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Original Article

## Morphological characterization of coronary plaques in young indian patients with acute coronary syndrome: A multicentric study

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## ABSTRACT

**Objectives:** The prevalence of atherosclerosis and acute coronary syndrome (ACS) is increasing in young Indians (18–50 years of age). However, the characteristics of atherosclerotic plaques in such individuals are poorly understood, presenting distinct challenges for the management of ACS. This study aims to analyze plaque characteristics in young Indian patients with ACS who underwent percutaneous coronary intervention (PCI) using optical coherence tomography (OCT) imaging.

**Methods:** This was a prospective, multicentric, non-interventional study on patients aged 18–50 years presenting with ST-elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction, or unstable angina, and were scheduled to undergo OCT-guided PCI. Major adverse cardiac events (MACE) were assessed post-procedure and at the 6-month and 12-month follow-ups.

**Results:** The study included 100 ACS patients (mean age =  $43.6 \pm 5.2$  years), with 51% presenting with STEMI. Pre-PCI OCT assessment showed that fibrous plaques (75%) were most common followed by plaques containing macrophages (27%), microchannels (20%), and calcified nodules (14%). In addition, plaque rupture, plaque erosion, and lipid-rich plaques, along with red, white, and mixed thrombi, were observed in 31%, 25%, 24%, 21%, 14%, and 17% (total thrombus occurrence = 52%) of the patients, respectively. At 12 months, the MACE (coronary artery bypass graft) rate was 1%.

**Conclusions:** Young Indian patients with ACS displayed a range of plaque morphologies identified through pre-PCI OCT. Among these, fibrous plaques were the most prominent type, followed by plaques containing macrophages. Additionally, plaque rupture, plaque erosion, and lipid-rich plaques were also observed in this population.

## 1. Introduction

Acute coronary syndrome (ACS) is a serious cardiovascular condition characterized by diminished myocardial blood flow, primarily caused by thrombi from atherosclerotic plaque rupture (PR) within the coronary arteries.<sup>1,2</sup> ACS manifests in three primary forms: ST-elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction

(NSTEMI), or unstable angina (UA).<sup>3</sup> Both the Million Death Study (India) and Global Burden of Disease (GBD) studies have reported that ACS and ischemic heart disease (IHD) are the most prevalent causes of hospitalization, morbidity, and mortality, posing major public health concerns worldwide and particularly in India, where in-hospital mortality ranges from 5% to 15%.<sup>4–7</sup> While PR is recognized as the main cause of ACS, accounting for 60%–75% of cases, plaque erosion (PE) and

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calcified nodules (CNs) are also known to trigger blood coagulation cascades, resulting in ACS.<sup>8,9</sup> In a study conducted on 298 patients with acute myocardial infarction (AMI), 25% of the cases were found to have PE.<sup>10</sup> Another study that examined blood vessels obtained from 84 autopsied human hearts reported the presence of CNs in 2%–7% of the patients with ACS.<sup>11</sup> Autopsy and imaging studies have revealed that PE and CNs have pathological features that differ from those of PR.<sup>2</sup> However, differentiating between these plaque morphologies requires advanced intravascular imaging techniques, such as optical coherence tomography (OCT).<sup>12,13</sup>

OCT is an intravascular imaging technique that provides high-resolution cross-sectional images of coronary arteries and enables tissue characterization of atherosclerotic plaques to identify PR, PE, and CNs in culprit lesions of patients with ACS.<sup>12,13</sup> OCT capabilities extend to identifying critical plaque features, such as thin-cap fibroatheroma (TCFA), macrophages, cholesterol crystals, and microvessels, which are indicators of plaque vulnerability and are associated with a higher risk of future disruption leading to occlusive thrombosis.<sup>14</sup>

The prevalence of ACS is on the rise among young Indian patients aged below 50 years, a demographic where gaps in cardiovascular care are becoming increasingly evident.<sup>6,7,15</sup> This study, therefore, aimed to gather data on the prevalence of different plaque characteristics in young Indian patients with ACS who underwent percutaneous coronary intervention (PCI) using OCT imaging.

## 2. Methods

### 2.1. Study design and participants

This prospective, multicentric, observational study enrolled 100 young patients aged between 18 and 50 years with ACS from eight different centers in India between January 2018 and September 2022 to report the prevalence of different plaque characteristics. The enrollment of patients was delayed due to the Coronavirus disease-19 (COVID-19) pandemic.

