



## Heart valve disease in elderly Chinese population: effect of advanced age and comorbidities on treatment decision-making and outcomes

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### Abstract

**Background** A considerable proportion of elderly patients with symptomatic severe heart valve disease are treated conservatively despite clear indications for surgical intervention. However, little is known about how advanced age and comorbidities affect treatment decision-making and therapeutic outcomes. **Methods** Patients ( $n = 234$ , mean age:  $78.5 \pm 3.7$  years) with symptomatic severe heart valve disease hospitalized in our center were included. One hundred and fifty-one patients (65%) were treated surgically (surgical group) and 83 (35%) were treated conservatively (conservative group). Factors that affected therapeutic decision-making and treatment outcomes were investigated and long-term survival was explored. **Results** Isolated aortic valve disease, female sex, chronic renal insufficiency, aged  $\geq 80$  years, pneumonia, and emergent status were independent factors associated with therapeutic decision-making. In-hospital mortality for the surgical group was 5.3% (8/151). Three patients (3.6%) in the conservative group died during initial hospitalization. Low cardiac output syndrome and chronic renal insufficiency were identified as predictors of in-hospital mortality in the surgical group. Conservative treatment was identified as the single risk factor for late death in the entire study population. The surgical group had better 5-year (77.2% vs. 45.4%,  $P < 0.0001$ ) and 10-year (34.5% vs. 8.9%,  $P < 0.0001$ ) survival rates than the conservative group, even when adjusted by propensity score-matched analysis. **Conclusions** Advanced age and geriatric comorbidities profoundly affect treatment decision-making for severe heart valve disease. Valve surgery in the elderly was not only safe but was also associated with good long-term survival while conservative treatment was unfavorable for patients with symptomatic severe valve disease.

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**Keywords:** Long-term survival; The elderly; Treatment outcomes; Valvular heart disease

## 1 Introduction

The prevalence of valvular heart disease increases with age and an estimated 13% of patients aged 75 years and over have heart valve disease.<sup>[1]</sup> Indications for surgical intervention are well defined in guidelines and symptomatic severe heart valve disease is a class I recommendation.<sup>[2,3]</sup> Valve surgery in the elderly is not only safe but also greatly improve the quality of life and expand the life span of those patients with heart valve disease.<sup>[4-9]</sup>

However, previous studies revealed that a large proportion of elderly patients with clear indication for surgical procedures refused or were not offered surgical treatment. Advanced age, comorbidities, perceived high surgical risk, and poor long-term outcomes post-surgery were common factors associated with conservative treatment.<sup>[10-16]</sup> These problems are getting more and more attention with the aggravation of the aging process.

In contrast with developed countries, rheumatic valve disease is still prevalent in the elderly in less developed countries like China.<sup>[17,18]</sup> Furthermore, little is known about the spectrum of valve disease in the elderly Chinese population and how treatment decisions are made in a real world setting. The present study aimed to determine how advanced age and comorbidities affect treatment decision-making and treatment outcomes, including long-term survival in elderly subjects with heart valve disease in China.

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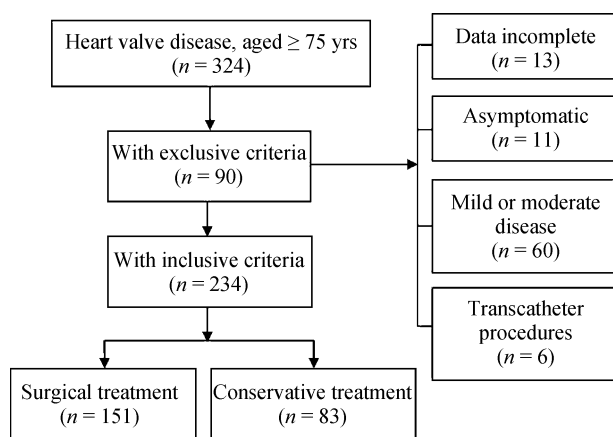
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## 2 Methods

### 2.1 Study population and treatment decision-making

The Institutional Review Board at our hospital waived the requirement for informed consent from patients and approved the protocol for this retrospective study.

