Clinical Benefit of Valvular Surgery in Patients with Chronic Kidney Disease

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Summary

Concomitant chronic kidney disease (CKD) is common in patients with significant valvular heart disease (VHD). This study sought to evaluate the clinical benefit of valvular surgery in patients with concomitant CKD.

We evaluated 349 patients with significant VHD who were referred for surgery. Patients were divided into those with CKD stage ≥ 3 (CKD patients; $n = 88$) and those with CKD stage 1 or 2 (no CKD patients; $n = 261$). 63 patients did not receive surgery, of which 20 patients had CKD and 43 had no CKD. Mortality and change in eGFR were assessed after a median follow-up of 21 months.

In the whole study population, 25% of the patients had CKD and these patients had higher mortality than those with no CKD. The annual mortality rates of patients with CKD who did and did not undergo surgery were 7.9% and 28.0%, respectively. In patients with no CKD, the annual mortality rates of those who did and did not undergo surgery were 1.8% and 2.3%, respectively. Importantly, surgery was associated with significant survival benefit in patients with CKD (log-rank test, $P < 0.01$), but was neutral in patients with no CKD. Multi-variable analysis confirmed the survival benefit of valvular surgery in all patients, which was most significant in patients with CKD. Furthermore, eGFR was preserved in patients who underwent valvular surgery but declined significantly in those who did not.

CKD is common in patients with significant VHD and, if left untreated surgically, these patients exhibit a high mortality.

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Key words: Renal dysfunction, Valvular heart disease, Estimated glomerular filtration rate, Outcome

Valvular heart disease (VHD) constitutes a special population in cardiovascular medicine and is subject of growing concern and focus because of its increased prevalence due to the aging population.¹⁾ Unlike heart failure and coronary artery disease, where medication is the mainstay of successful treatment, patients with significant VHD often require corrective valvular surgery to optimize long-term survival.^{2,3)} However, the decision between continued medical management and valvular surgery in patients with comorbidities is challenging for both patients and physicians. One of the determining factors is the presence of chronic kidney disease (CKD), likewise a rapidly growing health problem due to the aging population,⁴⁾ that is closely associated with morbidity and mortality following valvular surgery.^{5,6)} As a result, a significant number of patients have been denied surgery as they were considered too high risk due to concomitant CKD.

Although valvular surgery is associated with a dismal post-operative outcome, its long-term clinical outcome compared to that of continued medical therapy in patients with significant CKD has not been studied. The aim of the present study was thus to evaluate the clinical benefit of valvular surgery in patients with concomitant significant CKD.

Method

Study population: From January 2012 to February 2015, 414 consecutive patients with significant VHD for whom conventional surgical correction was indicated, including those with significant clinical symptoms, dilated left ventricular dimension, and/or impaired left ventricular function, were prospectively recruited.³⁾ Patients with a documented history of congenital heart disease ($n = 10$), acute

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infective endocarditis ($n = 4$), underlying renal parenchymal disease ($n = 23$), end-stage renal disease requiring dialysis ($n = 8$), or who refused to participate ($n = 20$) were excluded. A total of 349 patients suitable for final analysis were included. Indications for surgery in patients with VHD were evaluated according to the combined guidelines.^{2,3} The predominant left heart valvular lesion indicated for surgery was categorized as either single or mixed (defined as more than one valvular lesion with at least a moderate degree of severity). Concomitant tricuspid annuloplasty and coronary artery bypass graft during left heart valvular surgery was documented. The study was part of the Chinese Valvular Heart Disease Study to evaluate the pattern of disease, pathophysiology, and clinical outcome in Chinese patients with VHD.⁷ The study was approved by the ethics committee of the West Cluster Hospital Authority of Hong Kong, and all subjects gave written informed consent.

