Creatinine Score Can Predict Persistent Renal Dysfunction Following Trans-Catheter Aortic Valve Replacement

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Summary

Severe aortic stenosis (AS) is often accompanied by renal dysfunction, which portends a poor prognosis. Trans-catheter aortic valve replacement (TAVR) is an accepted therapy for patients with severe AS, whereas the prediction of persistent renal dysfunction following TAVR remains challenging. In this study, we aimed to evaluate the pre-procedural score to assess the reversibility of renal dysfunction following TAVR. A total of 2,588 patients with severe AS who received TAVR and were enrolled in the Optimized transCathEter vAlvular iNtervention (OCEAN-TAVI) multicenter registry (UMIN000020423) were retrospectively investigated and those with serum creatinine (Cre) data at baseline and one year following TAVR were included. The Cre score was calculated using the formula: $0.2 \times (\text{age [years]}) + 3.6 \times (\text{baseline serum Cre [mg/dL]})$. This score was evaluated to assess the risk of persistent renal dysfunction defined as serum Cre level > 1.5 mg/dL at one year following TAVR. Of the 1705 patients (84.3 ± 5.0 years old) included, 246 (14%) had persistent renal dysfunction following TAVR. The Cre score predicted the incidence of persistent renal dysfunction with an adjusted incidence rate ratio of 1.48 (95% confidence interval 1.42-1.56) with a cutoff of 21.4 (43% versus 5%, $P < 0.001$). The Cre score also predicted 4-year survival following TAVR (70% versus 52%, $P < 0.001$) with an adjusted hazard ratio of 1.75 (95% confidence interval 1.29-2.37). In conclusion, the Cre score identified those with a high risk of one-year persistent renal dysfunction following TAVR. The implication of Cre score-guided therapeutic strategy is the next concern.

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Key words: Renal disease, Heart failure, Hemodynamics

Severe aortic stenosis (AS) often accompanies renal impairment due to both diastolic dysfunction causing right-sided congestion and also from reduced organ perfusion.¹⁾ Such end-organ dysfunction further worsens patient prognosis, particularly for the elderly.²⁾ Recently, trans-catheter aortic valve replacement (TAVR) has become a widely utilized therapy for severe AS in patients with high operative risk due to advanced age.³⁾ Furthermore, a recent randomized trial has demonstrated comparable efficacy and safety of TAVR and surgical aortic valve replacement in certain subgroups of patients.⁴⁾

Renal function often improves following TAVR due to amelioration of both systemic congestion and organ

perfusion,⁵⁾ though severe renal impairment may remain in some patients despite undergoing TAVR. In the subset of patients with more than mild renal dysfunction, pre-procedural risk stratification of the reversibility of renal impairment would be useful to better select patients who may incur the most benefit post-procedure.

In this study, we investigated the applicability of the previously introduced creatinine (Cre) score, calculated using baseline age and serum Cre level,⁶⁾ to predict persistent renal dysfunction following TAVR in a Japanese multicenter prospective registry.⁷⁾

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Methods

Subjects and study design: A total of 2,588 patients with severe AS (defined as aortic valve area $< 1.0 \text{ cm}^2$ and mean pressure gradient $> 40 \text{ mmHg}$), who received TAVR at 14 large Japanese academic institutions between October 2013 and May 2017, were prospectively enrolled in the Optimized CathETER vAlvular iNtervention-Transcatheter Aortic Valve Implantation (OCEAN-TAVI) registry (UMIN000020423).⁷⁾ This retrospective study used the data of the OCEAN-TAVI registry, which is a prospective, multicenter, observational registry established to record clinical outcomes following TAVR.

Patients who had serum Cre levels measured at baseline and one year following TAVR were included. The ethics committee at each institution approved this study and written informed consent was obtained from all participants beforehand.

