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## Original article

## Albuminuria predicts worsening renal function after transcatheter aortic valve replacement



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## ABSTRACT

*Background:* The impact of albuminuria on worsening renal function (WRF) and clinical outcomes after transcatheter aortic valve replacement (TAVR) is unknown.

*Methods:* Overall, 142 patients who underwent TAVR for severe aortic stenosis were divided into two groups based on the preoperative urinary albumin-to-creatinine ratio (ACR): high (ACR  $\geq$ 30 mg/g) and low (ACR <30 mg/g). The incidence of WRF (an absolute increase in serum creatinine level of  $\geq$ 0.3 mg/dL or  $\geq$ 1.5-fold from baseline or dialysis initiation) at 6 months after TAVR and the incidence of all-cause death and heart failure readmission during follow-up were investigated.

*Results*: Half of the examined patients [n=71/142 (50.0%)] had a high ACR. Patients with a high ACR more frequently had WRF at 6 months than those with a low ACR (17.6% vs. 2.9%, p=0.004). Multivariate analysis showed a high ACR was independently associated with WRF (odds ratio, 7.76; 95% confidence interval, 1.62–37.30; p=0.01), whereas baseline estimated glomerular filtration rate <60 mL/min/1.73m<sup>2</sup> was not (odds ratio, 0.34; 95% confidence interval, 0.08–1.50; p=0.15). Patients with a high ACR had a higher risk of composite outcomes of all-cause death and heart failure readmission (p=0.002).

*Conclusions:* Preoperative albuminuria (ACR  $\geq$ 30 mg/g) was independently associated with WRF at 6 months after TAVR. Furthermore, patients with an ACR  $\geq$ 30 mg/g had higher risks of all-cause death and heart failure readmission than those with an ACR <30 mg/g.

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#### Introduction

Transcatheter aortic valve replacement (TAVR) is an established treatment for aortic stenosis (AS), and its treatment indications have expanded to younger and lower surgical risk patients [1]. Chronic kidney disease (CKD) is a major risk factor for poor clinical outcomes in patients with cardiovascular diseases, including AS undergoing TAVR [2–4]. Generally, when we assess the renal function, it is recommended to assess not only estimated glomerular filtration rate (eGFR) but also albuminuria [5]. Furthermore, some studies have reported that albuminuria is a stronger predictor of worse clinical outcomes than eGFR [6–8]. However, assessment of albuminuria is often missed in clinical practice [2], and its clinical

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significance among patients undergoing TAVR has not been well studied.

Previous studies showed worsening renal function (WRF) at chronic phase after TAVR was associated with subsequent poor prognosis [9–12]. This study aimed to investigate the impact of preoperative albuminuria on WRF at 6 months and clinical outcomes including all-cause death and heart failure readmission after TAVR.

## Materials and methods

This single-center observational study enrolled a total of 159 consecutive patients who underwent TAVR for severe AS between April 2018 and September 2020. None of the patients was on dialysis before TAVR. Patients whose urine data before TAVR were not available (n = 15) or who died in the hospital after TAVR (n = 2) were excluded. Finally, 142 patients were included in the analysis.

#### Table 1

Baseline characteristics of the patients.

