Original Article

Impact of Chronic Kidney Disease on Outcomes in Transcatheter Aortic Valve Implantation

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Abstract

Introduction: Chronic kidney disease (CKD) is a significant comorbidity in aortic stenosis (AS) patients. We examined the impact of baseline CKD, postoperative acute kidney injury (AKI) and CKD progression on clinical outcomes in patients who underwent transcatheter aortic valve implantation (TAVI). Materials and Methods: Consecutive patients with severe AS who underwent TAVI were classified into CKD stages 1–2 (≥60 mL/min/1.72m^2), 3 (30–59 mL/min/1.73m^2) and 4–5 (<30 mL/min/1.73m^2 or dialysis) based on estimated glomerular filtration rate (eGFR). Primary outcome was mortality and secondary outcomes included 1-year echocardiographic data on aortic valve area (AVA), mean pressure gradient (MPG) and aortic regurgitation (AR). Results: A total of 216 patients were included. Higher eGFR was associated with lower overall mortality (adjusted hazards ratio [AHR] 0.981, 95% confidence interval [CI] 0.968–0.993, P = 0.002). CKD 4–5 were associated with significantly higher mortality from non-cardiovascular causes (P <0.05). Patients with CKD 3–5 had higher incidence of moderate AR than those with CKD 1–2 (P = 0.010); no difference in AVA and MPG was seen. AKI patients had higher mortality (P = 0.008), but the effect was attenuated on multivariate analysis (AHR 1.823, 95% CI 0.977–3.403, P = 0.059). Patients with CKD progression also had significantly higher mortality (AHR 2.969, 95% CI 1.373–6.420, P = 0.006). Conclusion: CKD in severe AS patients undergoing TAVI portends significantly higher mortality and morbidity. Renal disease progression impacts negatively on outcomes and identifies a challenging subgroup of patients for optimal management.

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Key words: Acute kidney injury, Aortic stenosis, Transcatheter aortic valve replacement

Introduction

With improvements in device technology as well as increasing experience, transcatheter aortic valve implantation (TAVI) has replaced open surgical aortic valve implantation as the treatment of choice in severe symptomatic aortic stenosis (AS) patients who have prohibitive and high surgical risks.[1,2] TAVI has also gained increasing uptake in patients with intermediate surgical risk.[3]

Chronic kidney disease (CKD) is an established disease modifier in most major cardiovascular diseases[4] and portends significant mortality and morbidity in patients undergoing TAVI. Patients who have prohibitive and high surgical risks are known to have multiple comorbidities, of which CKD is prevalent.[4] However, in many landmark TAVI trials such as PARTNER, PARTNER 2 or CoreValve, only a minority (about 5%) of patients have baseline serum creatinine >2 mg/dL and end-stage renal failure (ESRF) patients were generally excluded.[1,2,5,6] Additionally, little information is available on the effects of postoperative acute kidney injury (AKI) and long-term renal function

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trajectory on valve haemodynamics and clinical outcomes. This study aimed to evaluate the impact of baseline CKD status, postoperative AKI and CKD progression on early and late outcomes and valve haemodynamics in severe AS patients undergoing TAVI.

Materials and Methods

This is a prospective registry of all consecutive patients with severe symptomatic AS who underwent TAVI in a single tertiary cardiac centre from October 2009 to August 2017. A heart team that comprised cardiothoracic surgeons, interventional cardiologists and cardiac imaging physicians were involved in the selection of patients, transcatheter valve type and study approach. Registry participation did not impact on clinical management. Written informed consent was obtained from all patients and the study was approved by the Institutional Review Board.

TAVI was performed according to previously published standard protocol.[6,7] After discharge, clinical review was done at 30 days, 3 months, 12 months and annually thereafter. All patients underwent echocardiographic evaluation at baseline prior to intervention and discharge, at follow-up 3 months later and yearly thereafter. Serum creatinine and estimated glomerular filtration rate (eGFR) were evaluated preoperatively, at 24–48 hours postoperatively and at similar intervals after discharge.

Using Cockcroft-Gault formula, eGFR was calculated based on serum creatinine. CKD was classified into 5 stages according to the guidelines of the Kidney Disease: Improving Global Outcomes workgroup[8] who used eGFR to determine them. The 5 stages are CKD 1 (eGFR ≥90 mL/min/1.72m^2), CKD 2 (eGFR 69–89 mL/min/1.72m^2), CKD 3 (eGFR ≥30–59 mL/min/1.72m^2), CKD 4 (eGFR ≥15–29 mL/min/1.72m^2) and CKD 5 or ESRF (eGFR <15 mL/min/1.72m^2).[8] Advanced CKD is defined as CKD 4 and above.

AKI was defined according to the Valve Academic Research Consortium (VARC) consensus on event definition (modified Risk, Injury, Failure, Loss of kidney function and End-stage kidney disease classification) as an absolute increase in serum creatinine of >0.3 mg/dL or an increase of >50% within 72 hours following TAVI.[9] Patients who developed AKI were classified according to severity into stage 1 (creatine 150–200% or >0.3 mg/dL), stage 2 (creatinine 200–300%) or stage 3 (creatinine >300%, creatinine >4.0 mg/dL with an increase of at least 0.5mg/dL or require renal replacement therapy).