Estimated glomerular filtration rate (eGFR): The serum creatinine level within 1 week of the echocardiography examination or surgery, whichever was closer, was used to calculate the baseline eGFR using the Modified Diet in Renal Disease Equation.⁸ Two categories of eGFR based on the National Kidney Foundation recommendations were compared: CKD stage 1 or 2 (eGFR ≥ 60 mL/minute/1.73 m²), classified as no CKD; CKD stage ≥ 3 (eGFR < 60 mL/minute/1.73 m²), classified as CKD according to prior studies.⁹⁻¹²

Clinical parameters: Clinical data on preoperative variables were collected from patient records by one investigator. The etiology of VHD was recorded as chronic rheumatic heart disease (CRHD), bicuspid aortic valve, mitral valve prolapse, and degenerative valvular disease according to the predominant lesion of the valve. The New York Heart Association (NYHA) classification was recorded as class I/II or III/IV, and the status of atrial fibrillation (AF) was also recorded for each subject. Conventional cardiovascular risk factors such as history of diabetes mellitus, hyperlipidemia, hypertension, and smoking status were documented. Data on prescription of angiotensin-converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB), beta blocker, calcium channel blocker, and statin were retrieved from the Hospital Authority records.

Clinical follow-up: All-cause mortality was retrieved from the inter-hospital computer medical system. Follow-up eGFR was calculated using the creatinine level measured at least 6 months after the baseline eGFR or that available at the time of death. Significant CKD progression was defined as a 30% reduction in eGFR from the baseline value.¹³ The annual rate of decline of eGFR (slope of eGFR over time) as a measure of CKD was also examined.

Conventional echocardiography: Detailed transthoracic echocardiography was performed in all subjects. Patients were imaged in the left lateral decubitus position using a commercially available echocardiography system (Vingmed E9, General Electric Vingmed Ultrasound; Milwaukee, WI, USA). A 3.5-MHz transducer was used to obtain images that were digitally stored in cine-loop format (5 cardiac cycles). Offline analysis was performed using

EchoPAC version 112.0 (General Electric Vingmed, Horten, Norway). The left ventricular (LV) systolic and diastolic volumes and ejection fraction were measured according to the modified biplane Simpson's rule.¹⁴

Statistical analysis: Continuous variables are expressed as mean $\pm$ standard deviation and were compared with the independent sample *t*-test. Categorical variables are reported as frequencies or proportions and were compared using the chi-squared or the Fisher's exact test if at least one cell had an expected cell count below 5.

A Kaplan-Meier curve was constructed and the percentage survival among patients with and without CKD and in those with and without valvular surgery were compared using the log-rank test. A Cox regression survival model adjusted for age, sex, diabetes mellitus, hypertension, hyperlipidemia, smoking, AF, ACEI/ARB use, and baseline eGFR was performed to evaluate the impact of valvular surgery on mortality. Logistic and linear regressions were used to assess the association of valvular surgery with CKD progression and annual rate of eGFR decline after adjusting for covariates. All statistical analyses were performed using the statistical package SPSS for windows (Version 20.0; SPSS, Chicago, IL, USA) and the *P* values reported are two-sided for consistency. A *P* value < 0.05 was considered statistically significant.

Results

Clinical demographics and prevalence of renal dysfunction: The mean age of the whole study population was 64 years and 56% were female (Table I). Nearly 70% of the patients had AF and over 60% had CRHD as the cause of valve pathology. The most common single valvular lesion was mitral regurgitation and 43.8% had mixed valvular disease. The mean eGFR of the whole population was 71.7 mL/minute/1.73 m², 88 patients (25%) had CKD (CKD stage ≥ 3) and 261 patients had no CKD (CKD stage 1 or 2). Patients with CKD were older and had a higher prevalence of diabetes mellitus and hypertension than those with no CKD. Nonetheless, the sex, NYHA class III/IV, etiology of VHD, and echocardiography parameters were similar between the two groups. For the whole study population, the prevalence of CKD increased with age and was present in up to 30% of the patients aged above 60 years (Figure 1), but was similar for males and females (23.8% versus 26.3%, *P* = 0.62).

