





BMJ Open Characteristics, interventions and outcomes of patients with valvular heart disease hospitalised in China: a cross-sectional study

Xinghe Huang ^{1,2,3} Sanket S Dhruva,⁴ Xin Yuan,⁵ Xueke Bai,² Yuan Lu ⁶, Xiaofang Yan,² Jiamin Liu,² Wei Li,² Danli Hu,² Runqing Ji,² Min Gao,² Fengyu Miao,² Jiaying Li,² Jinzhuo Ge,² Harlan M Krumholz ^{6,7,8} Jing Li ^{1,2}

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XH and SSD are joint first authors.
HMK and JL are joint senior authors.

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For numbered affiliations see end of article.

Correspondence to

Dr Jing Li; jing.li@wfoxford.org

ABSTRACT

Objectives Little is known about contemporary characteristics and management of valvular heart disease (VHD) in China. This study aimed to examine the clinical characteristics, aetiology and type of VHD, interventions and in-hospital outcomes of patients with VHD hospitalised in China.

Methods We used a two-stage random sampling design to create a nationally representative sample of patients with VHD hospitalised in 2015 in China and included adult patients with mild, moderate or severe VHD. We abstracted data from medical records, including echocardiogram reports, on patient characteristics, aetiology, type and severity of VHD, interventions and in-hospital outcomes. We weighted our findings to estimate nationally representative hospitalisations. We performed multivariable logistic regression analysis to identify factors associated with valve intervention.

Results In 2015, 38 841 patients with VHD were hospitalised in 188 randomly sampled hospitals, representing 662 384 inpatients with VHD in China. We sampled 9363 patients, mean age 68.7 years (95% CI 42.2 to 95.2) and 46.8% (95% CI 45.8% to 47.8%) male, with an echocardiogram. Degenerative origin was the predominant aetiology overall (33.3%, 95% CI 32.3% to 34.3%), while rheumatic origin was the most frequent aetiology among patients with VHD as the primary diagnosis (37.4%, 95% CI 35.9% to 38.8%). Rheumatic origin was also the most common aetiology among patients with moderate or severe VHD (27.3%, 95% CI 25.6% to 29.0% and 33.6%, 95% CI 31.9% to 35.2%, respectively). The most common VHD was mitral regurgitation (79.1%, 95% CI 78.2% to 79.9%), followed by tricuspid regurgitation (77.4%, 95% CI 76.5% to 78.2%). Among patients with a primary diagnosis of severe VHD who were admitted to facilities capable of valve intervention, 35.6% (95% CI 33.1% to 38.1%) underwent valve intervention during the hospitalisation. The likelihood of intervention decreased significantly among patients with higher operative risk.

Conclusions Among patients with VHD hospitalised in China, the predominant aetiology was degenerative in origin; among patients with moderate or severe VHD, rheumatic origin was the most common aetiology. Targeted strategies and policies should be promoted to address

Strengths and limitations of this study

- This is the first study to provide a comprehensive description of features and in-hospital outcomes of patients with valvular heart disease hospitalised in China.
- This study used a two-stage random sampling design to create a nationally representative sample of patients with valvular heart disease hospitalised in China.
- Because this study did not include military hospitals and some randomly sampled hospitals did not have any inpatients with valvular heart disease during the study period, the national numbers of patients with valvular heart disease may be underestimated.
- Patients may have undergone valve intervention at a subsequent hospitalisation in the same hospital or in another hospital, which was not captured by this study.
- This study did not collect enough information to evaluate the risks and benefits of intervention for valvular heart disease for individual patients.

degenerative VHD. Patients with severe VHD may be undertreated, particularly those with high operative risk.

INTRODUCTION

Valvular heart disease (VHD) is common and associated with increased morbidity and mortality.¹ Globally, more than 63.7 million people are affected by VHD.^{2 3} Rheumatic heart disease (RHD) is the principal cause of VHD in developing countries.¹ In 2015, approximately 33 million people globally suffered from RHD, resulting in 11 million disability-adjusted life-years.³ Additionally, population ageing is leading to an increased global burden of non-rheumatic VHD.^{2 4} Between 1990 and 2017, the Global Burden of Disease Study found the number of people with degenerative VHD doubled globally.²



As the world's most populous country, China faces challenges of a massive overall burden of VHD. One-fifth of all people with RHD reside in China, and RHD resulted in more than 70 000 deaths in 2015.³ The ageing of China's population suggests a likely increasing burden of VHD from degenerative aetiology. Meanwhile, advanced interventional techniques have been developed, including transcatheter aortic valve replacement; while this technology has been available since 2010, fewer than 700 patients had received it in China by the end of 2015.⁵ Despite the possible changing epidemiological pattern of VHD and availability of advanced interventional techniques, comprehensive national data about hospitalisations among patients with VHD in China are lacking. Previous studies in China have been from a single centre or province, focused on single aetiology (eg, RHD only), a specific valve (eg, mitral valve disease only) or focused on older patients.⁶⁻¹⁰ These prior studies have shown that rheumatic origin was the predominant aetiology.¹¹ In addition, despite the prevalence and relevance to treatment strategies of right-sided VHD,¹² it has been long ignored and only examined in a handful of international epidemiological studies.^{10 13 14} Therefore, there are important questions to be answered to better understand VHD in China, which could ultimately direct efforts to reduce the burden of these treatable diseases. These questions include: how many patients with VHD are hospitalised each year in China; what are comorbidities among these hospitalised patients; what is the aetiology, type and severity of VHD; are there differences by age and sex in aetiology and VHD type; what is the proportion of patients undergoing valve intervention; what factors are associated with valve intervention; and what are in-hospital outcomes of patients with VHD hospitalised in China.

