

Comparisons between female and male patients with mitral stenosis

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Abstract

Objective—To compare Doppler, echocardiographic, and clinical variables in female and male patients with mitral stenosis.

Design—Observational study in consecutive patients with mitral stenosis of cross sectional and Doppler echocardiographic and clinical variables and a retrospective search for a history of systemic embolism.

Setting—A medical centre with 3000 beds, serving both urban and rural populations.

Patients—500 consecutive patients with an echocardiographic mitral valve area of 2 cm² or less. 331 (66.2%) were female and 169 (33.8%) male (mean (SD) ages of 49 (13) and 48 (14) respectively).

Main outcome measures—Mitral valve areas by echocardiographic planimetry and Doppler pressure half-time method, peak early diastolic mitral velocity and pressure gradient, echocardiographic score of mitral valve, left atrial end systolic diameter, frequency of left atrial thrombus and smoky echoes as well as various valve lesions detected with Doppler and echocardiography, cardiac rhythm, symptomatic functional class of heart failure, and history of systemic embolism.

Results—The prevalence of significant tricuspid (22% v 9%, $P < 0.001$) and pulmonary regurgitation (5% v 1%, $P = 0.018$) was higher in the female patients than in the male patients. Female patients also had a higher peak regurgitant velocity (3.2 (0.7) v 2.9 (0.7) m/s, $P = 0.007$) and pressure gradient (41 (21) v 36 (19) mm Hg, $P = 0.010$) across the tricuspid valve. However, the male patients had a higher echocardiographic score (9.7 (2.4) v 7.0 (2.3), $P < 0.001$) and a smaller Doppler-derived mitral valve area (0.9 (0.4) v 1.0 (0.4) cm², $P = 0.027$). There were no differences between the female and the male patients in mitral valve area measured by planimetry, peak early diastolic mitral velocity and pressure gradient, and left atrial end systolic diameter or in the prevalence of atrial fibrillation, left atrial thrombus, left atrial smoky echoes, significant aortic stenosis, aortic regurgitation, or heart failure of New York Heart Association class III or IV.

Conclusions—Female patients not only had a higher prevalence of mitral stenosis but also had a higher prevalence of associated tricuspid and pulmonary regurgitation along with a higher velocity and gradient of tricuspid regurgitation. The echocardiographic score was higher in male patients, however. These findings suggest that the pathophysiology of mitral stenosis is different in the two sexes and that gender should be taken into account when therapeutic strategies are formulated.

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Keywords: mitral stenosis; gender; echocardiography.

Recently, attention has been focused on the relation between gender and cardiovascular diseases.¹ The recognition of physiological or pathological differences in male and female patients may lead to more appropriate treatments.

Despite its decline in developed countries rheumatic heart disease remains the leading cause of death from heart disease in those aged 5-24 in most part of the world.² Its incidence in Taiwan was 1.4 per 1000 children in 1970 and 0.6 per 1000 children in 1985.³ Mitral stenosis is more common in females than in males.⁴

We compared various Doppler, echocardiographic, and clinical variables in female and male patients with mitral stenosis to see whether gender affected the pathophysiology of this condition.

Patients and methods

PATIENTS

Consecutive patients who were older than 15 and had a mitral valve area of ≤ 2.0 cm² were enrolled in the study (331 female patients (66.2%) and 169 male (33.8%)). We excluded patients who had had open heart surgery or percutaneous balloon dilatation of the mitral valve.

CLINICAL VARIABLES

The clinical variables examined included age, body surface area, cardiac rhythm, and presence or absence of significant heart failure (defined as New York Heart Association class III or IV) history of systemic embolism, and current use of anticoagulant and diuretics.

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DOPPLER AND ECHOCARDIOGRAPHIC VARIABLES
Complete Doppler and echocardiographic examinations were performed with a Hewlett Packard Sonos 1000 ultrasound system using both 2.5 MHz and 5 MHz transducers from transthoracic windows. The examined variables included: mitral valve area; echocardiographic mitral valve score⁵; peak early diastolic mitral velocity; left atrial end systolic diameter; presence or absence of significant (more than a mild degree of) aortic stenosis, aortic regurgitation, mitral regurgitation, and pulmonary regurgitation; peak systolic velocity of tricuspid regurgitation; and the presence or absence of left atrial thrombus or smoky echoes. The mitral valve area was determined by two dimensional planimetry and the Doppler pressure half-time method.⁶⁻⁸ The left atrial end systolic diameter was measured on the M mode echocardiogram recorded in the parasternal long axis view. Measurements were made according to the American Society of Echocardiography recommendations.⁹ Left atrial thrombus was detected by a 2.5 MHz transducer from the transthoracic approach.¹⁰ We used a 5 MHz transducer to detect atrial smoky echoes¹¹⁻¹³ because it was more sensitive than a 2.5 MHz transducer.¹³ We prefer the term "smoky echoes" to "spontaneous echo contrast" because some patients with severe tricuspid regurgitation or right heart failure have bright moving spots (caused by microbubbles) in the inferior vena cava or hepatic vein identical to those appearing in contrast echocardiography. We reserve the term "spontaneous echo contrast" for this echo pattern and use the term "smoky echoes" for the finer, lighter whorling echoes (which probably originate from aggregated red blood cells)¹³ that appeared in the left atrium in patients with severe mitral stenosis. Significant aortic stenosis was defined as an