Clinical characteristic of patients with and without valvular surgery: In the whole study population, 286 patients underwent valvular surgery and 63 did not received surgery, of which 20 patients had CKD and 43 had no CKD. The reasons for not performing valvular surgery despite a positive indication at the time of assessment are as follows: declined by patient because of considering too high risk ($n = 33$) and those pending surgery ($n = 30$). For the patients who underwent surgery, the following valvular surgery was performed: mitral valve replacement ($n = 74$), mitral valve repair ($n = 76$), aortic valve replacement ($n = 45$), and dual valvular replacement ($n = 91$). Furthermore, all of them received cardiopulmonary bypass, 171 (59.8%) had concomitant tricuspid annuloplasty, and 20 (5.7%) received concomitant coronary artery by-

Table I. Clinical Characteristics of Patients

Variables	Total (<i>n</i> = 349)	CKD stage ≥ 3 (<i>n</i> = 88)	CKD stage 1 or 2 (<i>n</i> = 261)	<i>P</i>
Clinical demographics				
Age, years	64.4 $\pm$ 10.1	68.5 $\pm$ 8.0	63.0 $\pm$ 10.4	< 0.01
Male, <i>n</i> (%)	151 (43.3)	36 (40.9)	115 (44.1)	0.61
Diabetes mellitus, <i>n</i> (%)	61 (17.5)	23 (26.1)	38 (14.6)	0.01
Hypertension, <i>n</i> (%)	72 (20.6)	27 (30.7)	45 (17.2)	< 0.01
Hyperlipidemia, <i>n</i> (%)	61 (17.5)	20 (22.7)	41 (15.7)	0.13
Smoking, <i>n</i> (%)	58 (16.6)	17 (19.3)	41 (15.7)	0.43
Atrial fibrillation, <i>n</i> (%)	243 (69.6)	64 (72.7)	179 (68.6)	0.47
NYHA class III/IV, <i>n</i> (%)	86 (24.6)	26 (29.5)	60 (23.0)	0.22
Etiology of valvular heart disease, <i>n</i> (%)				
CRHD	210 (60.2)	51 (58.0)	159 (60.9)	0.43
Bicuspid aortic valve	7 (2.0)	1 (1.1)	6 (2.3)	
Mitral valve prolapse	86 (24.6)	27 (30.7)	59 (22.6)	
Degenerative valve disease	46 (13.2)	9 (10.2)	37 (14.2)	
Left sided valvular lesion, <i>n</i> (%)				
Single (<i>n</i> = 196)				
Mitral stenosis	33 (16.8)	8 (18.2)	25 (16.4)	0.64
Mitral regurgitation	113 (57.7)	28 (63.6)	85 (55.9)	
Aortic stenosis	29 (14.8)	4 (9.1)	25 (16.4)	
Aortic regurgitation	21 (10.7)	4 (9.1)	17 (11.2)	
Mixed (<i>n</i> = 153)	153 (43.8)	44 (50.0)	109 (41.8)	0.18
Predominant surgical details (<i>n</i> = 268), <i>n</i> (%)				
Mitral valve repair	76 (26.6)	26 (38.2)	50 (22.9)	0.08
Mitral valve replacement	74 (25.9)	15 (22.1)	59 (27.1)	
Aortic valve replacement	45 (15.7)	7 (10.3)	38 (17.4)	
Dual valvular replacement	91 (31.8)	20 (29.4)	71 (32.6)	
Combined tricuspid annuloplasty, <i>n</i> (%)	171 (59.8)	47 (69.1)	124 (56.9)	0.07
Renal function				
eGFR (mL/minute/1.73 m ²)	71.7 $\pm$ 18.3	49.8 $\pm$ 8.1	79.0 $\pm$ 14.5	< 0.01
Echocardiography parameters				
LVEDV (mL)	102.3 $\pm$ 49.6	102.5 $\pm$ 48.2	102.2 $\pm$ 50.2	0.97
LVESV (mL)	41.3 $\pm$ 27.2	42.7 $\pm$ 31.6	40.9 $\pm$ 25.6	0.59
LVEF (%)	60.6 $\pm$ 9.2	60.1 $\pm$ 10.0	60.8 $\pm$ 8.9	0.54
Drugs, <i>n</i> (%)				
ACEI/ARB	177 (50.7)	48 (54.5)	129 (49.4)	0.41
Calcium channel blocker	90 (25.8)	20 (22.7)	70 (26.8)	0.45
Beta blocker	187 (53.6)	49 (55.7)	138 (52.9)	0.65
Statin	122 (35.0)	95 (36.4)	27 (30.7)	0.33

