

Research Article

Patterns of Coronary Artery Disease in Patients under 40 with Acute Coronary Syndrome

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Received: 02.05.2026, Revised: 04.07.2026, Accepted: 12.07.2026

ABSTRACT

Background: In adult patients under 40 years of age, acute coronary syndrome can result in significant morbidity.

Objective: To identify the angiographic characteristics of coronary artery disease in young patients (< 40 years) with acute coronary syndrome.

Methods: This descriptive cross-sectional study involved 120 patients (18-39 years) with acute coronary syndrome (ACS) from March to August 2025 at Aga Khan University Hospital, Karachi. Demographic, risk factor, and coronary angiographic data were analyzed.

Results: The mean age was 34.2 ± 4.1 years, and 85.0% were male. The most common presentation (56.7%) was STEMI. The top risk factors were smoking (59.2%) and dyslipidemia (48.3%). Single-vessel disease was the most common (54.2%), and the left anterior descending artery was the most commonly affected (58.3%).

Conclusion: Single-vessel disease with LAD involvement predominated in young ACS patients and suggests the importance of early risk-factor control and prompt angiographic evaluation.

Keywords: Acute Coronary Syndrome, Coronary Artery Disease, Young Adults, Angiography, Risk Factors.

INTRODUCTION

Despite significant advances in preventive cardiology, diagnostic tools, pharmacologic therapy, and coronary revascularization techniques, acute coronary syndrome (ACS) continues to be one of the most important causes of morbidity and mortality in the world today. CAD and ACS are traditionally thought of as occurring mostly in older adults, and are becoming a major public health and clinical problem in younger people (1). Young patients with ACS are a special group as they have a significant socioeconomic burden, long-term disability, and a poor quality of life due to cardiovascular events occurring at the most productive years of life. While acute management has improved survival, the increasing prevalence of premature CAD highlights the importance of a better

understanding of the nature of the disease, angiographic patterns, associated risk factors, and clinical outcomes in younger patients (<40 years).

CAD is a multifactorial condition that begins with genetic susceptibility, metabolic disturbances, endothelial dysfunction, inflammation, thrombosis, and environmental factors (2). Stress echocardiographic and multimodality cardiovascular imaging techniques have expanded the ability to diagnose ischemia, myocardial viability, and functional significance of coronary lesions and have led to more accurate diagnosis and more individualized treatment plans than just anatomical evaluation. Advances in molecular medicine have further broadened the understanding of the pathogenesis of CAD. The results indicate that CAD is not just a vascular

disease but a systemic metabolic disease and provide new means for early detection and individual therapeutic strategies, especially in those without many traditional risk factors (3), who are also younger. The treatment of acute coronary syndrome has improved significantly since the publication of the evidence-based clinical guidelines, which focus on early diagnosis, rapid risk stratification, rapid reperfusion therapy, aggressive antithrombotic therapy, and comprehensive secondary prevention.

Current guidelines recommend urgent coronary angiography, customized revascularization techniques, optimization of lipid-lowering therapy, and long-term cardiovascular risk factor modification to decrease recurrent ischemic events and mortality. However, younger patients may also have more unusual clinical presentations, angiographic findings, and disease mechanisms, and require special consideration of age-specific disease characteristics (4). The ability to select patients for treatment and to customize therapy to each patient's specific circumstances remains crucial to maximizing long-term survival and minimizing adverse cardiovascular events (5). The morphology of the lesions, the composition of the plaques, the burden of the thrombus, the vascular remodeling, and the physiological characteristics are factors in the complexity of the procedure and in the prognosis. These angiographic patterns are particularly important in younger ACS patients, who tend to have different lesion characteristics than older patients, such as fewer vessels involved and more likely to have single-vessel disease (6).

