# Relevance of Syntax Score as a Marker of Complex Coronary Artery Disease and Plaque Burden in Young Coronary Artery Disease - A Single Centre Multifactorial Analysis

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## ABSTRACT

## BACKGROUND

Coronary Artery Disease (CAD) occurring in < 45 years of age is termed as young CAD. The prevalence of CAD in this age group among Indians is 5-10%, which is higher than the western average of 1.2%. Smoking is the most critical risk factor in young CAD. Two factors associated with adverse prognosis are current smoking and obesity. Angiographic studies have shown predominantly single-vessel disease and lesser atheroma burden.

## METHODS

It is a retrospective study conducted among young CAD adults aged between 20-45 years admitted for the acute coronary syndrome (ACS). We wanted to analyse the severity and extent of CAD by correlating with SYNTAX score and prevalence of conventional cardiovascular risk factors among those young Coronary Artery Disease patients.

#### RESULTS

In this study, 100 patients (83% male and 17% female), with a mean age of 39.9 years were included. Diabetes mellitus, hypertension, dyslipidaemia, hypothyroidism and history of young CAD and myocardial infarction were all positively related with a higher SYNTAX score (18%) but were statistically insignificant due to relatively small sample size. Ejection fraction was lower in patients with higher syntax score (>20%).

## CONCLUSIONS

In young CAD undergoing coronary angiography, non-modifiable cardiovascular risk factors such as male sex, as well as other risk factors like hypertension, hypothyroidism, and dyslipidaemia, were independently associated with CAD complexity as assessed by SYNTAX score. SYNTAX score may be a valid marker for CAD to establish relationships with potential risk factors of coronary atherosclerosis.

#### **KEY WORDS**

SYNTAX Score, Hypertension, Type 2 Diabetes Mellitus, Hypothyroidism, Dyslipidemia, Coronary Angiography, Coronary Artery Disease

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## BACKGROUND

Acute Coronary Syndrome (ACS) has increased morbidity and mortality in developed countries in recent years with growing health care costs. Whereas, in developed and developing countries, the leading cause of morbidity and mortality is Coronary artery disease (CAD). World Health Organisation reported that burden due to CAD is increasing globally from 47 million to 82 million in 2020. Among which young CAD contributes to 2-6% of all ACS.<sup>[1]</sup> Recently, one of the significant issue cardiologists addressing in risk stratification in patients with ACS was to study the severity and complexity of CAD.<sup>[2]</sup> A large number of scoring systems and laboratory parameters are in clinical practice to assess the severity and complexity of CAD. The most commonly used method is the SYNTAX.

SYNTAX is a significant scoring system predicting the prognosis and the need for revascularization. Also, it can determine the extent and severity of CAD.<sup>[3]</sup> The SYNergy between the percutaneous coronary intervention (PCI) with Taxus and cardiac surgery (SYNTAX) score calculated the complexity of CAD based on invasive coronary angiography (ICA).<sup>[3]</sup> The SYNTAX score can predict major adverse cardiac and cerebrovascular events (MACCEs) in populations with complex CAD (LM disease or 3-vessel disease).[4] It guides the optimal revascularization strategy. Among patients with complex CAD, Coronary artery By-pass grafting (CABG) remains as the standard of care for patients with high ( $\geq$ 33) or intermediate (23-32) SYNTAX scores, whereas PCI is an acceptable alternative in patients with the less complicated disease (SYNTAX score 22).<sup>[5]</sup> Although the scoring system has a large number of advantages, it requires an invasive method such as coronary angiography for performing the scoring. The Coronary Angiogram findings predict cardiac events and mortality in patients with CAD.<sup>[6,7]</sup> In this retrospective study on young CAD adults of age between 20-45 years with firsttime myocardial infarction, we analysed the severity and extent of CAD with syntax score and prevalence of conventional risk factors among those young CAD. The primary objective is to determine the severity of CAD among young CAD by correlating with syntax score. Other goals were to characterize the presence of cardiovascular risk factor among young patients admitted with myocardial infarction (MI) and to describe the coronary angiogram findings among young individuals with MI.

