

# Influence of Gender on the Etiology of Mitral Regurgitation

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Our aim was to investigate the prevalence of the different causes of severe mitral regurgitation and the influence of gender on that prevalence. We performed a prospective study of 272 consecutive patients with severe mitral regurgitation that had been detected echocardiographically. Their mean age was 70.2±13.8 years, and 143 were women (52.6%). Atrial fibrillation was present in 52.9%, 72.7% presented with heart failure, and 21.0% with previous myocardial infarction. The most common etiological factor was rheumatic disease (in 26.5%), with the etiology being unclear in 32 patients (11.8%). Rheumatic disease was more frequent in women, at 35.7%, than in men, at 16.3%, whereas other etiologies were less frequent in women ( $P<.001$ ). In all age groups, a rheumatic etiology was more frequent in women. Rheumatic heart disease remains the main cause of severe mitral regurgitation observed in women referred to hospitals similar to ours.

**Key words:** Mitral regurgitation. Gender. Rheumatic disease.

## Influencia del sexo en la etiología de la insuficiencia mitral

Para valorar la frecuencia actual de las distintas causas de insuficiencia mitral severa y la influencia del sexo en la etiología, realizamos un registro prospectivo de 272 pacientes consecutivos con insuficiencia mitral severa en el ecocardiograma. La edad media fue de 70,2 ± 13,8, con 143 mujeres (52,6%). El 52,9% presentaba fibrilación auricular, el 72,7% insuficiencia cardíaca y el 21,0%, infarto de miocardio previo. La etiología más frecuente fue la reumática (26,5%) y en 32 pacientes (11,8%) no se encontró una clara etiología de la regurgitación mitral. La enfermedad reumática fue más frecuente en mujeres (35,7%) que en varones (16,3%), mientras que otras etiologías fueron menos frecuentes en las mujeres ( $p < 0,001$ ). Para todos los grupos de edad, la etiología reumática era más frecuente en mujeres. La enfermedad reumática sigue siendo la causa principal de la insuficiencia mitral grave en las mujeres remitidas a un hospital de las características del nuestro.

**Palabras clave:** Insuficiencia mitral. Sexo. Enfermedad reumática.

## INTRODUCTION

The etiology of mitral regurgitation is changing. Although a rheumatic etiology is still very common in developing countries,<sup>1</sup> Western countries are experiencing a drastic reduction in the incidence of rheumatic fever,<sup>2</sup> a consequence of improved sanitary conditions and the generalized use of antibiotics. However, the longer life expectancy of the citizens of these countries has led to

an increase in the number of cases of degenerative mitral regurgitation due to valve prolapse; indeed, this is commonly thought to be the main cause of organic mitral regurgitation.<sup>3-5</sup> Although mitral regurgitation is the second most common valve disease in Europe,<sup>6</sup> the etiology of this problem has recently been investigated only in surgical patients; this selection does not allow the real prevalence of the different etiologies associated with this problem to be discerned. In Spain, the prevalence of such etiologies has not been investigated at all.

## METHODS

The data analyzed were obtained from the DECIMA (*Datos Ecocardiográficos y Clínicos de la Insuficiencia Mitral Avanzada*, ie, Advanced Mitral Regurgitation: Electrocardiographic and Clinical Information) registry. This is associated with a prospective study involving

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272 consecutive patients, all diagnosed at our center (between October 2004 and October 2005) with severe mitral regurgitation (determined via the use of transthoracic or transesophageal echocardiography). The severity of regurgitation was determined taking into account as least two variables from among the following: the size of the regurgitation orifice, the regurgitation fraction, the color Doppler area, and the flow inversion in the pulmonary veins. To quantify the mitral regurgitation, the approach recommended by the American Society of Echocardiography<sup>7</sup> was followed. Either a Sonos 5500 (Philips, Eindhoven, The Netherlands) or an Acuson Sequoia (Siemens, Munich, Germany) apparatus was used. Both instruments have second harmonic imaging potential, possess multifrequency transducers, and have pulsed and continuous Doppler capabilities. The patients were included after an echocardiogram was performed, at which time the results of this test plus demographic and clinical data were all recorded in a standardized file. The etiology of the mitral regurgitation was defined in agreement with the criteria of the echocardiographer. Patients were divided into five groups:

- Dilated cardiomyopathy: with no organic valve disease.
- Ischemic etiology: with normal valves and heartstrings but ischemic heart disease, generally due to a prior myocardial infarction.
- Valve prolapse: including flail leaflets.
- Rheumatic valve disease.
- Other etiologies: including prosthesis dysfunction, prior mitral valvuloplasty, and the sequelae of endocarditis or congenital heart disease.

In patients showing none of these etiologies, the cause of mitral regurgitation was recorded as unclear.