International guidelines stress the importance of aggressive preventive strategies in the early stages of (CAD) and the need to achieve lower low-density lipoprotein (LDL) cholesterol levels as early as possible after ACS to stabilize vulnerable plaques and reduce subsequent cardiovascular risk (7). Likewise, current recommendations for the management of stable coronary artery disease have emphasized the importance of thorough diagnostic work-up, functional testing, optimal medical management, and personalized decisions for revascularization. These recommendations acknowledge that CAD is a chronic progressive disease that needs to be managed beyond the acute phase and that recurrent ischemic events must be prevented and long-term cardiac function maintained (8). Another focus of interest is the difference in coronary plaque morphology by age. IVUS

studies have shown that plaque morphology is different in older and younger patients with ACS, with younger patients having more plaque erosion and different culprit lesion morphology. Recent studies have demonstrated strong correlations between exposure to microplastics, atherosclerotic burden, vascular complexity, and acute coronary syndrome, pointing to the possibility of environmental pollution as a novel pathway to the pathogenesis of cardiovascular diseases. These results extend the knowledge of cardiovascular risk beyond traditional clinical risk factors (10). Advances in the evaluation of coronary lesion severity have also been made by adding physiological measurements like the pressure wire. Functional assessment can give more information on the significance of the lesion than standard angiography and may impact clinical decisions for coronary intervention. There is evidence that incorporating physiological assessment into the standard clinical management of coronary artery disease (CAD) enhances the accuracy of diagnosis and assists in making more informed treatment decisions for patients with CAD (11). The epidemiological patterns emphasize the need for the identification of high-risk groups, such as younger adults with premature coronary artery disease (CAD) (12). Recurrent cardiovascular events are still a frequent occurrence after ACS, despite the progress in acute management. Long-term observational studies have shown that there are ongoing risks of myocardial infarction, stroke, repeat revascularization, heart failure, and cardiovascular death after the first event (13). The prognosis of cardiac function after coronary artery disease is also important. Reduced left ventricular (LV) ejection fraction continues to be one of the most powerful predictors of mortality and adverse cardiovascular outcomes, with reduced LV systolic function linked to increased risk of heart failure, recurrent ischemic events, and death.

Therefore, early diagnosis, successful reperfusion, and myocardial function preservation are important goals in the treatment of ACS to achieve a good long-term outcome (14). Advances in percutaneous treatment continue to drive surgical revascularization forward. Multi-arterial coronary bypass grafting has been shown in the long-term to have a greater survival rate and durability than single-arterial grafting, in certain patients. In younger ACS patients, because they are less likely to have extensive multivessel disease, understanding options for

revascularization is important when complex coronary anatomy is encountered (15). Studies specifically targeted at very young children with coronary artery disease consistently report unique clinical characteristics, including increased smoking, dyslipidemia, positive family history, obesity, and predominance of males, when compared to advanced age-related comorbidities (16). The role of inflammation has been identified as a new prognostic factor in ACS. A number of novel inflammatory markers, such as the systemic immune-inflammation index, have been found to have strong relationships with unfavorable cardiovascular outcomes, especially in individuals with concurrent chronic kidney disease.

The results confirm the increasing awareness that inflammatory pathways are an important component of plaque instability, thrombosis, and subsequent ischemic events, which may have future clinical implications for inflammation-based risk stratification (17). In the current European guidelines, the decision to undergo coronary revascularization is based on a multidisciplinary heart team discussion, patient characteristics, procedural risk, and coronary anatomy. The goal of evidence-based decision making for PCI versus CABG is to provide full revascularization with minimal procedural complications and maximal survival. In this context, the evaluation of the angiographic pattern of coronary artery disease in patients under 40 years old with acute coronary syndrome is crucial to understand the distribution of the disease, to direct the management, and to optimize preventive interventions in this growing population (18).

Objective: To describe the angiographic features of coronary artery disease in patients under 40 years of age with acute coronary syndrome and to assess the distribution of coronary lesion involvement in these patients.

MATERIALS AND METHODS

Study Design: Descriptive cross-sectional study.

Study Setting: Department of Cardiology, Aga Khan University Hospital, Karachi, Pakistan.

Duration of the Study: March 2025 to August 2025.

Inclusion Criteria: Patients with unstable angina, non-ST-elevation myocardial infarction (NSTEMI), or ST-elevation myocardial infarction (STEMI) aged 18 to 39 years with acute coronary syndrome (ACS) were included. Patients were enrolled only after giving informed consent and during coronary angiography.

Exclusion Criteria: Patients who were 40 years of age or older, had a previous diagnosis of coronary artery disease, myocardial infarction, previous percutaneous coronary intervention or coronary artery bypass grafting, congenital heart disease, cardiomyopathy, or inadequate angiographic information were excluded.