Accordingly, we conducted the China Patient-Centred Evaluative Assessment of Cardiac Events Retrospective Study of VHD (China PEACE-Retrospective VHD Study), drawing a random sample of patients with VHD who were hospitalised and examining their characteristics, aetiology and type of VHD, interventions and in-hospital outcomes through review of in-hospital medical records. Understanding these issues will help refine the focus of future research and ultimately improve clinical outcomes for patients with VHD.

METHODS

Study design

Our study is part of the National Studies of Major Chronic Disease in China in 2015. We obtained a nationally representative sample of VHD hospitalisations in 2015 using a two-stage random sampling design, similar to our previous study of myocardial infarction (online supplemental material).¹⁵ In the first stage, we identified all non-military hospitals in China and excluded prison hospitals, specialised hospitals without a division for cardiovascular disease, and specialised hospitals of

traditional Chinese medicine (online supplemental figure S1). The remaining hospitals were stratified into five groups by economic-geographical regions and urbanicity (eastern rural, central rural, western rural, eastern urban and central-western urban) because hospital volumes and clinical capacities differ between urban and rural areas and across Mainland China's three official economic-geographical regions. We grouped the central and western urban regions because incomes and health services capacity per person are similar. In the three rural strata, the sampling framework consisted of the central hospital (the general hospital with the largest clinical capacity) in each of the predefined rural areas. In the two urban strata, the sampling framework consisted of all secondary and tertiary hospitals in each of the predefined urban areas. We did not include primary hospitals, which typically lack capability to diagnose and treat VHD.

In the second stage, we identified all hospitalisations that began in 2015 with a discharge diagnosis of VHD from the sampled hospitals, using each local hospital's database. We then drew hospitalisations using systematic random sampling procedures with prespecified ratios based on annual volume. We identified a discharge diagnosis of VHD by searching International Classification of Diseases-Clinical Modification codes 10 (ICD-10-CM) (I05.x, I06.x, I07.x, I08.x, I09.801, I09.802, I33.x, I34.x, I35.x, I36.x, I37.x or I38.x); when ICD-10-CM codes were unavailable, we searched diagnosis terms in the medical record (details in online supplemental material).

We obtained an electronic copy of the medical record of each sampled hospitalisation for data abstraction. To ensure accuracy, data were centrally and independently abstracted using standardised definitions by two trained and certified abstractors. Any disagreement was resolved through review of the original medical records. Additionally, clinicians at the coordinating centre compared randomly selected records and abstractions to verify data accuracy.

Study population

We included adult patients (aged ≥ 18 years) with a discharge diagnosis of VHD, either as the primary diagnosis or as a comorbidity (secondary diagnosis). Patients with congenital VHD or with an uncertain diagnosis (ie, without an echocardiogram during the selected hospitalisation or without defined severity) were excluded (online supplemental figure S1). If a patient had multiple hospitalisations for VHD during 2015, we included only data from the first hospitalisation. Therefore, only one hospitalisation for each patient was included in this study.

Data elements and definitions

We abstracted data on patient characteristics, including age, sex and both cardiac and non-cardiac comorbidities. We defined comorbidities based on discharge diagnosis terms. We also abstracted types, potential aetiologies, severities of valvular lesions and details of echocardiographic findings.

VHD types were mitral stenosis, mitral regurgitation, aortic stenosis, aortic regurgitation, tricuspid stenosis, tricuspid regurgitation, pulmonary stenosis and pulmonary regurgitation. Multiple VHD was defined as moderate or severe valvular lesions occurring on ≥ 2 valves.^{16 17} Mixed VHD was defined as the combination of stenotic and regurgitant lesions on the same valve.¹⁶ We first determined VHD type by ICD-10-CM codes or discharge diagnosis terms (details in online supplemental material). If the diagnosis did not indicate which valve was affected, cardiologists at the coordinating centre reviewed the echocardiogram report to obtain this information.

VHD severities were classified as mild, moderate, and severe; these were determined by the discharge diagnosis, if the discharge diagnosis was unavailable, then parameters of the echocardiogram report, according to definitions in clinical practice guidelines (quantitative criteria in online supplemental material), were used to determine severity.^{18 19} We further verified the accuracy of the VHD severity abstracted from the discharge diagnosis with echocardiogram reports; overall, consistency was 95%. Among patients who received multiple echocardiograms during the hospitalisation, we included only the first echocardiogram. Aetiologies of VHD were determined according to discharge diagnosis or echocardiographic findings (criteria in online supplemental material).

We defined a hospital as having the capability to perform valve intervention if at least one sampled patient from that hospital underwent valve intervention (either surgical or percutaneous) during the study period. These interventions included valve repair and replacement. The in-hospital outcomes were length of hospital stay and death.

