

CARDIAC NURSING ROUNDTABLE

Acute Coronary Syndromes in the Young

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INTRODUCTION

The leading cause of death in developed countries is cardiovascular disease.¹ Acute coronary syndrome (ACS) is considered as a disease of the middle and old age. The knowledge for ACS is gained from research made in older aged patient groups.² However, heart disease exists also in younger ages.³ In recent decades, ACS appears more often in young people and increased clinical interest has emerged in this topic since it can lead to premature death.²

CLASSIFICATION AND MEANING OF ACUTE CORONARY SYNDROME

Myocardial ischemia is a general term which clinical syndromes caused by, belong to. According to the new classification of the 'acute coronary syndrome', it includes:

- Acute myocardial infarction (AMI) with ST-segment elevation – STEMI
- The non-ST segment elevation syndrome which covers two clinical entities:
 1. Unstable angina (absence of myocardial necrosis -negative cardiac troponin) and
 2. Non-ST segment elevation myocardial infarction (myocardial necrosis-evidence with increased cardiac troponin) – NSTEMI,^{4,6}

WHAT WE MEAN BY YOUNG PEOPLE?

At international level, the maximum age limit for the identification of young people with ACS is set to the age of 45.⁷ Few studies shift the age threshold to 60 years.

ETIOPATHOGENESIS

Acute coronary syndrome in young people can be divided into two categories, those with angiographically normal coronary arteries and young people with coronary heart disease with varied etiology.⁸

NORMAL CORONARY ARTERIES

The ACS event with the presence of normal coronary arteries, although uncommon for old ages, is more commonly encountered in young patients and it is estimated that concerns almost 20% of the total events.⁹ The pathophysiology remains unclear but may be attributed to coronary artery thrombosis, embolism, spasm,^{8,10} combination

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of these processes, syndrome X¹⁰ and myocardial bridging.

More specifically:

- *Coronary thrombosis* occurs in hypercoagulation as in nephrotic syndrome, antiphospholipid syndrome, lack of protein S and factor XII.⁸ Coronary artery thrombosis is shown below (Figure 1) in an otherwise normal coronary artery.¹¹
- *Embolism* of the coronary arteries is rare. It has been reported that in infective endocarditis septic embolism of vegetations of the mitral and/or aortic valve can cause myocardial infarction. Endocarditis is also caused by antiphospholipid syndrome and systemic lupus erythematosus with the difference that the vegetations may be non-septic. Such vegetations are treated with anticoagulation treatment. Thrombotic microembolism causing myocardial infarction has been reported in bacteremia and in the absence of endocarditis.⁸ Rarely, embolism of the otherwise normal coronary artery can be due to atrial fibrillation or flutter.
- *Coronary spasm*. The dominant mechanism that causes ACS is from the use of cocaine. Usually manifests itself as NSTEMI-ACS^{10,12,13}. Ischemic myocardial effects from cocaine can be caused through four main mechanisms:
 1. Increasing demand for O₂ because of the acute increase in systolic blood pressure (SBP) and heart rate caused by the positive inotropic action of cocaine.
 2. Coronary vasoconstriction caused by α₁-adrenergic properties and due to calcium direct vasoconstriction.
 3. Endothelial dysfunction predisposes to vasoconstriction and thrombosis.

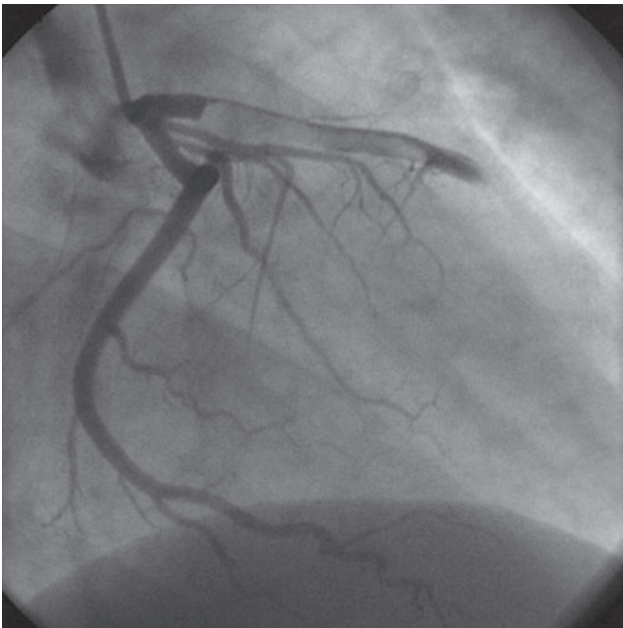


FIGURE 1. Intracoronary thrombus in left anterior descending artery with angiographically normal coronary arteries.

