# Differences in coronary heart disease according to sex and chest pain in primary care

**Diferencias en enfermedad coronaria según sexo y dolor torácico en atención primaria**

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## Abstract

Introduction: women who suffer a myocardial infarction present with more atypical symptoms than men. Chest pain remains an important common symptom of CAD.
Purpose: To assess the diagnostic value of non-acute chest pain characteristics for CAD in women and men.
Methods: A retrospective observational study was conducted to collect data from individual patients in primary care clinics.
Results: Sex-specific models showed better performance in females (ABC 0.89, 95 % CI 0.81 to 0.96).
Conclusions: The diagnostic value of non-acute chest pain characteristics was high in men and women.

Keywords: coronary arteries, myocardial infarction, sex,primary care. source: DeCS
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**Resumen**
Introducción: las mujeres que sufren un infarto de miocardio presentan síntomas más atípicos que los hombres, el dolor torácico sigue siendo un síntoma común importante de la EAC.
Objetivo: Evaluar el valor diagnóstico de las características del dolor torácico no agudo para la EAC en mujeres y hombres.
Método: Se realizó un estudio observacional retrospectivo donde se recopiló datos de pacientes individuales de clínicas de atención primaria.
Resultados: los modelos específicos de sexo mostraron un mejor rendimiento en las mujeres (ABC 0,89, IC del 95 %: 0,81 a 0,96) .
Conclusiones: Tanto en hombres como en mujeres, el valor diagnóstico de las

características del dolor torácico no agudo fue alto.

**Palabras clave**:arterias coronarias, infarto de miocardio,sexo,atención primaria fuente : DeCS

## Introduction

Although women with myocardial infarction are reported to have more atypical symptoms than men, chest pain remains an important common symptom of coronary artery disease (CAD) in both women and men[1]. The relationship between chest pain characteristics has been studied extensively in patients with acute chest pain but not comprehensively in patients with non-acute chest pain presenting to outpatient clinics[2].

Currently, approximately 1% of all patients consulting a general practitioner have complaints of chest pain as the main reason for their visit. However, only 8% to 12% of these patients have ischemic heart disease[3]. Forty percent of patients with chest pain are referred to a cardiologist for fear of missing the potentially fatal diagnosis of CAD and because of the difficulties in estimating the likelihood of CAD in these patients. In addition, additional noninvasive diagnostic tests are performed based on cardiologists' estimation of the probability of CAD. For structural evaluation of the coronary arteries, cardiac computed tomography (CT) or invasive coronary angiography (ICA) is used. Interestingly, in patients undergoing ICA, obstructive CAD is found twice as often in women as in men. Furthermore, approximately 50% of cardiac CT investigations show a calcium score of zero[4].

The high prevalence of normal imaging results raises the question of whether the presence of CAD could be estimated with more certainty to avoid unnecessary imaging. In addition, differences in outcome and clinical presentation between women and men may suggest that this estimate should consider sex-specific symptoms and risk factors. Chest pain characteristics are an important part of the diagnostic evaluation, as they are considered useful in estimating the likelihood of CAD[5]. However, their exact diagnostic value remains unclear. Furthermore, although outpatient clinics evaluate the largest proportion of patients with chest pain, most of the information on the diagnostic value of signs and symptoms is derived from hospitals. Little is known about the diagnostic value of chest pain characteristics for CAD in men and women with nonacute chest pain attending cardiology outpatient clinics[6]. Therefore, we evaluated the diagnostic value of nonacute chest pain characteristics in differentiating patients with CAD from patients without CAD in women and men attending cardiology outpatient clinics.

## Method

A retrospective observational study was conducted to collect data on individual patients from primary care clinics in the city of Ambato. Patients visited the clinics between April 2010 and February 2021. In addition, It included data from patients referred by their primary care physician due to non-acute chest pain, whose chest pain characteristics were recorded in a standardized manner using a questionnaire. The standard cardiovascular study for patients with chest pain consisted of an admission by a nurse who collected information on cardiovascular risk factors (age, sex, smoking history, history of cardiovascular disease, presence of diabetes mellitus, hypertension, dyslipidemia, body mass index (BMI), and signs of heart failure) and detection of ischemia by exercise ECG, followed by assessment by the cardiologist. This study was approved by the Universidad Regional Autónoma de Los Andes (UNIANDES).

Data records comprising the cardiologist's detailed and standardized documented description of the characteristics of nonacute chest pain (n = 1028) were retrieved from electronic health records. This contained appearance, location, radiation, onset, duration, frequency, progression, provoking and relieving factors, and concomitant symptoms. In addition, the cardiologist scored the available chest pain grade using the New

York Heart Association (NYHA) classification[7].

The diagnosis of CAD was based on available imaging reports or, if imaging was not performed, on the cardiologist's estimate of CAD. Patients not referred for imaging studies because of the cardiologist's low estimated probability of CAD after the standard cardiovascular study were considered not to have CAD. Significant stenosis (>50%) indicated CAD in patients referred for imaging studies.