Trans-catheter aortic valve implantation: Patient selection for TAVR was made by the heart valve team of each institute, which was comprised of cardiologists, cardiovascular surgeons, and anesthesiologists. Traditional surgical risk score models were considered to discuss the appropriateness of TAVR, according to the values of the European System for Cardiac Operative Risk Evaluation and Society of Thoracic Surgeons score.

Patients received Sapien 3 (Edwards Lifesciences Inc.), Evolut R (Medtronic, Dublin, Ireland), Sapien XT (Edwards Lifesciences Inc.), or CoreValve (Medtronic) via trans-femoral, trans-apical, transiliac, trans-subclavian, or direct aortic approaches under general or local anesthesia.^{8,9)}

Variables evaluated: Demographics, hemodynamics, echocardiography, and laboratory data collected just before TAVR were obtained. The Cre score was calculated as follows using the baseline serum Cre level: (Cre score) = $0.2 \times (\text{age} [\text{years}]) + 3.6 \times (\text{serum Cre} [\text{mg/dL}])$.⁶⁾ Serum Cre levels were obtained also at index discharge and one year following TAVR. Persistent renal dysfunction, which was a primary endpoint in this study, was defined as serum Cre level $> 1.5 \text{ mg/dL}$ at one year following TAVR. Four-year survival following TAVR was used as the secondary endpoint.

Rationale of the definition of primary endpoint: The original study defines a serum Cre level of 1.5 mg/dL as a primary endpoint following ventricular assist device implantation,⁶⁾ given that mortality following heart transplantation began to increase at serum Cre over 1.5 mg/dL .¹⁰⁾ The receiver operating characteristics analysis also demonstrated a cutoff of 1.5 mg/dL of the serum Cre level at a one-year follow-up associating with 4-year mortality in this study.

Statistical analysis: Continuous variables are expressed as the mean and standard deviation, and categorical variables are expressed as number and percentage. A value of $P < 0.05$ was considered statistically significant. Statistical analyses were performed using SPSS Statistics 22 (SPSS Inc, Armonk, IL, USA).

Receiver operating characteristics analyses were performed to calculate a cutoff of the Cre score to predict persistent renal dysfunction at one year following the

TAVR procedure. The incidence of persistent renal dysfunction was compared between the high Cre score group and the low Cre score group using negative binomial regression analysis. Trends of serum Cre level were analyzed using repeated analyses of variance.

Four-year survival following the TAVR procedure was stratified by the Cre score and compared between the two groups (i.e., high score versus low score). The impact of Cre score on the 4-year survival was also assessed using Cox proportional hazard ratio regression analysis. In the multivariable analyses, variables significantly different between the high and low Cre score groups were used for the adjustment.

Results

Baseline characteristics: Among 2,588 patients who received TAVR and were registered in the OCEAN-TAVI, 883 patients were excluded due to the lack of complete serum Cre data. The remaining 1,705 patients were included in this study (Table).

The mean age was 84.3 ± 5.0 years and 1,185 (70%) were males. The clinical frailty score and Society of Thoracic Surgeon score were 3.8 ± 1.2 and 7.5 ± 5.8 , respectively. Aortic valve area and mean pressure gradient were $0.63 \pm 0.17 \text{ cm}^2$ and $51.1 \pm 17.7 \text{ mmHg}$, respectively.

Calculation of the Cre score: The baseline serum Cre level was $0.99 \pm 0.44 \text{ mg/dL}$. The Cre score, which was calculated as $0.2 \times (\text{age} [\text{years}]) + 3.6 \times (\text{serum Cre level} [\text{mg/dL}])$, averaged 20.4 ± 1.9 , ranging between 14.5 and 35.2 (Figure 1).

Impact of Cre score on the persistent renal dysfunction following TAVR: The serum Cre level decreased significantly at the index discharge (down to 0.92 ± 0.42 , $P < 0.001$), but increased significantly at 1 year following TAVR (up to $1.08 \pm 0.51 \text{ mg/dL}$, $P < 0.001$). A total of 246 of the 1705 patients (14%) experienced persistent renal dysfunction (i.e., $> 1.5 \text{ mg/dL}$ of serum Cre level).

