

# Gender differences in the clinical presentation to the emergency department for chest pain

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## Key words:

Chest pain;  
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Risk factors;  
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Previous studies suggest that the presentation, treatment, and outcome of acute coronary syndromes differ between women and men. Women arriving to the emergency department for acute coronary syndromes are usually older, have a higher prevalence of diabetes and hypertension, show a longer delay from symptom onset and have a slightly higher in-hospital mortality than men. In our experience including 4843 emergency department admissions for chest pain, the time to presentation was longer and diagnostic mistakes more frequent in women than in men, whereas medical treatment and the rate of revascularization procedures were similar. The introduction of Chest Pain Units with pre-defined diagnostic and therapeutic procedures should facilitate the early identification of high-risk female patients, reduce inappropriate hospitalizations, and improve the diagnosis and outcome of coronary heart disease.

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The problem of evaluating female patients with ischemic heart disease was highlighted by Healy<sup>1</sup> in an editorial published in the *New England Journal of Medicine* in 1991. The problem consists of the higher probability of “diagnostic and therapeutic mistakes” in women admitted to the coronary care unit for acute coronary syndromes (ACS) compared to men. This phenomenon, described in the literature as the “Yentl syndrome”, has been related to a lower use of diagnostic and therapeutic procedures, to a lesser ability to identify patients at high risk for acute coronary events, to a lower rate of revascularization interventions, and to a higher morbidity and mortality in women than in men. These mistakes have been attributed to a number of factors: the lower prevalence of coronary artery disease in premenopausal women; the higher frequency of atypical symptoms in female patients; the lower diagnostic power of noninvasive testing because of more frequent false positive results in women; the scarcity of specific studies focusing on female patients<sup>2</sup>, and the very low number of women enrolled in clinical trials<sup>3</sup>.

An early and careful evaluation of women arriving to the emergency department (ED) with a clinical suspicion of ischemic heart disease is therefore the mainstay for their correct diagnostic and therapeutic management. The high prevalence

of the symptom “chest pain” as a cause of access to the ED makes this evaluation more difficult. Indeed, Pope et al.<sup>4</sup> reported that, of 10 689 patients arriving in 7 months to the ED for chest pain, only 17% were hospitalized with a recognized diagnosis of ACS (8% for acute myocardial infarction, and 9% for unstable angina), while 55% were discharged for noncardiac pain. These data are similar to those observed in our own hospital (San Camillo-Forlanini Hospital in Rome)<sup>5</sup> during the 12 months between January and December 2000: of 4843 admissions to the ED for chest pain, 16% were hospitalized for ACS (6% myocardial infarction, 10% unstable angina) and 58% were sent home.

## Epidemiology

In women the prevalence of ACS diagnosed in the ED is lower than in men, with different rates in the various studies depending on the clinical presentation at admission. In the MITRA registry<sup>6</sup> only one third of the patients hospitalized for acute ST-elevation myocardial infarction was of female sex, while in other studies<sup>7,8</sup> this percentage reached 40-45%. In our experience<sup>5</sup> women represented 41% of all hospitalized patients for acute myocardial infarction.

## Clinical presentation

Several studies<sup>5,6,9</sup> have shown that women arriving to the ED for ACS are usually older than men (in the MITRA registry 71 vs 62 years), although in other studies<sup>7</sup> this difference was not statistically significant.

The clinical history of patients with ACS in the ED shows that a previous myocardial infarction is less common in women than in men<sup>6</sup>. There is a higher prevalence of diabetes and hypertension in women<sup>6,7</sup>, and of smoking in men<sup>7</sup>. Gender differences in risk factors, however, are influenced by the population examined, particularly its age. A multicenter study<sup>10</sup> involving women arriving to the ED of 20 hospitals of the Lazio region in Italy for chest pain showed that smoking was the main risk factor in younger subjects (< 50 years), while hypertension, diabetes and dyslipidemia were more frequent in older patients; interestingly, 20% of women were unaware of their risk-factor profile<sup>10</sup>.

As to the clinical presentation, women with ACS frequently arrive to the ED with chest pain and with signs and symptoms of heart failure<sup>6</sup> (elevated heart rate, dyspnea). This presentation has for many years been considered "typical" of the female sex; recent data<sup>9,11,12</sup>, however, have definitely shown that the typical symptoms of myocardial ischemia (chest pain, cold sweats, pain extending to the arms and jaw) are strongly diagnostic in women too, and that their positive predictive value in identifying an ACS is higher in women than in men; on the contrary, atypical symptoms (dizziness, asthenia, atypical pain) do not significantly correlate with coronary heart disease, whereas perspiration during chest pain shows a high independent positive predictive value in the diagnosis of ACS. Data in the literature indicate that chest pain alone has little value in identifying women with coronary heart disease<sup>13</sup>.