Between January 2003 and June 2014, 324 patients aged  $\geq 75$  years who were diagnosed with heart valve disease and admitted to our hospital were included for analysis. Data regarding patient characteristics were reviewed. Etiology, severity of disease, and symptoms were evaluated according to guidelines.<sup>[2,3]</sup> As shown in Figure 1, 90 patients were excluded based on the following exclusion criteria: (1) had mild or moderate disease; (2) were asymptomatic; (3) underwent transcatheter procedures; or (4) clinical data were incomplete. Overall, 234 patients with symptomatic severe heart valve disease were included.



**Figure 1. Demographics of patients in the study.**

During the course of treatment decision-making, the attending practitioners explained the potential risks and benefits of surgical intervention or conservative treatment and gave patients advice. The choice was at the discretion of attending practitioners, the patients, and their relatives. Accordingly, a decision of surgical intervention was made for 151 patients (surgical group) while conservative treatment was decided on for 83 patients (conservative group).

### 2.2 Clinical data collection

The clinical data of all patients were reviewed. Variables including diagnosis, etiology, age, sex, weight, height, functional status, comorbidities, and medical history were recorded. The new European System for Cardiac Operative Risk Evaluation (EuroSCORE II) was used to calculate risk score.<sup>[19]</sup>

### 2.3 Follow-up

Follow-up started from the date of treatment decision-making to the date of death or the endpoint of the investigation. Information was obtained by telephone interview with patients or their relatives or, for some patients, by reviewing outpatient or inpatient records. Follow-up was completed for 94.0% (220/234) of patients with a mean duration of  $49.2 \pm 32.3$  months (range: 3 days to 130 months).

### 2.4 Statistics

All statistical analyses were performed using SPSS18.0 software. Continuous variables are expressed as the mean  $\pm$  SD or as interquartile ranges. Categorical variables are reported as numbers and percentages. Differences between two groups were analyzed using the Student's unpaired *t*-test, the chi-squared test, or the Fisher exact test, as shown in Table 1.

Variables with an associated *P* value  $< 0.10$  were subsequently submitted to a multivariate logistic regression procedure. Variables were selected using a backward procedure with a threshold of *P* = 0.05. The Kaplan–Meier method was used to compute overall survival and the two groups were compared using the log-rank test. We performed a propensity score analysis to reduce the effect of treatment selection bias. The propensity scores were estimated by using a multiple logistic regression model in which surgical treatment was the dependent variable, and variables which correlated with treatment decision-making or long-term outcomes were independent variables. These variables included age, weight, height, sex, coronary artery disease, history of prior myocardial infarction, chronic obstructive pneumonia disease (COPD), atrial fibrillation, hypertension, pulmonary arterial hypertension, diabetes, creatinine clearance, pneumonia, New York Heart Association functional class (NYHA class), left ventricular ejection fraction (LVEF) and emergent status. Matched propensity scores were then used to select pairs of patients in two groups (1: 1 match). Overall propensity score-adjusted survival in the matched groups was computed using the Kaplan–Meier method.

Finally, all variables were submitted to a Cox proportional hazard regression model using backward elimination procedure at the level of 0.10 to identify factors independently associated with treatment outcomes in each group. All remaining variables, together with the therapeutic decision, were submitted to a new Cox proportional hazard regression model to determine independent factors associated with long-term outcome in all patients. All tests were two-sided and a *P* value  $< 0.05$  was considered to be statistically significantly different.