aortic valve area of ≤ 1.2 cm² calculated by the continuity equation.¹⁴ Significant aortic regurgitation or pulmonary regurgitation was defined as a ratio of jet width to left or right ventricular outflow tract diameter of $\geq 25\%$.¹⁵ Significant mitral regurgitation or tricuspid regurgitation was defined as a ratio of jet width to left or right atrial area of $\geq 20\%$.¹⁵ The pressure gradient was calculated from the Bernoulli equation (pressure gradient = $4 \times$ square of velocity).

STATISTICAL ANALYSIS

Values are expressed as mean values (1 SD) for continuous variables. Comparisons between the two groups were made by a two-tailed Student's unpaired *t* test for continuous variables and by a χ^2 test for binary variables. Differences were regarded as significant when the *P* value was < 0.05 .

Results

In our study there were twice as many female patients as male patients. In Taiwan the sex ratio of the general population over 15 years of age is 0.93:1.¹⁶ The table shows comparisons of various Doppler, echocardiographic, and clinical variables in male and female patients. Tricuspid or pulmonary regurgitation were more common in the female patients (22% *v* 9%, *P* < 0.001 and 5% *v* 1%, *P* = 0.018, respectively). Female patients also had higher peak systolic velocity (3.2 (0.7) *v* 2.9 (0.7) m/s, *P* = 0.007) and pressure gradient of the tricuspid regurgitation jet (41 (21) *v* 36 (19) mm Hg, *P* = 0.010). Heart failure of New York Heart Association class III or IV tended to be more common in the female patients (42% *v* 34%, *P* = 0.064). The male patients had a higher echocardiographic score (9.7 (2.4) *v* 7.0 (2.3), *P* < 0.001) and smaller Doppler-derived mitral valve area (0.9 (0.4) *v* 1.0 (0.4) cm², *P* = 0.027). Important aortic regurgitation tended to be more common in the male patients (23% *v* 16%, *P* = 0.062). None the less, the mitral valve area measured by planimetry was similar in female and male patients (1.0 (0.4) *v* 1.0 (0.4) cm²). Nor were any of the other variables significantly different in the male and female patients.

Discussion

HIGHER PREVALENCE OF MITRAL STENOSIS IN FEMALE PATIENTS

The pathogenesis of rheumatic heart disease is not completely understood. Although it is an acquired disease caused by group A streptococcal infections,¹⁷⁻²⁰ it rarely develops even after the most virulent streptococcal infections. Consequently, the issue of host predisposition is often raised.^{21,22} The mechanisms leading to cardiac damage have not been clearly defined. What part does gender play? Our study confirmed the well known finding that rheumatic mitral stenosis is more common in female patients.⁴ A constitutional predisposition or sex linked inheritance may be involved.

Comparisons between female and male patients with mitral stenosis (mean (SD))

Variable	Females (n = 331)	Males (n = 169)	<i>P</i> value
Age (yr)	49 (13)	48 (14)	0.674
Body surface area (m ²)	1.50 (0.11)	1.72 (0.11)	$< 0.001^*$
Mitral area by echo (cm ²)	1.0 (0.4)	1.0 (0.4)	0.670
Mitral area by Doppler (cm ²)	1.0 (0.4)	0.9 (0.4)	0.027*
MS score	7.0 (2.3)	9.7 (2.4)	$< 0.001^*$
V of MS (m/s)	1.9 (0.4)	1.9 (0.4)	0.910
PG of MS (mm Hg)	15 (6)	15 (6)	0.810
LADs (mm)	50 (11)	51 (12)	0.674
Prevalence of:			
AF	248/331 (75%)	128/169 (76%)	0.676
Embolic	93/331 (28%)	51/169 (30%)	0.727
CHF (NYHA class III or IV)	139/331 (42%)	57/169 (34%)	0.064
LA thrombus	109/331 (33%)	47/169 (28%)	0.335
LA smoky echoes	63/331 (19%)	39/169 (23%)	0.252
AS	20/331 (6%)	15/169 (9%)	0.188
AR	53/331 (16%)	39/169 (23%)	0.062
MR	65/331 (20%)	28/169 (17%)	0.404
TR	73/331 (22%)	15/169 (9%)	$< 0.001^*$
PR	17/331 (5%)	2/169 (1%)	0.018*
V of TR (m/s)	3.2 (0.7)	2.9 (0.7)	0.007*
PG of TR (mm Hg)	41 (21)	36 (19)	0.010*
Use of anticoagulant	60/331 (18%)	41/169 (24%)	0.168
Use of diuretics	253/331 (76%)	113/169 (67%)	0.162

V and PG of MS, peak early diastolic velocity and pressure gradient (calculated by Bernoulli equation: $PG = 4V^2$) of mitral stenosis; LADs, left atrial end systolic diameter; AF, atrial fibrillation; CHF (NYHA class III or IV), congestive heart failure (New York Heart Association class III or IV); AS, aortic stenosis; AR, aortic regurgitation; MR, mitral regurgitation; TR, tricuspid regurgitation; PR pulmonary regurgitation; V and PG of TR, peak systolic velocity and pressure gradient (calculated by Bernoulli equation) of tricuspid regurgitation.

