Original Article

DOI: 10.7860/JCDR/2024/67673.19415

Risk Factors and Angiographic Syntax Score among Young Adults and Middle-aged Patients with Acute Coronary Syndrome: A Cross-sectional Study

Internal Medicine Section

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ABSTRACT

Introduction: Cardiovascular Disease (CVD) has become a major clinical and public health problem, with an increasing incidence and prevalence, particularly among the young adult population. Although there are well-established prevention strategies for reducing the incidence of Coronary Artery Disease (CAD), their effectiveness is diminished by several risk factors.

Aim: To investigate traditional and lifestyle CVD risk factors in young adults (18-30 years) and middle-aged (31-45 years) patients and to correlate them with the angiographic profile using the syntax score in these patients.

Materials and Methods: The study was designed as a cross-sectional study conducted at the Cardiology Department, Sri Venkateswara Institute of Medical Sciences (SVIMS), Tirupati, Andhra Pradesh, India, a teritary care teaching hospital during the period of August 2021 to July 2022. A total of 87 patients were included based on the study criteria. The study population was divided into two groups: Group-I (18-30 years) and Group-II (31-45 years). After obtaining informed consent, details regarding coronary risk factors such as smoking, Diabetes Mellitus (DM), hypertension, dyslipidaemia, obesity, family history of CAD, and details including physical inactivity were recorded. Coronary Angiography (CAG) was performed to determine obstructive coronary lesions, and the syntax score was calculated. All the collected data were recorded in Excel spreadsheets, and statistical analysis was carried out using Statistical Packages for Social Sciences version 25.0 software.

Results: A male preponderance was observed in the study population (84%) with a mean age of 38.7±5.5 years, and the youngest patient was a 19-year-old female. The majority of patients, 79 (90.8%), were in the middle-age group. Dyslipidaemia (94%) was the predominant modifiable risk factor in the study population ($p<0.05$), followed by obesity (65.5%). About half of the patients had smoking as the predisposing risk factor for CAD. The majority of patients presented with ST Elevation Myocardial Infarction (STEMI) (76.9%). Single Vessel Disease (SVD) was the most common finding (70.1%), and the common culprit vessel was the Left Anterior Descending (LAD) artery (24.1%). The angiographic syntax score was low (<16) in 70 (80.5%) of the patients, with only 6 (7%) of the patients having a higher syntax score (>22). The correlation of the mean syntax score with risk factors has shown an association with obesity (10.6), physical inactivity (10.6), followed by diabetes (10.5).

Conclusion: The study showed that middle age, male gender, and lifestyle risk factors including dyslipidaemia, obesity, physical inactivity, and smoking seem to correlate with angiographic lesions and CAD incidence. Therefore, the inclusion of healthy lifestyle changes such as regular physical activity and the control of modifiable risk factors, including smoking cessation, in this vulnerable middle-aged group is warranted.

Keywords: Coronary artery disease, Coronary angiography, Dyslipidaemia, Obesity

INTRODUCTION

Early onset of CAD is increasing over the past few decades. It is more prevalent in South Asians than in the Western population [1]. The underlying pathogenicity for the early incidence of CAD, especially in South Asians, is not fully understood [2]. Most of the knowledge about risk factors for CAD has been acquired from Western studies [3-5], and only limited data is available from India. Reports have revealed that risk factors for CAD among Asian Indians are 3-4 times higher than in other populations. Moreover, a conservative calculation ascertains that about 30 million CAD patients are expected in India [6,7]. The most concerning aspects of early CAD incidence are the increasing trend of Acute Myocardial Infarction (AMI), hospitalisation, and death rates [8]. The key drivers of CAD are mostly one or more modifiable risk factors like diabetes, dyslipidaemia, hypertension, and smoking. In Indians, the risk of developing CAD appears at a young age, and women also have a similar risk to that of men. Previous studies have shown that certain risk factors such as family history, obesity, dyslipidaemia, and the use of tobacco products are more potent predictors of outcomes of CAD in young individuals than in older counterparts [9,10]. Currently, most of the CVD risk profile assessments use age-old risk calculation tools that have been shown to underestimate the risk in young patients [11,12]. In addition to the traditional risk factors, the presentation of STEMI in young patients (35 years) was observed to be interconnected with abuse habits and non-convential risk factors. CAG data from a previous study indicate a preponderance of SVD or non-obstructive CAD in very young patients suffering from Acute Myocardial Infarcton (AMI) [13]. However, differences in the inherent characteristics of Acute Coronary Syndrome (ACS) presentation and CAG findings in young patients have not been studied compared to the elderly ACS patient population. This suggests the need for detailed risk assessment and improved identification of high-risk patients for early intervention [4]. Therefore, it is important to assess the risk profile in young patients presenting with CAD. The study aimed to investigate angiographic characteristics through syntax score calculation and correlate them with the risk factor profile of the ≤45 years of age CAD patients presenting to the tertiary healthcare center.