**Table 1. Baseline characteristics of the study population.**

Variables	All patients (n = 234)	Surgical group (n = 151)	Conservative group (n = 83)	P-value
Female	92 (39.3%)	51 (33.8%)	41 (49.4%)	0.024
Age, yrs	78.5 ± 3.7	77.4 ± 2.0	80.6 ± 4.9	< 0.0001
Weight, kg	59.2 ± 11.2	60.1 ± 10.9	57.5 ± 11.6	0.09
Height, cm	164.6 ± 6.7	164.3 ± 7.0	165.1 ± 6.1	0.431
Cc, mL/min	47.4 ± 15.5	50.4 ± 14.8	41.3 ± 15.2	< 0.0001
EuroSCORE II	6.0 ± 3.7	5.7 ± 3.5	6.4 ± 3.9	0.158
NYHA class				
II	37 (15.8%)	21 (13.9%)	15 (18.1%)	0.398
III	149 (63.7%)	109 (72.2%)	42 (50.1%)	0.001
IV	50 (21.4%)	23 (15.2%)	26 (31.3%)	0.004
LVEF	57.0% ± 12.5%	56.6% ± 11.9%	67.8% ± 13.7%	0.463
≤ 50%	73 (31.2%)	48 (31.8%)	26 (31.3%)	0.942
Valve disease				
Aortic	90 (37.2%)	65 (43.0%)	25 (30.1%)	0.052
Mitral	55 (23.5%)	33 (21.9%)	22 (26.5%)	0.422
Tricuspid	6 (2.6%)	3 (2.0%)	3 (3.6%)	0.748
Combined	84 (36.8%)	51 (33.8%)	33 (39.8%)	0.361
Etiology				
Degenerative	142 (60.7%)	94 (62.3%)	48 (57.8%)	0.508
Rheumatic	75 (32.1%)	52 (34.4%)	23 (27.8%)	0.292
Other	17 (4.7%)	10 (6.6%)	7 (8.4%)	0.610
Symptoms				
Dyspnea	169 (72.2%)	110 (72.8%)	59 (71.1%)	0.773
Syncope	33 (14.1%)	22 (14.6%)	11 (13.3%)	0.782
Angina	63 (26.9%)	39 (25.8%)	24 (28.9%)	0.610
Fatigue	95 (40.6%)	58 (38.4%)	37 (45.7%)	0.358
Edema	61 (26.1%)	39 (25.8%)	22 (26.5%)	0.910
Comorbidities				
CAD	51 (21.8%)	34 (22.5%)	17 (20.5%)	0.718
MI	18 (7.7%)	11 (7.3%)	7 (8.4%)	0.752
Hypertension	120 (54.7%)	81 (53.6%)	39 (47.0%)	0.330
Diabetes	47 (20.1%)	31 (20.5%)	16 (19.8%)	0.819
PAH	39 (16.7%)	20 (13.2%)	19 (22.9%)	0.058
Fibrillation	129 (55.1%)	85 (56.3%)	44 (53.0%)	0.629
COPD	29 (12.4%)	16 (10.6%)	13 (15.7%)	0.260
CRI	140 (59.8%)	76 (50.3%)	64 (77.1%)	< 0.0001
Pneumonia	26 (10.7%)	6 (4.0%)	20 (24.1%)	< 0.0001
*Emergent status	22 (9.0%)	6 (3.9%)	16 (19.3%)	< 0.0001

Data are presented as mean ± SD or n (%). \*Emergent status refers to patients who were admitted to the emergency department for acute MI, acute heart failure, respiratory failure, or thromboembolism. CAD: coronary artery disease; Cc: creatinine clearance; COPD: chronic obstructive pneumonia disease; CRI: chronic renal insufficiency; EuroSCORE II: System for Cardiac Operative Risk Evaluation II (2011); LVEF: left ventricular ejection fraction; MI: myocardial infarction; NYHA: New York Heart Association; PAH: pulmonary arterial hypertension.