Statistical analysis

To estimate the number of patients with VHD hospitalised nationally across China, we applied weights proportional to the inverse sampling fraction of hospitals within each stratum and the sampling fraction of patients within each hospital, similar to prior studies.¹⁵ We used the same weighting method to obtain nationally representative descriptive measures from our study sample. Normal distributed continuous variables are presented as means with 95% CIs, skewed distributed continuous variables are presented as medians with IQRs, and categorical variables are presented as percentages with 95% CIs. Comparisons between categorical variables were performed using the χ^2 test; comparisons between normal distributed continuous variables were performed using the Student's t-test or the one-way analysis of variance; comparisons between skewed distributed continuous variables were performed using the Mann-Whitney U test or the Kruskal-Wallis test. We compared the characteristics between patients with VHD as the primary diagnosis and as a secondary diagnosis, and among patients with different VHD severities and VHD types. We calculated the proportion of each aetiology and VHD type among all patients, and by age and sex. We calculated the age-specific and aetiology-specific

rate of hospitalisation as a weighted estimated number of patients with VHD hospitalised divided by the total population in the specific age group.²⁰ Among patients admitted to hospitals with the capability to perform valve interventions, we compared in-hospital outcomes between patients with and without valve intervention, and between patients with VHD as their primary diagnosis and those with VHD as a secondary diagnosis. We further performed multivariable logistic regression analysis among patients with VHD as the primary diagnosis to identify factors associated with valve intervention. A two-sided $p < 0.05$ was considered statistically significant. Statistical analyses were performed using SAS software (V.9.4; SAS Institute).

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

RESULTS

Among the 205 sampled hospitals, 8 had no VHD hospitalisations in 2015 and 9 declined to participate. From the remaining 188 hospitals (online supplemental figure S2), we identified 38 841 hospitalisations with a discharge diagnosis of VHD in 2015. After applying sampling weights, these patients represented 662 384 patients with VHD who were hospitalised in 2015 in China.

Patient characteristics

Of the 38 841 hospitalisations, we sampled 13 338 hospitalisations and obtained medical records for 13 138 hospitalisations (98.5%) (online supplemental figure S1). After excluding 3534 hospitalisations with an uncertain diagnosis, 60 hospitalisations with congenital VHD and 181 rehospitalisations for the same patient, our final study sample for analysis included 9363 patients with VHD who were hospitalised in 2015 and for whom echocardiogram results were available. Patient mean age was 68.7 years (95% CI 42.2 to 95.2) and 46.8% (95% CI 45.8% to 47.8%) were male (table 1). Heart failure (59.7%, 95% CI 58.7% to 60.6%), atrial fibrillation (33.0%, 95% CI 32.0% to 33.9%), hypertension (37.6%, 95% CI 36.7% to 38.6%) and coronary heart disease (23.9%, 95% CI 23.0% to 24.8%) were the most common comorbidities and 4.8% (95% CI 4.4% to 5.2%) of patients had undergone previous valve intervention.

There were 5404 (57.7%) patients with VHD as their primary diagnosis, representing 211 526 hospitalised patients with VHD as the primary diagnosis in 2015 in China. Compared with patients for whom VHD was the secondary diagnosis, those with VHD as the primary diagnosis were younger; more likely to have heart failure, atrial fibrillation, pulmonary hypertension and previous valve intervention; and less likely to have hypertension, coronary heart disease, chronic obstructive pulmonary disease and dyslipidaemia (table 1). The proportion of

Table 1 Characteristics of patients with valvular heart disease (VHD) hospitalised in China

	Total (n=9363)	Primary diagnosis of VHD (n=5404)	Secondary diagnosis of VHD (n=3959)	P value
Demographics				
Age, median (IQR), years	71 (60–79)	65 (56–75)	75 (65–81)	<0.001
Age, mean (95% CI), years	68.7 (42.2 to 95.2)	64.8 (41.3 to 88.3)	72.2 (44.2 to 100.2)	<0.001
Age, % (95% CI)				<0.001
18–44 years	5.0 (4.6 to 5.5)	6.8 (6.1 to 7.6)	3.4 (2.9 to 3.9)	
45–54 years	10.6 (10.0 to 11.2)	15.1 (14.0 to 16.2)	6.6 (5.9 to 7.3)	
55–64 years	19.2 (18.4 to 20.0)	25.5 (24.2 to 26.8)	13.6 (12.6 to 14.6)	
65–74 years	26.0 (25.2 to 26.9)	25.9 (24.6 to 27.2)	26.2 (25.0 to 27.4)	
≥75 years	39.0 (38.1 to 40.0)	26.6 (25.3 to 27.9)	50.1 (48.7 to 51.5)	
Male, % (95% CI)	46.8 (45.8 to 47.8)	43.2 (41.8 to 44.7)	50.0 (48.6 to 51.4)	<0.001
Comorbidities, % (95% CI)				
Heart failure	59.7 (58.7 to 60.6)	76.1 (74.8 to 77.4)	45.0 (43.6 to 46.4)	<0.001
Atrial fibrillation	33.0 (32.0 to 33.9)	45.2 (43.7 to 46.7)	22.0 (20.9 to 23.2)	<0.001
Pulmonary hypertension	10.7 (10.1 to 11.4)	13.0 (12.0 to 14.0)	8.7 (7.9 to 9.5)	<0.001
Hypertension	37.6 (36.7 to 38.6)	32.2 (30.8 to 33.6)	42.5 (41.2 to 43.9)	<0.001
Coronary heart disease	23.9 (23.0 to 24.8)	22.6 (21.4 to 23.9)	25.1 (23.9 to 26.3)	0.006
Chronic obstructive pulmonary disease	14.6 (13.9 to 15.3)	9.4 (8.5 to 10.3)	19.3 (18.2 to 20.4)	<0.001
Dyslipidaemia	10.6 (10.0 to 11.3)	8.1 (7.3 to 9.0)	12.9 (12.0 to 13.9)	<0.001
Type two diabetes	9.7 (9.1 to 10.3)	9.4 (8.5 to 10.3)	9.9 (9.1 to 10.8)	0.366
Previous valve intervention, % (95% CI)	4.8 (4.4 to 5.2)	7.5 (6.8 to 8.4)	2.3 (1.9 to 2.8)	<0.001
Aetiology, % (95% CI)				
				<0.001
Degenerative	33.3 (32.3 to 34.3)	15.2 (14.2 to 16.3)	49.4 (48.0 to 50.8)	
Rheumatic	22.2 (21.4 to 23.1)	37.4 (35.9 to 38.8)	8.7 (7.9 to 9.5)	
Ischaemic	3.1 (2.8 to 3.5)	3.2 (2.7 to 3.8)	3.0 (2.5 to 3.5)	
Infective	1.0 (0.8 to 1.2)	1.8 (1.4 to 2.2)	0.2 (0.1 to 0.4)	
Combined	12.5 (11.8 to 13.2)	14.0 (13.0 to 15.0)	11.2 (10.3 to 12.1)	
Unknown	27.9 (27.0 to 28.9)	28.4 (27.1 to 29.8)	27.5 (26.2 to 28.8)	
Disease type, % (95% CI)				
				<0.001
Single mitral valve disease	16.9 (16.1 to 17.6)	20.7 (19.5 to 21.9)	13.4 (12.5 to 14.4)	
Single aortic valve disease	13.8 (13.1 to 14.5)	12.7 (11.7 to 13.7)	14.8 (13.8 to 15.8)	
Single tricuspid valve disease	10.1 (9.5 to 10.8)	9.0 (8.2 to 9.9)	11.2 (10.3 to 12.1)	
Multiple valve disease	29.5 (28.6 to 30.4)	41.1 (39.6 to 42.5)	19.1 (18.0 to 20.3)	
Other	29.7 (28.8 to 30.7)	16.6 (15.5 to 17.7)	41.5 (40.1 to 42.9)	

