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Original Article

Gender specific echocardiographic prevalence of valvular stenosis and regurgitations in a large inpatient database of 24,265 patients

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Abstract: Introduction: Prevalence of different valvular pathologies has not been reported in female and male patients in large population-based studies. The goal of this study was to report the gender-specific prevalence of various valvular pathologies. Methods: We retrospectively analyzed 24,265 echocardiograms performed between 1984 and 1998. The prevalence of mitral regurgitation (MR) aortic valve regurgitation (AR) and stenosis (AS), and tricuspid regurgitation (TR) were calculated in female and male patients. Results: Echocardiograms were performed on 12,926 (53%) female and 11,339 (47%) male patients. Gender-specific echocardiographic prevalence of different valvular abnormalities was as follows: Prevalence of mitral regurgitations was similar in women and men (25% vs 24.7%). Aortic regurgitation was higher in males (5.5 vs 14.9%, P < 0.001). Aortic stenosis prevalence was similar between both genders (2.1 vs 2.3%). Tricuspid valve regurgitations were slightly higher in females (18.5 vs 16.7%, P < 0.001). Conclusion: In this study, we found a significantly higher prevalence of tricuspid valve regurgitation in women. Aortic regurgitation was more prevalent in men. Aortic stenosis and mitral regurgitation had similar prevalence in both genders.

Keywords: Echocardiography, aortic valve disease, mitral valve disease, valvular hear disease, valvular stenosis, valvular regurgitation, echocardiograms, tricuspid valve regurgitation, gender, valve disease, structural heart disease

Introduction

Valvular heart disease (VHD) is a common condition in the United States, with an estimated prevalence of 2.5% among adults [1-3]. The malfunctioning heart valves lead to backward flow in the case of regurgitation or increased pressures behind the stenotic valve in patients with valvular stenosis [4, 5]. Historically, rheumatic heart disease has been the predominant cause of heart valve failure. However, with the advent of anti-Group A Streptococcus treatments, the incidence of rheumatic heart disease in high-income countries has declined, and degenerative and functional diseases have become more prominent [6, 7].

Based on the findings of the Euro Heart Survey, aortic stenosis (AS) is reported to be the most frequent VHD [8], while the most prevalent VHD in the US is reported to be mitral regurgitation (MR) [1]. In addition to the discrepancies observed between countries, sex differences regarding the type of VHD have garnered significant attention. Conflicting reports on VHD showed that a greater proportion of women have mitral valve disease, while a greater proportion of males have aortic valve disease [9, 10]. Patients with early stages of chronic acquired valvular heart disease are usually asymptomatic unless infection occurs. Most patients will be symptomatic sometime in the course of their valve disease progression during the severe phase. Once symptoms arise, valvular interventions are necessary unless the patient has a poor life expectancy. Symptoms are usually consistent with shortness of breath and heart failure. In the case of aortic stenosis, angina can also occur without any significant coronary artery disease. Valve interventions are

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indicated when early cardiac abnormalities occur such as reduced left ventricular function or left ventricular dilatation even in the absence of symptoms. Diagnosis of valvular heart disease is based on echocardiographic studies using various techniques such as continuous Doppler and Color Doppler studies. Valve area can be calculated in the case of valvular stenosis using the Gorlin formula. Regurgitation severity can be measured using various techniques including the use of the PISA technique (Proximal Isovelocity Surface Area) to quantify the severity of valvular regurgitation, most commonly mitral regurgitation, by calculating the effective regurgitant orifice area (EROA) based on the size of the flow convergence zone seen on color Doppler imaging.

Given the significant impact of VHD on morbidity and mortality, understanding the gender-specific prevalence of these conditions is crucial for tailoring clinical interventions and improving patient outcomes. Previous studies have highlighted potential differences in the incidence and presentation of valvular abnormalities between men and women. However, comprehensive data from US national studies that could specify the gender- and type-specific prevalence remain limited. This study aims to fill this gap by providing a detailed analysis of the echocardiographic prevalence of valvular regurgitations and stenosis in a large population.