MATERIALS AND METHODS

It was a cross-sectional study carried out at the cardiology department, Sri Venkateswara Institute of Medical Sciences (SVIMS),

Tirupati, Andhra Pradesh, India, a tertiary care teaching hospital during the period of August 2021 to July 2022. The study was approved and accepted by the Institutional Ethics Committee (IEC) with the registration number Roc.No. AS/12/TPAC/SVIMS/2017. All the patients were explained about the study, and written informed consent was obtained from the study population.

Sample size calculation: Sample size was calculated by using the standard formula with the Confidence Interval (CI)

$$\text{Sample size}=\frac{Z_{1-\alpha/2}{}^2 p(1-p)}{d^2}$$

95%, error 5% (0.05), and the cardiac risk score in young-middle aged (20-59 years) with border line score was taken as 6% (0.06) [14].

Where,

$Z_{1-\alpha\ a/2}$=standard normal variate at 5% type 1 error=1.96

p=Cardiac risk score 6%

d=Absolute error or precision=5%

Inclusion criteria:

- Acute ST elevation myocardial infarction (STEMI)
- Non ST elevation myocardial infarction (NSTEMI)
- Unstable Angina (USA)
- Chronic stable angina.
- Patients aged between 18 and 45 years of both genders.
- Patients willing to participate.

Exclusion criteria:

- Patients aged >45 years
- Patients who underwent Percutaneous Coronary Intervention (PCI) or Coronary Bypass Surgery (CABG) previously.
- Previous Myocardial Infarction (MI)

Study Procedure

Detailed demographic and clinical data, including the history of smoking, diabetes, dyslipidaemia, hypertension, obesity, details of physical inactivity, and family history of CAD, were documented. All the patients were subjected to routine haematological and biochemical investigations, including troponin-I (0-0.04 ng/mL), HbA1c (<5.7%), fasting lipid profile (70 mg/dL-100 mg/dL). They were evaluated with electrocardiogram (ECG) and echocardiogram examinations. The study population was divided into two groups: Group-I: 18-30 years (young age); and Group-II: 31-45 years (middle age).

Coronary Angiographic (CAG) analysis: CAG was performed using standard percutaneous techniques either via the femoral or radial route after Allen's test. CAG was performed based on the American College of Cardiology/European Society of Cardiology indications for CAG [12].

Syntax score: The angiographic profile was obtained by calculating the syntax score. Each coronary lesion with a >50% luminal obstruction in vessels >1.5 mm is scored separately, and the scores were summed to provide the overall syntax score. Syntax score was calculated by a computer program consisting of sequential and interactive self-guided questions. The algorithm consists of twelve main questions. They can be divided into two groups: The first three determine the dominance, the total number of lesions, and the vessel segments involved per lesion, and they appear once. The last nine questions refer to adverse lesion characteristics and are repeated for each lesion. Angiographic severity was assessed in at least two orthogonal views using eye-balling, and the syntax score was calculated [15].