Single mitral valve disease includes mitral stenosis or mitral regurgitation; single aortic valve disease includes aortic stenosis or aortic regurgitation; single tricuspid valve disease includes tricuspid stenosis or tricuspid regurgitation; other includes mixed aortic valve disease, mixed mitral valve disease, single pulmonary disease and other combination of two or more mild valve disease.
VHD, valvular heart disease.

patients with heart failure, atrial fibrillation and pulmonary hypertension increased with VHD severity (online supplemental table S1). Detailed comparisons of patient characteristics across VHD types are shown in online supplemental table S2.

Aetiologies of VHD

Overall, 33.3% (95% CI 32.3% to 34.3%) of patients with VHD had degenerative origin and 22.2% (95% CI 21.4%

to 23.1%) had rheumatic origin (figure 1A). Rheumatic origin was the most frequent aetiology among patients with VHD as the primary diagnosis (37.4%, 95% CI 35.9% to 38.8%) and degenerative origin was the predominant aetiology among patients with VHD as the secondary diagnosis (49.4%, 95% CI 48.0% to 50.8%) (table 1). Degenerative origin was the most predominant aetiology in both sexes: 36.0% (95% CI 34.5% to 37.4% in males

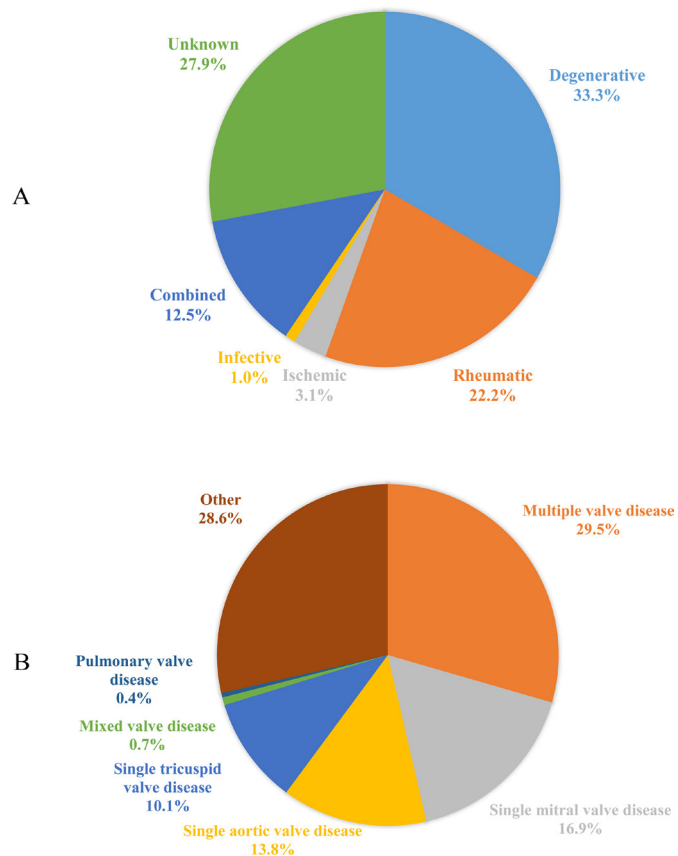


Figure 1 Aetioliology and type of valvular heart disease among patients hospitalised in China.

and 30.9% (95% CI 29.7% to 32.3%) in females (online supplemental figure S3). Rheumatic origin was more common in females (28.7%, 95% CI 27.5% to 30.0%) than males (14.8%, 95% CI 13.8% to 15.9%). Among patients with moderate or severe VHD, rheumatic origin was the most common aetiology (27.3%, 95% CI 25.6% to 29.0% and 33.6%, 95% CI 31.9% to 35.2%, respectively).