Receiver operating characteristic curves were constructed, and areas under the curve (ABC) were calculated to estimate model performance for women and men separately. Database and statistical processing of the data were performed and analyzed in SPSS 26 statistical software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used for the results collection, presentation and interpretation.

**Results**

The total study population comprised 1028 patients, of whom 505 (49%) were women. On average, women were two years older than men (58 years vs. 56 years, p=0.009). A history of cardiovascular disease (8.3% in women vs. 13.8% in men, p=0.007) and antihypertensive drugs (66.1% vs. 72.8%, p=0.04) were less frequent than in men. The prevalence of all other cardiovascular risk factors was similar for women and men.

After their clinic visit, 238 patients (23% of all patients, 44% women) were referred for cardiac CT (angiography) or ICA. Of these 238 referred patients, 99 were diagnosed with CAD (42% of all patients, 24% women).

Table 1 shows the prevalence of chest pain characteristics for women and men stratified by the presence of CAD. In women and men, daily chest pain of short duration was more frequent in the presence of CAD than without CAD. In women with CAD, daily chest pain was common in 63% versus 33% without CAD (p = 0.005). Daily chest pain was common in 51 % of men with CAD versus 28 % without CAD (p<0.001). Women with CAD reported short-duration chest pain in 96 % compared to 76 % without CAD (p<0.05). For chest pain of short duration, the prevalence was 93 % in men with CAD compared to 72 % in men without CAD (p<0.001). In addition, complaints were more frequently provoked by emotional or physical stress or extreme temperature and were relieved at rest in patients with CAD compared to patients without CAD. Provocation was prevalent in women in 75 % of CAD cases compared to 42 % of non-ACS cases (p=0.003) and in 88 % of men with CAD compared to 44 % of men without CAD (p<0.001).

Relief of chest pain complaints at rest was common in 75 % of women with CAD versus 39 % without CAD (p=0.001). In men, complaints were relieved at rest in 83 % with CAD and 37 % of men without CAD (p<0.001). The functional class of chest pain was higher in CAD cases than in non-ACE cases in both women and men: NYHA class II or higher in 54 % of women and 76 % of men with CAD compared to 30 % of women (p=0.025) and 23 % of men (p<0.001) without CAD.



Table 1. Relationship between chest pain characteristics and CAD.

| Features | Womenwith CAD (n=24) | No CAD (n=448) | p-value | Menwith CAD (n=75) | Without CAD (n=420) | p-value |
|---|---|---|---|---|---|---|
| Pressing nature, yes (%) | 22 (91,7) | 361 (80,6) | 0.278 | 72 (96,0) | 303 (72,1) | <0.001 |
| Radiation, yes (%) | 8 (33,3) | 198 (44,2) | 0.404 | 32 (42,7) | 129 (30,7) | 0.057 |
| Acute onset, | 13 (54,2) | 270 (60,3) | 0.704 | 37 (49,3) | 264 (62,9) | 0.037 |

| | | | | | | |
|---|---|---|---|---|---|---|
| yes (%) | | | | | | |
| Short duration, yes (%) | 23 (95,8) | 341 (76,1) | 0.046 | 70 (93,3) | 301 (71,7) | <0.001 |
| Dailyfrequency, yes (%) | 15 (62,5) | 146 (32,6) | 0.005 | 38 (50,7) | 117 (27,9) | <0.001 |
| Progressive, yes (%) | 10 (41,7) | 118 (26,3) | 0.159 | 40 (53,3) | 94 (22,4) | <0.001 |
| Provocation, yes (%) | 18 (75,0) | 190 (42,4) | 0.003 | 66 (88,0) | 184 (43,8) | <0.001 |
| Relief at rest, yes (%) | 18 (75,0) | 173 (38,6) | 0.001 | 62 (82,7) | 155 (36,9) | <0.001 |
| Vegetative symptoms, yes (%) | 2 (8.3) | 71 (15,8) | 0.483 | 7 (9.3) | 51 (12,1) | 0.616 |
| Dyspnea, yes (%) | 6 (25,0) | 66 (14,7) | 0.284 | 15 (20,0) | 39 (9,3) | 0.011 |
| NYHA class II or higher, yes (%) | 13 (54,2) | 135 (30,1) | 0.025 | 57 (76,0) | 97 (23,1) | <0.001 |



Source: statistical analysis, p ≤0.05 CAD, coronary artery disease; NYHA, New York Heart Association.

In thenet elastic analysis of women and men, the optimal model retained 4 of the 18 predictors with nonzero coefficients (α=0.68; λ=1 SD of the minimizer λ); age, provocation during stress or extreme stress temperature, relief at rest, and NYHA class. The model distinguished women and men with CAD from those without CAD with an ABC of 0.82 (95% CI 0.75 to 0.88). The ABC was 0.76 for women (95 % CI 0.68 to 0.85) and 0.83 (95 % CI 0.78 to 0.88) for men.