## METHODS

Patient Data collected from Sri Ramachandran Medical University database. The patients of both sex with age < 45 years, admitted with the acute coronary syndrome and have undergone coronary angiogram from January 2018 to January 2019 included in the study. Patients with raise or fall of cardiac biomarker > 1 value above the upper reference range, symptoms suggestive of ischemia, significant ST-T wave changes / LBBB, pathologic Q in ECG, image evidence of loss of viable or new RWMA and intracoronary thrombus by CAG included. The patients with known CAD, before MI/ PCI / CABG, severe renal dysfunction, myositis, acute PTE, stroke excluded from the study. Demographic and cardiovascular risk factors data collected from the medical records.

Hypertension is said to be present when systolic blood pressure was  $\geq$ 140 mmHg and/or diastolic blood pressure  $\geq$ 90 mmHg or if patients is on antihypertensive medications. Diabetes considered present if the subject if fasting blood glucose was  $\geq$ 110 mg or postprandial blood glucose  $\geq$ 140 mg at admission or treated with insulin or oral hypoglycaemic drugs. Dyslipidaemia defined as total cholesterol >200 mg/dl, low-density lipoprotein (LDL) cholesterol >130 mg/dl or on lipid-lowering medications.

#### **Coronary Angiography**

Details of coronary angiogram were obtained from cardiac catheterisation laboratory records and were evaluated. Coronary angiography (CAG) was performed on all our patients by either femoral or radial approach. A 6 F diagnostic catheter and iopromide as a contrast agent (Ultravist-370, Bayer Schering Pharma, Germany) was used in all subjects. A diameter of stenosis calculated as  $\geq$  50% with quantitative angiography accepted as significant. SYNTAX score was used to define the coronary atherosclerotic lesion. SYNTAX score calculated by two of three experienced cardiologists blinded in the study. If there was any controversy, the opinion of the third cardiologist was asked, and the last conclusion made with consensus. All coronary lesion with 50% diameter stenosis or more in arteries of at least 1.5 mm were scored. To assess the SYNTAX score most recently updated version used for the calculation (http://www.SYNTAXscore.com). SYNTAX score > 20 defined as high SYNTAX scores.

#### **Statistical Analysis**

Statistical analyses performed by SPSS (version 15.0, SPSS, Chicago, Illinois, USA). Quantitative variables expressed as the mean  $\pm$  standard deviation. Between-group differences of the categorical variable were analysed using the Chi-square test and the Student t-test for continuous variables. P-value < 0.05 was considered statistically significant.

## RESULTS

This retrospective study included data of 100 patients diagnosed with ACS and aged between 20 years to 45 years. Demographic data revealed ACS prevalence of 51%, 48% and 01% in patients between age group 31-40, 40-45, and 20-30, respectively. There was male preponderance in the prevalence of ACS with 83% in this study. Most of the study subjects (82%) had a SYNTAX score of  $\leq 20$  (Syn  $\leq 20$ ) and 18% exhibited SYNTAX score of  $\geq 20$  (Syn  $\geq 20$ ) [Table 1].

## CAG SYNTAX Score and Prevalence of Risk Factors

SYNTAX scores of ACS patients obtained from CAG findings categorized as Syn  $\leq$  20 and Syn > 20. The Syn  $\leq$  20 seen in 82 patients, which included 67 males and 15 females with a mean age of 39.58 years. The Syn > 20 seen in 18 patients, which included 16 males and two females with a mean age of 41.33 years. The gender distribution, mean age range between the two categories of SYNTAX scores were comparable and statistically insignificant the prevalence of risk factors associated between the two categories of SYNTAX scores

evaluated with the chi-square test. Prevalence of T2DM seen in 22 patients with Syn  $\leq$  20 and five patients with Syn > 20. History of dyslipidaemia seen in 10 patients with Syn  $\leq$ 20 and six patients with Syn > 20. Hypothyroidism reported by three patients with Syn  $\leq$  20. Hypertension diagnosed in 10 patients with Syn < 20 and 5 patients with Syn > 20. Totally four patients were smoking history, and all had syntax score  $\leq$ 20. Mean left ventricle ejection fraction was seen decreased in Syn > 20 when compared to Syn  $\leq$  20, but statistically insignificant (p-value = 0.07) [Table 2].