### Statistical Analysis

Data are presented as means (standard deviation [SD]). The  $\chi^2$  test was used in comparisons between groups for determining the relationship between sex and etiology. SPSS v. 11.0 software (SPSS Inc., Chicago, Illinois, USA) for Windows was used for all calculations.

## RESULTS

The majority of patients were women (n=143; 52.6%). The mean age of all patients was 70.2 years (interval 24-94 years), with the women slightly older than the men 71.9+14.4 compared to 68.3+12.8 years:  $P=.03$ ). The study involved patients admitted to hospital (163; 59.9%) as well as outpatients (109; 40.1%), who were selected by both cardiologists/heart surgeons (n=163; 59.9%) and other specialists (109; 40.1%).

Table 1 shows the cardiovascular profile of the patients, and records that cardiovascular risk factors or a history of cardiovascular problems were common. Table 1 also shows the echocardiographic findings for the patients, confirming the severity of their mitral regurgitation problems.

The most common etiology was rheumatic disease (26.5%). The etiology of the disease was unclear in 32 patients (11.8%). Rheumatic disease was particularly common in women (35.7% compared to 16.3% in men), whereas other etiologies were less common in women (Figure 1). No relationship was found between age and the frequency of rheumatic etiology, although for all age groups the latter was more common among women (Figure 2). The patients whose disease was rheumatic in origin commonly had other valve problems, although 14 (19.4%) with echocardiographic data highly indicative of rheumatic problems had no other significant valve disease (Table 2).

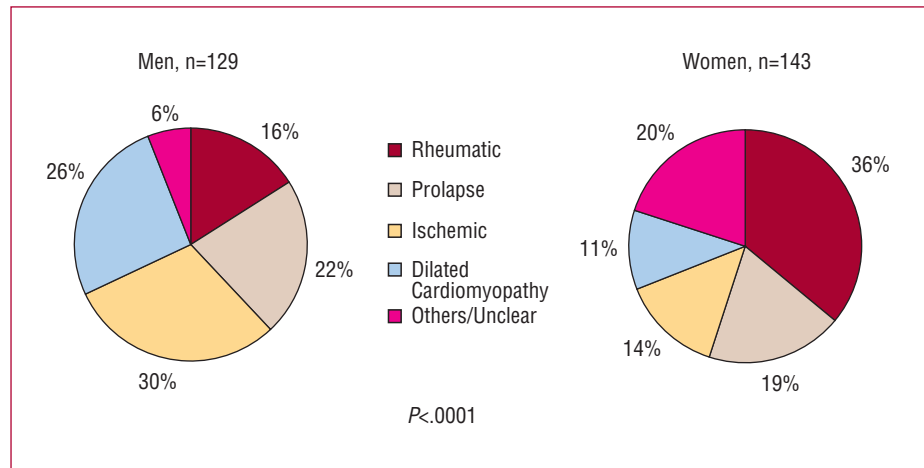
## DISCUSSION

Unlike in other reports involving patients who had undergone surgery, the members of the present population,

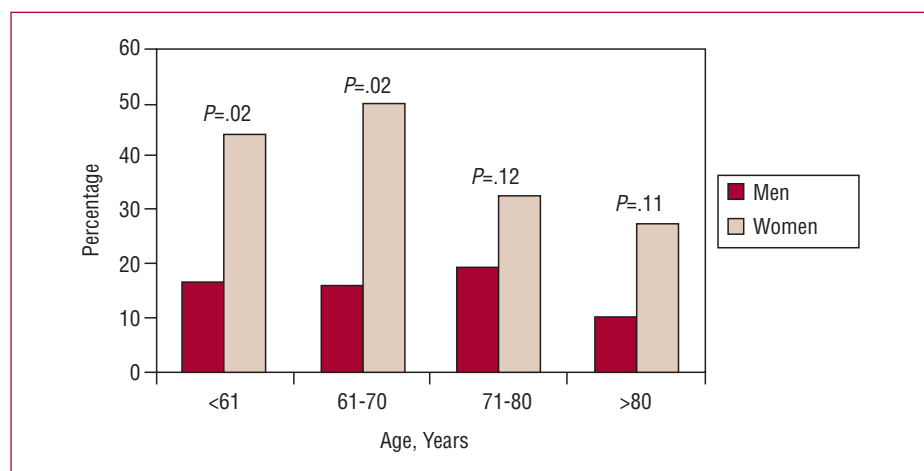
**TABLE 1. Patient Cardiovascular Profiles and Echocardiogram Results**