When examining age-specific hospitalisation rates for VHD, the peak rates of RHD were among patients aged 65–74 years, with a decrease with younger age. Rates of infective VHD were low across ages; while rates of other aetiologies increased with age (figure 2 and online supplemental tables S3 and S4). Similarly, among all patients with VHD, the proportion of patients with degenerative aetiology increased with age, from 6.1% (95% CI 4.1% to 8.6%) among patients <45 years to 56.6% (95% CI 55.0% to 58.2%) in those ≥ 75 years; the proportion who had RHD was 31.0% (95% CI 26.8% to 35.4%) among patients <45 years, 44.1% (95% CI 40.9% to 47.2%) in 45–54 years and then decreased with age (online supplemental figure S4). Aetiologies stratified by VHD type are presented in online supplemental figure S5.

Types and severities of VHD

Among all patients with VHD hospitalised in China, mitral regurgitation was the most frequent type of VHD (79.1%, 95% CI 78.2% to 79.9%; 44.1%, 95% CI 43.1% to 45.0% with mild severity), followed by tricuspid regurgitation

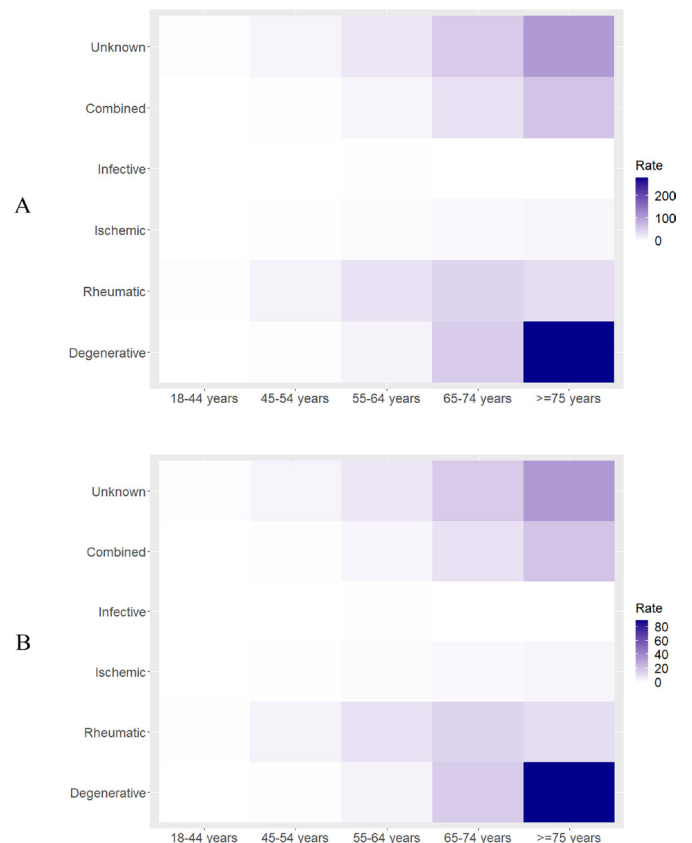


Figure 2 Rate of hospitalisation with valvular heart disease in age-specific and aetiology-specific groups (cases per 100 000). The age-specific and aetiology-specific rate of hospitalisation was the weighted estimated number of patients with valvular heart disease hospitalised divided by the total population in the specific age group (A) among all patients hospitalised with valvular heart disease; (B) among patients hospitalised with valvular heart disease as the primary diagnosis. Darker colour represents higher rates.

(77.4%, 95% CI 76.5% to 78.2%); 45.8% (95% CI 44.8% to 46.8%) with mild severity) and aortic regurgitation (70.6% (95% CI 69.7% to 71.6%); 47.7% (95% CI 46.7% to 48.7% with mild severity) (table 2).

Overall, 29.5% (95% CI 28.6% to 30.4%) of patients with VHD hospitalised had multiple VHD (figure 1B). The proportion of multiple VHD was higher among patients with VHD as the primary diagnosis compared with patients with VHD as the secondary diagnosis (41.1% vs 19.1%, $p < 0.001$) (table 1). The most frequent combination of multiple VHD was mitral regurgitation/tricuspid regurgitation, followed by aortic regurgitation/tricuspid regurgitation and mitral regurgitation/aortic regurgitation (online supplemental table S5). Data on VHD type by sex and age are presented in online supplemental figures S6 and S7.

Interventions for VHD

Thirty-eight hospitals included in our study had capability to perform valve intervention. Among patients with a primary diagnosis of mild, moderate and severe VHD who were hospitalised at these facilities during our study

