

Clinical Features of Precocious Acute Coronary Syndrome

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ABSTRACT

BACKGROUND: Acute coronary syndrome due to acute plaque rupture has been well described and is associated with established risk factors, including hypertension, diabetes mellitus, hyperlipidemia, and smoking. The prevalence of these risk factors in very young patients (aged ≤ 35 years) is not well known, and they may have other nontraditional risk factors. We hypothesized that acute coronary syndrome in very young patients may represent a thrombotic event independent of underlying atherosclerotic disease.

METHODS: We performed a dual-institution, retrospective study of consecutive patients aged ≤ 35 years who presented with acute coronary syndrome and underwent coronary angiography from January 2000 to December 2011. Standard demographics, risk factors, and detailed angiographic information were obtained.

RESULTS: A total of 124 patients met inclusion criteria. The mean age was 31 ± 4 years for both sexes. Approximately half (49%) of the patients were obese (body mass index ≥ 30 kg/m²); 90% of patients had at least 1 traditional risk factor, most commonly hyperlipidemia (63%) and smoking (60%); 52% of patients underwent re-vascularization, of which 94% were by percutaneous coronary intervention, and 42.9% of patients had intracoronary thrombus, of whom approximately one third had no detectable underlying coronary disease.

CONCLUSIONS: Very young patients with acute coronary syndrome tend to be obese, with a high prevalence of smoking and hyperlipidemia. The presence of thrombus in the absence of underlying coronary disease suggests a thromboembolic event or de novo thrombotic occlusion, which may reflect primary hemostatic dysfunction in a considerable number of these patients.

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Acute coronary syndrome is a leading cause of morbidity and mortality worldwide, and its incidence is projected to increase, especially in the developing world.¹ Approximately 3% to 10% of acute coronary syndrome occurs in young patients (aged < 45 years)^{2,3}; however, this risk is often underappreciated.^{4,5} Autopsy studies have shown that the asymptomatic atherosclerosis burden present in young patients increases with modifiable cardiovascular disease risk factors, but it is unknown why some patients develop precocious acute coronary syndrome.⁶ The prevalence of traditional cardiovascular disease risk factors, such as hypertension, hyperlipidemia, diabetes, and smoking status, in very young patients (aged ≤ 35 years) is not well known.

Furthermore, this population may have additional nontraditional risk factors contributing to acute coronary syndrome events. An examination of patients with non-ST-segment elevation myocardial infarction revealed that 9% were found to have insignificant coronary artery disease, suggesting a pathophysiologic mechanism distinct from progressive plaque rupture that may drive acute coronary syndrome events.⁷ Hypercoagulable states (high fibrinogen, high D-dimer) also have been associated with premature acute coronary syndrome, suggesting a different pathophysiologic mechanism of acute coronary syndrome in this population, possibly via de novo thrombotic occlusion.⁸ Thus, we conducted a dual-institution, observational study to determine the clinical characteristics of very young patients who present with acute coronary syndrome.

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MATERIALS AND METHODS

We performed a retrospective observational study of consecutive adult patients (aged ≥ 18 to ≤ 35 years) with the