Materials and methods

Echocardiographic evaluations

We conducted a retrospective analysis of 24,265 echocardiograms that were carried out between 1984 and 1998. These echocardiograms were requested by clinicians at the University of California, Irvine Medical Center for different medical reasons. Echocardiographic studies included echocardiograms that were performed as in or outpatients. The functional evaluation of heart valves was made by interpreting echocardiograms using various parameters. Pulse and continuous wave Doppler in apical views and if available suprasternal notch were utilized when evaluating valvular stenosis. Aortic and mitral valve areas could be calculated using the Gorlin formula. For regurgitation, the color Doppler flow imaging was used to estimate regurgitation severity based on the degree of the color flow and when was feasible, the PISA technique (Proximal Isovelocity Surface Area) was utilized to quantify the severity of valvular regurgitation by calculating the effective regurgitant orifice area (EROA) based on the size of the flow convergence zone seen on color Doppler imaging. Furthermore, two-dimensional and Doppler echocardiography was used to measure valve area for the stenotic valve and regurgitation orifice for valvular regurgitations. Regurgitation fraction calculation could further define regurgitation severity. The definitive final diagnoses and the severity reported by board certified cardiologist that were accessible and utilized for our investigation. The reports were produced by clinical cardiologists who have received training in the analysis of echocardiograms. The diagnostic of regurgitations and stenoses encompassed a range from mild to severe, excluding only trace regurgitations that are typically found in healthy individuals.

Statistical analysis

We conducted our study using univariate analysis to examine the gender-specific prevalence of VHDs. Hence, the prevalence of aortic valve regurgitation (AR) and stenosis (AS), mitral regurgitation (MR), and tricuspid regurgitation (TR) were calculated in female and male patients. The prevalence of mitral stenosis has already been reported previously from our database.

The statistical analysis was performed using the SPSS version 17. A p-value below 0.05 was statistically significant. The variables were examined using a chi-square test. This study was approved by the institutional review board of the University of Arizona, Irvine. Included were all echocardiograms of patients between the ages of 16-99 that were performed for various clinical reasons and a final report about their valve conditions was available. Exclusions were any echocardiograms that had no report about valve conditions or patients that were outside the age range of 16-99 years old.

Results

In this study, we analyzed the gender-specific echocardiographic prevalence of various VHDs among 24,265 patients who had an echocardiogram in our institution between 1984 and

Table 1. Prevalence of different types of valvular heart disease (VHD) in overall and by sex

Type of Valvular Disease	Prevalence in Females (%)	Prevalence in Males (%)	Overall Prevalence (%)
MR, all	24.4	25.0	24.7
MR, mild	16.5	16.5	16.5
MR, moderate	6.1	6.3	6.2
MR, severe	1.9	2.2	2.0
MS, all**	1.6	0.4	1.0
AR, all	5.5	14.9	15.2
AR, mild**	11.5	10.1	10.9
AR, moderate	2.6	2.5	2.6
AR, severe**	0.4	1.0	0.7
AS, all	2.1	2.3	2.2
TR, all**	18.5	16.7	17.7
TR, mild	11.9	11.6	11.7
TR, moderate*	4.4	3.7	4.0
TR, severe**	2.3	1.5	1.9

*P < 0.01. **P < 0.001.

1998. The females constituted 12,926 (53%), while the males were 11,339 (47%).

Mitral regurgitation (MR)

Females had a relatively similar overall prevalence of MR to males, at 24.7% (females-24.4%, males-25.0%). When stratified by severity, mild mitral regurgitation was found to affect both genders at equal percentages -16.5%. Besides that, it was observed that moderate MR among females stood at 6.1% relative to 6.3% for males respectively whereas severe MR was seen in 1.9% of females and 2.2% of males respectively. No significant gender differences were seen across all grades of severity (**Table 1**).

Mitral stenosis (MS)

The prevalence of MS was significantly higher among women with an overall prevalence of 1.6%, while men recorded only 0.4%. This finding has been reported previously by us in detail in a manuscript published in 2006 which is not a new finding [11]. For comparison to other valvular prevalence, we are adding these numbers to our table for completeness (**Table 1**).