-			
	ACR <30 mg/gN=71	ACR $\geq$ 30 mg/gN=71	p-value
Age, years	83 (80-86)	84 (81-87)	0.17
Male sex, n (%)	27 (38.0%)	23 (32.4%)	0.48
Height, cm	150 (145-157)	148 (144-156)	0.52
Body weight, kg	50.0 (41.8-59.0)	49.0 (43.0-56.0)	0.87
Body mass index	21.5 (19.3-24.7)	22.0 (20.1-24.5)	0.46
Hypertension, n (%)	52 (73.2%)	60 (84.5%)	0.10
Dyslipidemia, n (%)	41 (57.7%)	41 (57.7%)	1.00
Diabetes mellitus, n (%)	18 (25.4%)	24 (33.8%)	0.27
History of smoking, n (%)	19 (26.8%)	19 (26.8%)	1.00
Atrial fibrillation, n (%)	11 (15.5%)	12 (16.9%)	0.82
Obstructive pulmonary disorder, n (%)	8 (11.3%)	20 (28.2%)	0.01
Extracardiac arteriopathy, n (%)	6 (8.5%)	16 (22.5%)	0.02
Previous stroke /transient ischemic attack, n (%)	9 (12.7%)	11 (15.5%)	0.63
Previous cardiovascular surgery, n (%)	5 (7.0%)	5 (7.0%)	1.00
Previous PCI	9 (12.7%)	14 (19.7%)	0.26
Serum creatinine, mg/dL	0.93 (0.75-1.20)	1.01 (0.76-1.30)	0.32
eGFR, mL/min/1.73 m <sup>2</sup>	49.8 (34.8-64.8)	47.9 (32.4-58.1)	0.15
eGFR <60 mL/min/1.73m², n (%)	49 (69.0%)	57 (80.3%)	0.12
PCR $\geq$ 150 mg/g, n (%)	9 (12.7%)	53 (74.6%)	< 0.001
Pre-operative medication			
ACE-I/ARB, n (%)	31 (43.7%)	36 (50.7%)	0.40
Calcium blocker, n (%)	26 (36.6%)	42 (59.2%)	0.007
Beta blocker, n (%)	20 (28.2%)	19 (26.8%)	0.85
Loop diuretic, n (%)	28 (39.4%)	32 (45.1%)	0.50
Tolvaptan, n (%)	7 (9.9%)	13 (18.3%)	0.15
Aldosterone antagonist, n (%)	17 (23.9%)	17 (23.9%)	1.00
Thiazide, n (%)	6 (8.5%)	7 (9.9%)	0.77
NYHA III/IV	40 (56.3%)	38 (53.5%)	0.74
SIS	4.7 (3.1-6.8)	6.3 (4.4-8.2)	0.002
EUROScorell	3.2 (2.0-5.0)	4.4 (3.4-5.8)	0.001
LogisticEuroSCORE	10.1 (7.5-15.6)	12.0 (9.5-17.0)	0.07
Echocardiography	0.00 (0.40.070)	0.00 (0.40, 0.70)	0.00
Aortic valve area, cm <sup>2</sup>	0.60(0.46-0.70)	0.60(0.40-0.70)	0.86
Peak velocity, III/s	4.22 (4.00-5.00)	4.20 (4.00-4.70)	0.47
Mean prossure gradient, miling	/1.0 (04.0-100.0)	/0.0 (04.0-88.4)	0.47
Left ventricular ejection fraction %	45.2 (50.0-55.0)	42.0 (50.0-51.5)	0.35
Computed tomography	05.0 (00.0-71.2)	05.5 (57.0-08.0)	0.45
Appulue area cm <sup>2</sup>	414+69	125 + 72	0.00
Annulus area, cili	$414\pm00$	455±75 74.4±6.2	0.09
Procedural characteristics	72.0±J.9	74.4±0.5	0.12
Prosthetic value type			
SAPIFN XT/3 n (%)	43 (60.6%)	45 (63.4%)	0.73
Evolut R/Pro $n$ (%)	28 (39.4%)	26 (36.6%)	0.75
Prosthetic valve size	20 (33.1%)	20 (30.0%)	
20  mm n (%)	4 (5.6%)	1 (1 4%)	035
23  mm  n (%)	28 (39.4%)	25 (35 2%)	0.55
26 mm n (%)	25 (35.2%)	24 (33.8%)	
29 mm n (%)	14 (19.7%)	21 (29.6%)	
Approach site	11(101/10)	21 (2010/0)	
Transfemoral, n (%)	68 (95.8%)	69 (97.2%)	0.50
Non-transfemoral, n (%)	3 (4.2%)	2 (2.8%)	
Pre-operative hydration, n (%)	71 (100%)	71 (100%)	-
Amount of contrast, ml	70 (50-90)	66 (40-100)	0.88
<sup>†</sup> Procedural complication	. /		
Disabling/ non-disabling stroke, n (%)	3 (4.2%)	4 (5.6%)	0.50
Life-threatening/disabling bleeding, n (%)	0 (0.0%)	1 (1.4%)	0.50
Major vascular complication, n (%)	0 (0.0%)	0 (0.0%)	-
New pacemaker implantation, n (%)	4 (5.6%)	9 (12.7%)	0.15
Acute kidney injury	1 (1 4%)	4 (5.6%)	0.18