4. Worsening of atherosclerosis.⁸

The vasoconstrictor effect of cocaine, and more specifically directly to the smooth muscle cells of the blood vessels, has been confirmed in vivo and in vitro. The 24-hour ECG monitoring of patients in rehabilitation departments showed ST elevation the first 2 weeks. The results from coronary angiography in patients showed that they had normal coronary arteries. These patients are usually under 40 years old, male smokers, without other known risk factors for coronary heart disease, with reports of using cocaine several hours or just before the onset of symptoms.¹⁰ All new patients presenting with symptoms suggestive of myocardial ischemia should be asked if they have used cocaine.⁹ Since after the use of cocaine increased mobility and possible injury of skeletal muscle or even rhabdomyolysis exists, CK and CK-MB markers are unreliable in the diagnosis of ACS. Cardiac troponins I and T are more specific and reliable and should be checked at regular intervals (every 6 hours). Dissection of the aorta and coronary arteries has been reported as further complications of vascular spasm from the use of cocaine.¹⁰

Alcohol and amphetamines have been also implicated in coronary spasm with subsequent MI.⁸ It is proven that Prinzmetal angina is due to epicardial vessel spasm, resulting in induction of myocardial ischemia. Spasm may involve otherwise normal vessels. It concerns younger people who are often heavy smokers. The symptom is usually severe and can lead to syncope. Vasoconstrictive angina attacks usually occur between 00:00 and 08:00 hours. Epicardial artery spasm leading to transmural ischemia is the key feature of Prinzmetal angina.

The Tako Tsubo syndrome refers to an event of NSTEMI-ACS with normal epicardial vessels and apical ballooning of the left ventricle. It is associated with severe emotional stress, toxic effects of catecholamines may also be related but the precise pathophysiology is not known. It is fully reversible within a few weeks to months.

- *Syndrome X* includes angina: caused by physical effort, accompanied by ST segment depression on stress test, has normal epicardial vessels and may display unstable angina's standard characters. As a cause of this situation can be a disordered endothelial-dependent vasodilatation, impaired NO production, hypersensitivity to sympathetic stimulation and hypersensitivity to pain. Generally, it has a good prognosis.¹⁰
- *Myocardial bridging*. It is an anomaly characterized by a typical intramyocardial route of a segment of one of the major coronary arteries. This can prevent the flow of blood during systole which may persist during diastole resulting in myocardial ischemia and thus myocardial infarction.

ABNORMAL CORONARY ARTERIES

Early atherosclerosis

Many young patients may have typical atherosclerosis. The appearance of advanced atherosclerosis in the young has not

been explained satisfactorily. Various factors such as smoking, hypertension, obesity, family history, etc., which will be discussed below, may predispose to premature atherosclerosis. Hyperlipidemia and hyperhomocysteinemia are implicated in premature atherosclerosis. A mutation in the gene encoding of low density lipoprotein receptor causes familial hypercholesterolemia, an autoimmune disorder clinically characterized by high cholesterol and premature atherosclerosis.

Spontaneous rupture of the coronary arteries

It occurs as idiopathic, in conjunction with atherosclerotic plaque, and as a rare cause of heart attack with higher incidence in young women, particularly during the postpartum period.

Aneurysms, anatomical abnormalities of the coronary

They have been associated with myocardial infarction in young adults, although the mechanism is not clear. Kawasaki disease is an example,⁸ anomalous origin of the left coronary artery arising from the pulmonary artery (ALCAPA) as shown in Figure 2 or congenital coronary artery/arteriovenous fistula (CAF) as shown in Figure 3.