Table 2 Types and severities of valvular heart disease

	Total, % (95% CI)	Mild, % (95% CI)	Moderate, % (95% CI)	Severe, % (95% CI)
Mitral regurgitation	79.1 (78.2 to 79.9)	44.1 (43.1 to 45.0)	17.2 (16.5 to 18.0)	15.6 (14.8 to 16.3)
Mitral stenosis	19.6 (18.8 to 20.5)	5.7 (5.3 to 6.2)	8.0 (7.5 to 8.5)	5.4 (4.9 to 5.9)
Aortic regurgitation	70.6 (69.7 to 71.6)	47.7 (46.7 to 48.7)	14.3 (13.6 to 15.0)	6.7 (6.2 to 7.2)
Aortic stenosis	14.8 (14.1 to 15.6)	6.3 (5.8 to 6.8)	4.1 (3.7 to 4.5)	4.1 (3.7 to 4.5)
Tricuspid regurgitation	77.4 (76.5 to 78.2)	45.8 (44.8 to 46.8)	16.1 (15.4 to 16.9)	13.3 (12.6 to 14.0)
Tricuspid stenosis	0.1 (0.1 to 0.2)	0.1 (0 to 0.2)	0 (0 to 0.1)	0 (0 to 0.1)
Pulmonary regurgitation	12.9 (12.2 to 13.6)	11.0 (10.4 to 11.7)	1.3 (1.1 to 1.6)	0.2 (0.1 to 0.3)
Pulmonary stenosis	0.4 (0.3 to 0.5)	0.1 (0.1 to 0.2)	0.1 (0.1 to 0.2)	0.1 (0.1 to 0.2)

period, 5.5% (95% CI 3.3% to 8.5%), 21.0% (95% CI 18.2% to 24.0%) and 35.6% (95% CI 33.1% to 38.1%) underwent valve intervention during the index hospitalisation, respectively (figure 3). Only four patients (2.2%) underwent valve intervention during a rehospitalisation within the study period. For mitral and aortic valve disease, most patients underwent valve replacement; for tricuspid valve disease, most patients underwent valve repair (table 3).

Compared with those younger than 45 years, older patients (OR 0.58, 95% CI 0.42 to 0.80 for age 45–54 years; OR 0.35, 95% CI 0.25 to 0.48 for age 55–64 years; OR 0.10, 95% CI 0.07 to 0.14 for age 65–74 years; OR 0.01, 95% CI 0.01 to 0.03 for age \geq 75 years) were less likely to undergo valve intervention. Patients with mild (OR 0.12, 95% CI 0.08 to 0.20) or moderate (OR 0.43, 95% CI 0.34 to 0.54) VHD severity were less likely to undergo valve intervention compared with those with severe VHD. Hypertension (OR 0.71, 95% CI 0.53 to 0.93), type 2 diabetes (OR 0.44, 95% CI 0.27 to 0.72), chronic obstructive pulmonary disease (OR 0.41, 95% CI 0.22 to 0.77) and previous valve intervention (OR 0.65, 95% CI 0.42 to 0.99) were associated with lower likelihood of valve intervention. In

contrast, patients with pulmonary hypertension (OR 1.69, 95% CI 1.29 to 2.23) were more likely to undergo valve intervention (figure 4).

In-hospital outcomes

Among 4182 patients hospitalised at facilities with capability to perform valve intervention, the median length of hospital stay was 10 days (IQR 7–16) and in-hospital death was 1.3% (95% CI 1.0% to 1.7%) (online supplemental table S6). The median length of hospital stay among patients with and without valve intervention was 24 days (IQR 18%32) and 9 days (IQR 6%13), respectively ($p<0.001$). In-hospital death occurred in 1.4% (95% CI 0.7% to 2.5%) and 1.3% (95% CI 1.0% to 1.7%) of patients who underwent and did not undergo valve intervention, respectively ($p=0.862$). Details of in-hospital outcomes between patients with VHD as the primary diagnosis and as the secondary diagnosis are shown in online supplemental table S7.

DISCUSSION

This nationally representative study provides the first comprehensive picture of patients with VHD who are hospitalised in China, including data on patient characteristics, aetiology and type, interventions and in-hospital outcomes. We estimate that more than 662 384 patients with VHD were hospitalised in China in 2015. We are the first to find that degenerative origin was the most frequent aetiology among patients with VHD hospitalised in China, compared with previous single-centre studies, which have shown that rheumatic valve disease was the predominant aetiology.^{6 21} However, among patients with VHD as the primary diagnosis and among patients with moderate or severe VHD, rheumatic valve disease was the predominant aetiology. The most common VHD was mitral regurgitation, followed by tricuspid regurgitation; almost one-third of patients suffered from moderate or severe tricuspid regurgitation. Among patients with a primary diagnosis of severe VHD who were hospitalised at facilities capable of valvular intervention, only one-third underwent valve intervention during the hospitalisation, with lower intervention rates among those with advanced age, more comorbidities or previous valve intervention.

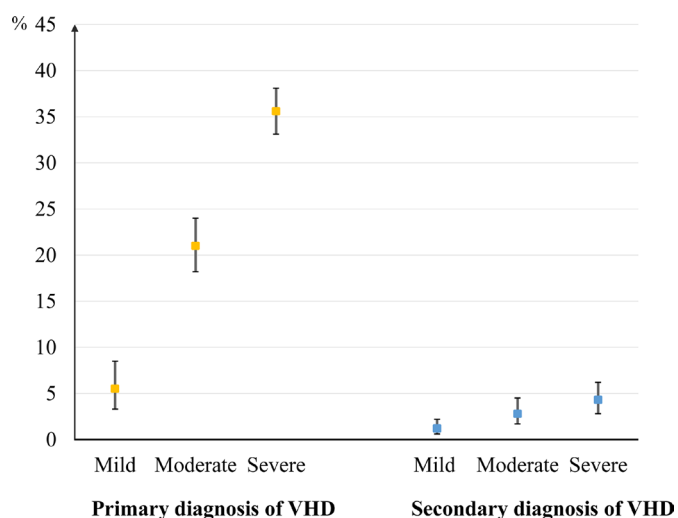


Figure 3 Proportion of patients hospitalised with valvular heart disease (VHD) in hospitals capable of valve intervention who underwent intervention. Each square represents the point estimate, and the line shows the 95% CI.