As described above, the general model, including both sexes, achieved an ABC of 0.76 (95 % CI 0.68 to 0.85) in women and 0.83 (95 % CI 0.78 to 0.88) in men. However, a comparison of the performance of the overall model with that of the sex-specific models showed better performance in women (ABC 0.89, 95 % CI 0.81 to 0.96) and only minimal improvement in men (ABC 0.83, 95 % CI 0.73 to 0.90).

**Discussion**

This study shows that nonacute chest pain characteristics are useful in identifying CAD in both women and men referred to cardiology outpatient clinics. Their diagnostic value appears to be reasonably high. Moreover, if non-acute chest pain is present, women and men with CAD have relatively similar characteristics for chest pain. However, small differences were observed between women and men for the features selected in the sex-specific models and their diagnostic performance. In women, dyspnea, BMI, hypertension and smoking were stronger predictors of the presence of CAD compared to men. In men, functional class and history of diabetes were more important than women. The performance of chest pain characteristics in diagnosing CAD improved when stratified by sex.

The analysis is based on routine care data from patients presenting to the primary care and cardiology outpatient clinic and undergoing an extensive standardized cardiovascular workup. First, this provided a unique representative sample of the general population presenting to cardiology outpatient clinics with nonacute chest pain without any selection bias that can occur in cohort studies in which many patients may not participate because of poor quality of life[8,9]. Second, the study contained an almost equal number of women and men, allowing to study women and men with equal power.

In the primary care setting, Bösneret al.[3] evaluated sex differences in clinical characteristics of chest pain. The investigators observed that some characteristics of chest pain, e.g., pain that worsened with exercise, were equally relevant for men and women. However, in women, prolonged chest pain was positively associated with CAD, whereas in men, shorter duration showed a positive association. These characteristics of chest pain are different from those reported in our study, dyspnea in women and functional class in men. This difference could be due to dissimilarity in the domain, as women and men presented to outpatient cardiology clinics were already referred by their general practitioners. In a further study,[10] results support the high diagnostic value of chest pain characteristics in differentiating patients with CAD from patients without CAD that we observed in both sexes, as well as the small sex differences in chest pain characteristics associated with CAD. This suggests that using a sex-stratified method may improve the diagnostic approach in these patients.

Several studies in the emergency department showed a similar high diagnostic value of clinical symptoms and cardiovascular risk factors for CAD in patients presenting with chest pain[11,12].In addition, they showed that women and men presented quite similarly if they presented with chest pain. On the other hand, Ferry et al. [2] reported that typical symptoms were more prevalent in patients with a diagnosis of myocardial infarction and had greater predictive value in women than in men. Consistent with our findings and those already mentioned in primary care, van der Meer et al.and Gimenez et al.also found small sex differences in the characteristics of chest pain associated with CAD[11,13].

Interestingly, although the pressing nature of chest pain is often considered one of the most typical and suspicious features in assessment, this feature was not retained in the overall elastic net model, which is similar to a previous report[14]. Although the pressor nature differentiated between CAD and non-ACE in both men and women in our univariate analysis, it was reduced to zero in our more optimal elastic net model. Furthermore, radiation was not significantly different between women and men with and without CAD in our univariate analyses, as shown in previous research[15].

The study shows that chest pain characteristics have diagnostic value in women and men presenting with non-acute chest pain in outpatient cardiology clinics. Furthermore, these results were comparable to the acute setting in the emergency department and primary care setting, implying that these easy-to-obtain chest pain characteristics are equally predictive in high-and low-risk populations.[16]

Within the outpatient clinics evaluated in this study, CT or ICA is the preferred method for evaluating CAD. However, noninvasive stress imaging is also recommended and frequently performed for CAD evaluation in patients presenting with chest pain in current clinical care[17,18]. To improve the diagnostic approach in patients presenting with chest pain beyond anatomic CAD assessment by CT or ICA, it would be interesting to evaluate whether clinical features could be added to the assessment of ischemia in patients presenting with chest pain as well and could be useful to improve patient selection for noninvasive stress imaging.

Cardiologists may have only recorded the characteristics of chest pain when chest pain was the predominant complaint. The conclusion may not apply to patients with mild dyspnea and chest discomfort. In addition, some characteristics of chest pain (e.g., vagal symptoms) were underreported to be studied. Moreover, not all patients in our study were referred for imaging, and we assumed that these non-referred women and men were free of CAD, which may not have been the case. This may have resulted in the misclassification of patients[19,20]. This misclassification of CAD may have resulted in an underestimation of the diagnostic value of chest pain features for CAD. As such, the diagnostic



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value of chest pain characteristics may be greater than reported in this study.

**Conclusions**

The diagnostic value of nonacute chest pain characteristics and risk factors in differentiating CAD from no CAD was high in men and women. Temperature or stress provocation, relief at rest, and functional class of chest pain were the most powerful in diagnosing CAD. Furthermore, when presenting with non-acute chest pain, women and men with CAD have similar chest pain characteristics. Nevertheless, our data show small sex differences in chest pain characteristics, and stratified by sex, the model performance improved, especially in women.

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