The originally proposed cutoff Cre score of 14.1 could not stratify the primary endpoint, given that all patients had a Cre score above 14.1. A newly calculated cutoff of the Cre score to predict persistent renal dysfunction (defined as serum Cre $> 1.5 \text{ mg/dL}$ at 1 year) was 21.4 with a sensitivity of 0.758, a specificity of 0.830, and area under the curve of 0.870 (Figure 2). The Cre score had an area under the curve of 0.883 in the women cohort and 0.847 in the men cohort. The estimated glomerular filtration rate had an area under the curve of 0.802, which is numerically lower than the Cre score.

Among all the subjects, 407 (24%) had a Cre score above 21.4 (Figure 1). Among the patients with a higher Cre score, 175/407 (43%) experienced persistent renal dysfunction; whereas persistent renal dysfunction occurred in only 61/1298 (5%) in the low Cre score group (Figure 3A), with an adjusted incidence rate ratio of 1.48 (95% confidence interval 1.42-1.56, $P < 0.001$).

The associations between age, baseline serum Cre level, and achievement of persistent renal dysfunction (red dot) are shown in Figure 3B. The blue line represents the predicted cutoff line of 21.4. For example, when a patient has an age of 75 years and baseline serum Cre of 1.7 mg/

Table. Baseline Characteristics

	Total (n = 1705)	High Cre score (score > 21.4) (n = 407)	Low Cre Score (score ≤ 21.4) (n = 1298)	P value
Demographics				
Age, years	84.3 ± 5.0	87.8 ± 4.1	83.3 ± 4.8	< 0.001*
Male sex	1185 (70%)	244 (60%)	941 (72%)	< 0.001*
Body mass index	22.4 ± 3.6	22.4 ± 3.6	22.4 ± 3.5	0.006*
Clinical frailty score	3.8 ± 1.2	4.0 ± 1.2	3.7 ± 1.2	< 0.001*
MMSE	25.0 ± 4.6	24.3 ± 4.8	25.2 ± 4.5	0.007*
Logarithm of EuroScore	15.4 ± 11.1	20.0 ± 13.6	13.9 ± 9.8	< 0.001*
STS score	7.5 ± 5.8	11.0 ± 8.2	6.4 ± 4.2	< 0.001*
Comorbidities				
Hypertension	1333 (78%)	342 (84%)	991 (76%)	0.001*
Dyslipidemia	761 (45%)	158 (39%)	603 (46%)	0.004*
Diabetes mellitus	341 (20%)	80 (20%)	261 (20%)	0.45
Atrial fibrillation	331 (19%)	110 (27%)	221 (17%)	< 0.001*
Peripheral artery disease	221 (13%)	69 (17%)	152 (12%)	0.005*
Chronic obstructive pulmonary disease	241 (14%)	67 (16%)	174 (13%)	0.073
Medications				
Beta-blocker	566 (33%)	164 (40%)	402 (31%)	< 0.001*
ACEI or ARB	922 (54%)	236 (58%)	686 (53%)	0.039*
Diuretics	886 (52%)	291 (71%)	595 (46%)	0.039*
Laboratory data				
Albumin, g/dL	3.8 ± 0.5	3.7 ± 0.5	3.9 ± 0.4	< 0.001*
Total bilirubin, mg/dL	0.7 ± 0.4	0.6 ± 0.3	0.7 ± 0.4	0.002*
Sodium, mEq/L	140.0 ± 3.4	140.0 ± 3.2	139.9 ± 3.5	0.54
Cre, mg/dL	0.99 ± 0.44	1.50 ± 0.58	0.83 ± 0.21	< 0.001*
B-type natriuretic peptide, pg/mL	432.3 ± 571.2	581.0 ± 635.5	385.6 ± 541.4	< 0.001*
Echocardiographic data				
Aortic valve area, cm ²	0.63 ± 0.17	0.62 ± 0.17	0.64 ± 0.17	0.039*
Aortic valve peak velocity, m/sec	4.60 ± 0.76	4.60 ± 0.77	4.59 ± 0.76	0.92
Aortic valve mean pressure gradient, mmHg	51.1 ± 17.7	51.2 ± 18.0	51.1 ± 17.6	0.95
Left ventricular end-diastolic diameter, mm	44.3 ± 6.5	45.4 ± 6.6	43.9 ± 6.4	< 0.001*