At 3 months, repeat renal panel was performed. Renal disease progression was defined as an increase in CKD stage from baseline or new requirement for renal replacement therapy.

During hospitalisation, operative success and major perioperative complications from TAVI were assessed. Echocardiographic outcomes were analysed at discharge and 12 months and included aortic valve (AV) area, mean AV pressure gradient and AV regurgitation (graded as none/trace, mild, moderate and severe). Mortality and its aetiology (cardiovascular vs non-cardiovascular) were obtained from national registries and classified into early (up to 30 days) and cumulative (inclusive of 30 days until last follow-up) mortality. All outcomes were defined according to VARC-2 criteria.[10]

Continuous variables were subjected to 1-way analysis of variance and results were expressed as mean and standard deviation (SD). Categorical variables were analysed using chi-square test and the findings were expressed as counts and percentages. Logistic regression was used to compare outcomes between groups for in-hospital/30-day outcomes; Cox proportional hazards regression was used to analyse cumulative outcomes. Multivariate analysis was used to derive odds ratio (OR) for logistic regression, hazards ratio (HR) for Cox regression and 95% confidence intervals (CI) for predictive variables. Survival curves were presented. All statistical analyses were performed using SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). A value of P <0.05 was considered statistically significant.

Results

A total of 216 severe symptomatic AS patients who underwent TAVI were included; 55 (25.5%) were CKD 1–2, 100 (46.3%) were CKD 3 and 61 (28.2%) were CKD 4–5 (24 were on dialysis). Mean and median follow-up were 2.63 years (SD 2.11) and 2.23 years (interquartile range 0.83–4.14 years) years, respectively. Baseline and procedural characteristics according to CKD severity are shown in Tables 1 and 2, respectively.

Patients with advanced CKD were older (P = 0.001), had lower body mass index (P = 0.001) and poor effort tolerance of at least New York Heart Association (NYHA) class III–IV (P = 0.002). No significant differences were noted in baseline cardiovascular risk factors, atrial fibrillation, ischaemic heart disease, prior cerebrovascular accidents or peripheral vascular disease (PVD). There was a commensurate increase in

Table 1. Baseline Characteristics According to CKD Severity

Variable	Aggregate (n = 216)	CKD 1 – 2 (n = 55)	CKD 3 (n = 100)	Advanced CKD (n = 61)	*P* Value
Mean age, years (SD)	75.5 (9.3)	70.3 (8.5)	78.2 (7.3)	75.6 (11.0)	<0.001
Male gender (%)	106 (49.1)	25 (45.5)	53 (53)	28 (45.9)	0.992
Mean body mass index, kg/m^2 (SD)	23.9 (4.7)	26.2 (4.6)	23.4 (4.2)	22.8 (4.9)	<0.001
NYHA class (%)					0.002
I – II	90 (41.7)	31 (56.4)	42 (42)	17 (27.9)	
III – IV	126 (58.3)	24 (43.6)	58 (58)	44 (72.1)	
Smoker (%)	41 (19)	8 (14.5)	25 (25)	8 (13.1)	0.788
Diabetes mellitus (%)	86 (39.8)	25 (45.5)	35 (35)	26 (42.6)	0.793
Hypertension (%)	177 (81.9)	44 (80)	81 (81)	52 (85.2)	0.457
Hyperlipidaemia (%)	165 (76.4)	44 (80)	72 (72)	49 (80.3)	0.928
Prior ischaemic heart disease (%)	127 (58.8)	33 (60)	60 (60)	34 (55.7)	0.634
Prior coronary artery bypass (%)	49 (22.7)	13 (23.6)	20 (20)	6 (26.2)	0.717
Atrial fibrillation (%)	45 (20.8)	7 (12.7)	24 (24)	14 (23)	0.189
Prior stroke (%)	27 (12.5)	4 (7.3)	15 (15)	8 (13.1)	0.362
Peripheral vascular disease (%)	35 (16.2)	5 (9.1)	17 (17)	13 (21.3)	0.077
Chronic obstructive lung disease (%)	22 (10.2)	4 (7.3)	16 (16)	2 (3.3)	0.424
Mean eGFR, mL/min/1.72m^2 (SD)	45.8 (26.1)	80.2 (19.5)	44.3 (8.1)	17.3 (8.4)	<0.001
Mean STS risk score (SD)	6.5 (6.1)	3.5 (2.1)	6.1 (7)	9.8 (5.2)	<0.001
Mean Logistic EuroSCORE (SD)	16.1 (14.2)	11.1 (10.7)	15.5 (12.1)	21.7 (17.8)	<0.001
Mean EuroSCORE II (SD)	6.2 (7.6)	3.4 (3.1)	5.8 (8.0)	9.4 (8.5)	<0.001
Mean AV calcium score in Agatston units, n = 104 (SD)	2634 (1943)	2153 (1041)	2690 (1820)	3045 (2804)	0.046

AV: Aortic valve; CKD: Chronic kidney disease; eGFR: Estimated glomerular filtration rate; EuroSCORE: European System for Cardiac Operative Risk Evaluation; NYHA: New York Heart Association; SD: Standard deviation; STS: Society of Thoracic Surgeons

surgical risk on the Society of Thoracic Surgeons risk score, Logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) and EuroSCORE II with increasing CKD severity ($P = 0.001$). CKD severity was also associated with heavier AV calcification on AV calcium score ($P = 0.046$). For procedural characteristics, no significant differences were noted in the different stages of CKD severity in TAVI approach, size and type of prostheses and procedural contrast volume used.