### 3 Results

#### 3.1 Population characteristics

A total of 234 patients (female, 39.3%) with symptomatic severe heart valve disease were included in the present investigation. The mean age of all patients was 78.5 ±

3.7 years (range 75–100 years); six patients (2.7%) were aged ≥ 90 years. As shown in Table 1, degenerative disease was the most common (60.7%) etiology; however, rheumatic valve disease was the second most common (32.1%) cause of heart valve disease in the study population. Three of the most prevalent comorbidities were chronic renal in-

sufficiency (59.8%), atrial fibrillation (55.1%), and hypertension (54.7%). There were no differences between the two treatment groups with respect to height, weight, overall functional class, LVEF, EuroSCORE II risk score, type of diseases, etiology, and symptoms. However, patients in the conservative group were older, had lower creatinine clearance, and a greater frequency of functional class IV, emergent status, and pneumonia.

### 3.2 Therapeutic decision-making

In the conservative group, 52 patients (62.6%) were considered by physicians as too high risk to undergo a surgical procedure and were not referred to a cardiac surgeon, only 37.4% of this group (31/83) were referred to a cardiac surgeon. Among them, 21.7% (18/83) declined surgical intervention and 15.7% (13/83) were recommended conservative treatment by the cardiac surgeon because of contraindication for surgical intervention. Patients in the conservative group were treated with pharmacotherapy to control their condition. In the surgical group, 136 patients were recruited from the cardiac surgery outpatient clinic and 15 patients were referred by physicians and recruited from a medical ward; these 15 patients were initially referred for conservative treatment but subsequently received surgery. One hundred and sixteen patients underwent isolated valve procedures and 29 patients underwent a valve procedure combined with coronary artery bypass grafting (CABG). Six patients underwent other procedures including two aortic replacement combined ascending aorta repair, two Bentall procedures, and two aortic valve replacements in combination with semi-aortic arch replacement.

**Table 3. Early outcomes in the surgical group.**

Variables	Isolated valve procedures	Valve procedures combined CABG	Other procedures	Total
Patients	116 (76.8%)	29 (19.2%)	6 (4.0%)	151 (100%)
In-hospital death	5 (4.3%)	3 (10.3%)	0	8 (5.3%)
Hospital stay, days	21.4 ± 10.2	24.8 ± 20.5	23 ± 6.1	21.9 ± 12.7
ICU stay, days	13.3 ± 8.9	13.5 ± 10.3	10.8 ± 3.1	13.3 ± 9.0
In-hospital complications				
MI	6 (5.2%)	2 (6.9%)	0	8 (5.3%)
Stroke	8 (6.9%)	2 (6.9%)	1 (16.7%)	11 (7.3%)
Dialysis	1 (0.9%)	1 (3.4%)	0	2 (1.3%)
Bleeding	18 (15.5%)	7 (24.1%)	1 (16.7%)	26 (17.2%)
Rethoracotomy	8 (6.9%)	3 (10.3%)	0	11 (7.3%)
Low cardiac output	11 (9.5%)	3 (10.3%)	0	14 (9.3%)
Permanent pacemaker	1 (0.9%)	0	0	1 (0.7%)
Wound infection	6 (5.2%)	1 (3.4%)	1 (16.7%)	8 (5.3%)
Pneumonia	14 (12.1%)	4 (13.8%)	1 (16.7%)	19 (12.6%)
Tracheotomy	5 (4.3%)	2 (6.9%)	1 (16.7%)	8 (5.3%)
Respiratory failure	6 (5.2%)	2 (6.9%)	0	8 (5.3%)

Data are presented as mean ± SD or *n* (%). CABG: coronary artery bypass grafting; ICU: intensive care unit; MI: myocardial infarction.

According to multivariate logistic regression analysis, age ≥ 80 years, pneumonia, chronic renal insufficiency, emergent status, and female sex were identified as predictive factors associated with a decision of conservative treatment; while isolated aortic valve disease was an independent factor for choosing surgical treatment (Table 2).