Values are mean $\pm$ SD or *n* (%). ACEI indicates angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; CRHD, chronic rheumatic heart disease; eGFR, estimated glomerular filtration rate; LVEDV, left ventricular end diastolic volume; LVEF, LV ejection fraction; LVESV, LV end systolic volume; and NYHA, New York Heart Association.

pass graft. The predominant surgical types were no difference between patients with and without CKD (Table I). For patients with CKD, those who did not receive surgery were more likely to have mixed valvular disease (Table II). For patients with no CKD, those who did not receive surgery were more likely to be older, have single valvular disease, a smaller LV dimension, and less AF compared to those who received surgery.

Clinical outcome: The median follow-up was 21 months (range 1-44 months) and death occurred in 26 patients: all were due to a cardiovascular cause (24 heart failure-related and two sudden cardiac deaths). The annual mortality rates for patients with and with no valvular surgery were 3.3% and 8.1%, respectively.

The Kaplan-Meier survival curves comparing the prognostic value of valvular surgery in patients with and

with no CKD are shown in Figure 2. The annual mortality rates of CKD patients with and with no valvular surgery were 7.9% and 28.0%, respectively. In patients with no CKD, the annual mortality rates of those with and with no surgery were 1.8% and 2.3%, respectively. In the whole study population, patients with CKD had a higher mortality than those with no CKD (Figure 2A, *P* < 0.01). Importantly, surgery was associated with a significant survival benefit in patients with CKD (solid line, Figure 2B) but was neutral in patients with no CKD (dotted line, Figure 2B). Furthermore, patients with CKD who did not undergo surgery had the worst prognosis among all subgroups (Figure 2B). Among the 33 patients who declined surgery, mortality occurred in 4/10 (40%) patients who had CKD compared to only 2/23 (8.7%) patients with no CKD (*P* = 0.05). Similarly, among the 30 patients who

Figure 1. Percentage of patients with significant renal dysfunction defined as chronic kidney disease (CKD) stage ≥ 3 according to different age groups.

were pending surgery, 3/10 (30%) with CKD died during the waiting period (median 2 months, range 1-3 months) compared with none of those with no CKD ($P = 0.03$). Multivariable Cox regression confirmed the survival benefit of valvular surgery in all patients (Table III). Importantly, the adjusted survival benefit was most significant for patients with CKD but neutral for those with no CKD.

CKD progression in patients with and without valvular surgery: In the whole population, the mean eGFR declined from 71.7 ± 18.3 to 70.3 ± 22.8 mL/minute/1.73 m². The eGFR was preserved in patients who underwent valvular surgery (72.4 ± 18.6 to 72.1 ± 23.1 mL/minute/1.73 m², $P = 0.78$), but declined significantly in those who did not (68.4 ± 16.7 to 62.1 ± 19.6 mL/minute/1.73 m², $P < 0.01$). Comparison with those who underwent valvular surgery revealed that the distribution of eGFR percentage change in patients without surgery was more skewed towards a negative value, indicating a more prevalent decline in eGFR (Figure 3). Furthermore, the incidence of $>30\%$ eGFR loss and the annual rate of eGFR decline was greater in patients with no surgery than in those who underwent valvular surgery, even after multivariable adjustment (Table IV).