Findings of univariate analysis showed that CKD 1–2 (OR 0.192, 95% CI 0.040–0.921, $P = 0.039$) and CKD 3 (OR 0.052, 95% CI 0.006–0.414, $P = 0.005$) were associated with significantly lower 30-day mortality than advanced CKD. After adjusting for diabetes mellitus, PVD and non-transfemoral TAVI approach, findings of multivariate analysis showed that the relationship was attenuated in CKD 1–2 patients against advanced CKD patients (adjusted OR [AOR] 0.257, 95% CI 0.047–1.390, $P = 0.115$); however, it remained significant in CKD 3 patients vs advanced CKD patients (AOR 0.047, 95% CI 0.005–0.414, $P = 0.006$). Higher eGFR was also significantly associated with lower 30-day mortality (OR 0.967, 95% CI 0.939–0.996, $P = 0.024$), but the effect was similarly attenuated on multivariate analysis (AOR 0.969, 95% CI 0.938–1.000, $P = 0.053$). At 30 days, CKD 3 was associated with significantly

Table 2. Procedural Characteristics According to CKD Severity

Variable	CKD 1 – 2 (n = 55)	CKD 3 (n = 100)	Advanced CKD (n = 61)	*P* Value
Approach (%)				0.414
Transfemoral	44 (80)	79 (79)	45 (73.8)	
Non-transfemoral	11 (20)	21 (21)	16 (26.2)	
Trans-apical	7 (12.7)	18 (18)	11 (18)	
Direct-aortic	3 (5.5)	3 (3)	5 (8.2)	
Trans-subclavian	1 (1.8)	0 (0)	0 (0)	
Prosthesis type (%)				0.959
Self-expandable	24 (43.6)	47 (47)	27 (44.3)	
Balloon-expandable	31 (56.4)	53 (53)	34 (55.7)	
Valve generation (%)*				0.613
Early	45 (93.8)	86 (90.5)	52 (88.1)	
New	3 (6.3)	9 (9.5)	7 (11.9)	
Prosthesis size (%)				0.247
23 mm	19 (35.2)	34 (34)	26 (42.5)	
25 mm	2 (3.7)	2 (2)	1 (1.6)	
26 mm	18 (33.3)	47 (47)	23 (37.7)	
27 mm	1 (1.9)	0 (0)	0 (0)	
29 mm	11 (20.4)	16 (16)	9 (14.8)	
31 mm	3 (5.6)	1 (1)	2 (3.3)	
Mean contrast volume, mL (SD)	139 (68)	143 (77)	116 (56)	0.070
Device success (%)	53 (96.4)	95 (95)	60 (98.4)	0.549

CKD: Chronic kidney disease; SD: Standard deviation
*Early-generation valves refer to CoreValve, SAPIEN and SAPIEN XT. New-generation valves refer to CoreValve Evolut R, CoreValve Evolut Pro and SAPIEN 3. A total of 8 Lotus, 3 Portico and 2 Engager valve cases were excluded from analysis.

lower odds of new permanent pacemaker implantation (PPM) than advanced CKD (3% vs 13.1%, OR 0.205, 95% CI 0.052–0.805, P = 0.023). A trend towards lower odds in new PPM implantation in CKD 1–2 vs advanced CKD (3.6% vs 13.1%, OR 0.250, 95% CI 0.051–1.233, P = 0.089) patients was observed. No significant differences were seen in length of hospitalisation, major vascular complications, stroke or bleeding rates (Table 3).

At 1 year, the mortality rates in CKD 1–2, CKD 3 and advanced CKD patients were 9.1%, 9% and 23%, respectively; at 3 years, the overall mortality rates in the 3 groups were 16.4%, 24% and 45.9%, respectively. In patients who were on dialysis, the 1- and 3-year mortality rates were 16.7% and 50%, respectively. After adjusting for left ventricular ejection fraction (LVEF) and NYHA status, findings of multivariate analysis showed that CKD 1–2 (adjusted HR [AHR] 0.366, 95% CI 0.168–0.797, P = 0.011) and CKD 3 (AHR 0.467, 95% CI 0.267–0.817, P = 0.008) were significantly associated with lower overall mortality than advanced CKD. Higher eGFR was also associated with lower overall mortality (AHR 0.981, 95% CI 0.968–0.993, P = 0.002). Increased mortality (Fig. 1) was attributed to non-cardiovascular causes in CKD 1–2 vs advanced CKD (AHR 0.360, 95% CI 0.132–0.979, P = 0.045)