Sl. No.	Characteristics	Frequency (n)	Percentage (%)		
	SYNTAX Score				
1	≤20	82	82		
	>20	18	18		
	Sex				
2	Male	83	83		
	Female	17	17		
	Age				
2	20-30	01	01		
3	31-40	51	51		
	41-45	48	48		
Table 1 Patient Characteristics of the Study Group					

Sl. No.	<b>Risk Factors</b>	SYNTAX Score ≤20	SYNTAX Score >20	р		
1	Male (n)	67	16	0.825		
2	Female (n)	15	2	0.527		
3	Age (Mean ± SD)	$39.58 \pm 4.21$	41.33 ± 3.08	0.482		
4	T2DM (n)	22	5	0.984		
5	Hypothyroidism (n)	3	0	0.418		
6	HTN (n)	10	5	0.166		
7	DLP (n)	10	6	.0738		
8	LVEF (%) (Mean ± SD)	54.87 ± 9.84	49.64 ± 13.56	0.075		
9	Smoking	4	0	0.491		
Table 2. SYNTAX Scores and Prevalence of Risk Factors						

## DISCUSSION

Prevalence of Coronary artery disease over the last few decades increased in young age (Below 45 years) due to increase in risk factors in the populations. The prognosis as well as longevity after an acute coronary episode in this age group is varied compared to conventional age. In this study, SYNTAX score was calculated for all patients and the severity of CAD were measured with SYNTAX scores. This study evaluated the relationship between SYNTAX score obtained from CAG and conventional CV risk factors, in young CAD diagnosed with acute coronary syndrome. This study demonstrated a positive correlation of SYNTAX score with age, diabetes mellitus, dyslipidaemia, hypertension, and hypothyroidism. In our study persons with syntax score more than 20 had lower ejection fraction by echocardiogram compared to persons syntax score less than 20. SYNTAX score has become an reliable method to evaluate CAD complexity.<sup>[8,9,10]</sup> SYNTAX score was chosen for this study, due to its strict anatomical based design to assess CAD complexity.<sup>[1]</sup> Despite its limitations<sup>[11]</sup> and criticism in current clinical practice, SYNTAX trial still applies.[12] SYNTAX score used as a surrogate marker which sought to establish correlations of several clinical and biochemical variables with coronary atherosclerosis.[13,14,15] However, the SYNTAX score in this context has not validated correctly. Framingham Heart study and many landmark studies has established the role of age, male gender, diabetes mellitus, hypertension, hypothyroidism, and lipid abnormalities as risk factors for CAD.<sup>[16,17,18]</sup> This study suggests a positive association of these parameters with the complexity of CAD, as expressed through

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SYNTAX score. Male preponderance (83%) might be associated with progressive endothelial dysfunction, occurring earlier in males, presumably due to the protective role of oestrogens in premenopausal women.<sup>(19,20)</sup> In diabetes hyperglycaemia, insulin resistance and free fatty acid release have been shown to lead to increased oxidative stress and therefore accelerate atherosclerosis.<sup>(21,22,23,24,25)</sup> In the present study, 22 of 82 patients had a history of T2DM with SYN≤20, and five of 18 patients had a history of T2DM with SYN>20. The score should be applied for major epicardial coronaries, including mainly coronary lesions located in vessels with diameters >1.5 mm. Therefore, CAD extensiveness in diabetic patients underestimated with this method. Due to prevention strategies, the well-known vascular risk factors like dyslipidaemia or hypertension not associated with the score. Lack of correlation is mainly due to prior treatment with statins to reduce the concentration of LDL-c, triglyceride, Apo-B, increase in HDL-c and treatment with angiotensin-II receptor blocking agents to lower the rate of plaque burden and coronary atheroma progression.(26,27) As mentioned above, the SYNTAX score is used as a surrogate marker of CAD. Variables like fasting blood glucose, monocyte subtypes, red cell distribution width or bilirubin levels were compared with SYNTAX score in the development of coronary atherosclerosis. (28,29,30,31,32) We believe that the demonstrated relationship of 'non-modifiable' risk factors with the complexity of CAD, justifies the use of SYNTAX score in assessing the severity of coronary artery disease in young patients.

## CONCLUSIONS

In young CAD undergoing coronary angiography, nonmodifiable cardiovascular risk factors such as male sex, as well as other risk factors like hypertension, hypothyroidism, and dyslipidaemia, were independently associated with CAD complexity as assessed by SYNTAX score. SYNTAX score seems to be a valid marker of CAD to establish relationships with potential risk factors of coronary atherosclerosis.

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