### 3.3 Treatment outcomes and long-term survival

In-hospital mortality was 5.3% (8/151) in the surgical group and the mean duration of in-hospital stay was 21.9 ± 12.7 days. Early treatment outcomes in the surgical group are summarized in Table 3. Compared with isolated valve procedures, valve procedures combined with CABG had a

**Table 2. Independent factors associated with a decision for conservative treatment.**

Variable	Odds ratio	95% CI	<i>P</i> value
Age (≥ 80 years)	5.34	2.31–12.34	< 0.0001
Sex (female)	5.47	2.33–12.85	< 0.0001
*Emergent status	6.45	1.81–23.02	0.004
PAH	4.65	0.83–26.03	0.080
COPD	1.78	0.59–5.39	0.310
Pneumonia	14.45	2.43–85.89	0.003
CRI	2.32	1.00–5.41	0.049
Functional class IV	1.94	0.67–5.60	0.220
Isolated aortic valve disease	0.07	0.02–0.24	< 0.0001

\*Emergent status refers to patients who were admitted to the emergency department for acute myocardial infarction, myocardial infarction, acute heart failure, respiratory failure, or thromboembolism. COPD: chronic obstructive pulmonary disease; CRI: chronic renal insufficiency, creatinine clearance ≤ 50 mL/min; PAH: pulmonary arterial hypertension.

**Table 4. Independent factors associated with surgical mortality.**

Variable	Odds ratio	95% CI	P-value
<b>Preoperative</b>			
Age ≥ 80 yrs	1.34	0.94–3.46	0.067
Atrial fibrillation	1.02	0.67–2.12	0.453
PAH	1.23	0.86–2.03	0.684
COPD	1.58	0.59–4.93	0.531
CAD	1.56	0.78–5.39	0.078
CRI	2.82	1.05–6.41	0.041
Functional class IV	1.44	0.91–3.53	0.522
<b>Postoperative</b>			
Low cardiac output	2.54	1.27–9.23	0.032
Hemodialysis	1.01	0.72–2.56	0.642
Rethoracotomy	1.03	0.32–2.23	0.456
Dialysis	1.89	1.05–4.39	0.072

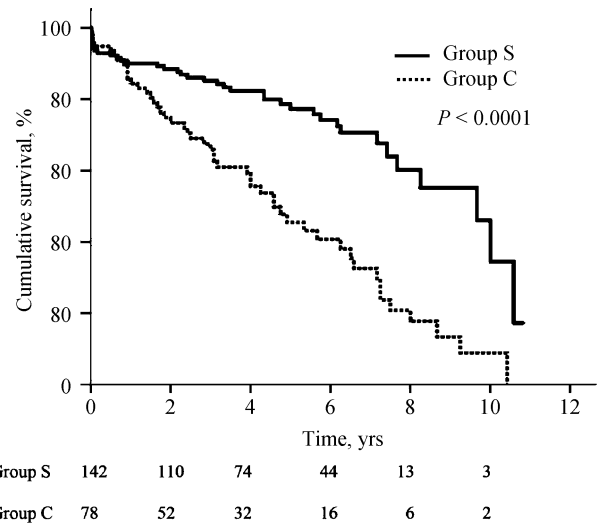
CAD: coronary artery disease; COPD: chronic obstructive pneumonia disease; CRI: chronic renal insufficiency, creatinine clearance ≤ 50 mL/min; PAH: pulmonary arterial hypertension.

higher in-hospital mortality rate, longer in-hospital stay, longer intensive care unit (ICU) stay, and more complications. However, these differences did not reach statistical significance. Low cardiac output syndrome and chronic renal insufficiency were identified as independent risk factors for surgical mortality (Table 4). Three (3.6%) sudden cardiac deaths occurred in the conservative group during initial hospitalization. If symptoms of the conservative group were relieved, patients were discharged after a mean hospital stay of 12.3 ± 7.6 days, while 45% of patients were readmitted to the hospital within the next year for severe myocardial infarction, heart failure, or other heart-related comorbidities.

Patients in the surgical group experienced an obvious improvement in exercise tolerance and quality of life. The NYHA class of 82% of surviving patients improved to class I or II within one year post-surgery. Unfortunately, patients in the conservative group suffered recurrent disease and their exercise tolerance was seriously limited.