Table 3. Outcome at 30 Days According to CKD Severity

Variable	CKD 1 – 2 (n = 55)	CKD 3 (n = 100)	Advanced CKD (n = 61)	*P* Value
Mean hospital stay in days (SD)	9.8 (14.5)	9.9 (10.7)	11.4 (11.7)	0.711
30-day mortality (%)	2 (3.6)	1 (1)	10 (16.4)	0.003
Major vascular complications (%)	6 (10.9)	11 (11)	11 (18)	0.244
Major bleeding (%)	4 (7.3)	4 (4)	5 (8.2)	0.803
Minor bleeding (%)	2 (3.6)	10 (10)	6 (9.8)	0.240
Stroke (%)	1 (1.8)	1 (1)	0 (0)	0.307
New pacemaker (%)	2 (3.6)	3 (3)	8 (13.1)	0.038
Acute kidney injury (%)				0.008
Total	3 (5.5)	19 (19)	15 (40.5)*	
Stage 1	2 (3.6)	10 (10)	9 (24.3)*	
Stage 2	1 (1.9)	1 (1)	2 (5.4)*	
Stage 3	0 (0)	8 (8)	4 (10.8)*	
Dialysis	0 (0)	5 (5)	4 (10.8)*	

CKD: Chronic kidney disease; SD: Standard deviation
*Exclude 24 patients who were already on dialysis.

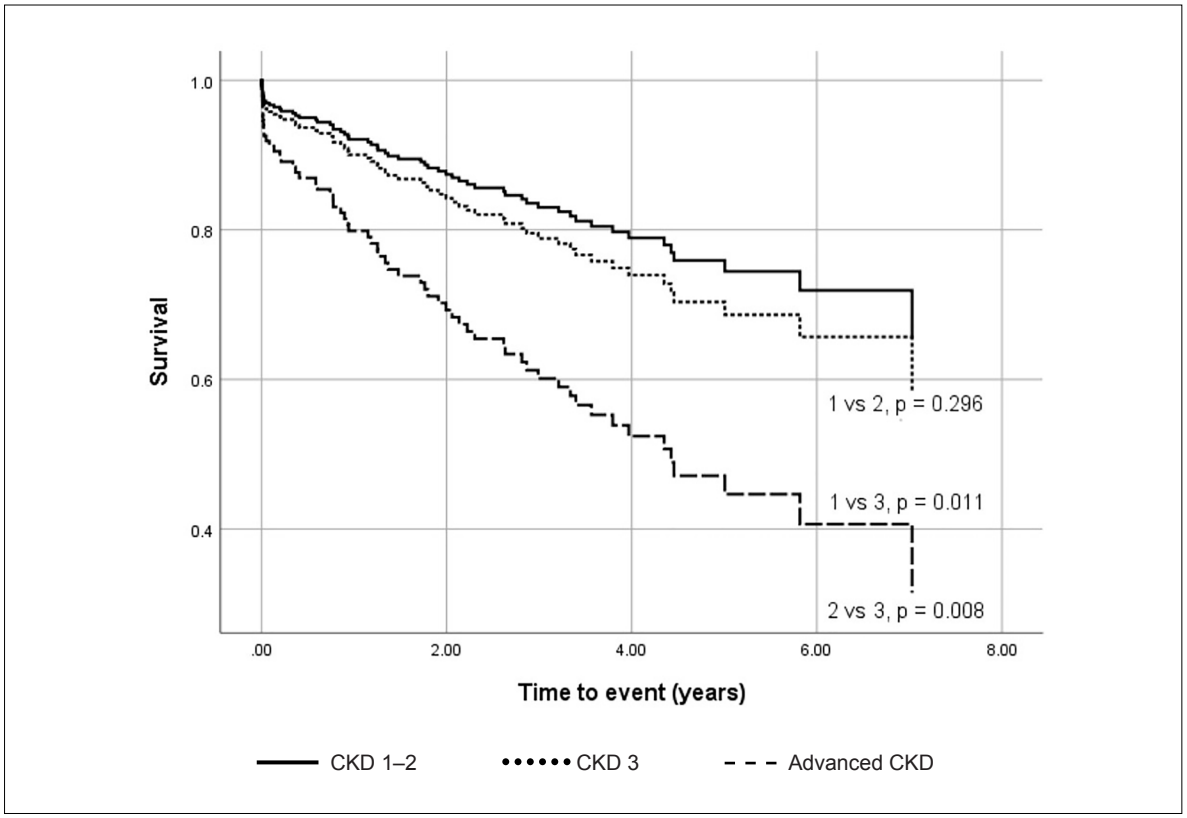

Fig. 1. Survival curves for cumulative overall mortality in patients with chronic kidney disease (CKD) stages 1–2 (solid line), stage 3 (dotted line) and advanced stages (4–5) or end-stage renal failure (dashed line).

patients and in CKD 3 vs advanced CKD (AHR 0.314, 95% CI 0.146–0.675, P = 0.003) patients, particularly with progression of kidney disease (P = 0.008) and non-respiratory sepsis (P = 0.003) (Table 4).