The study was initiated following ethics committee approval from the respective institutes and was conducted in accordance with the

principles of the Declaration of Helsinki and its revisions, the International Conference on Harmonization Good Clinical Practice (ICH-GCP) guidelines, and all other federal and local laws. Written informed consent was obtained from all participants. The study was also registered under the Clinical Trials Registry of India (CTRI/2018/01/011150). The inclusion and exclusion criteria used in this study are shown in Fig. 1.

### 2.2. Study procedures

The patients first underwent coronary angiography, following standard protocols. All the patients who underwent OCT-guided PCI were included in the analysis. OCT was performed using a Dragonfly™ OPTIS™ imaging catheter (Abbott Vascular, Santa Clara, CA, USA). The plaque characteristics were recorded across the length of the treated lesion. Where feasible, FFR was assessed in non-culprit vessels using a Pressure Wire™ X (Abbott Vascular, USA). The patients were followed up at 6 and 12 months. The major adverse cardiac events (MACE) rates, hospitalization events, and revascularization events after the initial PCI were recorded during follow-ups.

### 2.3. Outcomes

The primary outcome of this study was to assess the prevalence of different plaque characteristics in young Indian patients with ACS. The secondary outcome of this study was to evaluate the MACE rate at 6 and 12 months. MACE was defined as the cumulative incidence of myocardial infarction, revascularization, and cardiovascular death.

### 2.4. Statistical analysis

This study was designed to provide preliminary data on the prevalence of different plaque morphologies. As no hypothesis was tested in this study, the sample size was not calculated. Considering a 10 % loss to follow-up and expecting minimum follow-up data for 90 patients, 100 patients were enrolled in the study.

Categorical variables are presented as numbers (percentages), while continuous data are expressed as mean ± standard deviation. Plaque

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> <li>• Patient is ≥18 and ≤50 years of age and going for PCI.</li> <li>• At least ≥1 de novo lesion in a native coronary segment with a visually estimated diameter stenosis ≥40%.</li> <li>• Patient has documented ACS (UA, NSTEMI, or STEMI).</li> <li>• Patient demonstrates an LVEF of ≥30% as measured prior to enrolment.</li> <li>• Patient understands and agrees to comply with all specified study requirements and provides written informed consent.</li> </ul>	<ul style="list-style-type: none"> <li>• Patient has a life expectancy of &lt;12 months due to another medical condition.</li> <li>• Patient exhibits cardiogenic shock (systolic pressure &lt;80 mmHg and PCWP &gt;20 mmHg or cardiac index &lt;1.8 L/min/m<sup>2</sup>; or intra-aortic balloon pump or intravenous inotropes are needed to maintain a systolic pressure &gt;80 mmHg) for any time within 24 hours prior to index procedure.</li> <li>• Patient demonstrates evidence of acute or chronic renal dysfunction (serum creatinine &gt;2.0 mg/dL or 177 μmol/L).</li> <li>• Planned cardiac surgery procedure ≤6 months post-index procedure.</li> <li>• Cerebrovascular accident including stroke or TIA within the last 3 months.</li> <li>• Patient with contraindications to aspirin, clopidogrel, prasugrel, or ticagrelor.</li> <li>• Female of childbearing potential with a positive pregnancy test within 7 days before the index procedure; or lactating; or intends to become pregnant during the 6-month-post-index procedure.</li> <li>• Patient not clinically appropriate for OCT evaluation as per the opinion of the investigator.</li> </ul>

ACS: Acute coronary syndrome; LVEF: Left ventricular ejection fraction; NSTEMI: Non-ST-elevation myocardial infarction; OCT: Optical coherence tomography; PCI: Percutaneous coronary intervention; PCWP: Pulmonary capillary wedge pressure; STEMI: ST-elevation myocardial infarction; TIA: Transient ischemic attack; UA: Unstable angina.

Fig. 1. List of inclusion and exclusion criteria.

morphology between age groups was analyzed using the Fisher's exact test. A *p*-value of <0.05 was considered to be statistically significant. R software (Version 4.3.2) was used to analyze the data.