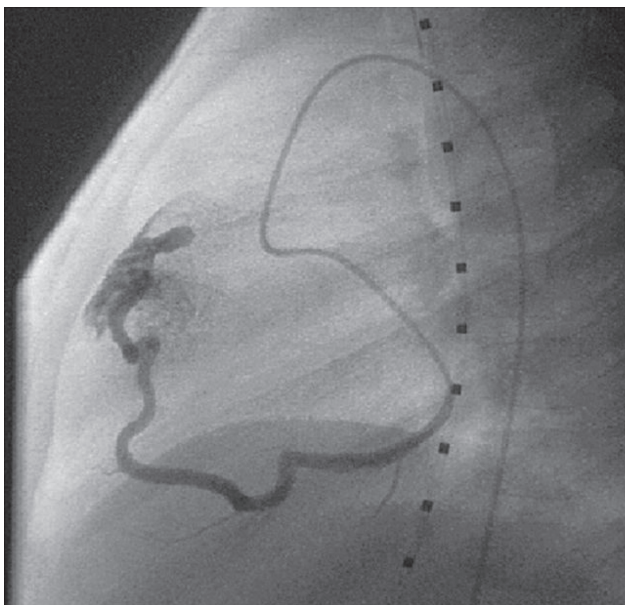


FIGURE 2. Dilated right coronary artery associated with ALCAPA.

RISK FACTORS

SMOKING

It is the most common risk factor for ACS in young people.

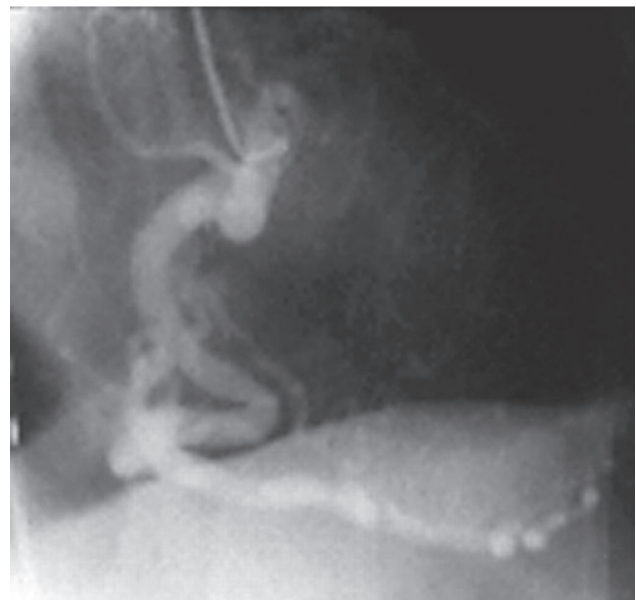


FIGURE 3. Coronary angiogram in a patient with CAF.

Mechanisms of ACS from smoking:

- Atherosclerosis, thrombosis: By causing endothelial dysfunction, increases the risk of atherosclerosis. Also it is contributing to the occurrence of thrombotic phenomena as it enhances platelet adhesion to the endothelium.
- Spasm: Smoking even one cigarette can cause sudden coronary spasm, as found during coronary angiography. Also, it may contribute in causing myocardial infarction and vasospastic angina in patients with insignificant atherosclerosis.
- Disorder of O₂ transport: Nicotine in tobacco increases the release of catecholamines, which in turn cause an increase in blood pressure and heart rate. Cigarette smoke contains 2-6% carbon monoxide, which in combination with hemoglobin produces carboxyhemoglobin and prevents the O₂ transport. According to the above, it adversely affects the balance of supply and demand for O₂ in the myocardium leading to ischemic event.¹⁰

GENETIC FACTORS

A positive family history of coronary artery disease (defined as early onset of the disease in first degree relatives), is an important, after smoking, risk factor for ACS in young patients with percentage that varies between 14 to 69%. The influence of heredity in the formation of early atherosclerosis in young people is not clear.

LIPID DISORDERS

These include hyperlipidemia, hypercholesterolemia and hypertriglyceridemia.

OBESITY

In the Framingham study, among men and women under 50, the incidence of cardiovascular disease was two times greater in obese men and nearly 2.5 times higher in obese women compared with the flimsy people.⁹

USE OF CONTRACEPTIVES

Combined oral contraceptives interfere with three mechanisms that are substantially presented as predisposing factors for development of ACS: Lipids metabolism; Carbohydrate metabolism; Mechanism of hemostasis. What is generally observed is the significant correlation between the use of oral contraceptives and smoking with ACS. Recent studies indicate an increased risk for myocardial infarction in women taking oral contraceptives and simultaneously being smokers.¹⁴