Table 3 Intervention types among patients who underwent valve intervention during hospitalisation

	Valve replacement, % (95% CI)	Valve repair, % (95% CI)	Percutaneous valve intervention, % (95% CI)
Mitral valve (n=488)	81.1 (77.6 to 84.3)	17.3 (14.3 to 20.8)	1.5 (0.7 to 2.9)
Aortic valve (n=248)	97.3 (94.6 to 98.9)	2.7 (1.1 to 5.4)	–
Tricuspid valve (n=211)	6.0 (3.4 to 9.8)	94.0 (90.2 to 96.6)	–
Pulmonary valve (n=6)	–	79.0 (40.2 to 97.8)	21.0 (2.2 to 59.8)

This is the first study of patients with VHD hospitalised in China using nationally representative data. When including all VHD (including mild), we found that degenerative valve disease is the predominant aetiology. In the USA and Europe in recent decades, RHD incidence has fallen substantially, and degenerative VHD has replaced RHD as the leading cause of VHD.^{1 17 22} Given the increase in life expectancy and the current lack of validated prevention strategies, the burden of degenerative VHD has increased in Asia-Pacific countries as well.^{1 23} We found more than one-third of patients with VHD hospitalised in China had a degenerative origin of their VHD. This proportion reached three-fifths among patients aged ≥ 75 years, extending findings from a cohort of older VHD patients in China.⁹ China's ageing population means degenerative VHD prevalence will continue increasing in the future.^{24 25} Although most degenerative VHD was mild, 38.4% was moderate or severe. Some mild degenerative VHD, such as mild aortic stenosis, may progress to severe VHD. Thus, given the high burden of degenerative VHD, more attention should be paid to detection and mitigation in order to reduce adverse clinical consequences. RHD usually begins during childhood as the long-term sequela of acute rheumatic fever.²⁶ Although RHD was the dominant aetiology among patients with VHD as the primary diagnosis and when limiting to patients with moderate or severe VHD, we found the rate of hospitalisation with RHD substantially decreased with younger age, supporting RHD prevalence has decreased in China. This decrease is likely related to improvements in prevention and treatment of acute rheumatic fever over the past decades through improved socioeconomic status, living conditions and antibiotic prophylaxis,²⁵ and the Global Burden of Disease Study showed death from RHD in China decreased by 47% from 1990 to 2016.²⁷ Because there is still a high burden of RHD, prevention strategies and effective care of affected patients should still be strengthened in China.

To the best of our knowledge, our study is the first to document details about tricuspid regurgitation among patients with VHD hospitalised in China. Nearly half of patients with tricuspid regurgitation had moderate or severe severity. Tricuspid valve disease is associated with decreased long-term survival,^{28 29} however, it has received less attention than left-sided VHD and has often been excluded from epidemiological studies of VHD.^{17 21 30} For these reasons, the tricuspid valve is often referred to as the 'forgotten valve'.³¹ The management recommendations

in current clinical practice guidelines for tricuspid valve disease lack evidence from rigorous randomised controlled trials;^{19 32} thus, there is an urgent need for further prospective research on this topic given the high burden of tricuspid valve disease found in our study. We found that mitral regurgitation was the most common VHD among patients with VHD hospitalised in China, in line with the results of a cohort of older adults with VHD in China.³³ Similar to our study, a US population-based study found the most frequent VHD was mitral regurgitation, while in Europe, aortic stenosis was the most frequent.^{22 30}

There may be undertreatment with valve repair or replacement among patients hospitalised at facilities with the capability to perform valve interventions. Only one-third of patients with a primary diagnosis of severe VHD underwent valve intervention, and just an additional 2.2% later in the year within the same hospital. Undertreatment of VHD has been reported in other international studies.^{17 34–37} The decision to perform valve intervention is complex and encompasses many factors including life expectancy, comorbidities, surgical risk, feasibility of successful intervention and patient preferences.^{9 30 38 39} We found the likelihood of intervention decreased among patients with high operative risk, including older age, more comorbidities or previous valve intervention.^{30 38 40} The low rate of valve intervention for patients with VHD suggests a need for better promotion of both traditional surgical and advanced interventional techniques. Although less invasive valve therapies such as transcatheter aortic valve replacement and transcatheter mitral valve repair were at an early stage in 2015, mainly available in very large medical centres in China,⁴¹ there may be opportunities to use these interventions in appropriately selected patients who meet evidence-based criteria. Enhancing multidisciplinary collaboration for VHD may offer potential to reduce the burden of VHD and its clinical sequelae.

Limitations

This study should be considered in the context of multiple limitations. First, our study was based on data collected in 2015; however, it is the first to provide a comprehensive national picture of patients with VHD hospitalised in China. Second, we may underestimate the national numbers of patients with VHD for the following two reasons: (1) we did not include military hospitals which also provide care for VHD because these data are