### 3. Results

#### 3.1. Baseline and clinical characteristics

Of the 100 ACS patients, 94 % (*n* = 94) were male. The study population had a mean age of  $43.6 \pm 5.2$  years. Among the study population, 28 patients (28%) were aged between 31 and 40 years, 72 patients (72%) were aged between 41 and 50 years, and 13 patients (13%) were smokers. A history of hypertension was reported in 40 (40%) patients, 31 (31%) patients had diabetes mellitus, 23 (23%) had a history of familial hypercholesterolemia of coronary artery disease (CAD), and 12 (12%) had dyslipidemia. Additionally, 10 participants (10%) had a history of PCI, and one (1%) had a coronary artery bypass graft (CABG). The most common clinical presentation was STEMI (*n* = 51, 51%), followed by UA (*n* = 25, 25%) and NSTEMI (*n* = 24, 24%). The baseline and clinical characteristics of the study population are summarized in Table 1.

#### 3.2. Lesion characteristics

The culprit target vessel was the LAD coronary artery in 63% of the patients, followed by the right coronary artery (RCA) and left circumflex artery (LCX) in 23% and 11% of the patients, respectively. The non-target vessel was the LAD in 12% of the patients. In the non-culprit vessel, an FFR value > 0.8 was observed in 25 patients who presented with 27 lesions. The lesion characteristics are presented in Table 2.

**Table 1**

Baseline and clinical characteristics of the study population (*n* = 100).

Characteristics	Patients ( <i>n</i> = 100)
<b>Demographics and vitals</b>	
Age, Mean $\pm$ SD (years)	43.6 $\pm$ 5.2
BMI, Mean $\pm$ SD (kg/m <sup>2</sup> )	22.2 $\pm$ 3.5
SBP, Mean $\pm$ SD (mmHg)	127 $\pm$ 12.3
DBP, Mean $\pm$ SD (mmHg)	78.7 $\pm$ 8.7
<b>Gender</b>	
Male, n (%)	94 (94)
Female, n (%)	6 (6)
<b>Age Group</b>	
<45 years, n (%)	49 (49)
45–50 years, n (%)	51 (51)
<b>Current Smoker</b>	
Yes, n (%)	13 (13)
No, n (%)	87 (87)
<b>Medical History</b>	
Diabetes Mellitus, n (%)	31 (31)
Dyslipidemia, n (%)	12 (12)
Hypertension, n (%)	40 (40)
FH of CAD, n (%)	23 (23)
Renal Insufficiency, n (%)	0 (0)
Peripheral Vascular, n (%)	0 (0)
Stroke, n (%)	0 (0)
TIA, n (%)	0 (0)
Congestive Heart Failure, n (%)	0 (0)
Previous CABG, n (%)	1 (1)
Previous PCI, n (%)	10 (10)
<b>Clinical Presentation</b>	
NSTEMI, n (%)	24 (24)
STEMI, n (%)	51 (51)
UA, n (%)	25 (25)

BMI: Body mass index; CABG: Coronary artery bypass graft; CAD: Coronary artery disease; DBP: Diastolic blood pressure; FH: Family history; NSTEMI: Non-ST elevation myocardial infarction; PCI: Percutaneous coronary intervention; SBP: Systolic blood pressure; SD: Standard deviation; STEMI: ST-elevation myocardial infarction; TIA: Transient ischemic attack; UA: Unstable angina.

**Table 2**

Lesion characteristics of the study population (*n* = 100).

Parameters	Patients ( <i>n</i> = 100)
<b>Target Vessel</b>	
LAD, n (%)	63 (63)
LCX, n (%)	11 (11)
LM, n (%)	2 (2)
PLVB, n (%)	1 (1)
RCA, n (%)	23 (23)
<b>Non-Target Vessel</b>	
LAD, n (%)	12 (12)
LCX, n (%)	5 (5)
OM, n (%)	2 (2)
RCA, n (%)	7 (7)
<b>FFR Value (Non-Culprit Vessel)—N=25 patients, 27 lesions</b>	
>0.8	25 (25)

FFR: Fractional flow reserve; LAD: Left anterior descending artery; LCX: Left circumflex artery; LM: Left main; OM: Obtuse marginal; PLVB: Posterior left ventricular branch; RCA: Right coronary artery.

