary centers caring for young CAD patients are needed. We did not attempt any physiological study on the coronary lesions for decision regarding significance of borderline lesions. We did not use any professional QCA software for our angiographic analysis. The visual and native quantitative analysis programs on board the angiography machines also may have confounded our analysis.

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**Conflict of Interest - None.**


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