<sup>†</sup> Procedural complications were evaluated according to VARC-2 criteria (Valve Academic Research Consortium-2) [23]. Acute kidney injury was defined as an increase in serum creatinine  $\geq 0.3$  mg/dL or  $\geq 1.5$ -fold from baseline within 48 hours after TAVLACR, urinary albumin to creatinine ratio; eGFR, estimated glomerular filtration rate; PCR, urinary total protein to creatinine ratio; PCI, percutaneous coronary intervention; ACE-1, angiotensinconverting enzyme inhibitor; ARB, angiotensin II receptor blocker; STS, Society of Thoracic Surgeons; NYHA, New York Heart Association.

This study complied with the Declaration of Helsinki and was approved by our institutional ethics committee.

A spot urine sample was collected at any time of the day before TAVR and used to calculate the urinary albumin-to-creatinine ratio (ACR). The patients were divided into two groups according to ACR: high ( $\geq$ 30 mg/g) and low (<30 mg/g) [5]. The urinary total protein-to-creatinine ratio (PCR) was also calculated, and patients were divided into  $\geq$ 150 mg/g and <150 mg/g groups according to the Japanese CKD guidelines and a previous report [13].

The primary outcome was WRF at 6 months after TAVR (defined as an absolute increase in serum creatinine levels  $\geq$ 0.3 mg/dL or  $\geq$ 1.5-fold from baseline or dialysis initiation) [9, 10]. The sec-

Table 2	
Clinical	outcomes.

ACR $<30 \text{ mg/g}$	ACR $\geq$ 30 mg/g	p-value
N=70	N=68	
0.93 (0.74-1.17)	1.08 (0.80-1.42)	0.03
48.5 (37.5-63.3)	43.5 (31.4-54.8)	0.02
2 (2.9%)	12 (17.6%)	0.004
0	1 (1.5%)	0.49
N=71	N=71	
1	11	
1	5	
0	7	
	ACR <30 mg/g N=70 0.93 (0.74-1.17) 48.5 (37.5-63.3) 2 (2.9%) 0 N=71 1 1 0	$\begin{array}{c c} ACR < 30 \mbox{ mg/g} & ACR \geq 30 \mbox{ mg/g} \\ \hline N=70 & N=68 \\ \hline 0.93 \ (0.74-1.17) & 1.08 \ (0.80-1.42) \\ 48.5 \ (37.5-63.3) & 43.5 \ (31.4-54.8) \\ 2 \ (2.9\%) & 12 \ (17.6\%) \\ 0 & 1 \ (1.5\%) \\ N=71 & N=71 \\ 1 & 11 \\ 1 & 5 \\ 0 & 7 \\ \hline \end{array}$

ACR, urinary albumin to creatinine ratio; eGFR, estimated glomerular filtration rate; WRF, worsening renal function.

For the evaluation of renal function at 6 months, patients who died within 6 months (n=2) and whose laboratory data regarding renal function at 6 months were not available (n=2) were excluded and 138 patients were evaluated.

ondary outcome was the composite outcomes of all-cause death and readmission due to heart failure during the follow-up period. For the secondary outcome in patients with multiple events, the first event was evaluated. eGFR was calculated using the following revised Japanese equation: eGFR (mL/min/1.73 m<sup>2</sup>) = 194 × serum creatinine<sup>-1.094</sup> × age<sup>-0.287</sup> × 0.739 (for females) [14].