PR was noted in 31% of the culprit lesions, followed by PE and CNs in 25% (*n* = 25) and 14% (*n* = 14) of the lesions, respectively. Most of the plaques exhibited a fibrous composition, accounting for 75% of the instances, and 27% showed a macrophage-rich composition. Fibrocalcific plaques were evident in 17% of the cases, while lipidic plaques were noted in 24% of the cases. TCFAs were identified in 16% and cholesterol crystals were observed in 11% of the patients. Microchannels were observed in 20% while layered plaques were identified in 8% of the cases. Red, white, and mixed thrombi were observed in 21 (21%), 14 (14%), and 17 (17%) of the patients, respectively (Figs. 2 and 3).

A comparison of the plaque characteristics between the three different ACS types is shown in Fig. 4. Fibrous plaques were most prevalent in all three (UA, NSTEMI, and STEMI) conditions (67%, 79%, and 88%, respectively). In addition, the lesions in these patients most commonly exhibited PR (49%, 21%, and 4%, respectively) and PE (35%, 17%, and 12%, respectively).

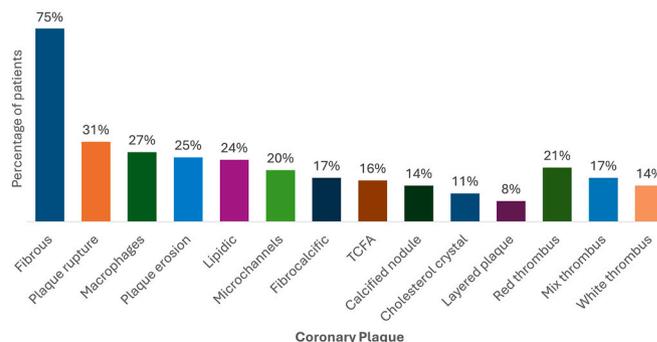
#### 3.3. Plaque characteristics across age groups

All plaque characteristics across the two age groups (<45 years and 45–55 years) were similar (Fig. 5), except those for lipidic plaques. Lipidic plaques were significantly higher in the patients in the <45 years age group as compared to those in the 45–55 years age group.

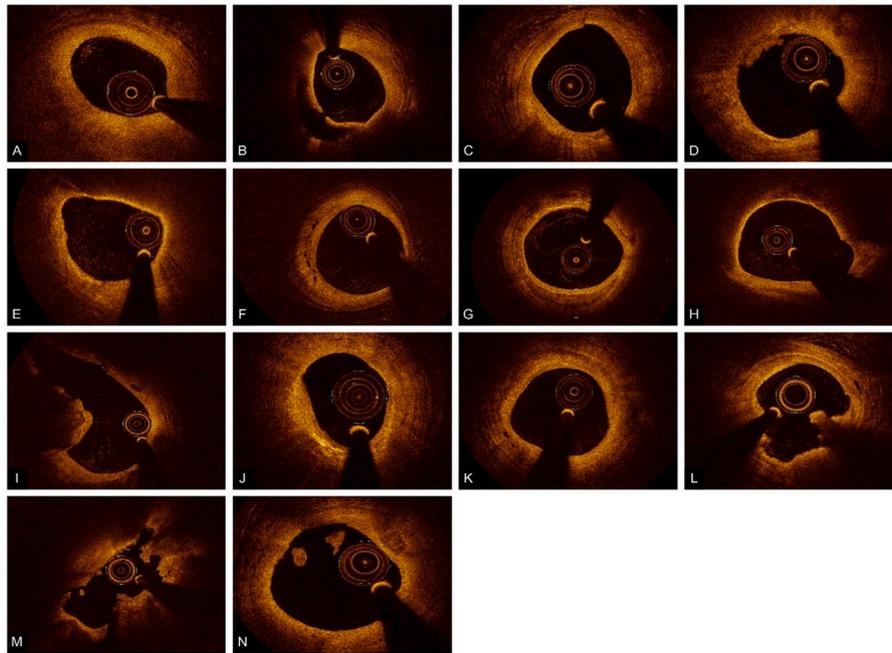
#### 3.4. Post-procedure assessment

##### 3.4.1. Cardiac medications

Patients were followed up at 6 and 12 months. All patients (*n* = 100) were using aspirin and purinergic receptor P2Y G-protein coupled 12 protein (P2Y12) inhibitors before the procedure. After the procedure, there was a decrease in the usage of P2Y12 inhibitors from 100 to 90 patients, while aspirin use remained unchanged. At the 6-month follow-