Cre indicates creatinine; MMSE, mini-mental state examination; STS, Society of Thoracic Surgeons; ACEI, angiotensin converting enzyme inhibitor; and ARB, angiotensin receptor II blocker. Continuous variables are expressed as mean and standard deviation and were compared using unpaired t-test. Categorical variables are expressed as number and percentage and were compared using Fisher's exact test. * $P < 0.05$.

dL, the plot is located below the blue line, and he/she is expected to avoid persistent renal dysfunction. When another patient has an age of 95 years and baseline serum Cre level of 0.8 mg/dL, the plot is located above the blue line, and he/she is expected to experience persistent renal dysfunction, despite preserved baseline renal function.

Trends of serum Cre levels stratified by the Cre score: The trends of serum Cre levels are stratified by the Cre score in Figure 4. Serum Cre level in the high Cre score group remained elevated, although it declined slightly at index discharge.

Impact of Cre score on survival: During the 4-year observational period, 489 patients died. The Cre score significantly stratified the 4-year survival following TAVR at a cutoff of 21.4 (70% versus 52%, $P < 0.001$; Figure 5) with an unadjusted hazard ratio of 2.11 (95% confidence interval 1.76-2.52) and an adjusted hazard ratio of 1.75 (95% confidence interval 1.29-2.37).

Discussion

In this study, we investigated the implication of the Cre score, which consists of age and baseline serum Cre

level, in predicting post-procedural persistent renal dysfunction, defined as serum Cre level > 1.5 mg/dL at 1 year following TAVR. The major findings are as follows: (1) The Cre score at baseline was widely distributed; (2) The Cre score distinguished persistent renal dysfunction following TAVR when stratified at a newly-calculated cutoff of 21.4; and (3) The Cre score also stratified 4-year survival following TAVR.

The concept of Cre score: The concept of Cre score was originally developed to predict the reversibility of renal dysfunction following durable ventricular assist device implantation.⁶⁾ The score is particularly important in situations where a patient is being considered as a bridge to transplant candidate versus destination therapy. Patients who will have persistent renal dysfunction cannot receive durable ventricular assist device therapy as a bridge to transplant.

The reversibility of renal dysfunction is largely affected by age.¹¹⁾ Even in the setting of apparent severe renal dysfunction, normalization can occur if a patient is younger, whereas the odds of renal recovery in elderly patient are less likely. This is the concept behind the Cre score, for which the basis is simply dependent on age and

baseline serum Cre level.⁶⁾ In this previous study, the Cre score had a better predictability over the serum Cre level alone and estimated glomerular filtration ratio. This is a rationale why we preferred to use the Cre score. In this study, we validated a cutoff of serum Cre 1.5 mg/dL associating with 4-year mortality using a receiver operating characteristics analysis.

Prediction of persistent renal dysfunction using Cre score: The Cre score predicted persistent renal dysfunction at a cutoff of 21.4, which is higher than the original cutoff of 14.3 as defined in the ventricular assist device literature.⁶⁾ This may be due to differences in cohort-derived age, comorbidities (original cohort with patients < 65 years age), procedure (ventricular assist device versus TAVR), and the protocol (original cohort observed for 6 months).