* Statistically significant.

HIGHER ECHOCARDIOGRAPHIC SCORE AND SMALLER DOPPLER-DERIVED MITRAL VALVE AREA IN MALE PATIENTS

The higher echocardiographic score suggests a more severe mitral abnormality in male patients. The smaller Doppler-derived mitral valve area in the male patients accords with this suggestion. However, the mitral valve area derived from pressure half-time method may be inaccurate in various conditions.²³⁻²⁵ For example, chronic clinically significant aortic regurgitation may lead to underestimation of mitral valve area by the pressure half-time method.²⁵ In our study, there was a trend (that did not achieve statistical significance) that more male patients had important aortic regurgitation (table). This might explain why the males had smaller Doppler-derived mitral area, whereas by planimetry the mitral valve areas were similar in the male and the female patients. Nevertheless, because the body surface area in the male patients ($1.72(0.11) \text{ v } 1.50(0.11)\text{m}^2$, $P < 0.001$) was larger their mitral valve area may still be smaller in relation to body surface area. In any case the pathological changes of the mitral valve in the male patients are likely to be more severe, because of their higher levels of physical activity.

HIGHER PREVALENCE OF ASSOCIATED TRICUSPID AND PULMONARY REGURGITATION AND HIGHER PULMONARY PRESSURE IN THE FEMALE PATIENTS

The higher prevalence of associated tricuspid and pulmonary regurgitation and the higher peak velocity and pressure gradient of tricuspid regurgitation jet suggest that pulmonary arterial pressure (by Bernoulli equation: pressure gradient = $4 \times$ square of velocity) was higher in the female patients. If the mitral valve lesion is less severe in the female patients, the higher pulmonary pressure suggests higher pulmonary resistance. There are three possible mechanisms leading to pulmonary hypertension in patients with mitral stenosis: (a) passive backward transmission of the raised left atrial and pulmonary venous pressures; (b) reactive arteriolar vasoconstriction, which presumably is triggered by the increase in pulmonary venous pressure (reactive pulmonary hypertension); and (c) organic obliterative changes in the pulmonary vasculature, which may be caused by a longstanding increase in pressure. In this study, the higher pulmonary pressure in the female patients is unlikely to be caused by backward transmission of left atrial pressure, because the mitral valve lesion may be more severe in the male patients than in the female patients. The higher pressure may be due to a higher reactivity and/or more organic obliterative changes of the pulmonary vasculature in the female patients.

CLINICAL IMPLICATIONS

This study showed pathophysiological differences between female and male patients with mitral stenosis. This means that it may be necessary to take gender into account in for-

mulating therapeutic strategies for mitral stenosis. For example, interventions, such as percutaneous balloon dilatation of the mitral valve, may be needed at an earlier stage in female patients to prevent the development of severe pulmonary hypertension. In addition, the success rate may be higher in the female patients because their echocardiographic scores are lower. Further studies are required to confirm these speculations.

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Comment

Chiang *et al* studied 500 consecutive patients with clinically important mitral stenosis to determine whether or not there are significant differences between the sexes in some of the echocardiographic variables commonly used in the clinical evaluation of patients with valvar heart disease. The data are of interest, if only because such an extensive characterisation of severe rheumatic mitral valve disease could no longer be undertaken in the western world—where the incidence of rheumatic heart disease has fallen and new cases are more likely to be detected at an earlier stage of the disease process.

Possible gender differences in the presentation and management of coronary artery disease have aroused considerable interest in recent years. Chiang *et al* suggest that gender differences extend to the manifestations of rheumatic mitral stenosis and that female patients had a higher prevalence and severity of tricuspid regurgitation although male patients (probably) had more severe mitral stenosis. They suggest that the pulmonary vascular response to mitral stenosis is greater in female patients, perhaps because the vascular reactivity of the pulmonary vascular bed is increased.

Whether these findings indicate a real gen-

der difference or not is uncertain. The results suggest that mitral stenosis was more severe in males, but only just—mitral valve area estimated by Doppler echocardiography (pressure half-time method) was slightly less in males and the echocardiographic score was higher. This score, however, is a purely descriptive and subjective assessment. The mitral valve area measured by planimetry, the forward velocity across the valve, the pressure gradient, and left atrial diameter were the same in both sexes. The difference in peak tricuspid regurgitation velocity between the sexes (0.3 m/s) is within the limits of the error of measurement of the technique. Consequently, the higher pressure gradient across the tricuspid valve in female patients (41 *v* 36 mm Hg) may well have been overinterpreted. However, Chiang *et al* point out that if mitral valve area was corrected for body size, the gender difference in valve area would be even greater. There are examples where vasomotor tone of certain vascular beds is greater in female patients. Whether or not the data presented here are part of the same phenomenon is open to interpretation.

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