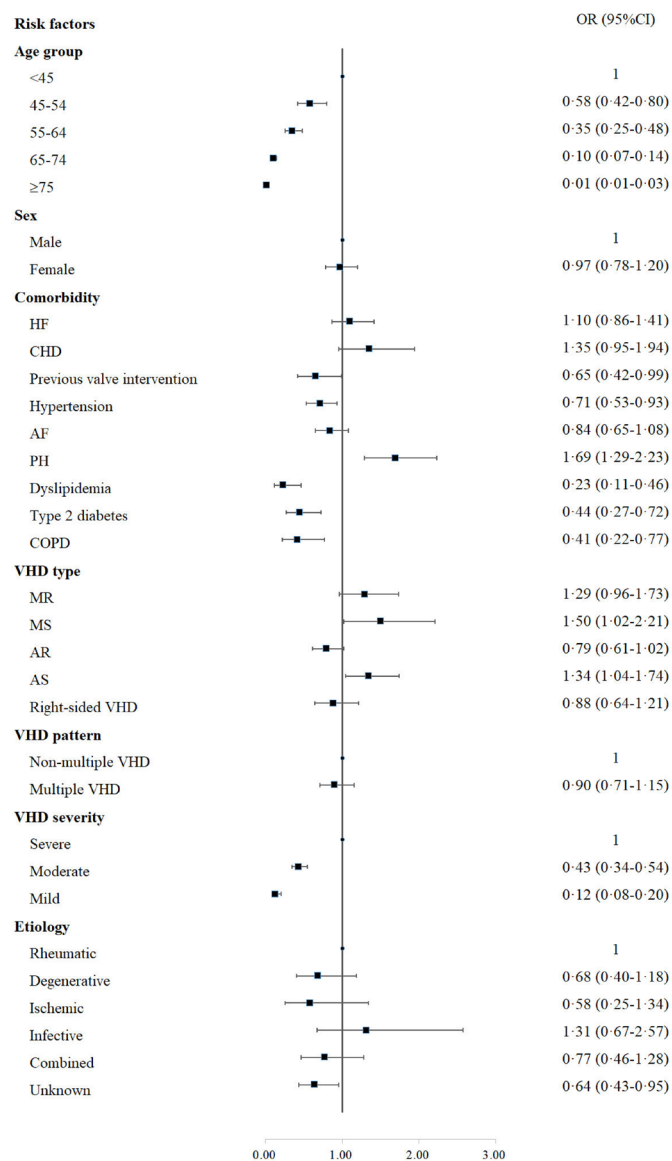


Figure 4 Factors associated with intervention during hospitalisation. The strength of effect is shown along the horizontal axis, with the vertical line demarcating an OR of 1 (ie, no association); estimates to the right (ie, >1) are associated with greater likelihood of intervention, while those to the left (ie, <1) indicate association with less likelihood of intervention. Each square represents the point estimate of the effect of that variable in the model, while the line shows the 95% CI. AF, atrial fibrillation; AR, aortic regurgitation; AS, aortic stenosis; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; HF, heart failure; MR, mitral regurgitation; MS, mitral stenosis; PH, pulmonary hypertension; VHD, valvular heart disease.

unavailable; (2) some randomly sampled hospitals did not have any inpatients with VHD during the study period, which suggests they may lack capability of diagnosing VHD. Third, we only obtained information from medical records; thus, for approximately 27.9% of patients, we could not identify aetiology of VHD. Fourth, patients may have undergone valve intervention at a subsequent hospitalisation in the same hospital or in another hospital,

which was not captured by our study. However, we were able to account for rehospitalisations at the same hospital in 2015 and only 2% were rehospitalised and a total of four patients underwent valve intervention at the subsequent hospitalisation in the same hospital during the study period. Fifth, we did not collect enough information to evaluate the risks and benefits of intervention for VHD for individual patients; however, the small proportion of patients undergoing valve intervention likely indicates some degree of undertreatment of VHD.

CONCLUSION

This contemporary study provides the first comprehensive description of patient characteristics, aetiology, disease features, interventions and in-hospital outcomes of patients with VHD hospitalised in China in 2015. Degenerative origin is the dominant aetiology of VHD. Mitral regurgitation is the most frequent VHD, followed by tricuspid regurgitation; nearly one-third of VHD patients have moderate or severe tricuspid regurgitation. Patients with severe VHD may be undertreated, especially those with high operative risk, which calls for the use of surgical and interventional techniques among patients who meet evidence-based criteria. These findings highlight the opportunities to improve care and outcomes for patients with VHD in China.

Author affiliations

¹Fuwai Hospital, Chinese Academy of Medical Sciences, Shenzhen, People's Republic of China

²National Clinical Research Center for Cardiovascular Diseases, Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, National Center for Cardiovascular Diseases, Beijing, People's Republic of China

³School of Nursing, Peking Union Medical College, Beijing, People's Republic of China

⁴Department of Medicine, University of California, San Francisco School of Medicine and Section of Cardiology, San Francisco Veterans Affairs Medical Center, San Francisco, California, USA

⁵Department of Cardiovascular Surgery, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, Chinese Academy of Medical Science and Peking Union Medical College, National Center for Cardiovascular Diseases, Xicheng District, People's Republic of China

⁶Center for Outcomes Research and Evaluation, Yale-New Haven Hospital, and Department of Internal Medicine, Yale University School of Medicine, New Haven, Connecticut, USA

⁷Department of Health Policy and Management, Yale University School of Public Health, New Haven, Connecticut, USA

⁸Section of Cardiovascular Medicine, Department of Internal Medicine, Yale University School of Medicine, New Haven, Connecticut, USA

Twitter Harlan M Krumholz @hmk Yale

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ORCID iDs

Xinghe Huang <http://orcid.org/0000-0002-3664-8779>

Yuan Lu <http://orcid.org/0000-0001-5264-2169>

Harlan M Krumholz <http://orcid.org/0000-0003-2046-127X>

Jing Li <http://orcid.org/0000-0002-8840-8638>

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