STATISTICAL ANALYSIS

Descriptive statistics for the categorical variables were performed by computing the means and frequencies in each category. Continuous variables were expressed as mean±Standard Deviation (SD). A 95% Confidence Interval (CI) was estimated, and a global significance level of α=5% was chosen. A p-value ≤ 0.05 was considered significant. Statistical Package for the Social Sciences (SPSS software version 25.0) was used.

RESULTS

Among the 87 patients included in the study, the majority were males (n=73). The mean age of the study population was 38.7±5.5 years. In both genders, the mean age of males and females was 39.2±4.9 and 36.7±7.7 years, respectively. Most patients, 79 (90.8%) were in the age group of 31-45 years (Group-II). Group-II was observed to be the predominant age range among patients. The mean age of this group was 40.11±3.5 years [Table/Fig-1].

Age distribution N=87, (18-45 years)	Frequency n (%)	Mean±SD	Significance
18-30 years	08 (9.1%)	25.62±4.3	p<0.05*
31-45 years	79 (90.8%)	40.11±3.5	

[Table/Fig-1]: Age distribution of patients (N=87).
Note: "*"Asterisk mark indicates the statistical significance; Student's t-test

The prevalence of dyslipidaemia was predominant in patients, accounting for 94% (n=82), with Group-II constituting 88.5%. High Density Lipid (HDL) cholesterol levels were low in most patients (65.5%), followed by higher levels of triglycerides (61%). Obesity was observed in 57 patients (65.5%). These findings suggest a concurrent relationship between lifestyle and traditional risk factors. Diabetes and hypertension were found to be secondary traditional risk factors in this population, accounting for 34.5% each. Young patients (Group-I) (aged 18-30 years) were less likely to have hypertension and diabetes. Most risk factors, including dyslipidaemia, obesity, hypertension, and diabetes, were observed predominantly in Group-II, comprising middle-aged patients, and showed a significant difference compared to young-aged patients (p<0.001) [Table/Fig-2]. The majority of patients, 67 (76.9%), presented with STEMI, and chest discomfort was the most reported complaint in 83 patients (95%). Among the STEMI patients, 45 (51.7%) presented with Anterior Wall Myocardial Infarction (AWMI), and 30% of patients were thrombolysed [Table/Fig-3].

Characteristics	Total population N=87 n (%)	18-30 years n (%) (n=08)	31-45 years n (%) (n=79)	p-value
Gender, Male	73 (84)	4 (4.6)	69 (79.3)	p<0.0001
Diabetes Mellitus (DM): FBS >100 mg/dL	30 (34.5)	1 (1.1)	29 (33.3)	p=0.06
Hypertension: >120/80 (mmHg)	30 (34.5)	0	30 (34.5)	p<0.05
Smoking	43 (50.0)	3 (3.4)	40 (46)	p<0.05
Obesity: BMI >30.0	57 (65.5)	3 (3.4)	54 (62)	p<0.001
Dyslipidaemia	82 (94.0)	5 (5.7)	77 (88.5)	p<0.05
Physical inactivity	27(31)	8 (9.2)	19 (21.8)	p=0.4
Family history	14 (16.0)	2 (2.3)	12 (13.8)	p=0.3
Total Cholesterol >200 mg/dL	32 (37)	2 (2.3)	30 (34.4)	p=0.06
Triglycerides >150 mg/dL	53 (61)	5 (5.7)	48 (55.1)	p<0.05
LDL-Cholesterol >100 mg/dL	26 (30)	2 (2.3)	24 (27.6)	p=0.1
HDL-Cholesterol <50 mg/dL	57 (65.5)	6 (6.9)	51 (58.6)	p<0.05

[Table/Fig-2]: Demographic and baseline characteristics in groups (N=87).
FBS: Fasting blood sugar; BMI: Body mass index (kg/m^2); LDL: Low density lipid; HDL: High density lipid Student's t-test

The angiographic findings revealed that most patients (67.8%) had obstructive CAD (>70% stenosis), with the LAD artery being the most common culprit vessel, and 32.2% had non-obstructive CAD