Categorical variables are presented as number and percentage, and continuous variables are presented as mean  $\pm$  standard deviation or median (interquartile range). To compare categorical variables, the chi-square test or Fisher's exact test was used. Continuous variables were compared between the two groups using the *t*-test or Mann-Whitney U test. To compare baseline and 6month postoperative renal function, the paired t-test was used. A univariate logistic regression analysis was performed to obtain the odds ratio (OR) to predict WRF for the appropriate variables. A multivariate logistic regression analysis of variables with pvalues <0.05 in the univariate analysis or clinical significance was performed. Time-to-event data were evaluated using the Kaplan-Meier method, and the differences in event rates between patients with high and low ACR and PCR, and eGFR above and below 60 mL/min/1.73 m<sup>2</sup> were evaluated using the log-rank test. Each OR is presented with its 95% confidence interval (CI). Statistical significance was set at *p*-values <0.05. All statistical analyses were performed using SPSS version 27.0 (SPSS, Chicago, IL, USA).

## Results

Table 1 presents the patients' baseline characteristics. Half of the patients [n = 71/142 (50.0%)] had a high ACR. Age, body mass index, proportion of male sex, hypertension, and diabetes mellitus were not significantly different between the two groups. Serum creatinine and eGFR were not significantly different, either. The prevalence of obstructive pulmonary disorder, extracardiac arteriopathy, preoperative use of calcium blockers, and mean Society of Thoracic Surgeons score and EuroSCOREII were higher in the high ACR group than in the low ACR group. Forty-four percent of patients had a PCR  $\geq$ 150 mg/g, and the rate was higher in the high ACR group than in the low ACR group. Preoperative hydration was ensured for all patients, and the incidence of acute kidney injury was not significantly different between the two groups [high ACR, n = 4/71 (5.6%); low ACR, n = 1/71 (1.4%); p = 0.18].

Renal function at 6 months is shown in Table 2. To evaluate WRF at 6 months after TAVR, patients who died within 6 months (n = 2) and whose laboratory data regarding renal function at 6 months were not available (n = 2) were excluded; thus, a total of 138 patients were evaluated. Serum creatinine level was higher and eGFR was lower at 6 months in the high ACR group than in the low ACR group [serum creatinine: high ACR: 1.08 (0.80–

Table 3						
Comparison of renal	function	between	baseline	and	6	months.

	Baseline	6 months	p-value
ACR <30 mg/g (n=70)			
Serum creatinine, mg/dL	0.93 (0.75-1.20)	0.93 (0.74-1.17)	0.98
eGFR, mL/min/1.73 m <sup>2</sup>	50.5 (34.5-64.9)	48.5 (37.5-63.3)	0.51
ACR $\geq$ 30 mg/g (n=68)			
Serum creatinine, mg/dL	0.96 (0.76-1.24)	1.08 (0.80-1.42)	0.001
eGFR, mL/min/1.73 m <sup>2</sup>	49.9 (32.5-58.9)	43.5 (31.4-54.8)	0.005

ACR, urinary albumin-to-creatinine ratio; eGFR, estimated glomerular filtration rate.

1.42) mg/dL, low ACR, 0.93 (0.74–1.17) mg/dL, p = 0.03; eGFR: high ACR, 43.5 (31.4–54.8) mL/min/1.73 m<sup>2</sup>, low ACR, 48.5 (37.5–63.3) mL/min/1.73 m<sup>2</sup>, p = 0.02]. In the low ACR group, neither serum creatinine level nor eGFR differed significantly between baseline and 6 months after TAVR [serum creatinine: baseline, 0.93 (0.75-1.20) mg/dL, 6 months, 0.93 (0.74–1.17) mg/dL, p = 0.98; eGFR: baseline, 50.5 (34.5-64.9) mL/min/1.73 m<sup>2</sup>, 6 months, 48.5 (37.5-63.3) mL/min/1.73 m<sup>2</sup>, p = 0.51]. In the high ACR group, serum creatinine level was higher and eGFR was lower at 6 months after TAVR than at baseline [serum creatinine: baseline; 0.96 (0.76-1.24) mg/dL, 6 months, 1.08 (0.80–1.42) mg/dL, p = 0.001; eGFR: baseline, 49.9 (32.5-58.9) mL/min/1.73 m<sup>2</sup>, 6 months, 43.5 (31.4-54.8) mL/min/1.73 m<sup>2</sup>, p = 0.005] (Table 3). The incidence of WRF at 6 months after TAVR was higher in the high ACR group than in the low ACR group [17.6% (12/68) vs 2.9% (2/70), respectively; p = 0.004] (Table 2, Fig. 1A). Meanwhile, there were no significant differences in the incidence of WRF at 6 months between patients with a baseline eGFR  $\geq$ 60 versus <60 mL/min/1.73 m<sup>2</sup> [11.1% (4/36) vs. 9.8% (10/102), respectively; p = 0.82] and between patients with a PCR  $\geq$ 150 versus <150 mg/g [13.3% (8/60) vs. (7.7%) 6/78; p = 0.28] (Fig. 1B,C).