The Cre score is unique in that it incorporates only age and baseline serum Cre level. Although the estimated glomerular filtration ratio is also calculated by age and serum Cre, its predictability was inferior to that of the Cre

score. When a patient is 75 years old, a baseline Cre of 1.78 mg/dL may avoid post-procedural persistent renal dysfunction (i.e., > 1.5 mg/dL of serum Cre at 6 months), whereas a 90-year-old patient with a baseline Cre of 0.94 mg/dL is at higher risk for post-procedural persistent renal dysfunction.

Interestingly, the serum Cre level worsened following TAVR irrespective of the Cre score, which is in contrast to data observed in ventricular assist device patient cohorts and a prior TAVR registry.^{5,6)} Despite hemodynamic improvement following TAVR (data not shown),¹²⁾ renal function may not improve significantly due to the influence of age on renal recovery.

Clinical implication of the Cre score: Among the patients with a Cre score ≤ 21.4, 95% did not develop persistent renal dysfunction. The Cre score could, therefore, be a useful tool to select candidates for TAVR whose risk of post-procedural renal dysfunction is low. Among the patients with a Cre score > 21.4, 43% had persistent renal

Figure 1. Distribution of Cre score. Cre indicates creatinine.

Figure 2. Cutoff of Cre score to achieve the primary endpoint (serum creatinine level > 1.5 mg/dL at one year following TAVR) in the receiver operating characteristics analysis.

Figure 3. Association among age, baseline serum creatinine level, and the achievement of primary endpoint (A); the incidence of the primary endpoint stratified by the Cre score (B). The blue bar indicates the cutoff line of the Cre score = $0.2 \times (\text{age}) + 3.6 \times (\text{baseline serum Cre level}) = 21.4$. The incidence rate ratio was adjusted for variables significantly different in the Table except for serum Cre level. * $P < 0.05$.

Figure 4. Trends of serum creatinine level stratified by the Cre score at baseline, discharge, and one year following TAVR. Variables were compared with baseline using the paired *t*-test in each group. **P* < 0.05.

dysfunction, which should be considered in clinical decision-making given an apparent higher risk of post-procedural renal dysfunction as well as worse survival. Early intervention with TAVR for patients with severe AS might, therefore, be recommended before deterioration of baseline renal function to prevent post-procedural renal dysfunction and potentially improve survival. Preoperative efforts to preserve renal function via definitive antihypertensive treatment, restrictive use of diuretics, and aggressive use of SGLT2 inhibitor, might improve post-procedural renal outcomes.

We should state that various other variables also affect post-TAVR renal function,¹³⁾ although the Cre score is actionable and simple to widely apply to TAVR candidates. Nevertheless, uninvestigated peri-procedural factors including the procedural time or approach sites could potentially affect the risk of post-procedural deterioration of renal function.

Limitations: The OCEAN-TAVI registry includes Japanese patients with severe AS and high-risk comorbidities, including older age. The applicability of our findings to other cohorts remains unknown. We defined persistent renal dysfunction as a serum Cre level > 1.5 mg/dL at 1 year following TAVR given the original definition, but the impact of Cre score on other endpoints (i.e., different Cre value, acute kidney injury, or different observational period) remains unknown.¹⁴⁾ Also, the definition of persistent renal impairment varies in each study.^{15,16)} The Cre score just consists of age and baseline serum Cre level for simplicity to calculate, but many other parameters including the etiology of renal dysfunction could also impact the endpoint.^{5,13)} We excluded those who died during the observational period, except for the survival analysis, which may have led to considerable selection bias.

Conclusions

The Cre score, calculated using age and baseline serum Cre level, identified those with a high risk of one-year persistent renal dysfunction following TAVR. A prospective study is warranted to validate the clinical utility

Figure 5. Four-year survival stratified by the Cre score. **P* < 0.05 by Cox proportional hazard ratio regression analyses.

of this score.

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Disclosure

Conflicts of interest: Dr. Imamura receives grant support from JSPS KAKENHI: JP20K17143. Dr. Yamamoto, Dr. Tada, Dr. Naganuma, Dr. Shirai, Dr. Mizutani, Dr. Ueno, and Dr. Watanabe are clinical proctors for Edwards Lifesciences and Medtronic. Dr. Araki, Dr. Tabata, Dr. Takagi, and Dr. Hayashida are clinical proctors of Edwards Lifesciences. The remaining authors have nothing to disclose.