At 1-year post-TAVI, echocardiographic outcomes were available in 173 (80.1%) patients; no significant differences in valve area and mean transvalvular valve gradient were observed across all CKD groups. However, CKD 3 (20%) and CKD 4–5 (22%) patients had higher incidence of AR of at least moderate severity than CKD 1–2 (2.2%) patients (P = 0.010). Except for 1 case of transvalvular regurgitation, all AR cases had paravalvular regurgitation (Table 4).

Seven patients experienced severe TAVI valve leaflet degeneration; 6 were restenosis and 1 was mixed stenosis with regurgitation. Two patients were on dialysis and the remaining 5 were in CKD 1–3. In the dialysis patients, valve degeneration occurred at between 1.5–2 years; in remaining patients, it occurred at between 3.75–6 years. Three patients underwent repeat TAVI and another 3 passed away. Six patients underwent either a transoesophageal echocardiogram and/or computed tomography, except for 1 patient who did not undergo further investigations due to poor premorbid status. In 5 of them, thrombosis was ruled out and they were not anticoagulated. In 1 patient, embolic phenomenon was suspected and low molecular weight heparin was initiated, but patient passed away during that admission (Table 5).

After excluding patients who were already on dialysis, 37 (19.3%) patients developed AKI postTAVI; 21 (10.9%), 4 (2.1%) and 12 (6.3%) patients were in AKI stages 1, 2 and 3, respectively. Among AKI stage 3 patients, 4 required dialysis. No significant differences were noted in amount of contrast volume used during TAVI in AKI (mean 133 mL, SD 64) and non-AKI (mean 140 mL, SD 96) patients (P = 0.113). A significant association between severity of baseline CKD (OR 5.014, 95 CI 1.074–23.403, P = 0.040) and occurrence of AKI was seen. Findings of univariate analysis showed that AKI patients had higher overall mortality (43.2% vs 25.1%, HR 2.275, 95% CI 1.237–4.185, P = 0.008), but the effect was attenuated after adjustment for LVEF and NYHA status (AHR 1.823, 95% CI 0.977–3.403, P = 0.059). No significant interaction was found for mortality ($p_{interaction}$ = 0.851) between AKI and baseline CKD status (Fig. 2).

After patients who were already on dialysis were excluded, findings of renal panel at 3 months showed that 138 (71.9%) patients had stable CKD and 37 (19.3%) patients had progressive CKD. In patients

Table 4. Cumulative Outcomes According to CKD severity

Variable	CKD 1 – 2		CKD 3		Advanced CKD		*P* Value
	N = 46	N = 55	N = 82	N = 100	N = 45	N = 61	
1-year echocardiographic outcomes							
Mean AV area (SD)	1.57 (0.38)		1.58 (0.38)		1.69 (0.49)		0.290
Mean AV pressure gradient, mmHg (SD)	12.6 (5.9)		11.6 (5.8)		11.2 (6.0)		0.494
≥2+ aortic regurgitation (%)	1 (2.2)		18 (22)		9 (20)		0.021
Overall mortality		9 (16.4)		24 (24)		28 (45.9)	<0.001
Cardiovascular mortality		4 (7.3)		14 (14)		8 (13.1)	0.447
Non-cardiovascular mortality		5 (9.1)		10 (10)		20 (32.8)	0.006
Respiratory		0 (0)		3 (3)		2 (3.3)	0.414
Malignancy		2 (3.6)		4 (4)		2 (3.3)	0.972
Kidney failure		1 (1.8)		0 (0)		5 (8.2)	0.008
Bleeding		0 (0)		1 (0)		0 (0)	0.558
Non-respiratory sepsis		1 (1.8)		2 (2)		8 (13.1)	0.003

AV: Aortic valve; CKD: Chronic kidney disease; SD: Standard deviation

Table 5. Clinical Characteristics of Patients with TAVI Valve Degeneration

Patient Number	Initial TAVI Valve	Duration from TAVR to Diagnosis of Degeneration	CKD Stage	Degeneration Type (AS, AR, Mixed)	Outcome	Investigation	Anticoagulation
1	SAPIEN, 23 mm	7 years	3	Severe AS	Repeat TAVI with CoreValve Evolut R, 23mm	TEE: severe prosthesis stenosis, no thrombus CT: No thrombus	No
2	SAPIEN XT, 26 mm	2 years	Peritoneal dialysis	Severe AS	Repeat TAVI with CoreValve Evolut Pro, 26mm	TEE: severe prosthesis stenosis with reduced leaflet mobility, no thrombus CT: No thrombus	No
3	SAPIEN, 23 mm	6 years and 11 months	1	Severe AS	Repeat TAVI with Corevalve Evolut R, 23mm	TEE: severe prosthesis stenosis with reduced leaflet mobility CT: No thrombus.	No
4	SAPIEN, 26 mm	6 years and 11 months	3	Severe AS	Medical therapy (poor overall prognosis)	No TEE/CT given due to poor premorbid status	No
5	SAPIEN, 26 mm	6 years	1	Severe AS	CV mortality	TEE: restricted leaflet excursion, no thrombus	No
6	SAPIEN XT, 26 mm	3 years and 9 months	2	Severe AS	CV mortality	CT: restricted leaflet excursion, no thrombus	No
7	CoreValve Evolut R, 29 mm	1 year and 7 months	Haemodialysis	Mixed severe AS and AR	CV mortality	TEE: moderate transvalvular >paravalvular AR CT: no definite thrombus	Yes, trial of anticoagulation was given in view of suspected embolic phenomenon