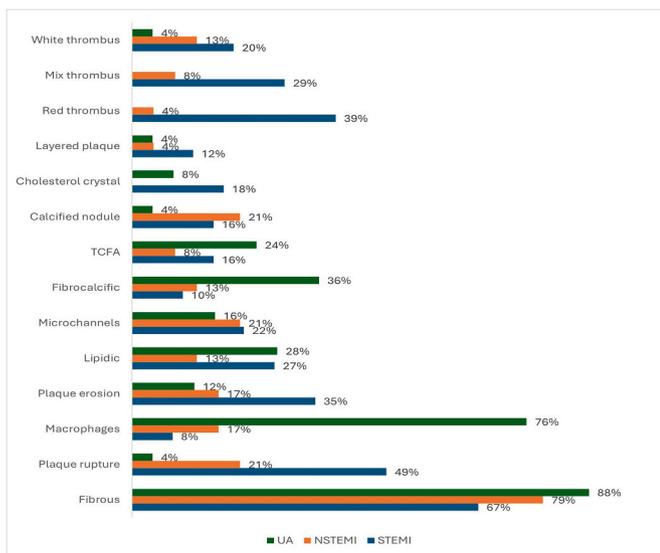


**Fig. 2.** Plaque morphology in ACS patients.



A—Fibrous; B—Plaque rupture; C—Macrophages; D—Plaque erosion; E—Lipid rich; F—Microchannels; G—Fibrocalcific; H—Thin-cap fibroatheromas; I—Calcified nodule; J—Cholesterol crystal; K—Layered plaque; L—Red Thrombus; M—Mix thrombus; N—White thrombus.

Fig. 3. Coronary plaque characteristics.



ACS: Acute coronary syndrome; NSTEMI: Non-ST-elevation myocardial infarction; STEMI: ST-elevation myocardial infarction; TCFA: Thin cap fibroatheroma; UA: Unstable angina.

Fig. 4. Plaque morphology in different indications among ACS patients.

up, aspirin and P2Y12 inhibitors were used by 73 and 78 patients, respectively. At the 12-month follow-up, aspirin and P2Y12 inhibitors were used by 72 and 71 patients, respectively.

3.4.2. Clinical outcomes

No in-hospital MACE were reported. All patients were followed up at 6 months, at which time, 1 case (1%) of MACE related to CABG was reported, and no other safety events or rehospitalizations were reported even at 12 months.

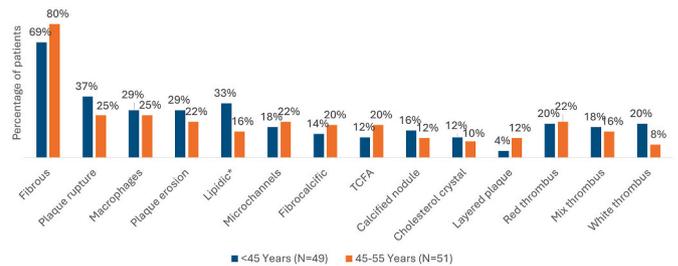


Fig. 5. Plaque morphology in different age groups among ACS patients.

4. Discussion

The findings from this study of 100 young Indian patients with ACS who underwent PCI using OCT imaging revealed that the major component of plaque observed in culprit lesions was PR (31%), followed by PE (25%) and CNs (14%). In 75% of the patients, the plaques were fibrous. Post-procedural monitoring of events revealed a low occurrence of adverse events (AEs) at both the 6- and 12-month follow-ups.