Table 4 shows the results of the univariate and multivariate logistic regression analysis for WRF at 6 months. A baseline ACR  $\geq$  30 mg/dL and preoperative medication with a loop diuretic were significant in the univariate analysis. Neither a PCR  $\geq$ 150 mg/g nor eGFR <60 mL/min/1.73m<sup>2</sup> was significant. The multivariate analysis showed an ACR  $\geq$  30 mg/g (OR, 7.76; 95% CI, 1.62–37.30; p = 0.01) and loop diuretic (OR, 5.67; 95% CI, 1.40–22.89; p=0.02) were independent predictors of WRF, but baseline eGFR <60 mL/min/1.73m<sup>2</sup> was not (OR, 0.34; 95% CI, 0.08–1.50; p = 0.15).

The incidence of secondary outcomes is listed in Table 2. The secondary outcome occurred in 1 patient in the low ACR group and in 11 patients in the high ACR group. Fig. 2 shows the Kaplan-Meier curve of the secondary outcomes in patients with low and high ACR, PCR, and eGFR. During the median follow-up period of 366 (226–551) days, the incidence of the composite outcome of



Fig. 1. Incidence of WRF at 6 months. (A) Patients with a high ACR ( $\geq$ 30 mg/g) versus low ACR (<30 mg/g). (B) Patients with a baseline eGFR <60 versus  $\geq$ 60 mL/min/1.73 m<sup>2</sup>. (C) Patients with a PCR  $\geq$ 150 versus <150 mg/g.

ACR, urinary albumin-to-creatinine ratio; eGFR, estimated glomerular filtration rate; PCR, urinary total protein-to-creatinine ratio; WRF, worsening renal function.

#### Table 4

Univariate and multivariate analysis for the prediction of worsening renal function at 6 months after transcatheter aortic valve replacement.

	Univar	Univariate		Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
Age	1.06	0.94 - 1.19	0.37			
Male sex	0.73	0.22 - 2.46	0.61			
Body mass index	1.00	0.87 - 1.15	0.96			
Hypertension	-	0.00	1.00			
Dyslipidemia	1.30	0.41 - 4.11	0.66			
Diabetes mellitus	0.62	0.16 - 2.34	0.48			
Atrial fibrillation	0.87	0.18 - 4.17	0.86			
Obstructive lung disorder	2.58	0.79 - 8.44	0.12			
Extracardiac arteriopathy	0.92	0.19 - 4.45	0.92			
Previous PCI	0.38	0.05 - 3.04	0.36			
eGFR <60 mL/min/1.73m <sup>2</sup>	0.87	0.26 - 2.97	0.82	0.34	0.08 - 1.50	0.15
ACR $\geq$ 30 mg/g	7.29	1.57 - 33.92	0.01	7.76	1.62 - 37.30	0.01
PCR $\geq$ 150 mg/g	1.85	0.60 - 5.64	0.28			
Pre-operative medication						
ACE-I/ARB	3.24	0.96 - 10.90	0.06			
Ca blocker	1.52	0.50 - 4.63	0.46			
Beta blocker	2.35	0.76 - 7.32	0.14			
Loop diuretic	4.10	1.22 - 13.80	0.02	5.67	1.40 - 22.89	0.02
Tolvaptan	0.52	0.06 - 4.24	0.54			
Aldosterone antagonist	2.97	0.94 - 9.34	0.06			
NYHA III/IV	1.58	0.50 - 4.99	0.43			
STS score	1.06	0.92 - 1.23	0.40			
EuroSCOREII	1.03	0.91 - 1.16	0.62			
Left ventricular ejection fraction	0.99	0.94 - 1.03	0.56			
Procedural characteristics						
Prosthetic valve type (Evolut R/Pro)	0.43	0.12 - 1.63	0.22			
Non-transfemoral approach	0.00	0.00	1.00			
Amount of contrast	1.01	1.00 - 1.02	0.14			