AR: Aortic regurgitation; AS: Aortic stenosis; CT: Computed tomography; CV: Cardiovascular; TAVI: Transcatheter aortic valve implantation; TAVR: Transcatheter aortic valve replacement; TEE: Transesophageal echocardiography

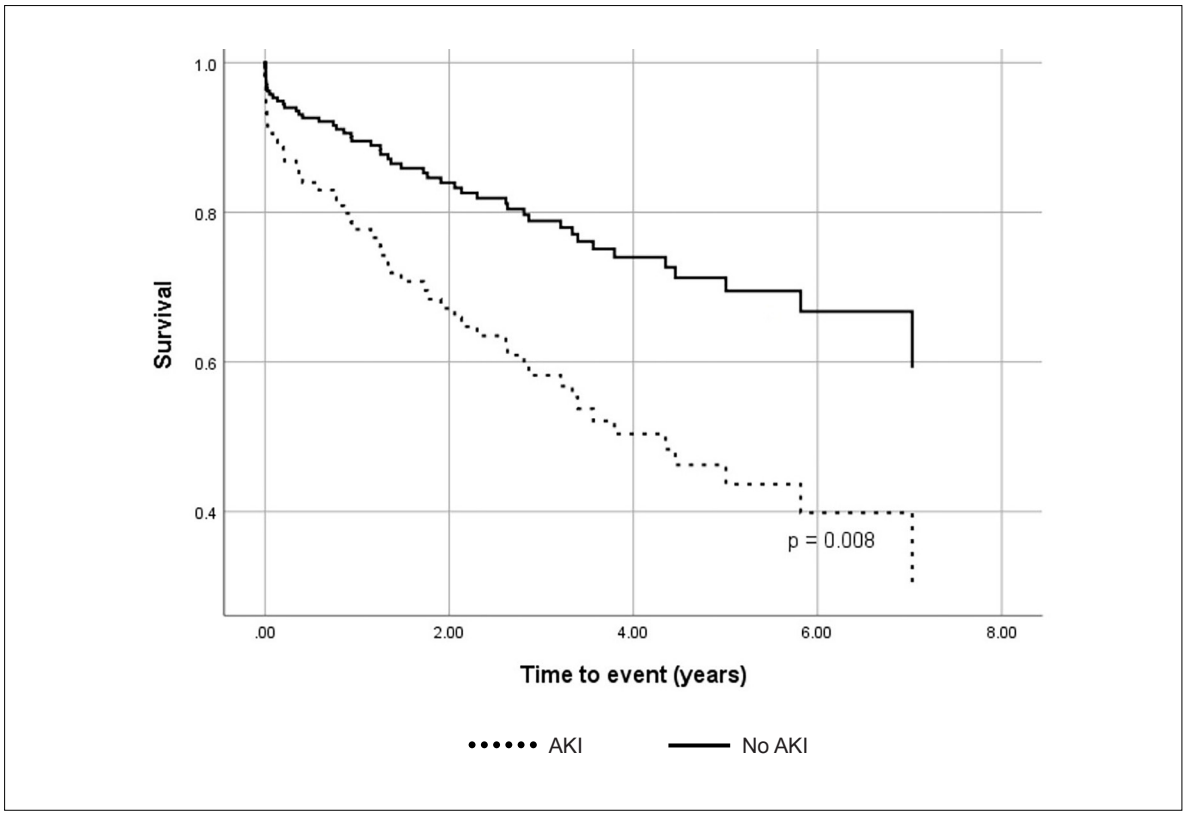

Fig. 2. Survival curves for cumulative overall mortality between acute kidney injury (AKI) patients (dotted line) and non-AKI patients (solid line).

with progressive CKD, findings of multivariate analysis revealed that they had significantly higher overall mortality (AHR 2.883, 95% CI 1.321–6.290, P = 0 .008). No significant interaction was found for mortality ($p_{interaction}$ = 0.157) between CKD progression and baseline CKD status.

In this study, 19 (8.8%) patients underwent TAVI with new-generation valves that included CoreValve Evolut R (Medtronic Inc., Minneapolis, MN, USA), CoreValve Evolut PRO (Medtronic Inc., Minneapolis, MN, USA) and SAPIEN 3 (Edwards Lifesciences Corp., Irvine, CA, USA). No significant differences in the use of new-generation valves were found among CKD 1–2 (6.3%), CKD 3 (9.5%) and CKD 4–5/ESRF (11.9%) patients (P = 0.613). Additionally, newer-generation valves did not impact any early or late outcomes (Table 6).