Table II. Clinical Characteristics of Patients with and without Valvular Surgery

	CKD stage ≥ 3 ($n = 88$)			CKD stage 1 or 2 ($n = 261$)		
	Surgery ($n = 68$)	No surgery ($n = 20$)	P	Surgery ($n = 218$)	No surgery ($n = 43$)	P
Age, years	68.3 ± 6.9	69.2 ± 11.0	0.74	62.1 ± 10.1	67.2 ± 10.6	< 0.01
Male, n (%)	27 (39.7)	9 (45.0)	0.67	93 (42.7)	22 (51.2)	0.31
Diabetes mellitus, n (%)	17 (25.0)	6 (30.0)	0.66	33 (15.1)	5 (11.6)	0.55
Hypertension, n (%)	20 (29.4)	7 (35.0)	0.63	38 (17.4)	7 (16.3)	0.86
Hyperlipidemia, n (%)	16 (23.5)	4 (20.0)	0.74	35 (16.1)	6 (14.0)	0.73
Smoking, n (%)	12 (17.6)	5 (25.0)	0.52	37 (17.0)	4 (9.3)	0.21
Atrial fibrillation, n (%)	48 (70.6)	16 (80.0)	0.41	156 (71.6)	23 (53.5)	0.02
NYHA class III/IV, n (%)	20 (29.4)	6 (30.0)	0.96	55 (25.2)	5 (11.6)	0.06
Etiology of valvular heart disease, n (%)						
CRHD	39 (57.4)	12 (60.0)	0.73	139 (63.8)	20 (46.5)	0.08
Bicuspid aortic valve	1 (1.4)	0 (0)		6 (2.8)	0 (0)	
Mitral valve prolapse	22 (32.4)	5 (25.0)		45 (20.6)	14 (32.6)	
Degenerative valve disease	6 (8.8)	3 (15.0)		28 (12.8)	9 (20.9)	
Left sided valvular lesion, n (%)						
Single						
Mitral stenosis	7 (17.9)	1 (20.0)	0.74	21 (17.4)	4 (12.9)	0.28
Mitral regurgitation	24 (61.5)	4 (80.0)		64 (52.9)	21 (67.7)	
Aortic stenosis	4 (10.3)	0 (0)		23 (19.0)	2 (6.5)	
Aortic regurgitation	4 (10.3)	0 (0)		13 (10.7)	4 (12.9)	
Mixed	29 (42.6)	15 (75.0)	0.01	97 (44.5)	12 (27.9)	0.04
Predominant surgical details, n (%)						
Mitral valve repair	26 (38.2)	-	-	50 (22.9)	-	-
Mitral valve replacement	15 (22.1)	-	-	59 (27.1)	-	-
Aortic valve replacement	7 (10.3)	-	-	38 (17.4)	-	-
Dual valvular replacement	20 (29.4)	-	-	71 (32.6)	-	-
Combined tricuspid annuloplasty, n (%)	47 (69.1)	-	-	124 (56.9)	-	-
LVEDV (mL)	102.3 ± 46.7	103.5 ± 54.2	0.92	104.4 ± 53.0	91.5 ± 30.4	0.03
LVESV (mL)	43.3 ± 29.9	40.7 ± 37.8	0.75	42.3 ± 27.2	33.6 ± 13.0	< 0.01
LVEF (%)	59.4 ± 9.9	62.5 ± 10.4	0.24	60.3 ± 9.2	63.1 ± 7.0	0.06
ACEI/ARB	39 (57.4)	9 (45.0)	0.33	106 (48.6)	23 (53.5)	0.56
Calcium channel blocker, n (%)	15 (22.1)	5 (25.0)	0.77	57 (26.1)	13 (30.2)	0.58
Beta blocker, n (%)	40 (58.8)	9 (45.0)	0.27	116 (53.2)	22 (51.2)	0.81
Statin, n (%)	21 (30.9)	6 (30.0)	0.94	80 (36.7)	15 (34.9)	0.82

Values are mean $\pm$ SD or n (%). Abbreviations similar to those of Table I.