OR, odds ratio; CI, confidence interval; PCI, percutaneous coronary intervention; eGFR, estimated glomerular filtration rate; ACR, urinary albumin to creatinine ratio; PCR, urinary total protein to creatinine ratio; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; NYHA, New York Heart Association; STS, Society of Thoracic Surgeons.

all-cause death and heart failure readmission was higher in the high ACR group than in the low ACR group (p = 0.002) (Fig. 2A). Patients with high PCR were also at higher risk of secondary outcomes than those with low PCR (p=0.004) (Fig. 2C). Meanwhile, there was no significant difference in the incidence of secondary outcomes between the patients with eGFR above and below 60 mL/min/1.73 m<sup>2</sup> (Fig. 2B).

## Discussion

This study evaluated the relationship between preoperative albuminuria and WRF at 6 months after TAVR. An ACR  $\geq$ 30 mg/dL was independently associated with WRF at 6 months after TAVR. Furthermore, patients with an ACR  $\geq$ 30 mg/dL had higher risks of composite outcomes of all-cause death and heart failure readmission than those with an ACR < 30 mg/dL.

In the assessments of renal function, testing for albuminuria or total proteinuria is important as well as eGFR; however, it is often forgotten in clinical practice. Among patients with hypertension, less than 10% underwent routine testing for albuminuria [2]. In this study, half of the patients had an ACR  $\geq$ 30 mg/dL. It seems particularly important to focus on albuminuria in patients undergoing TAVR since half of them had albuminuria. Several studies have shown the relationship between pre- or postprocedural eGFRs or serum creatinine levels and clinical outcomes after TAVR [3, 4, 9-12]; however, the influence of albuminuria or total proteinuria on TAVR has not been investigated. To our knowledge, this is the first study to show the relationship between albuminuria or total proteinuria before TAVR and clinical outcomes.



**Fig. 2.** Cumulative event rate of secondary outcome (composite of all-cause death and heart failure readmission) among patients with a high ACR ( $\geq$  30 mg/g) versus low ACR (< 30 mg/g) (A), with eGFR < 60 versus  $\geq$  60 mL/min/1.73 m<sup>2</sup> (B), and with a high PCR ( $\geq$  150 mg/g) versus low PCR (< 150 mg/g) (C). The median follow-up period was 366 (226–551) days.

ACR, urinary albumin-to-creatinine ratio; eGFR, estimated glomerular filtration rate; PCR, urinary total protein-to-creatinine ratio.