No significant differences in the use of self-expandable valves (SEV) and balloon-expandable valves (BEV) were seen in CKD patients (P = 0.959). Mean contrast volume was 123 mL (SD 76) in BEV, which was significantly lower than 146 mL (SD 62) in SEV (P = 0.020). At 1 year, echocardiographic studies showed that AV area was lower in BEV (mean 1.50, SD 0.35) than SEV (mean 1.72, SD 0.44, P = 0.001); AV gradient was also higher in BEV (mean 12.9 mmHg, SD 5.1) than SEV (mean 10.4 mmHg, SD 6.5, P = 0.001). No significant differences were observed in development of moderate AR and pacemaker, stroke and mortality rates (Table 7).

Discussion

This study evaluated the impact of baseline CKD status, postoperative AKI and CKD progression on early and late outcomes and valve haemodynamics in severe AS patients undergoing TAVI. The significant findings included: 1) CKD had a negative impact on cumulative overall mortality that was attributed to non-cardiovascular mortality and this effect was seen as early as at 30 days, but was more pronounced on long-term follow-up; 2) CKD resulted in significantly higher AR and PPM implantation rates; 3) postoperative AKI had a negative impact on overall mortality, but this effect was attenuated after adjustment for

Table 6. Valve Haemodynamic Outcomes in Early- and New-Generation TAVI Valves at 30 Days and 1 Year

Variable	Early-Generation Valves			New-Generation Valves			*P* Value
	N = 183	N = 164	N = 147	N = 19*	N = 15	N = 14	
Mean contrast volume, mL (SD)	126 (65)			163 (54)			0.021
30-day mortality (%)	13 (7.1)			0 (0)			0.230
Stroke (%)	1 (0.5)			0 (0)			0.747
New pacemaker (%)	11 (6.0)			0 (0)			0.272
Acute kidney injury (%)†							0.219
Total		32 (19.5)			1 (6.7)		
Stage 1		18 (11)			0 (0)		
Stage 2		3 (1.8)			0 (0)		
Stage 3		3 (1.8)			0 (0)		
Dialysis		8 (4.9)			1 (6.7)		
1-year overall mortality	24 (13.1)			1 (5.3)			0.323
1-year cardiovascular mortality	11 (6.0)			0 (0)			0.272
1-year echocardiographic outcomes							
Mean AV area (SD)			1.62 (0.42)			1.69 (0.28)	0.527
Mean AV pressure gradient, mmHg (SD)			11.6 (5.9)			10.2 (3.8)	0.381
≥2+ aortic regurgitation (%)			22 (15.0)			2 (14.3)	0.946

AV: Aortic valve; SD: Standard deviation; TAVI: Transcatheter aortic valve implantation
*A total of 8 Lotus, 3 Portico and 2 Engager valve cases were excluded from analysis.
†Exclude 24 patients who were already on dialysis.

confounders; and 4) renal disease progression was independently associated with higher overall mortality.

CKD can portend worse outcomes in patients who undergo TAVI.[5] Several studies have established that CKD severity prognosticates acute and long-term mortality.[11–15] In their study of 41,025 patients who underwent TAVI, Gupta et al reported higher in-hospital mortality in CKD and ESRF patients than non-CKD patients.[16] In their study of CKD 1–2, CKD 3 and advanced CKD patients, Allende et al found a significant difference in mortality of 15.6%, 20% and 27.5–35.5%, respectively, at 1 year.[17] Similarly, this study found that advanced CKD was associated with higher mortality at 30 days and more salient differences were observed on long-term follow-up; at 1 year, the mortality rates were 9.1%, 9% and 23% in CKD1–2, CKD3 and advanced CKD patients, respectively.

Dialysis has been shown to be a marker of worse outcomes.[18] In their study, Allende et al reported slightly higher mortality of 20% at 1 year and up to approximately 65% at 3 years in ESRF patients.[17] In their study of 66 dialysis patients who underwent TAVI, Codner et al also noted higher risk of mortality of close to 24.2% at 1 year.[19] In our dialysis patients, the mortality rates at 1 and 3 years were 16.7% and 50%, respectively.

In patients with advanced CKD, this study found higher non-cardiovascular mortality rates that were attributed to non-respiratory sepsis and renal disease progression, a finding similar to that of Allende et al.[17] Patients with renal disease are at higher risk of sepsis than the general population[19] and the reasons include reduced immunity and vaccine efficacy, increased comorbidities, more visits to healthcare facilities and treatment of the disease itself.[21] CKD is a well-established risk factor for cardiovascular disease and mortality.[20,22,23] Although other studies had found higher cardiovascular mortality rates in TAVI patients with