METHODS

Upon getting approval from the Institutional Ethical Review Committee, all eligible patients fulfilling the inclusion criteria were included in the study using a consecutive non-probability sampling technique. All participants signed informed consent forms prior to participation. Coronary angiography was performed in all patients by experienced interventional cardiologists using standard institutional procedures. Angiographic findings were analyzed to assess the pattern of coronary artery disease, whether single-vessel, double-vessel, triple-vessel, or left main coronary artery disease. All the data was entered and analyzed using SPSS version 26.0.

RESULTS

The study included 120 patients under 40 years of age with ACS. The age of the participants was 34.2 ± 4.1 years, ranging from 21 to 39 years. The majority of participants were male (102, 85.0%) and female (18, 15.0%). The age group with the highest number of patients ($n = 77$, 64.2%) was 35–39. As for clinical presentation, 68 (56.7%) patients had ST-elevation myocardial infarction.

Table 1. Demographic and Clinical Characteristics of Patients (N=120)

Characteristics	Frequency	Percentage
Age 20–29 years	14	11.7%
Age 30–34 years	29	24.1%
Age 35–39 years	77	64.2%
Male	102	85.0%
Female	18	15.0%
STEMI	68	56.7%

NSTEMI	34	28.3%
Unstable angina	18	15.0%

The most common cardiovascular risk factor was smoking, which was reported in 71 (59.2%) patients. 58 (48.3%) had dyslipidemia, while 45 (37.5%) had a family history of premature

coronary artery disease. Hypertension was present in 39 (32.5%) patients, diabetes mellitus in 27 (22.5%), and obesity in 25 (20.8%).

Table 2. Distribution of Cardiovascular Risk Factors

Risk factor	Frequency	Percentage
Smoking	71	59.2%
Dyslipidemia	58	48.3%
Family history of premature CAD	45	37.5%
Hypertension	39	32.5%
Diabetes mellitus	27	22.5%
Obesity	25	20.8%

In 105 (87.5%) patients, coronary angiography revealed obstructive coronary artery disease, and 15 (12.5%) patients had normal or

nonobstructive coronary arteries. The most frequent angiographic pattern was single-vessel disease in 65 (54.2%) patients.

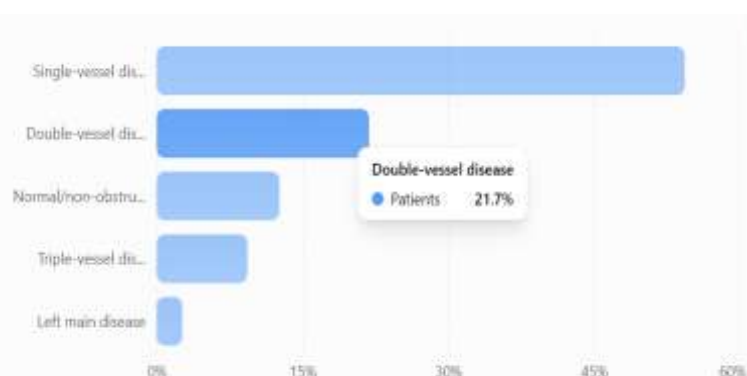


Figure 1. Angiographic Patterns of Coronary Artery Disease

The left anterior descending artery was the most common coronary artery involved in 70 (58.3%) patients. In 42 (35.0%), the right coronary artery was involved, and in 30

(25.0%), the left circumflex artery was involved. In some cases, more than one vessel was involved.

Table 3. Angiographic Findings among Study Participants

Angiographic finding	Frequency	Percentage
Single-vessel disease	65	54.2%
Double-vessel disease	26	21.7%
Triple-vessel disease	11	9.2%
Left main disease	3	2.5%
Normal/non-obstructive arteries	15	12.5%
Left anterior descending involvement	70	58.3%
Right coronary artery involvement	42	35.0%
Left circumflex artery involvement	30	25.0%

Overall, young ACS patients were mostly male and presented with STEMI. The most common risk factors were smoking and dyslipidemia, and the most common angiographic pattern was single-vessel disease with involvement of the left anterior descending artery.