diagnosis of acute coronary syndrome, including ST-elevation myocardial infarction, non-ST-elevation myocardial infarction, and unstable angina, who underwent coronary angiography between January 1, 2000, and December 31, 2011. Patients were identified from the Northwestern University Enterprise Data Warehouse by the International Classification of Diseases, Ninth Revision codes for acute myocardial infarction (410.0-411.91) and the Vanderbilt University cardiac catheterization laboratory database. Study data were collected and managed using REDCap electronic data capture tools hosted at Vanderbilt University.⁹ Diagnosis of the different types of acute coronary syndrome was based on the American College of Cardiology clinical data standards.¹⁰ Patients who had received heart transplants were excluded. Baseline characteristics were collected, including demographics, medical history, medications, physical examination, and laboratory data. Diabetes was defined as having a reported history of diabetes, treatment with anti-diabetic medications, or a fasting blood glucose of 126 mg/dL or greater. Hypertension was defined as having a history of hypertension or treatment with any antihypertensive drug. Hyperlipidemia was defined as a history of dyslipidemia, treatment with an anti-hyperlipidemic medication, or serum lipid levels meeting diagnostic criteria for dyslipidemia according to the Adult Treatment Panel III guidelines.¹¹ A positive family history of coronary artery disease was defined as documented medical history of coronary artery disease in a first-degree relative before 55 years of age. Obesity was defined as body mass index ≥ 30 kg/m². Renal impairment was defined as a history of chronic kidney disease or an estimated glomerular filtration rate of <60 mL/min. Detailed angiographic information, including the presence of thrombus, was obtained from cardiac catheterization reports. Culprit and nonculprit lesions were classified according to the modified American Heart Association/American College of Cardiology lesion classification scheme¹² and electrocardiographic changes. SPSS (SPSS Inc, Chicago, Ill) was used for calculation of descriptive statistical analysis.

RESULTS

Of 13,072 patients who presented with acute coronary syndrome during the study period, 124 (3%) met inclusion criteria with a mean age of 31 ± 4 years for both sexes (Table 1). Approximately half (49%) of the patients were obese (mean body mass index, 31.5 ± 8.5 kg/m²). Ninety percent of patients had at least 1 traditional cardiovascular disease risk factor, most commonly hyperlipidemia (63%)

and smoking (60%). Hypertension was present in 58% of patients. Cocaine abuse was present in 10.7% of patients, exclusively in men.

Acute coronary syndrome presentation was unstable angina in 34.7% of patients, followed by non-ST-elevation myocardial infarction in 33.8% of patients, and ST-elevation myocardial infarction in 31.5% of patients (Table 2). Coronary angiography demonstrated that 59.8% of patients had coronary artery disease. Intracoronary thrombus was present in 33 (42.9%) of the 77 patients with angiographic comment on the presence of thrombus, approximately one third of whom ($n = 10$) had no underlying angiographic coronary artery disease (Figure 1). Revascularization was performed in 52.0% of patients, mainly by percutaneous coronary intervention (93.8%).

CLINICAL SIGNIFICANCE

- Acute coronary syndrome in young patients is characterized by a high rate of traditional risk factors, particularly hyperlipidemia and smoking.
- Of patients with intracoronary thrombus, a significant portion had no evidence of underlying coronary artery disease.
- Acute coronary syndrome in young patients may be a result of underlying hypercoagulability or fibrinolytic dysfunction.

DISCUSSION

Young patients comprise 3% to 10% of all cases of acute coronary syndrome^{2,3} and represent an important population to study because they serve potentially to gain the most benefit in terms of risk factor modification for secondary prevention. We performed an observational study to evaluate clinical characteristics, which included traditional cardiovascular risk factors, presentation, and outcomes of 124 young patients who presented with acute coronary syndrome and underwent coronary angiography. The patients tended to be obese with a high prevalence of smoking and hyperlipidemia. Despite a significant intracoronary thrombus burden, a significant number of these patients had no underlying angiographically apparent coronary disease.

The current study demonstrates that baseline risk factors have an important role in identifying very young patients at risk for acute coronary syndrome. Approximately 80% to 90% of patients with coronary artery disease in traditional acute coronary syndrome populations possess established risk factors, including hypertension, diabetes, hyperlipidemia, and smoking.¹³ In our study, although these risk factors were all observed, smoking and hyperlipidemia were most common. At the time of angiography, 43% of patients had evidence of intracoronary thrombus. Although the majority of these patients had underlying coronary artery disease, approximately one third of patients had no demonstrable atherosclerotic disease. This suggests that acute de novo thrombosis may occur independently of a plaque rupture phenomenon. This information could be useful in initiating public health interventions that target younger patients for more aggressive smoking cessation awareness, lipid management, and antiplatelet therapy.

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