

Acute Coronary Syndrome in a Young Woman

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When should an acute coronary event be suspected in a young woman with chest pain? Coronary artery disease is not common in such patients, but the possibility should not be discounted. Correct characterization of the pain, along with presence of known risk factors for CAD, can lead to an accurate diagnosis, even though the presentation may be atypical. [Rev Cardiovasc. 2001;2(3):166–171]

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A 38-year-old female presented to her community hospital complaining of chest pain.

History

She had been well until 1 week prior to admission when she had three episodes of transient substernal chest burning occurring at rest, radiating to her back. The night before admission, she had a mild episode of chest discomfort for which she took antacids and then went to sleep. On the morning of admission, she again experienced chest discomfort, now moderate in intensity and radiating to the throat. After 1 hour with no improvement in her symptoms, she drove to the emergency department of her local hospital.

Her past medical history was notable for an anxiety disorder, for which she was taking paroxetine, and palpitations attributed to mitral valve prolapse, for which she was taking propranolol. She denied tobacco or illicit drug use, hypertension, and diabetes. She had a history of mild hypercholesterolemia. The family history was notable for a father with a myocardial infarction (MI) and coronary artery bypass surgery at age 39, and a mother with an MI at age 60. The review of systems was non contributory. The patient was active in sports; she had played soccer within the past 2 weeks without chest pain or dyspnea.



Figure 1. Resting 12-lead ECG on admission to the local hospital.

Physical Exam

In the emergency department, the physical exam was normal. There was no chest wall tenderness. The lungs were clear. The cardiac exam was notable for the absence of an S3 or S4, murmurs, clicks, or rubs. The abdomen was soft. The extremities were free of edema, with full distal pulses.

The electrocardiogram (ECG) is shown in Figure 1. With the exception of the suggestion of peaked T waves in the precordial leads, there were no abnormalities. The chest x-ray was normal.

Treatment

The patient was treated initially with antacids and ranitidine without relief. Subsequently, she was given sublingual nitroglycerin, which relieved her chest discomfort completely. Aspirin and nitroglycerin paste were also started. Initial laboratory tests were normal, with the exception of an elevated cholesterol level (241 mg/dL). Initial creatine kinase (CK) concentration with MB fraction and troponin I were normal. The patient was admitted to a telemetry bed for observation.

Several hours after being admitted, the patient became unresponsive and had a seizure. She was found to be in rapid polymorphic ventricular tachycardia, for which she was cardioverted successfully. She subsequently complained of chest pain and now had transient 1- to 2-mm ST-segment elevation on her ECG. She was treated with heparin and intravenous nitroglycerin and was transferred to a tertiary medical center for further evaluation.

At the tertiary hospital, her ECG showed anterior Q waves with persistent ST-segment elevation sugges-

tive of MI (Figure 2). Bedside echocardiogram demonstrated severely reduced left ventricular function with apical and anterior akinesis and an ejection fraction of 25%. The mitral valve was normal. The CK level was now 1,276 mg/dL with a positive MB fraction. The patient underwent urgent cardiac catheterization. Left ventriculography revealed moderately reduced left ventricular function, with akinesis of the apex and anterolateral wall (Figure 3). Coronary angiography revealed a total occlusion of the mid-left anterior descending artery with evidence of thrombus. The lesion was successfully dilated using an intracoronary stent (Figure 4). There were no other significant coronary lesions. The patient received abciximab at the time of stent placement and was placed on clopidogrel for 4 weeks.

The remainder of the patient's hospital course was uneventful. She was placed on a beta-blocker and angiotensin-converting enzyme inhibitor therapy. She was treated for hypercholesterolemia with atorvastatin. A follow-up echocardiogram showed dyskinesia of the apex but only hypokinesia of the anterior wall, with an improved ejection

Figure 2. Resting 12-lead ECG on admission to the tertiary hospital.