DISCUSSION

The major results indicated that the majority of patients were male, aged 35–39 years, and most commonly suffered from ST-elevation myocardial infarction. The results suggest that clinically relevant coronary atherosclerosis may

develop at a young age and is closely linked to modifiable cardiovascular risk factors. This is consistent with a large analysis of young South Asian patients with acute coronary syndrome, who were mostly male and typically had a myocardial infarction, reflecting the increasing burden of premature coronary artery disease in this population (1). The current study showed that the majority of the patients experienced STEMI, indicating that younger patients can have sudden and severe coronary occlusion with relatively mild atherosclerotic disease compared to older patients.

The critical importance of early recognition of ischemia is that it can cause more myocardial injury and compromise ventricular function if delayed. In addition to coronary angiography, which is the main diagnostic tool in the diagnosis of ACS, stress echo and other functional imaging modalities have an important role in evaluating residual ischemia, myocardial viability, and suspected coronary disease after stabilization. These approaches might be especially useful in younger patients with atypical symptoms or in those who do not have obstructive coronary arteries (2). In addition to traditional risk factors, complex metabolic abnormalities are likely to play a role in the development of coronary artery disease in young adults. This study found that dyslipidemia and obesity were prevalent, which could be a sign of abnormalities in lipid metabolism, insulin sensitivity, oxidative stress, and energy utilization.

In metabolomics studies, patients with coronary artery disease and cardiovascular events have been found to have common and event-specific metabolic changes. This evidence suggests that biochemical changes can occur before clinically apparent atherosclerosis, and may help to identify high-risk young people before they have an acute event (3). The high percentage of STEMI patients also emphasizes the need for timely diagnosis and treatment in accordance with guidelines. The current acute coronary syndrome guidelines suggest prompt risk assessment, antiplatelet/anticoagulant therapy, intensive lipid-lowering therapy, and prompt invasive therapy based on clinical presentation. Clinicians should not dismiss symptoms or delay coronary angiography in younger patients due to the potential for significant long-term morbidity, decreased productivity, and repeated cardiovascular events occurring over many decades for premature ACS (4).

In the current study, the majority of patients had single-vessel disease, and relatively smaller numbers had double, triple-vessel, or left main disease. This distribution has direct therapeutic implications because focal single-vessel disease is generally suitable for percutaneous coronary intervention, whereas complex multivessel or left main disease may require multidisciplinary assessment and surgical revascularization. In the left main disease, comparative studies of PCI and coronary artery bypass grafting (CABG) suggest that age alone should not be the basis for treatment decision-making, and that the anatomical complexity of the disease, clinical presentation, procedural risk, and expected long-term outcomes should be taken into account. The severity of the stenosis is not the only factor that determines the outcome of the procedure. Coronary lesions vary in the burden of plaque, in calcium, in thrombus, in diffuse disease, and in physiological properties. These pathophysiological patterns may affect immediate PCI success and the risk of complications.

The high prevalence of focal lesions in young ACS patients may be helpful for interventions to be successful, but high thrombus burden or unstable plaque may make interventional procedures more challenging. Detailed lesion assessment may help to select treatment and procedural planning (6). In the present study, smoking was the most prevalent risk factor, followed by dyslipidemia. Both can be prevented and should be emphasized in the hospital and in follow-up. In young patients, particularly, aggressive lipid reduction is especially important as they may have a longer period of high low-density lipoprotein cholesterol during their lifetime. The current expert guidelines are to start intensive statin therapy early and to use ezetimibe or PCSK9 therapy in addition to statins when lipid targets are not met. Structured secondary prevention programs should include smoking cessation, dietary changes, physical activity, and medication compliance (7).

The results also support the notion that coronary artery disease is a chronic disease and not an isolated acute event. Patients are still at risk for progression in untreated vessels, recurrent ischemia, and future cardiovascular complications even after successful reperfusion. Treatment of stable coronary disease is based on optimal medical management, functional assessment (if indicated), and personalized revascularization. Therefore, long-term cardiology follow-up, monitoring of risk factors,

and ongoing lifestyle intervention are indicated for young survivors of ACS (8). The male predominance in this study may be partly attributed to differences in plaque characteristics related to sex and age. Intracoronary imaging research has shown that there are age and sex differences in the morphology of the culprit plaque, such as differences in plaque rupture, erosion, lipid content, and fibrous cap characteristics.