Aortic regurgitation (AR)

AR was more common in men (14.9%) than women (15.5%), with a total rate of 15.2%. A higher proportion of females had mild AR compared to their male counterparts, the difference being significant at P < 0.001. Patients with moderate AR were found almost equally among females (2.6%) and males (2.5%). Severe AR had a higher prevalence in males than females, and this difference was also statistically significant at P < 0.001 (**Table 1**).

Aortic stenosis (AS)

The percentage occurrence for AS remained relatively similar among the sexes; it was found to be 2.1% in the female population while the male counterpart registered a figure of just 2.3% resulting in an average tally of about 2.2%. Gender did not significantly determine one's chances of having AS (**Table 1**).

Tricuspid regurgitation (TR)

Females had a high overall prevalence of TR as compared to males, where it was 18.5% and 16.7% respectively, culminating in a total prevalence rate of 17.7% (P < 0.001). In terms of severity, women had the same proportion of mild TR (11.9%) as men did but most of them were suffering from moderate TR with P < 0.01, i.e., more females suffered from this problem than men at a probability level of less than 1%. Similarly, severe TR was found in more females than males with a significance level of P < 0.001 (**Table 1**).

Summary of significant findings

In female patients with MS or moderate-to-severe TR, there was a significantly higher frequency. Severe AR was also significantly common among male subjects. There was no significant difference between both genders in the general prevalence values for MR and AS (**Table 1** and **Figure 1**).

Discussion

In this large-scale retrospective study, we evaluated the gender-specific prevalence of VHDs in an echocardiographic database of 24,265 patients. We demonstrated a significant difference in the prevalence of MS (previously reported), mild and severe AR, and TR between males and females. Degenerative mitral regurgitation has less regional variation compared to calcific aortic stenosis, perhaps due to its greater independence from atherosclerotic risk factors in