USE OF ERGOGENIC AIDS

In users of ergogenic aids for enhancing athletic performance, both prohibited (doping substances) and licit substances, increased rates of cardiovascular disorders with onset of ACS has been reported, even sudden cardiac death. Users are athletes, professionals and amateurs, as well exercisers in fitness or recreational activities. The most commonly used prohibited substances by athletes are: androgen - anabolic steroids, erythropoietin and stimulants of the central nervous system (CNS), while nutrition supplements are most commonly used from the licit substances. Anabolic steroids have atherogenic, vasoconstrictor, thrombogenic and direct toxic effect on the myocardium, thus contributing to the ACS event. CNS stimulants and nutrition supplements are acting through sympathomimetic effect.^{15,16}

HYPERTENSION - DIABETES MELLITUS

They are less common risk factors in young patients than in older patients.⁹

DEPRESSION

The direct effects of depression on body's physiology and hence in the occurrence of ACS involves three mechanisms: Hypercortisolism; Significant platelet disorders; The autonomic activity, such as conduction and rhythm abnormalities.^{17,18} The CARDIO2000 study highlighted the adverse impact of depression on the likelihood of ACS in the Greek population with relative risk increased by 12%. The analysis by gender showed that the relative risk differs significantly between men and women (OR-men=1.09 versus OR-women=1.19, P<0.01). Statistically significant correlations affecting additively the risk for ACS in young, was observed between depression and smoking (the cardiovascular risk increases by 25%), alcohol consumption (+97%), physical inactivity (+137%) and obesity (+127%). Also, the interaction between depression and various social parameters such as income, education, etc., increases coronary risk by 55 to 132%, while the effect of bad

family situation increases the previous to 167% in men and to 123% in women.¹⁷

SOCIO-ECONOMIC FACTORS

Evaluation of the statistics from health insurance funds on those who become unemployed showed that hospital admissions due to heart attacks increased during unemployment. The relative risk was 1.49 in the first eight months of unemployment, 1.82 after 8-16 months and 3.08 after more than 16 months. So it's clear that the long period of unemployment increases the risk of cardiovascular and mental diseases.¹⁹ Today, as a result of the economic crisis, unemployment rates are significantly increased. This might explain the higher frequency of ACS in young people in the last years.²⁰

NOVEL RISK FACTORS

Since no satisfactory explanation has been given by the classical risk factors for provocation of ACS in young by acute atheromatic plaque rupture, arises that for this population there may be additional risk factors.¹¹ Today, after extensive research and a better understanding of classical risk factors and their mechanisms, the so-called novel risk factors are admitted (Table 1). Of course, they are treated with caution by a part of the scientific community regarding their acceptance as risk factors.³

CHARACTERISTICS OF ACS IN YOUNG PEOPLE

The ACS in the young usually presents some characteristics with respect to its occurrence in more advanced ages. Most young people have the typical atherosclerotic disease which is most often manifested as a vessel disease as shown by the Coronary Artery Surgery Study. The usual localization of MI is the lower wall. In the electrocardiogram, it usually appears as STEMI in contradiction to the older people that it appears more often as NSTEMI-ACS.²¹ The main complication of ACS to young people is arrhythmias.²²

TABLE 1. Novel risk factors.

Novel risk factors
1) Elevated homocysteine levels
2) Increased levels of triglycerides
3) Elevated levels of lipoprotein a Lp(a)
4) Hypercoagulability and decreased activity of the fibrinolytic mechanism
5) Left ventricular hypertrophy
6) Infectious agents-inflammatory markers e.g. CRP
7) Oxidative stress

**EPIDEMIOLOGICAL DATA FOR ACS
IN YOUNG PEOPLE**

FREQUENCY OF OCCURRENCE

From current available data, new patients represent 0.4% - 19% of total ACS cases and only 2% of patients is under 35 years.⁷

ACS AND GENDER

The general rule is that between the two sexes there is a phase difference at the maximum frequency of about 10 years, with women being affected later than men, especially after menopause.³

Euro Heart Survey analyzed 10,253 patients who were hospitalized due to ACS in order to investigate gender differences in younger and older aged patients. This evaluation showed that in younger patients with ACS, women were less likely to present MI with ST elevation and more likely to be diagnosed with unstable angina. In older ages, men and women had no differences in their clinical picture. Both older and younger women had less extensive atherosclerotic lesions as shown angiographically. The findings of this evaluation suggest a different pathophysiology of ACS in younger but not in older women.²³

Acute coronary syndromes, although still rare in women of childbearing age, according to the latest researches an increase in occurrence during pregnancy was observed which has been attributed to the modern trend of childbearing at older ages as the result of educational and employment goals now placed by young women leading to postpone childbearing for later.²⁴