More intracoronary imaging studies may help to better understand the mechanisms of ACS in very young patients (9). Other environmental exposures, such as emerging ones, can also play a part in premature atherosclerosis. Exposure was not quantified in the current study, but these results imply that air pollution, industrial contaminants, and other environmental exposures may interact with smoking, metabolic abnormalities, and inflammation to drive coronary disease in younger individuals (10). Single-vessel disease is the predominant disease, which is why accurate assessment of lesions is important.

Anatomical information is obtained with conventional angiography, but this technique may fail to define the functional significance of intermediate stenoses. Pressure-wire assessment may be helpful in deciding if a lesion is causing ischemia and may avoid unnecessary intervention. The RIPCORD 2 trial showed that the routine use of physiological assessment can change the diagnosis and management, but this should be individualized in acute coronary artery disease (CAD) (11). Population-level trends also reinforce the need to investigate premature cardiovascular disease. A large study in the UK revealed significant trends in the prevalence of various cardiovascular diseases over 20 years. Although some age-standardized rates have decreased, cardiovascular disease remains a significant burden. The early age of ACS onset (before 40 years) is especially alarming because it indicates early exposure to preventable risk factors and also leaves a long window for recurrent events to occur (12).

Clinically important recurrent cardiovascular risk is present even after initial successful treatment. There have been continued risks of recurrent myocardial infarction, stroke, heart failure, repeat revascularization, and mortality among large post-ACS cohorts. The young age of patients in the present study population should not be read as a good prognosis for the rest of their lives. Rather, it is a chance for intensive prevention, because the control of

smoking, lipid levels, blood pressure, glucose, and body weight could substantially lower cumulative cardiovascular risk (13). Another important factor determining outcome after ACS is left ventricular function. If not reperfused, patients with STEMI can suffer significant myocardial injury. Reduced EF has been shown to be associated with mortality or cardiovascular events in patients with coronary artery disease.

Ejection fraction was not one of the primary angiographic endpoints of the present study, but should be assessed as part of routine assessment, as it is used to guide prognosis and the use of heart failure therapies (14). The more extensive multivessel and left main disease has only been seen in a small number of patients in the present study, but these results are clinically relevant. In some young patients, coronary artery bypass grafting may be necessary, especially if the disease is complex. There are good long-term survival and durability data for multi-arterial grafting in suitable surgical patients. The durability of revascularization is especially important when surgical therapy is being considered, since younger patients are likely to have a longer life expectancy (15). The overall angiographic pattern seen in this study is similar to the findings of previous studies of very young coronary artery disease patients, which found that men were more common, that smoking and dyslipidemia were common risk factors, and that single-vessel disease occurred in a significant proportion.

The left anterior descending artery has also been frequently found to be the main vessel involved. The similarities point to a clinical profile of premature CAD, but the strength of the association among the various risk factors may vary between different geographical and socioeconomic groups (16). An alternative explanation for acute plaque instability in younger patients may be inflammation. The systemic immune-inflammation index has been linked with poor outcomes in patients with ACS, especially those with chronic kidney disease. This study did not assess inflammatory biomarkers, but future studies should explore the association between lesion burden, vessel involvement, and prognosis in young adults. These markers can be used to better stratify risk in combination with traditional cardiovascular risk factors (17).

Last but not least, complex coronary anatomy should be treated according to current revascularization guidelines and a

multidisciplinary approach. Current European guidelines for review recommend a balanced approach to PCI versus CABG in LMD, especially when both options are technically viable. While left main involvement was rare in the current study, it was found in patients younger than 40 years, showing that coronary disease is not restricted to older patients. In conclusion, the study underscores the importance of early detection of risk factors, early invasive assessment, appropriate revascularization, and lifelong secondary prevention in younger patients with acute coronary syndrome (18).

CONCLUSION

Among patients under 40, acute coronary syndrome was associated with coronary artery disease, and was more common in men, especially those aged 35-39. The most frequent clinical presentation was that of ST-elevation myocardial infarction, suggesting that young adults can suffer severe and sudden coronary events. Comparatively less common but clinically important were double-vessel disease, triple-vessel disease, and left main coronary disease. The results of this study highlight the importance of early screening, early implementation of aggressive management of modifiable risk factors, early diagnosis, and early coronary angiography in young patients with suspected ACS. Recurrent cardiovascular events and clinical outcomes can be minimized by long-term secondary prevention and periodic follow-up.

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