Eighty-seven patients died during the follow-up period, 38 (eight died during surgical intervention) in the surgical group and 49 (3 died during initial hospitalization) in the conservative group. Heart failure was the most common cause of death in all patients during the follow-up period including 19 patients in the surgical group and 38 patients in the conservative group.

According to Kaplan–Meier analysis, the overall 1-year, 5-year, and 10-year survival in the surgical and conservative groups was 90.1% vs. 84.4%, 77.2% vs. 45.4%, and 34.5% vs. 8.9%, respectively (log-rank  $P < 0.0001$ ) (Figure 2). Cox



**Figure 2. Kaplan–Meier survival analysis of the two treatment groups.** Group S: surgical group; Group C: conservative group.

**Table 5. Cox regression analysis of risk factors associated with late mortality in all study patients.**

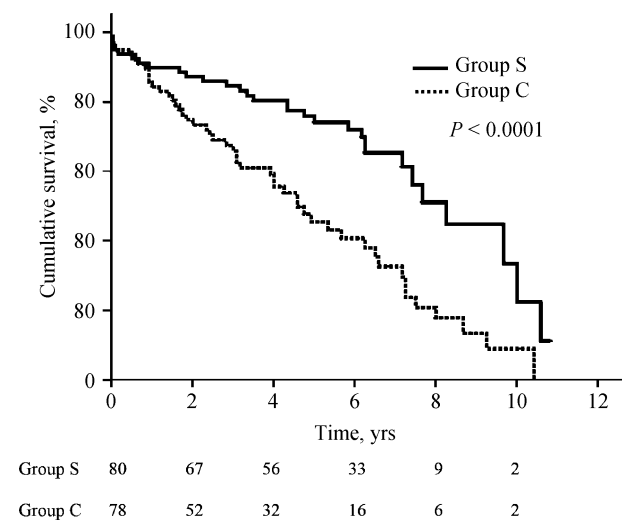
Variables	Hazard ratio	95%CI	P-value
Sex (female)	0.75	0.39–1.98	0.112
LVEF	0.68	0.43–1.69	0.421
CAD	1.53	1.01–7.54	0.076
COPD	0.72	0.056–2.48	0.153
NYHA class IV	1.57	0.98–5.49	0.067
CRI	1.19	0.58–4.45	0.463
EuroSCORE II	0.82	0.54–1.56	0.072
Conservative treatment	9.23	3.17–31.24	< 0.0001

CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; CRI: chronic renal insufficiency, creatinine clearance ≤ 50 mL/min; EuroSCORE II: System for Cardiac Operative Risk Evaluation II (2011); LVEF: left ventricular ejection fraction; NYHA: New York Heart Association functional class.

regression analysis revealed that conservative treatment was the single risk factor associated with poor long-term outcomes in the overall series of patients (Table 5).

### 3.4 Propensity score analysis

Seventeen baseline covariates were entered into a logistic model for individual propensity score estimation. The model had an area under the receiver operating characteristic curve of 0.841. Propensity score matching for all patients (1: 1 match) yielded 83 pairs of matched patients. Seventy-eight in the conservative group and 80 in the surgical group were followed up. Kaplan–Meier analysis showed better long-term survival in the surgical group (log-rank  $P < 0.0001$ ) (Figure 3).



**Figure 3. Kaplan–Meier survival analysis of propensity score-matched patients.** Group S: surgical group; Group C: conservative group.

## 4 Discussion

Although surgical intervention for patients with symptomatic severe heart valve disease is clearly stated in guidelines, a large number of elderly patients with symptomatic severe heart valve disease are treated conservatively.<sup>[15]</sup> In the present investigation, we included 234 patients aged 75 years and over with symptomatic heart valve disease in a Chinese population. We found that 35% of patients with a clear indication for surgical intervention were treated conservatively. Further assessment showed that advanced age, as well as cardiac and geriatric comorbidities, not only affected therapeutic decision-making but also influenced treatment outcomes and long-term survival.