Characteristics	Total population N=87 n (%)	18-30 years n (%) (n=08)	31-45 years n (%) (n=79)	p-value
AWMI	45 (51.7)	1 (1.1)	44 (50.6)	p<0.05*
IWMI	22 (25.3)	2 (2.3)	20 (22.3)	p=0.1
NSTEMI	15 (17.3)	3 (3.4)	12 (13.8)	p=0.4
USA	05 (5.7)	0	05 (5.7)	p=0.4
Chest pain	83 (93)	8 (9.2)	75 (86.2)	p<0.0001*
Dyspnea	19 (21.8)	5 (5.7)	14 (16)	p=0.4
Troponin-I (0-14 ng/L)	79 (90.8)	7 (8)	72 (82.8)	p<0.0001*
Ejection Fraction, (EF%) (50-70%)	56 (64.4)	6 (6.9)	50 (57.5)	p<0.05*

[Table/Fig-3]: Clinical and echo findings of the patients (N=87).
Notes: AWMI: Anterior wall myocardial infarction; IWMI: Inferior wall myocardial infarction; NSTEMI: Non ST elevation myocardial infarction; USA: Unstable angina
"*"Asterisk mark indicates the statistical significance
Student's t-test

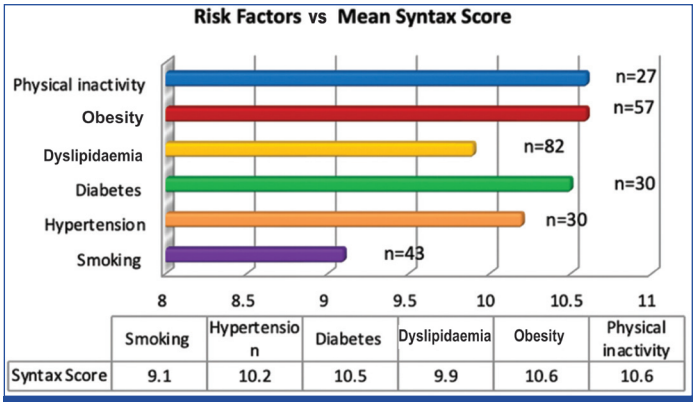
[Table/Fig-4]. The mean syntax score of present study population was 9.6±6.7. The majority of patients, especially in Group-II, had a low syntax score of 6.8±3.7. A syntax score above 22 was observed in only six patients [Table/Fig-5]. The correlation of the mean syntax score with risk factors showed an association with obesity (10.6), physical inactivity (10.6), followed by diabetes (10.5) [Table/Fig-6].

Variables	Number	Percentage
Obstructive Coronary Artery Disease (CAD)	59	67.8%
Single vessel disease 34		
LAD	21	24.1%
LCX	9	9.2%
RCA	4	4.6%
Double vessel disease 14		
LAD, LCX	3	3.4%
LAD, RCA	9	10.3%
LCX, RCA	2	2.3%
Triple vessel disease 11		
LAD, LCX, RCA	11	12.6%
Non-obstructive CAD	28	32.2%
LAD	6	6.9%
Spontaneous dissection of RCA	3	3.4%
Normal Coronaries	14	16.0%
LCX	5	5.7%

[Table/Fig-4]: Coronary Angiographic (CAG) characteristics of the patients (N=87).
LAD: Left descending artery; LCX: Left circumflex artery; RCA: Right coronary artery

Syntax score	Total population N=87, Mean±SD (n)	18-30 years (n=08) Mean±SD (n)	31-45 years (n=79) Mean±SD (n)
Mean Syntax score	**9.6±6.7 (87)**	**7.3 ±6.8 (8)**	**9.9±6.8 (79)**
Low <16	6.85±3.3 (70)	7.3±6.8 (8)	6.8±3.7 (62)
Intermediate (16-22)	18.3±1.6 (11)	00	18.3±1.6 (11)
High (>22)	23.8±1.9(6)	00	23.8±1.9 (6)

[Table/Fig-5]: Syntax score grading in the groups.