Table III. Cox Regression Analysis of Valve Surgery in Association with Mortality

	All patients		CKD stage ≥ 3		CKD stage 1 or 2	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Unadjusted	0.37 (0.17 to 0.84)	0.02	0.32 (0.12 to 0.84)	0.02	0.66 (0.14 to 3.20)	0.61
Adjusted*	0.45 (0.19 to 1.04)	0.06	0.32 (0.12 to 0.86)	0.02	0.87 (0.17 to 4.64)	0.87
Adjusted [§]	0.39 (0.16 to 0.92)	0.03	0.33 (0.12 to 0.93)	0.04	0.91 (0.14 to 5.91)	0.92

Adjusted*: adjusted age, sex. Adjusted[§]: adjusted age, sex, diabetes mellitus, hypertension, hyperlipidemia, smoking, atrial fibrillation, ACEI/ARB, and baseline eGFR. Abbreviations similar to those of Table I.

Discussion

The present study demonstrates that significant CKD is common in patients with significant VHD and increases with age. Importantly, valvular surgery in patients with concomitant significant CKD improved survival compared with continued medical therapy. The survival benefit of valvular surgery was, however, neutral in patients with no CKD. Furthermore, valvular surgery preserved renal function, whereas patients left untreated surgically had a significant decline in renal function.

Renal dysfunction is highly prevalent in patients with

cardiovascular disease and has been reported to affect 25% to 56% of patients with chronic heart failure and 32% of patients with coronary artery disease.^{9,11} The present study demonstrated that, compared with other cardiovascular diseases, renal dysfunction was present in 25% of patients with significant VHD. Furthermore, the presence of renal dysfunction was most likely to occur in elderly patients (up to 30% of the patients aged over 60 years). As the etiology of VHD now shifted toward degenerative from CRHD, patients presented with VHD will be more often elderly and thus the presence of concomitant CKD will be increasingly seen.¹⁾

Table IV. Change in Renal Function in Patients with and without Valvular Surgery

	eGFR decline > 30%			Annual rate of eGFR decline		
	<i>n</i> (%)	OR (95% CI)	<i>P</i>	Median (Interquartile range)	B (95% CI)	<i>P</i>
Surgery (<i>n</i> = 286)	19 (6.6)		0.02	0.4 (-6.2 to 7.3)		< 0.01
Without surgery (<i>n</i> = 63)	10 (15.9)			-4.6 (-23.0 to 0)		
Regression model (surgery versus without surgery)						
Unadjusted		0.38 (0.17 to 0.86)	0.02		-22.66 (-34.74 to -10.59)	< 0.01
Adjusted*		0.46 (0.20 to 1.09)	0.08		-20.01 (-32.25 to -7.86)	< 0.01
Adjusted ^{&}		0.40 (0.16 to 0.98)	0.04		-21.67 (-33.98 to -9.39)	< 0.01

Adjusted*: adjusted age, sex. Adjusted[&]: adjusted age, sex, diabetes mellitus, hypertension, hyperlipidemia, smoking, atrial fibrillation, ACEI/ARB, and baseline eGFR. Abbreviation similar to Table I.