Table 7. Valve Haemodynamic Outcomes in BEV and SEV at 30 Days and 1 Year

Variable	SEV			BEV			*P* Value
	N = 98	N = 86	N = 77	N = 118	N = 106	N = 96	
Mean contrast volume, mL (SD)	146 (62)			123 (76)			0.020
30-day mortality (%)	2 (2.0)			11 (9.3)			0.025
Stroke (%)	1 (1.0)			1 (0.8)			0.895
New pacemaker (%)	9 (9.2)			4 (3.4)			0.075
Acute kidney injury (%)*							0.429
Total		14 (16.3)			22 (20.8)		
Stage 1		7 (8.1)			13 (12.3)		
Stage 2		1 (1.2)			3 (2.8)		
Stage 3		2 (2.3)			1 (0.9)		
Dialysis		4 (4.7)			5 (4.7)		
1-year overall mortality	12 (12.2)			16 (13.6)			0.775
1-year cardiovascular mortality	6 (6.1)			6 (5.1)			0.740
Cumulative overall mortality	24 (24.5)			37 (31.4)			0.264
Cumulative cardiovascular mortality	13 (13.3)			13 (11.0)			0.613
1-year echocardiographic outcomes							
Mean AV area (SD)			1.72 (0.44)			1.50 (0.35)	0.001
Mean AV pressure gradient, mmHg (SD)			10.4 (6.5)			12.9 (5.1)	0.001
≥2+ aortic regurgitation (%)			14 (18.2)			14 (14.6)	0.523

AV: Aortic valve; BEV: Balloon-expandable valve; SD: Standard deviation; SEV: Self-expandable valve
*Exclude 24 patients who were already on dialysis.

advanced CKD,[17,19] an insignificant trend was found by this study that could be attributed to smaller sample size.

Advanced CKD has been linked to platelet dysfunction and coagulopathy that contribute to higher risk of bleeding events, especially the use of dual antiplatelet agents or vitamin K antagonists.[24,25] Unlike other studies,[13,26] this study did not show an increase in minor or major bleeding events in patients with advanced CKD at 30 days. A longer duration of follow-up is needed to evaluate differences in the longer term.

The postTAVI PPM implantation rate of 6% reported by this study was comparable to the rate of 2–51% reported in the literature.[27] The finding that postTAVI PPM implantation was more common in advanced CKD patients than non-CKD patients also concurred with findings reported in the literature.[16] It could partly be attributed to increased calcification that is commonly seen in CKD patients and is caused by hormonal and metabolic derangements such as increased parathyroid hormone, calcium-phosphate products and 1,25-dihydroxyvitamin D.[28] During valve deployment, increased calcification in the left ventricular outflow tract could compress the conduction system and lead to conduction blockages that necessitate the need for PPM implantation.

In the literature, findings on the outcome of advanced CKD on valve haemodynamics are mixed. While some studies reported rapid deterioration in valve haemodynamics in advanced CKD patients, others[29,30] did not report significant differences between these patients and non-CKD patients.[13] Although this study did not find significant changes in AV area and mean gradient at 1 year, there were, however, 2 cases of

"early" TAVI failure that had significant valve stenosis <2 years after TAVI was performed (Table 5). Both occurred in ESRF patients who were on dialysis and the phenomenon could be attributed to deranged and increased calcification.[28] Larger long-term studies are needed to evaluate the clinical significance of early TAVI failure in dialysis patients.

PostTAVI, moderate AR was seen in more advanced CKD patients and was attributed to increased calcification.[28] When calcification is present in the aortic annulus, it may prevent adequate sealing of the valve. Postoperative AR is not benign and has been identified as an independent predictor of all-cause and cardiovascular mortality after TAVI.[31,32] It can affect the functional status of patients such as effort tolerance and trigger symptoms of heart failure.[33]

In this study, the findings of an AKI incidence of approximately 19% and CKD 4 patients with the highest risk of developing it were consistent with those reported in the literature.[34,35] Findings of univariate analysis showed that AKI was a significant predictor of mortality, but its effect was attenuated by multivariate analysis. In their study, Allende et al reported that AKI was a significant predictor of overall mortality.[17] A few reports had described renal trajectory and outcomes post-TAVI. In this study, the finding that CKD progression led to higher mortality at 3 months suggested that care should be taken to minimise AKI during: 1) the preoperative/perioperative phase through avoidance of haemodynamic instability and nephrotoxic agents but with provision of adequate hydration; and 2) the subacute and chronic phases post-TAVI to retard CKD progression since it heralds poorer long-term outcomes.

In this study, BEV had lower AV area and higher AV gradients with no differences in AR at 1 year compared to SEV, a result that was also reported by the CHOICE trial.[36] However, the FRANCE-TAVI registry reported that SEV patients had higher risk of developing paravalvular leak than BEV patients and higher all-cause mortality at 2 years, irrespective of valve generation.[37] These differences need to be validated in future studies.

A limitation of this study was the small sample size that limited extrapolation of its findings. The results will need to be validated in bigger patient cohorts. Since data was only available on renal trajectory at 3 months, more study is required to examine the long-term effects of renal disease progression. Nevertheless, this study had raised some interesting hypotheses and findings that can guide future research. Due to the non-randomised nature of the study, there is possibility of bias from confounding factors. The high incidence of valve degeneration in those who underwent TAVI was attributed to the predominant use of SAPIEN valves in the early phase of our TAVI programme.

Conclusion

In severe AS patients undergoing TAVI, CKD portends higher mortality and morbidity. In the long term, renal disease progression impacts negatively on outcomes. Dedicated preventive and management efforts should be undertaken to optimise outcomes in this group of patients.

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