The study predominantly involved male participants (94%) with an average age of  $43.6 \pm 5.2$  years, consistent with regional findings. For instance, a study of 90 young ACS patients <45 years of age reported a 78.9% male prevalence with an average age of  $39.79 \pm 5.15$ .<sup>16</sup> Another study from Chandigarh found that 96.2% of ACS patients <40 years were male, with an average age of  $35.5 \pm 4.7$  years,<sup>15</sup> while a Kerala study observed a 76% male predominance among ACS patients aged <55 years, with an average age of 46.02 years.<sup>17</sup> These studies confirm male predominance in younger ACS demographics, frequently associated with modifiable risk factors such as hypertension, diabetes, smoking, and dyslipidemia.<sup>18</sup>

In this cohort, 13% of the patients were smokers, 40% had hypertension, 31% had diabetes mellitus, and 12% had dyslipidemia. These numbers align with those from a national registry analysis that reported

smoking rates of 16.5% and 18.4% among Indian STEMI and NSTEMI patients, respectively.<sup>19</sup> Additionally, a Saudi Arabian study found that 33.3% of ACS patients were smokers, and 45.2% and 32.3% of them had hypertension and diabetes, respectively.<sup>20</sup> An Indian study highlighted smoking as the primary risk factor among males (62.16%) with ACS, with notable gender differences in the prevalence of hypertension, diabetes, and dyslipidemia.<sup>17</sup> These observations underscore the critical impact of these risk factors on ACS incidence across diverse populations.<sup>1,19,20</sup>

OCT provides substantial advantages in characterizing plaque phenotypes within culprit lesions of patients with ACS.<sup>21</sup> In this study, the most commonly affected target vessel was the LAD coronary artery, identified in 63% of the patients, followed by the RCA and LCX in 23% and 11% of the patients, respectively. This aligns with another OCT study where PEs were predominantly found in the LAD (54.5%), the LCX (47.2%), and the RCA (23.1%),<sup>22</sup> which furthers our understanding of plaque distribution within coronary arteries.

Our findings revealed that PR was the most common type of plaque, occurring in 31% of the lesions, followed by PE and CNs in 25% and 14% of the lesions, respectively. This is similar to a report on 43 young Indian ACS patients, where PR was observed in 51.2% and PE in 37.2% of the cases.<sup>23</sup> Notably, PR and PE often lead to thrombus formation and significantly impact the pathophysiology of ACS and influence treatment strategies.<sup>24</sup>

However, the prevalence of PR in our study differs from that of the FORMIDABLE registry, which reported PR in 70% of young ACS patients ( $\leq 50$  years) and 64% of older patients ( $> 50$  years).<sup>25</sup> Additionally, the registry reported that fibrotic and fibrocalcific plaques were less frequent in younger patients (32% and 17%, respectively) compared to older patients (57% and 36%), while our study reports a higher prevalence of fibrotic plaques (75%) in young patients.<sup>25</sup> TCFAs were identified in 16% of the cases in the current study, contrasting with the 70% and 58% reported in younger and older patients, respectively, in the FORMIDABLE registry.<sup>25</sup> These differences may reflect varying population characteristics even within Indian patients. In addition, other aspects, such as lifestyle factors and the baseline risk profile of the study population, may also contribute to these differences.

In this study, fibrous plaques were predominant, accounting for 75% of the total plaques, and were the most prevalent in various ACS conditions—67% in STEMI, 79% in NSTEMI, and 88% in UA patients. Thrombus assessment indicated that 21%, 14%, and 17% of the thrombi were red, white, and mixed, respectively. A comparative study by Chandra et al (2021) involving OCT imaging in 43 ACS patients from Uttar Pradesh, India, found that 79.1% of the plaques were fibroatheromatous while 16.3% were fibrous, with red, mixed, and white thrombi in 27.9%, 25.6%, and 20.9% of patients, respectively.<sup>23</sup> In addition, the present study also shows that like the results from the FORMIDABLE registry, younger patients have fewer fibrotic and fibrocalcific plaques, although these differences were not statistically significant in the present study.<sup>25</sup> However, the plaque characteristics across age groups reported in the present study are different from those reported by Chaudhary et al, whose work showed that older patients ( $> 35$  years of age) had significantly higher macrophages and microchannel prevalence than younger patients ( $< 35$  years of age).<sup>26</sup> Similarly, the present study results, which indicate that lipidic plaques occur significantly more frequently in younger patients ( $< 45$  years) than older patients (45–55 years of age) differ from those of Bambagioni et al, who have reported that lipidic plaques occurred just as frequently in younger patients as older patients (across an age range of  $< 50$  to  $> 75$  years).<sup>27</sup>

Additionally, the positioning and nature of the plaque significantly influence thrombus formation and platelet activation.<sup>28</sup> In our study, FFR values  $> 0.8$  were noted in 27 lesions (from 25 patients) categorized as non-culprit, aligning with an observational study where 43.2% of 217 non-culprit lesions (from 156 patients) had FFR values  $> 0.8$ .<sup>29</sup> These findings underline the variability in plaque and thrombus characteristics among ACS patients and underscore the importance of continued

research to refine treatment strategies.