[Table/Fig-6]: Risk factors and mean syntax score in patients.

DISCUSSION

The ACS is a life-threatening condition characterised by coronary artery narrowing and thrombus formation. It is reported that the majority of young MI patients have at least one of the cardiovascular risk factors [16]. Young patients have different characteristic features and risks for CAD compared to older patients. Over the past three decades, the prevalence of CV risk factors, including smoking, diabetes, hypertension, and dyslipidaemia, has markedly increased in India [17]. There are few age-related studies reporting the risk factors and angiographic profile in CAD patients [13,18,19], but there are very few Indian studies evaluating risk factors in association with the angiographic syntax score [16,20]. Therefore, in present study, authors aimed to assess the relationship between risk factors and the severity of the angiographic syntax score. Since there is no universal age cutoff to define young age (<45 years) [21,22], we have divided the ACS patients into two groups (18-30 years (Group-I) as young and 31-45 years (Group-II) as middle-aged).

In present prospective study, the majority of patients comprised middle-aged patients (31-45 years, Group-II). A study by Morillas P et al., reported that 25% of AMI cases in India occur under the age of 40 and 50% under the age of 50 years [23]. Older age alone was a strong independent risk factor for the incidence of CAD, as evident in present findings. Most patients were observed under Group-II, indicating that increased age is a risk factor for developing co-morbidities and the severity of CAD. It is clear that Group-II patients were more likely to experience CV morbidity than the younger population.

An individual's lifestyle has a significant influence on the predisposition to CAD. Dyslipidaemia was found to be present in 82 (94%) of patients, with low HDL-cholesterol, high LDL, and triglyceride levels. A study by Akanda MAK et al., reported the prevalence of dyslipidaemia in about 60% of patients, indicating the risk of atherosclerotic lesions [24]. Additionally, Sinha SK et al., reported that the frequency of dyslipidaemia data from different studies ranged from 20-80% [13]. Similarly, a recent study revealed that atherosclerotic disease severity was largely influenced by dyslipidaemia (80%) in young adults [25]. Recent research has explained the importance of inherent biological differences in lipid and glucose metabolism, inflammatory states, genetic predispositions, and epigenetic influences on the increased risk [26]. These findings are consistent with this study, which reported 88.5% of dyslipidaemia patients. Based on this, it is recommended to follow a nutritional and balanced diet based on BMI to increase HDL-C levels.

Most of the patients in Group-II (62%) were found to be obese with a BMI of >30. Lakka HM et al., (in their study) have acknowledged that central obesity is an independent risk factor in middle-aged ACS male patients in connection with smoking and increases the risk of coronary events by 5.5 times [27]. There appears to be a significant association between dyslipidaemia and obesity, as most obese patients were found to be dyslipidemic. The findings of the present study are consistent with previous studies that show clustering of key cardiovascular risk factors predominating the risk in young patients with CAD [28,29]. A recent study by Kumar V et al., revealed that the prevalence of obesity was only 33.3% in young STEMI patients, which was consistent with the AMIYA study [16]. The higher rate of obesity in present study can be attributed to the inclusion of ACS (STEMI, NSTEMI, and USA) patients. It can be inferred that a sedentary lifestyle and physical inactivity have a significant influence on the development of CAD. A recent review suggests that primordial preventive measures at an early age should be followed by adopting healthy lifestyle changes such as a good diet, yoga, and meditation. Therefore, it is necessary to engage in regular physical activity to ensure heart health [30].

Cigarette smoking is a well-recognised behavioural risk factor for CAD morbidity and mortality. Among present study population, smoking habits were present in 50% of Group-II patients. However, the prevalence of smoking in these patients was lower compared to the study by Lakka HM et al., which comprised 78.5% of the population [27]. Hypertension and diabetes accounted for 34.5%, which was consistent with the South Asian cohort of the INTERHEART study (31.1%), as the population subgroup was different [31].