The prognostic value of CKD in patients who undergo valvular surgery has been extensively reported,^{5,6)} and thus the assessment of eGFR has been implemented in risk-scoring systems such as EuroScore II and the Society of Thoracic Surgeons score to calculate the post-operative mortality risk. A significant number of patients have consequently been denied surgery because they were considered to be too high risk, partly due to renal dysfunction. In agreement with the Euro Heart Survey on VHD, surgery was denied to 33% of patients with severe aortic stenosis¹⁵⁾ and 49% of patients with severe mitral regurgitation.¹⁶⁾ In addition to older age and impaired LV ejection fraction, comorbidities such as renal dysfunction were characteristic of patients who were denied surgery. In the present study, surgery was denied to 33 patients, of which over 30% had concomitant CKD and did not undergo surgery despite clinically indicated. These findings thus confirmed that renal dysfunction was common in patients who were denied surgery.

The survival benefit of valvular surgery in patients who are symptomatic or with LV remodeling is well proven. However, the survival benefit of surgery in patients with concomitant CKD, a group that is considered having high post-operative risk, has not been evaluated. The present study confirms that patients with concomitant CKD had a high risk of adverse events following surgery. Importantly, those who had CKD but did not receive surgery experienced the highest mortality rate. Notably, compared to patients who were managed medically, valvular surgery provided significant survival benefit to those with CKD. Collectively, these findings imply that in patients with significant VHD who are referred for surgery, the presence of CKD should not be considered only a risk factor for post-operative complications but rather an indicator of mortality if only treated medically. In addition, up to 30% of patients with CKD died while waiting for surgery. This finding thus suggests that patients with significant valvular disease and concomitant CKD had an unstable cardiac condition and were at high risk of mortality. A timely surgery is thus indicated to those with CKD in order to prevent premature mortality during the waiting period. Furthermore, due to the short follow-up period (median 21 months) of the current study, the positive impact of valvular surgery may not be reflected in patients without CKD.

Although renal dysfunction is strongly associated with mortality,¹⁷⁾ worsening of eGFR remains common

among patients with heart failure.¹⁸⁾ Studies have failed to demonstrate any effective treatment that can prevent the worsening of renal function.^{19,20)} The present study demonstrated that in patients with VHD, renal function was preserved in those who underwent surgery but rapidly declined in those who did not. This finding is further evidence that surgical correction of the valvular status is an effective means to prevent progression of renal dysfunction in patients with VHD. Importantly, the rapid decline in eGFR in those without surgery confirms the causative role of significant VHD in the development of renal dysfunction, and that medical treatment alone will not be sufficient to slow the progress.

Clinical implications: The optimal timing of valvular surgery relies on individual risk-benefit analysis, and the decision-making process is generally based upon clinical experience. While guidelines recommend the severity of symptoms and worsened echocardiography parameters as major indications for surgery, the role of renal dysfunction in this regard has not been addressed.^{2,3)} The present study demonstrated that renal function declines rapidly in patients with significant VHD, and once renal dysfunction has developed, mortality is alarmingly high if surgery is not performed. Based on these observations, it is recommended that renal function should be evaluated frequently in patients with significant VHD and renal dysfunction as well as considered an important indication for early valvular surgery.

Limitations: The present study did not systemically calculate the Society of Thoracic Surgeons (STS) score or EuroScore II, and did not perform hemodynamic measurements to assess pre-surgical cardiac output and central venous pressure. These measures should be elucidated by future studies. Additionally, the present study included patients referred for valvular surgery with various etiologies and surgical procedures, and the results should thus be verified in individual types of VHD. Furthermore, the present evaluation is a comparative effectiveness study and, therefore, a randomized trial would be required to control for all confounders. A larger sample size is required to determine the best cutoff value of renal function in association with mortality in order to better define the optimal timing of surgery. Finally, renal function was evaluated in the present study by eGFR; studies using biomarkers such as cystatin C and microalbuminuria are required to provide additional information on renal function.

Conclusions

The present study demonstrates that renal dysfunction is common in patients with significant VHD. Patients with significant VHD that was not corrected surgically exhibited a rapid decline in renal function and mortality was high once renal dysfunction developed. Monitoring renal function and identifying patients with CKD is, therefore, recommended. The latter should be considered an important indication for early surgery in patients with VHD.

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