To reduce selection bias, we recruited all patients who presented with symptomatic severe heart valve disease from our hospital data base, which guaranteed consistency of the medical condition. Echocardiograms, symptoms, disease, and etiology were reviewed according to guidelines, and all the patients included in the study had a clear indication for surgical intervention.<sup>[2,3]</sup> In addition, we made use of a propensity score matching analysis to reduce selection bias in this retrospective observational study. Finally, this study included a large number of Chinese elderly patients and investigated the spectrum of heart valve disease in this subgroup. Interestingly, different from developed countries, rheumatic heart valve disease was still prevalent and accounted for 32.1% in the elderly.<sup>[20,21]</sup> We also found that more than 50% of patients had concomitant chronic renal insufficiency, atrial fibrillation, and hypertension.

There is a paucity of literature about the effect of ad-

vanced age and comorbidities on treatment decision-making and outcomes of elderly patients with heart valve disease, especially in less developed countries. Furthermore, therapeutic decision-making for these patients is complex in the real world setting.<sup>[22,23]</sup> Individual cardiac and geriatric characteristics of patients in our study lead to considerable variability in mortality and morbidity, as well as life expectancy and quality of life. Consequently, treatment decisions should be reached based on an estimation of benefit–risk ratio instead of only relying on an estimation of treatment risk.<sup>[24]</sup> However, in accordance with other studies, we found that physicians were generally lacking knowledge about the risks and results of surgical intervention, and many patients with a clear-cut indication for surgical intervention were recommended for conservative treatment.<sup>[5]</sup> In the present study, almost two-thirds (62.7%) of patients in the conservative group were not even evaluated by a cardiac surgeon. Accordingly, we advocate that the optimal therapeutic option for elderly patients with heart valve disease should be made following an integrated discussion with a heart team.

To analyze the process of treatment decision-making objectively, we compared objective characteristics of patients in addition to reasons given by attending practitioners. We found that aged  $\geq 80$  years, pneumonia, chronic renal insufficiency, emergent status, and female sex were independent factors associated with a decision for conservative treatment. However, patients with isolated aortic valve disease tended to be treated surgically.

Advanced age is associated with various complications including renal insufficiency, respiratory dysfunction, and a subsequent reduction in life expectancy.<sup>[8]</sup> Consequently, advanced age raises the risks associated with surgical intervention and is a predictor of conservative treatment for elderly patients with heart disease.<sup>[5,6,11,25]</sup> An investigation showed that advanced age was taken into consideration by attending practitioners as a significant factor for conservative treatment.<sup>[26]</sup> However, advanced age was no longer a risk factor associated with poor long-term survival when compared with an age-matched population.<sup>[6,12,20]</sup> Importantly, guidelines state that advanced age alone should not be a contraindication for surgical intervention.<sup>[2,3]</sup>

Cardiac and non-cardiac comorbidities in elderly patients with heart disease are frequent. The present study showed that more than 50% of patients had comorbid chronic renal insufficiency, atrial fibrillation, and hypertension. Comorbidities not only affected treatment decision-making but also influenced early treatment outcomes and long-term survival.<sup>[27]</sup> Our data indicated that chronic renal insufficiency was independently associated with a decision of

conservative treatment. Chronic renal insufficiency was also identified as a predictor of in-hospital mortality in the surgical group. Previous studies have shown that chronic renal insufficiency is a predictor of operative mortality and poor long-term survival, especially during cardiac surgery in the elderly.<sup>[4,15]</sup> Together with our results, this suggests that caution should be exercised when contemplating surgical intervention for elderly patients with heart valve disease.

Left ventricular dysfunction is a predictor of surgical mortality and poor long-outcomes.<sup>[28,29]</sup> Therefore, poor left ventricular function is an important factor in discouraging surgical intervention in clinical practice.<sup>[25]</sup> However, patients with symptomatic heart valve disease accompanied by impaired left ventricular function always had poorer late outcomes if conservative treatment was adopted. Moreover, such patients benefited more from surgical intervention than those with normal left ventricular function.<sup>[6]</sup> Nevertheless, decision-making is complicated in the real world and the benefit–risk ratio is hard to evaluate for patients with impaired left ventricular function. In the present study, left ventricular function had not been taken into consideration when making treatment decisions. This is most likely because there were no significant differences between the two treatment groups regarding left ventricular function and there were no patients with a very low LVEF (< 30%) among our study population.