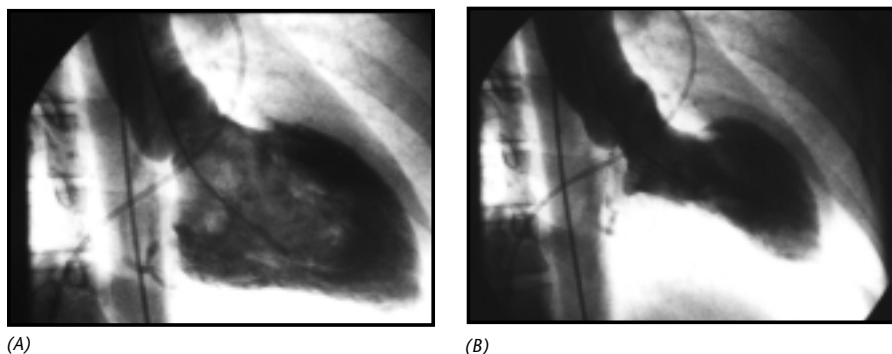


Figure 3. Single-frame left ventriculogram in the right anterior oblique projection. (A) end-diastole (B) end-systole.

fraction of 45%. The patient was discharged on hospital day 6 and is presently participating in a cardiac rehabilitation program without symptoms.

Discussion

Despite the numerous advances in the treatment of cardiac disorders, cardiovascular disease is the leading cause of death among men and women and accounts for approximately half of all female deaths.¹ Furthermore, although mortality from acute coronary syndromes has decreased over the past several decades in men, this trend has been less pronounced in women,¹ and due to the aging of the population and the longer survival of women, the absolute number of deaths due to cardiovascular disease is actually higher in women.²

As in men, the incidence of CAD in women increases with age. However, the prevalence of CAD in women is lower than that in men, and the clinical manifestations of the disease present 10-20 years later in women.³ Therefore, women present at an older age, often with a heavier burden of comorbid conditions. Women are also known to be more likely to present with atypical chest pain, without ST-segment elevation, or to have nondiagnostic ECGs or exercise stress tests.⁴ In addition, the specificity of

chest pain is lower in women than in men, and there is a higher likelihood of normal findings or insignificant CAD on angiography in women.⁵

The greater age of women in comparison to men when the clinical manifestations of CAD appear may have a negative impact on clinical outcomes following a coronary event. However, knowledge of the increased prevalence of CAD in older women may also translate into a barrier against prompt diagnosis and aggressive treatment in younger women presenting with coronary symptoms. The present case illustrates the hazard of translating characteristics of populations to an individual patient. Based on the initial therapy given (antacids and H₂ blockers), it is apparent that

the initial working diagnosis was dyspepsia rather than angina. This may, in part, be due to the perceived rarity of CAD in women of this patient's age. While data from the Framingham Heart Study show that the biennial rate of CAD morbidity in women ages 35-44 is one sixth that in men, the absolute difference is relatively small (1.2 versus 8.2/1,000 population).³ The fact that the patient had a large component of indigestion with a relatively benign ECG also likely contributed to a delay in pursuing the correct diagnosis. Similarly, the history of anxiety as well as a suspicion of mitral valve prolapse (not confirmed by physical exam or echocardiogram) may also have tended to suggest a noncardiac (or noncoronary) etiology.

There were, however, clinical indicators that pointed to a higher-than-expected likelihood of CAD. The patient had several risk factors for coronary artery disease, including a history of premature CAD in both parents and a history of dyslipidemia. The traditional risk factors for CAD that are operative in men are also operative in women: hypertension (including systolic hypertension), cigarette smoking, elevated low-density lipoprotein (LDL) cholesterol, low high-density