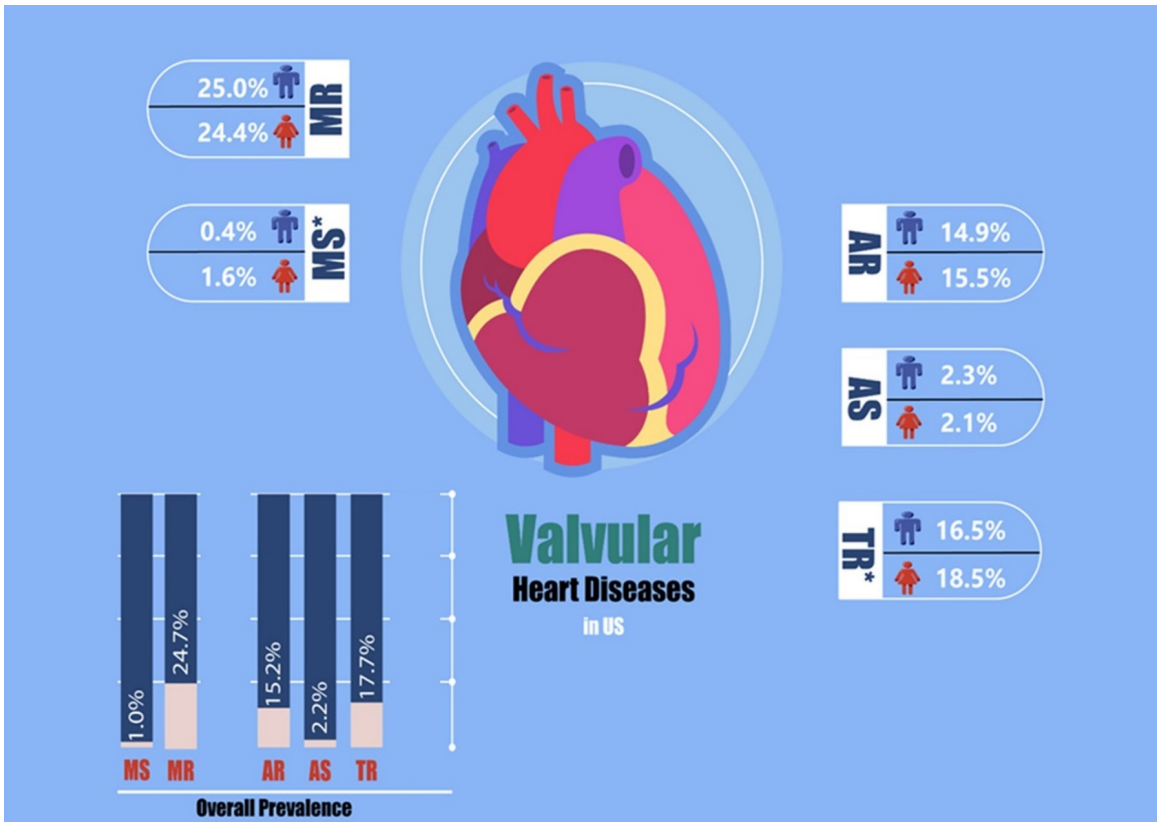

Figure 1. Gender-based prevalence of valvular regurgitations and stenosis in the United States. This figure illustrates the distribution of valvular heart diseases among 24,265 echocardiograms, including Aortic Regurgitation (AR), Aortic Stenosis (AS), Mitral Regurgitation (MR), Mitral Stenosis (MS), and Tricuspid Regurgitation (TR). The percentages indicate the prevalence of each condition, * indicates a significant difference in prevalence between genders ($P < 0.01$).

terms of its pathophysiology [12]. In industrialized nations, mitral valve (MV) disorders account for approximately 25% of all VHD, with MR being more prevalent than MS [13]. In line with our findings, MR is the most prevalent VHD globally, impacting approximately 1% to 2% of the global population. However, the prevalence of MR rises from 7% to 9% among individuals aged 75 years and beyond [1].

In our study, although the overall prevalence of MR was 24.7%, the moderate and severe cases constituted 8.2% of patients. This far division from global prevalence can be attributed to our examined population. Since our examined population was not naïve and was referred for evaluation based on their symptoms, it is expected that they would experience more MR. Studies reported that MV disorders including MS have a female predilection [11, 13, 14]. Our finding support the significant female predilection of MS that was reported previously from this database. The exact underlying reason for this predilection has not been fully understood. However, since rheumatic heart disease is a major cause of MS and disproportionately affects girls and women, it can contribute to this predilection [15].

It was found that AR was more common in males than in women, with a prevalence of 44% in men compared to 29% in women ($P < 0.001$) [16]. This could be related to the fact that men have a greater likelihood of experiencing BAV-related health problems, such as AR, endocarditis, aneurysm formation, and aortic dissection, compared to women [17, 18].

Aortic regurgitation is the fourth most common VHD globally [4], although in affluent countries with low incidence of rheumatic fever, it ranks third among non-rheumatic VHDs [13].

The prevalence varies, perhaps because asymptomatic patients are not being detected.

Among UK subjects aged over 65 years old, the prevalence is 1.6% [19], whereas among participants in the United States, Framingham research found to be 4.9% [20]. In our large-scale population, the overall prevalence of moderate and severe AR was 3.3% and there was no gender-specific difference in the prevalence of AR. However, the mild and severe forms were exhibited conversely; the prevalence of severe AR was significantly higher in males (1% versus 0.4%), while the mild AR rate was significantly higher in females (11.5% versus 10.1%).

A large proportion of patients diagnosed with AS in the United States currently have calcific degeneration of the tricuspid aortic valves. While men are generally more susceptible to developing AS than women, there is a growing prevalence of AS in older women. The majority of AS patients over the age of 80 are women [6, 13, 21-23]. These two opposite trends - the higher incidence of BAV in men and the higher incidence of AS in elderly women - may explain the relatively equal distribution of AS between men and women in our population.