ACS AND NATIONALITY

ACS is a global health problem as it occurs to all nationalities with some differences in respect to age of onset, mortality rates, etc. AIR study is of particular interest as the risk factors for ACS were investigated for Indian patients hospitalized to a cardiology unit of South African during 15 years, from 1995 to 2010. According to the findings of this study, ACS in Indian patients showed increased frequency at young age as the result of the complexity of risk factors to this population.²⁵

**ACS IN THE CORONARY CARE UNIT
OF “EVAGELISMOS” HOSPITAL**

In the Coronary Care Unit of “EVAGELISMOS” hospital, a total of 760 hospitalized patients were diagnosed with ACS in the last two years. From these patients, 158 were young people and the majority of them were men. More specifically, in the year 2012, 377 patients were admitted from both cardiology clinics, and 81 patients were under 50 years of age. In the year 2013, a total of 383 patients were hospitalized with ACS. From

these, 77 were younger than 50 years old.

ACS TREATMENT

**TREATMENT OF ACS IN YOUNG PEOPLE
INCLUDES:**

Thrombolysis

Successful thrombolysis in hypercoagulable states is reported in the bibliography. In case of spasm from use of cocaine, thrombolysis should be done if there is no immediate resolution of symptoms and changes in the ST interval after administration of sufficient doses of vasodilators.

Angioplasty

Because of the wide spectrum of causes for ACS in young people, diagnostic angiography should be performed in all cases to confirm the cause and suggest the most suitable treatment.⁸ Performing promptly a coronary angiography in young patients compared with the elderly, is a lifesaving treatment that has been proven after several investigations in hospitals equipped with catheterization laboratory.²⁵ There are reports of successful angioplasty with or without stent placement in the antiphospholipid syndrome. In these patients with accelerated atherosclerosis, early intervention with primary angioplasty has better results compared to thrombolysis. Percutaneous transluminal coronary angioplasty (PTCA) and stent insertion should be considered in spontaneous rupture of coronary artery and myocardial bridging.

An antiplatelet and antithrombotic therapy

Aspirin is recommended in most cases. Anticoagulant treatment should be considered in the nephrotic syndrome, if the serum albumin is less than 20 g/l. In Hughes syndrome, after a heart attack long anticoagulant treatment is necessary.

B-blockers

These drugs are best to be avoided in case of parallel use of

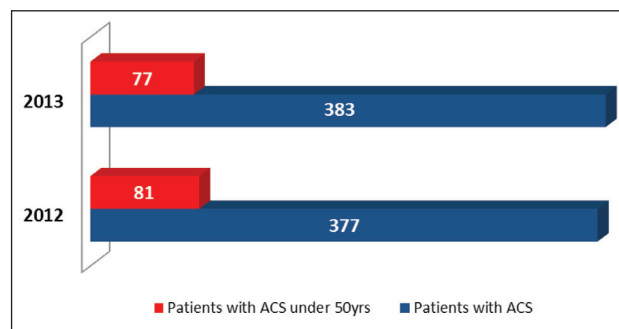


TABLE 2. ACS in Coronary Care Unit of G.H.A “EVAGGEMISMOS”.

cocaine and amphetamines, as there is risk with concomitant alpha1-adrenergic activity, worsening of coronary spasm.⁵

The best treatment of ACS in young people is the prevention of risk factors (smoking, obesity, dyslipidemia).

PROGNOSIS

Young patients with ACS have more favorable prognosis than the elderly ones. The young age is an independent indicator of good prognosis for these patients. The rate of in-hospital mortality of young patients with EM is about 1-6%, while for the elderly patients it ranges from 8-22%.⁸ Also, the incidence of complications such as cardiogenic Shock, stroke and dysfunction of the left ventricle is lower in young patients.^{21,25}

CONCLUSION

The occurrence of ACS in young people, although is not a common condition compared to older people, is a reality which is often overlooked during clinical examination of a young patient. While the ACS due to atherosclerosis has been studied and sufficiently linked to the classical risk factors, the data are limited and the prevalence of these factors among young people has not been adequately explained. This reflects the need for further investigation and potential modification of risk factors in order to address the increasing appearance in recent years of ACS in the younger population. Monitoring the young patient with ACS is a particular challenge for health care professionals as they help them to improve life expectancy and quality of life, with their contribution to the adjustment of lifestyle to the new data of the present disease, because as we know the young people are undergoing a productive period which requires an adequate level of health by at least minimizing the modifiable risk factors.

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