References

- Raggi P, Boulay A, Chasan-Taber S, *et al.* Cardiac calcification in adult hemodialysis patients. A link between end-stage renal disease and cardiovascular disease? *J Am Coll Cardiol* 2002; 39: 695-701.
- Denegri A, Mehran R, Holy E, *et al.* Post procedural risk assessment in patients undergoing trans aortic valve implantation according to the age, creatinine, and ejection fraction-7 score: Advantages of age, creatinine, and ejection fraction-7 in stratification of post-procedural outcome. *Catheter Cardiovasc Interv* 2019; 93: 141-8.
- Leon MB, Smith CR, Mack M, *et al.* Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010; 363: 1597-607.
- Mack MJ, Leon MB, Thourani VH, *et al.* Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients. *N Engl J Med* 2019; 380: 1695-705.
- Calca R, Teles RC, Branco P, *et al.* Impact of Transcatheter Aortic Valve Implantation on Kidney Function. *Arq Bras Cardiol* 2019; 113: 1104-11.
- Imamura T, Kinugawa K, Shiga T, *et al.* Preoperative levels of bilirubin or creatinine adjusted by age can predict their reversibility after implantation of left ventricular assist device. *Circ J* 2013; 77: 96-104.
- Yamamoto M, Watanabe Y, Tada N, *et al.* Transcatheter aortic

- valve replacement outcomes in Japan: Optimized Catheter vA-lvular iNtervention (OCEAN) Japanese multicenter registry. *Cardiovasc Revasc Med* 2019; 20: 843-51.
8. Webb JG, Pasupati S, Humphries K, *et al.* Percutaneous transarterial aortic valve replacement in selected high-risk patients with aortic stenosis. *Circulation* 2007; 116: 755-63.
9. Grube E, Schuler G, Buellesfeld L, *et al.* Percutaneous aortic valve replacement for severe aortic stenosis in high-risk patients using the second- and current third-generation self-expanding CoreValve prosthesis: device success and 30-day clinical outcome. *J Am Coll Cardiol* 2007; 50: 69-76.
10. Stehlik J, Edwards LB, Kucheryavaya AY, *et al.* The Registry of the International Society for Heart and Lung Transplantation: Twenty-eighth Adult Heart Transplant Report--2011. *J Heart Lung Transplant* 2011; 30: 1078-94.
11. Schmitt R, Coca S, Kanbay M, Tinetti ME, Cantley LG, Parikh CR. Recovery of kidney function after acute kidney injury in the elderly: a systematic review and meta-analysis. *Am J Kidney Dis* 2008; 52: 262-71.
12. Douglas PS, Leon MB, Mack MJ, *et al.* Longitudinal Hemodynamics of Transcatheter and Surgical Aortic Valves in the PARTNER Trial. *JAMA Cardiol* 2017; 2: 1197-206.
13. Langfritz M, Shahin M, Nietlispach F, *et al.* Baseline Predictors of Renal Failure in Transcatheter Aortic Valve Implantation. *J Invasive Cardiol* 2019; 31: E289-97.
14. Franzone A, Stortecky S, Pilgrim T, *et al.* Incidence and impact of renal dysfunction on clinical outcomes after transcatheter aortic valve implantation. *Int J Cardiol* 2018; 250: 73-9.
15. Thongprayoon C, Cheungpasitporn W, Mao MA, *et al.* Persistent acute kidney injury following transcatheter aortic valve replacement. *J Card Surg* 2017; 32: 550-5.
16. Blair JA, Brummel K, Friedman JL, *et al.* Inhospital and Post-discharge Changes in Renal Function After Transcatheter Aortic Valve Replacement. *Am J Cardiol* 2016; 117: 633-9.