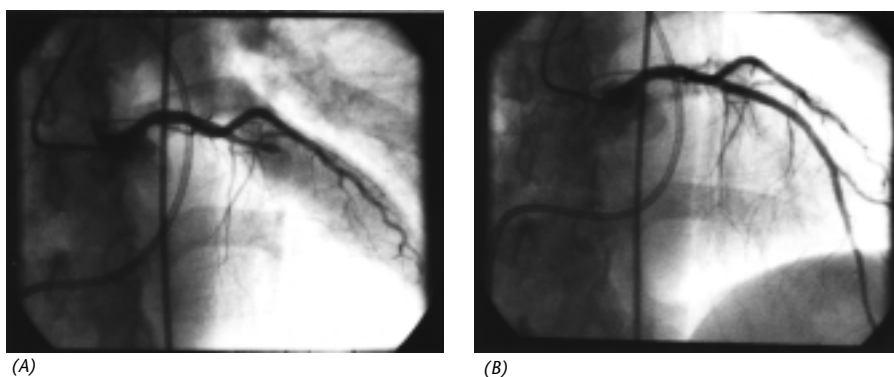


Figure 4. Single-frame cineangiogram of the left coronary artery in the right anterior oblique projection with cranial angulation. The left anterior descending artery (A) is occluded in its mid-portion. Following intracoronary stent deployment, there is no residual stenosis (B).

lipoprotein (HDL) cholesterol, family history of premature CAD, diabetes, and sedentary lifestyle.⁶ In addition, early menopause in women has been documented as a risk factor.⁷ It is of note that some risk factors may be more important in women than in men. Diabetes is associated with a 3- to 7-fold increase in risk of CAD in women, compared to a 2- to 3-fold increase in men.² High LDL cholesterol is an important risk factor for CAD in women, especially those less than 65 years old,⁸ and low HDL cholesterol is a stronger predictor of CAD mortality in women than in men.²

The presence of chest pain was also suggestive of CAD. Despite the

lower specificity of chest pain, it is the most common presenting symptom of coronary syndromes in women.³ In the Myocardial Infarction Triage and Intervention Registry, almost 90% of women with MI had chest pain as a feature of the initial clinical presentation. Women were also more likely than men to have symptoms such as abdominal pain, dyspnea, nausea, or fatigue as a component of their presentation.⁹ In the Coronary Artery Surgery Study (CASS), characterizing chest pain as definite angina, probable angina, or nonanginal pain was shown to be useful. Sixty-two percent of women with definite angina had CAD, while 40% with

probable angina and 4% with nonanginal pain had CAD.⁴ Thus, the presence of chest pain other than clearly nonanginal chest pain suggests at least a moderate risk of having the disease. In the presence of typical anginal chest pain and of other risk factors, use of a diagnostic algorithm suggested by Douglas and Ginsburg¹⁰ may further define the likelihood of CAD in women (Tables 1 and 2). The presence of 2 or more major determinants or 1 major and more than 1 intermediate or minor determinant suggests more than an 80% likelihood of the presence of CAD. The absence of any major and no more than 1 intermediate or 2 minor

Table 1
Characteristics of Typical and Atypical Angina

Typical

Substernal
Characterized by a burning, heavy, or squeezing feeling
Precipitated by exertion or emotion
Promptly relieved by rest or nitroglycerin

Atypical

Located in the left chest, abdomen, back or arm in the absence of mid-chest pain
Sharp or fleeting
Repeated, very prolonged
Unrelated to exercise
Not relieved by rest or nitroglycerin
Relieved by antacids
Characterized by palpitations without chest pain

Adapted from Douglas and Ginsburg.¹⁰

Table 2
Determinants of Coronary Artery Disease in Women with Chest Pain

Major

Typical angina pectoris
Postmenopausal status without hormone replacement
Diabetes mellitus
Peripheral vascular disease

Intermediate

Hypertension
Smoking
Lipoprotein abnormalities, especially low HDL cholesterol levels

Minor

Age (65 years)
Obesity, especially central obesity
Sedentary lifestyle
Family history of CAD
Other risk factors for CAD (eg, psychosocial or hemostatic)

Adapted from Douglas and Ginsburg.¹⁰

determinants suggests a low (less than 20%) likelihood of having the disease. Using this approach, this patient would be said to have had 1 major, 1 minor, and 1 intermediate determinant, suggesting a moderate to high likelihood of CAD. Therefore, this patient was appropriately admitted for further evaluation. The outcome would likely have been far worse had the patient been discharged based on her benign ECG and negative initial enzymes and the low prevalence of CAD in her age group.