Functional status is not only an important factor associated with treatment risk and long-term survival, but also a significant factor which should be taken into consideration when treatment decisions are made. In our study, universal analysis disclosed that NYHA class IV was frequently linked with therapeutic decision, but this difference did not reach statistical significance in multivariate analysis. This could be partly explained because an assessment of the functional status of elderly patients does not always reflect the real condition. With increasing age, daily activities decrease and lifestyle changes. Consequently, it is difficult for the attending practitioner to accurately assess the functional status of elderly patients with heart disease, especially those with a long-term medical history or an emergent status.<sup>[30,31]</sup>

Our data indicated that pneumonia and emergent status were independent components which affected the treatment decision-making process. However, pneumonia and emergent status merely reflected the immediate condition of patients when they were admitted to the hospital. Nevertheless, physicians did not recommend surgical intervention for such patients, even when the pneumonia and emergent status were under control. This phenomenon once again suggests that an interdisciplinary discussion should be enforced to optimize the treatment strategy for elderly patients with heart valve disease.

Previous studies showed that female sex was associated with morbidity, mortality, and adverse long-term outcomes in patients who underwent cardiac surgery.<sup>[32–34]</sup> However, sex differences were not taken into consideration by attending practitioners when the treatment decision was made.<sup>[26]</sup> In contrast with previous investigations which discussed treatment decision-making for elderly patients with cardiac disease, our data revealed that female sex was independently associated with a decision of conservative treatment (OR = 5.47, 95% CI: 2.33–12.85,  $P < 0.0001$ ). This is probably related to a higher risk score, limited activity and organ dysfunction in aged females. Nevertheless, this reminds us that more research, both basic and clinical, is needed to highlight the effect of sex on treatment outcomes and long-term prognosis of patients with heart disease.

Bhamidipati, *et al.*<sup>[4]</sup> showed that isolated mitral and combined procedures in octogenarians have higher complications and costs. In accordance with this, our investigation indicated that patients with isolated aortic valve disease tended to be treated surgically. More interestingly, we found that although isolated aortic valve disease was the most common disease in the entire study population, mitral disease and combined heart valve disease accounted for more than 60%. This is probably because of the prevalence of rheumatic valve disease in the elderly in China and rheumatic disease always involves mitral and combined valves. However, although rheumatic valve disease was prevalent in our study population, it did not affect treatment decision-making and outcomes.

#### 4.1 Study limitations

The limitations of this retrospective survey should be acknowledged. First, patients included in the study were recruited from inpatient wards, and most of the patients in the surgical group were evaluated by surgeons in cardiac surgery outpatient clinics, and almost all of them were in a stable condition. Conversely, patients in the conservative group were mostly in an unstable condition when they were admitted to the hospital. Second, despite the absence of any significant differences between the two groups in EuroSCORE II scores, and the use of propensity score matching to reduce selection bias, unaccounted for confounding factors may have contributed to our results.

#### 4.2 Conclusions

This retrospective analysis of elderly patients with symptomatic severe heart valve disease in China showed that more than one-third were treated conservatively, despite a clear indication for surgical intervention. Advanced age as well as cardiac- and age-related comorbidities profoundly

affected treatment decision-making, treatment outcomes, and long-term prognosis. Valve surgery in the elderly is associated with good early outcomes and excellent long-term survival, in addition to distinct improvements in quality of life. Conversely, conservative treatment seemed unfavorable for long-term survival and improvement of quality of life. An assessment of the benefit-risk ratio for elderly patients with heart disease is complicated and interdisciplinary discussions should be enforced to optimize treatment strategies.

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