Tricuspid valve regurgitation can be classified as either primary, resulting from inherent valve defects, or secondary, frequently produced by dilatation of the right ventricle or tricuspid annulus [24]. The causes of primary TR, which is less prevalent in adults, encompass valve injury resulting from surgical operations, infective endocarditis, trauma, and congenital disorders [25]. In contrast, secondary TR is more common and occurs due to the enlargement of the right ventricle and the dilatation of the tricuspid annulus, despite having a previously normal valve [26]. Although over 1.6 million Americans suffer from moderate or severe TR, only a small number of repair surgeries are conducted each year [27]. Significant TR was discovered in 0.55% of a US community cohort undergoing echocardiography for clinical purposes (and related with other cardiac pathology in 92% of patients) [28], and in 2.7% of a UK cohort of older persons without known VHD [19]. In the Framingham Heart Study, 18% of women were found to have mild or more severe TR, with a male-to-female ratio of 1 to 1.6 [29]. This female predominance for TR has also been observed in other community-based cross-sectional investigations [28]. However, certain factors such as congenital TR, right-sided endocarditis, carcinoid cardiac disease, and device-related TR may have a higher prevalence in men [30-32]. Likewise, our findings show that the overall TR rates are higher in females, with moderate and severe TR showing a statistically significant higher prevalence in females. The similar prevalence of mild TR between men and women may be due to the fact that once women present with mild TR, their disease progresses rapidly to moderate and severe forms [33]. The global effect of valvular heart disease on different populations are discussed in detail in a recent studies which is beyond the scope of this manuscript [34, 35].

In French, aortic stenosis was the most prevalent valvular disease followed by mitral regurgitation [36].

The prevalence of valvular heart disease in China also showed gender discrepancy with the proportion of aortic regurgitation, aortic stenosis, and bicuspid aortic valve found to be higher in male patients with moderate or severe VHD than those in female patients [37]. Looking at the burden of rheumatic valve disease in the world, it remains unfortunately very high in Africa [38] requiring more resource allocation to African nations in order to reduce this completely preventable valve disease. Reducing cardiovascular risk factors may affect valvular heart disease. In a large series of 11,862 patients, more than 20% VHD patients had at least two conventional cardiovascular risk factors [39]. Furthermore, many inflammatory diseases have high correlations with aortic valve regurgitation and stenosis warranting further investigation for the role of inflammation in VHD [40-42]. Gender gap in performing valve surgery [43] remains a major issue that needs to be resolved with improvement of this gender gap in recent years [44]. From our perspective, future research should focus on discovering preventive measures that could help to reduce the burden of all VHDs including aortic stenosis and regurgitations.

Limitation

The present study is subject to numerous limitations. At the starting point, the retrospective nature of the study may have introduced selection bias, as echocardiograms were conducted

for a variety of clinical purposes. It also failed to substantiate the referring diagnosis of VHD with independent data. Additionally, this dataset was associated with referral bias due to its origination from a tertiary care referral center. Dependence on previous studies led to non-uniform assessments of echocardiographic abnormalities. Standardization was not implemented for VHD diagnoses, and there were no clear criteria available to diagnose or grade the condition. Furthermore, older devices used in our population probably had a lower sensitivity for VHD detection than their contemporary counterparts. Adjustments for potential confounders, such as comorbidities and socioeconomic factors, are not possible due to the absence of initial clinical characteristics in this database. It is also possible that there was significant inter-observer variability, as the echocardiographic interpretations were conducted by various cardiologists. Finally, the generalizability of the results beyond this restricted population is not appropriate. These limitations underscore the importance of a detailed interpretation of the results. These findings require confirmation and extension to other populations in future prospective studies that employ standardized diagnostic criteria and involve more diverse populations. Nevertheless, this investigation can provide valuable gender-specific prevalence data regarding valvular heart disease. This indicates the primary distinctions that should be taken into account in the practice of medicine.

Conclusion

In this extensive examination which was based on a large-scale study consisting of 24,265 echocardiograms, we reported that the prevalence of various VHDs regarding regurgitations and stenosis varies significantly based on gender. Nevertheless, women were more likely to experience MS, whereas males were more likely to experience severe AR. In contrast, the study demonstrated that females were more likely to have mild AR and moderate-to-severe TR.

Disclosure of conflict of interest

None.

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