Cardiovascular profile, n (%)	
High blood pressure	157 (57.7)
Smoker/previous smoker	117 (43.1)
Hyperlipidemia	86 (31.6)
Diabetes	68 (25.0)
Obesity	59 (21.7)
Family background of ischemic heart disease	54 (19.9)
Antecedents, n (%)	
Dyspnea: functional class >I	198 (72.7)
Chronic atrial fibrillation	144 (52.9)
Previous myocardial infarction	57 (21.0)
Percutaneous coronary intervention	37 (13.6)
Previous heart surgery	37 (13.6)
Ictus	28 (10.3)
Peripheral artery disease	26 (9.6)
Previous mitral surgery	19 (7.0)
Echocardiogram results, mean (SD)	
Color Doppler area, cm <sup>2</sup>	12.2 (4.1)
Regurgitation orifice, cm <sup>2</sup>	0.30 (0.13)
Left ventricular ejection fraction, %	46.8 (17.4)
Diameter of the left atrium, mm	52.4 (8.9)
End-diastolic ventricular diameter, mm	55.5 (10.3)
End-systolic ventricular diameter, mm	40.0 (12.3)
Estimated systolic blood pressure in the pulmonary artery, mm Hg	55.9 (16.3)

SD: standard deviation



**Figure 1.** Etiology of mitral regurgitation according to gender.



**Figure 2.** Percentage of patients with rheumatic etiology according to sex and age.

all of whom had severe mitral regurgitation, were selected because of a referral for an echocardiogram. The mean age of the present population was high (over 70 years), and cardiovascular comorbidities were common. However, a high percentage of the patients were monitored by specialists who were not cardiologists (40%); this is probably related to the fact that the majority of the patients admitted to our hospital due to heart failure come from outside its own cardiology unit.<sup>8</sup>

The main finding of this work is that the etiology of mitral regurgitation in Spain is still most commonly rheumatic (27% of all cases). This disagrees with the current movement towards considering valve prolapse as the main culprit. Previous studies performed with surgical patients reported the great predominance of valve prolapse (up to 60%).<sup>3</sup> However, apart from the inherent geographical differences in these studies, it should be remembered that surgical patients represent a highly selected population that might well show a greater percentage of mitral prolapse problems; this problem is associated with the best surgical results and the highest valve repair rate.

**TABLE 2. Other Significant Valve Lesions in Patients With and Without Rheumatic Etiology**

	With Rheumatic Etiology (n=72), n (%)	Without Rheumatic Etiology (n=200), n (%)
None	14 (19.4)	-
Mitral stenosis	37 (51.4)	-
Mitral and aortic stenosis	8 (11.1)	-
Aortic stenosis	12 (16.7)	5 (2.5)
Aortic regurgitation	1 (1.4)	9 (4.5)

Although it cannot be ruled out that the increase in the immigrant population of Madrid (which now makes up some 10%-15% of the city's entire population) may have caused an upturn in the frequency of rheumatic etiology, the mean age of the present patients was advanced, indicating this not to be a determining factor.

The present data indicate that mitral regurgitation is more commonly of rheumatic etiology in women than in men; in fact the frequency of rheumatic valve disease

in women was more than double that in men. Olson et al.,<sup>4</sup> who worked with surgical patients, also found a greater frequency of rheumatic disease among women. The cause of this sex-related disparity is not clear, although age does not appear to play an important role. Possibly the greater prevalence of ischemic heart disease in men may have some influence.<sup>9</sup> Finally, it should be noted that, although this was a prospective study designed to investigate the etiology of mitral regurgitation, the cause of this malady remained unclear in 11.8% of patients. This shows the need for further research into the etiological diagnosis of mitral valve dysfunction; etiological knowledge is important in the choice of treatment and has prognostic implications.<sup>10</sup> Kumar et al.,<sup>1</sup> who employed a methodology similar to that of the present work and whose patient sample reflected a high incidence of rheumatic etiology (44%), also found a similar percentage (10%) with disease of unclear etiology. It is possible that several factors that contribute towards mitral regurgitation may be at work in some of these patients. In the present study, the etiology was most often unclear in women; this may be partly the fault of the breasts reducing the quality of the echocardiographic window.

### Limitations

Including only patients referred for an echocardiographic study at a hospital that is also the surgical reference center may have introduced a bias towards selecting the most symptomatic etiologies. However, this would have been small compared to the great selection bias of previous studies involving surgical patients. A background of acute rheumatic fever was not systematically checked for; thus etiological diagnoses were based only on the structural data for the mitral valve shown by the echocardiogram, and the presence of other significant valve disease. In

conclusion, the present patients with severe mitral regurgitation were of advanced age and they commonly showed signs of cardiovascular comorbidities. In Spain, rheumatic disease still appears to be the main cause of severe mitral regurgitation in women referred to hospitals with characteristics similar to those of our own.

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