The MITRA registry<sup>6</sup> reported in women a more frequent presentation with acute anterior myocardial infarction, with less extensive coronary involvement, and with a better left ventricular systolic function in women compared to men; in contrast, ST-segment elevation is more frequent in men than in women<sup>12</sup>.

## Timing

Women with ACS usually arrive to the ED with a longer delay from symptom onset than men (45 min later in the MITRA registry<sup>6</sup>); fewer women reach the hospital during the first hour from the onset of symptoms (7.6% of women vs 12.6% of men<sup>6</sup>); this greater delay is influenced by age and social status<sup>11,14</sup>.

Data from the San Camillo-Forlanini Hospital in Rome<sup>5</sup> show that 84% of men but only 68% of women with ACS reach the hospital within 12 hours of symptom onset; this difference is even greater in women > 55 years, among whom more than one third arrive after 12 hours.

## Treatment

One of the most common explanations given for the "Yentl syndrome" is the different use of invasive procedures in men and women with coronary heart disease<sup>15</sup>: for similar clinical conditions, both thrombolysis and coronary angioplasty were performed less frequently in women than in men<sup>6,11,13</sup>. Several recent studies, however, have questioned this explanation: first of all, women arriving to the ED for ACS are older, have a longer time to presentation, and more often have co-morbidities than men<sup>6</sup>. These coexisting clinical variables can sometimes represent contraindications to early revascularization; after adjustment for these variables, in fact, the differences in the rate of revascularization between men and women<sup>7,16</sup> were no longer statistically significant. Secondly, with the advent of stenting, the improved results of percutaneous revascularization (more evident in women, who have a higher risk of adverse events after coronary angioplasty compared to men<sup>17</sup>) have stimulated the use of angiography in women to a similar extent as in men.

In the study from the San Camillo-Forlanini Hospital in Rome<sup>5</sup> neither the percentage treated by urgent revascularization for ACS (41% of men vs 38% of women) nor the success rate of the procedure (post-procedural TIMI 3 flow in 94% of men vs 97% of women) were significantly different between men and women.

Finally, among patients with unstable angina, the use of aspirin, heparin and antianginal drugs is similar in female and male patients<sup>7</sup>.

## Mortality

The in-hospital mortality among women with acute myocardial infarction tends to be greater than in men<sup>5,6,11,14</sup>. A trend towards higher in-hospital mortality is particularly evident among female patients < 50 years<sup>4,6,18</sup>. One of the causes for this trend could be the missed diagnoses of ACS among young women<sup>19</sup> and the consequent admission to inappropriate departments<sup>9,16</sup>. In the study conducted at the San Camillo-Forlanini Hospital<sup>5</sup>, the mortality for acute myocardial infarction was significantly higher in women than in men on univariate analysis (17.9 vs 8.8%,  $p < 0.05$ ), but not after adjustment for age.

## Role of Chest Pain Units

The recent institution of Chest Pain Units, with well-established diagnostic measures, has yielded good results in the United States, decreasing mortality and medical costs, with a sharp reduction in inappropriate admissions, and shorter hospitalizations.

At the San Camillo-Forlanini Hospital, guidelines for the management of chest pain have been introduced into

clinical practice. These require an effective collaboration between ED physicians and cardiologists. The patients are quickly evaluated and classified as “low”, “medium” and “high risk”, depending on the results of clinical and instrumental exams (ECG, clinical history, markers of myocardial damage, hemodynamic status, etc.); medium and high-risk patients are admitted to the coronary care unit and cardiology ward. Low-risk patients are kept under observation in the Chest Pain Unit and monitored for 24-48 hours. At the end of the observation period, in the absence of signs and symptoms of ACS, patients undergo a stress test and, if this is negative, are discharged. In women the stress test is dobutamine echocardiography, because it is noninvasive, with the best cost/effectiveness ratio for diagnosing coronary artery disease in the female sex, and because exercise ECG stress testing has a lower predictive value in women than in men<sup>2,20</sup>.

## Conclusions

The diagnosis of ACS in subjects of both sexes who arrive to the ED is an important public health problem. Every effort has to be made, and in a short time span, to avoid the early discharge of patients at high risk of cardiac events<sup>8</sup>. Pope et al.<sup>4</sup> showed that the percentage of patients arriving to the ED for chest pain who were inappropriately discharged with an unrecognized ACS is globally low (2.1%), but higher in women, particularly if young. In our experience<sup>10</sup>, too, 56% of women arriving to the ED for chest pain are discharged without having undergone further examinations other than ECG and markers of myonecrosis, even when the ECG is described as “abnormal” by a cardiologist. Notably, 7.6% of these had a major cardiac event within 6 months<sup>10</sup>. The main problem, therefore, is the lack of a careful clinical and diagnostic evaluation of female patients arriving to the ED with the suspicion of an ACS, especially considering that the clinical presentation and prognosis do not significantly differ between men and women.

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