Albuminuria is one of the major risk factors for a decline in renal function or cardiovascular disease independent of eGFR [6]. Albuminuria precedes and is associated with a decline in eGFR and is associated with the progression to end-stage kidney disease [7]. Furthermore, macroalbuminuria was a strong predictor of readmission due to heart failure in patients with type 2 diabetes mellitus [15]. Although the mechanisms of albuminuria causing cardiovascular events are not well understood, albuminuria is believed to occur because of glomerular damage and represent systemic vascular damage [16]. This study showed that preoperative albuminuria was an independent risk factor for WRF at 6 months after TAVR. Previous studies demonstrated that WRF at 30 days, 3-6 months, and 1 year after TAVR were associated with increased mortality [9– 12]; therefore, patients with albuminuria are considered to have an increased risk of mortality. We also showed a relationship between albuminuria and the composite outcome of all-cause death and heart failure readmission and suggested that patients with an ACR  $\geq$  30 mg/g had a higher risk of renal and cardiac events after TAVR. Based on the results, firstly we need to recognize patients with albuminuria are high-risk subjects and consider careful management to prevent deterioration of renal function and cardiovascular events. Although it might be difficult to clarify specific approaches for such high-risk patients, several possible interventions can be considered. Previous studies showed acute kidney injury and blood transfusion were associated with deterioration of renal function [10, 12], thus maximum effort should be made to reduce the amount of contrast and bleeding. In addition, some medical therapies, such as angiotensin-converting enzyme inhibitor (ACE-I), angiotensin II receptor blocker (ARB), sodium glucose cotransporter 2 inhibitor, or finerenone can improve the prognosis of the patients with albuminuria [17–21]. However, the effectiveness and safety of these medications have not been validated yet in the elderly TAVR patients. Actually, our result of univariate analysis showed medication of ACE-I / ARB tended to have negative impact on the incidence of WRF. Further investigations should be required to determine the optimal approach to TAVR patients with albuminuria.

Preoperative CKD defined by eGFR is a well-known risk factor for poor clinical outcomes in patients undergoing TAVR [3, 4]. In this study, albuminuria was a significant predictor of WRF at 6 months in the multivariate analysis, but eGFR was not. In addition, patients with ACR  $\geq$ 30 mg/g were at higher risk of all-cause death and heart failure readmission but those with eGFR <60 mL/min/1.73 m<sup>2</sup> were not. Although this is partially because of the small number of patients, it suggests that albuminuria was more clinically significant than eGFR. Previous studies have shown that albuminuria is more associated with a decline in renal func-

tion and cardiovascular outcomes than eGFR [6–8]. As albuminuria increased, the rate of renal decline was high, regardless of eGFR [7]. One meta-analysis showed that ACR improved the prediction of cardiovascular events beyond established risk factors, and the improvement of ACR was greater than that of eGFR [6]. Furthermore, in patients without diabetes mellitus, hypertension, or cardiovascular disease, albuminuria was a stronger predictor of cardiovascular outcomes than eGFR [8]. Our results were consistent with those of these studies.

According to the Japanese CKD guidelines, PCR of 150 mg/g can be used as a substitute for ACR of 30 mg/g. This study showed patients with PCR  $\geq$ 150 mg/g had a higher incidence rate of secondary outcomes (all-cause death and heart failure readmission) than those with PCR <150 mg/g. However, PCR  $\geq$ 150 mg/g was not a significant risk factor for WRF. Although several studies have shown that total proteinuria is a useful marker equivalent to albuminuria for predicting clinical events [13, 22], albuminuria is considered more sensitive to glomerular injury than total proteinuria [2]. Our result of ACR being associated with both WRF and secondary outcomes would support the theory and ACR may be a more sensitive marker for cardiorenal events than PCR. Future studies investigating the relationships between ACR / PCR and cardiorenal events with a larger number of subjects are expected.

This study had several limitations. First, this was a single-center study with a limited number of patients. A regression analysis of the secondary outcome was not conducted because of the limited number of events. Second, preoperative urine samples could not be obtained from all TAVR patients during the study period. Third, the spot urine sample was collected at any time of the day and diurnal or day-to-day variations may exist. Regardless, there is limited evidence of an association between albuminuria and WRF after TAVR, and our results would be of importance in daily practice.

#### Conclusions

Preoperative albuminuria (ACR  $\geq$  30 mg/dL) was independently associated with WRF at 6 months after TAVR. Furthermore, patients with an ACR  $\geq$  30 mg/dL had a higher risk of the composite outcomes of all-cause death and heart failure readmission than those with an ACR <30 mg/dL. Our findings suggest that preoperative albuminuria can be a useful marker for predicting cardiac and renal events after TAVR in daily practice.

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