The patient's subsequent course of treatment for her coronary disease was standard once the diagnosis of acute coronary syndrome was made. However, there is evidence that the treatment and outcome in women are often different than they are in men. Two recent reports highlight such differences.

Analysis of the Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes (GUSTO) IIb trial¹¹ revealed that women with acute coronary syndromes were more likely to present with unstable angina than men were and that among those presenting with MI, women were less likely to have ST-segment elevation. Women also were older, had more

comorbid conditions, and were more likely to have complications (eg, hypotension and pulmonary edema) than men. Women were less likely than men to undergo cardiac catheterization (53% vs 59%; $P < .001$) and had a higher overall mortality rate (6% vs 4% $P < .001$). After adjustment for differences in baseline characteristics, women with the diagnosis of unstable angina had a statistically better survival rate than men, probably due to the higher likelihood of finding nonobstructive CAD in these patients. However, there was a strong trend toward a worse outcome in women presenting with ST-elevation MI.

In a recently published study¹² from the National Registry of Myocardial Infarction 2, involving 155,000 women and 229,000 men hospitalized with MI, the women were again found to be older, less likely to have ST-segment elevation at presentation, and less likely to receive thrombolytic or other reperfusion therapy. In-hospital mortality was higher for women (16.7% vs 11.5%). What was surprising was that while the mortality rate for older women was similar to that of older men, younger women (particularly the youngest) died at a much higher rate than younger men. This

held true even after adjusting for baseline characteristics.

Other factors relating to treatment of acute coronary syndromes that may have an impact on outcome are worth noting. Women are less likely to receive proven treatments such as aspirin, beta-blockers, and reperfusion therapy.¹³ There may also be variations in the response to treatment such as thrombolytic therapy. A review of the large-scale placebo-controlled trials of thrombolysis in acute MI revealed that although intravenous thrombolytic therapy significantly reduced mortality rates in both women and men, there was less of a reduction in women and mortality rates were higher among women than among men in both the placebo and the treatment groups.¹⁴ Older age in women and a higher incidence of hemorrhagic complications, including stroke, have been reported to account for much of this gender difference in outcomes.¹⁵⁻¹⁷

Other forms of revascularization have shown similar benefit for both sexes. In a comparison of primary angioplasty versus thrombolytic therapy, men and women had equally superior results with primary angioplasty.¹⁸ Similarly, in patients undergoing multivessel

Main Points

- Cardiovascular disease accounts for about half of all deaths in females.
- The prevalence of CAD in women of a given age is about that in men 10 to 20 years younger.
- Women are more likely to present with atypical chest pain or without ST-segment elevation or to have indefinite results on diagnostic tests.
- Clinicians may have a lower index of suspicion for CAD in younger females.
- Women are less likely than men to receive proven treatments and may respond to treatment differently.
- Diabetes and low HDL cholesterol are stronger risk factors for CAD in women than in men.
- An algorithm based on typical angina and on other risk factors can help determine the likelihood of CAD in women presenting with chest pain.
- Women with MI are less likely to have ST-segment elevation and have worse outcomes following the event.

angioplasty or coronary artery bypass grafting in the Bypass Angioplasty Revascularization Investigation (BARI), women fared as well as or even better than men after adjustment for baseline characteristics.¹⁹

Acute coronary syndromes, particularly MI, represent significant health problems in women. Biological differences and advanced age in women contribute to clinical presentations, responses to therapy, and outcomes different from those of men. Increased primary prevention, better diagnosis of existing disease, more aggressive application of proven therapies, and further refinement of the treatment of acute coronary syndromes will likely result in improved outcomes in women. ■

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