In this study, the usage of P2Y12 inhibitors decreased from 100 to 90 patients after the procedure, while the use of aspirin remained consistent. By the 6- and 12-month follow-ups, both aspirin and P2Y12 inhibitor usage had reduced by approximately 30%. Initially, 87% of the patients were prescribed antiplatelet therapy during hospital discharge, which was to be continued till the 12-month follow-up. This contrasts with data from the Acute Coronary Syndrome Quality Improvement in Kerala (ACS QUIK) trial, which involved 4762 patients and reported pre-hospitalization aspirin use as 16.8%. In-hospital usage rates for aspirin and P2Y12 inhibitors were 97.7% and 98.2%, respectively, with continued post-discharge usage at 98.7% for aspirin and 97.9% for P2Y12 inhibitors.<sup>30</sup>

The incidence of AEs in this study was 1% at the 6-month follow-up, with no AEs reported at the 12-month mark. This is lower than the findings from Khraishah et al (2022), which showed that 1.9% of ACS patients aged  $\leq 50$  years experienced in-hospital MACE, and 3.1% had MACE within 30 days among a cohort of 4762 patients.<sup>30</sup> The lower AE incidence in our study could be attributed to OCT-guided PCI. Monitoring post-procedural AEs is critical in ACS patients undergoing PCI, given the associated risks of MACE.<sup>31</sup>

This study provides valuable information on plaque morphology in young patients with ACS from India. The strength of this study is that it reports real-world data obtained using advanced OCT imaging techniques and post-procedural parameters for follow-up periods of 6 and 12 months. However, a limitation of this study was the small sample size (100 patients), which may affect the generalizability of the findings to a broader population of young Indian patients with ACS. Therefore, further studies with larger cohorts are necessary to validate these findings. Most study participants were male; therefore, this study sample does not adequately represent the female population with different risk profiles and disease manifestations. Additionally, the risk of selection bias should be considered while interpreting the results. The prolonged enrollment period was influenced by the COVID-19 pandemic due to operational challenges.

## 5. Conclusion

The use of OCT in PCI procedures for young Indian patients with ACS provides valuable information regarding lesion characteristics and safety profiles of PCI procedures. PR has emerged as the primary culprit, followed by PE and CNs in causing ACS. Fibrous plaques were prevalent in 75% of the cases. However, the prevalence of PR, TCFAs, and lipidic plaques was lower, and that of fibrous plaques was higher in this cohort compared to data from Western populations. This difference underscores the potential regional variations in the pathophysiology of ACS, suggesting that young Indian patients may exhibit different plaque compositions, which may influence clinical presentations and responses to therapies. Young ACS patients in India tend to be predominantly male, with high rates of smoking, hypertension, diabetes, and dyslipidemia. The findings reveal the remarkable advantages of OCT in characterizing plaque phenotypes and contribute valuable real-world data to enhance our understanding of ACS in the Indian context, emphasizing the need for further research and comprehensive risk factor management and treatment strategies. Such studies are essential for developing comprehensive risk factor management and treatment approaches optimized for the specific needs of the Indian population and similar demographics.

## 6. What is already known?

Atherosclerosis and ACS are increasing among young Indians, necessitating comprehensive plaque analysis for effective ACS management. Current insights reveal diverse plaque features in this demographic, highlighting thrombus diversity and plaque vulnerabilities. OCT enables precise characterization of plaque components, informing

potential treatment strategies.

## 7. What this study adds?

This study adds to the literature comparing population demographics, plaque characteristics and outcomes in OCT-guided PCI in young Indian ACS patients. The study attempts to highlight the role of intravascular imaging in proposing tailored medical and interventional approach on the basis of lesion morphological finding especially in Young ACS patients.

## Author contribution

All authors equally contributed to the study and manuscript development and finalization.

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## Conflict of interest

All authors declare that they do not have any conflict of interest. MN is an employee of Abbott Healthcare Pvt Ltd.

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