The CAG data showed that most patients had obstructive CAD (vessel lumen stenosis ≥70%) in 67.8% of cases. SVD had a higher frequency followed by double and triple vessel disease. These findings are consistent with the studies by Saghir T et al., and Hong MK et al., [32,33]. Among patients with single-vessel disease, the artery LAD was the most common infarct-related artery (47.1%), while the LCX was involved in 11.5% and the RCA in 10.3%. Similarly, Badran HM et al., and Al-Mayali AH et al., also found a similar distribution of lesion arteries in the angiographic profile [7,34]. The low prevalence of double vessel disease suggests that extensive coronary involvement is not a common finding in young adults presenting with ACS. Available literature also indicates that young adults with ACS are characterised by less extensive coronary disease, mainly in the single-vessel form [7,35].

The angiographic Syntax score is a valuable tool for scoring lesions that has been used to assess the severity and complexity of CAD in order to determine the appropriate revascularisation strategy [15,36]. It is used not only for identifying luminal stenosis but also for assessing plaque vulnerability, which is an important aspect of coronary artery anatomy in patients with acute STEMI [37]. In present study, the mean Syntax score of the study population was 9.6±6.7. The majority of patients (n=70) had a low Syntax score (<16), and only 7% of patients had a high Syntax score (>22). Although there was no significant relation between coronary lesion grade and risk factors, upon correlating with the mean Syntax score, physical activity, obesity, and diabetes were found to be associated with coronary lesion grade. The difference in the grading of angiographic lesions can be attributed to poor functional capacity in these patients, as reported in the study by Tang WHM et al., [38]. Recent studies have reported that the Syntax score can serve as an independent predictor of both morbidity and mortality in MI patients [37,39,40]. Therefore, the Syntax score in these patients can be used to predict future risk and long-term prognosis.

Cameron SJ et al., have reported a case study where the risk and severity of CAD are lower in patients with a healthy lifestyle [41]. Also, recent studies emphasise the importance of focusing on lifestyle factors in addition to conventional risk factors for CAD, as they play a crucial role in the pathways of CVD. Kalra A et al., have reported that adopting a multifaceted and universal approach to CVD prevention involves controlling risk factors in different population groups [26]. Therefore, it is recommended to focus on lifestyle modifications, including a healthy diet and regular physical activity, for effective prevention of early CAD risk in young to middle-aged patients [38,42].

Limitation(s)

There was no control group, so the statistical significance of each risk factor could not be analysed. Being an observational study, certain confounding variables may have played a role. Factors such as a family history of coronary heart disease may have introduced bias. Novel risk factors were not evaluated. This was a single-centre study, and authors only analysed patients who reached the hospital, so it may not be a true representative of the population. Therefore, the results cannot be generalised to the community. Like in many other studies, authors used eye-balling to grade angiographic stenosis.

CONCLUSION(S)

The present study showed that CAD in young individuals occurred predominantly in males with hypertriglyceridemia, obesity, and a history of smoking as commonly occurring risk factors. The rapid changes in lifestyle, unhealthy habits such as smoking, sedentary lifestyle, and dietary factors are considered to be responsible for the increase in CAD in young adults. The incidence of critical CAD at a young age leads to the loss of workdays, transition from an active to a sedentary working life, and decreased efficiency. Therefore, greater emphasis should be placed on lifestyle modifications such as smoking cessation and regular physical activity for the primary prevention of MI in the young population, which is the best way to decrease mortality and morbidity related to ACS.

Acknowledgement

The authors would like to acknowledge the contrubution of the Departments of Cardiology and Biochemistry at Sri Venkateswara Institute of Medical Sciences, Tirupati.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Sep 23, 2023
- Manual Googling: Feb 24, 2024
- iThenticate Software: Mar 14, 2024 (12%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Sep 23, 2023**
Date of Peer Review: **Dec 14, 2023**
Date of Acceptance: **Mar 18, 2024**
Date of Publishing: **May 01, 2024**