

Long-term outcomes after transcatheter aortic valve replacement with minimal contrast in chronic kidney disease

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Abstract

Background: Patients with renal insufficiency have poor short-term outcomes after transcatheter aortic valve replacement (TAVR).

Methods: Retrospective chart review identified 575 consecutive patients not on hemodialysis who underwent TAVR between September 2014 and January 2017. Outcomes were defined by VARC-2 criteria. Primary outcome of all-cause mortality was evaluated at a median follow-up of 811 days (interquartile range 125–1,151).

Results: Preprocedural glomerular filtration rate (GFR) was ≥ 60 ml/min in 51.7%, 30–60 ml/min in 42.1%, and < 30 ml/min in 6.3%. Use of transfemoral access (98.8%) and achieved device success (91.0%) did not differ among groups, but less contrast was used with lower GFR (23 ml [15–33], 24 ml [14–33], 13 ml [8–20]; $p < .001$). Peri-procedural stroke (0.7%, 2.1%, 11.1%; $p < .001$) was higher with lower GFR. Core lab analysis of preprocedural computed tomography scans of patients who developed a peri-procedural stroke identified potential anatomic substrate for stroke in three out of four patients with GFR 30–60 ml/min and all three with GFR < 30 ml/min (severe atheroma was the most common subtype of anatomical substrate present). Compared to GFR ≥ 60 ml/min, all-cause mortality was higher with GFR 30–60 ml/min (HR 1.61 [1.00–2.59]; aHR 1.61 [0.91–2.83]) and GFR < 30 ml/min (HR 2.41 [1.06–5.48]; aHR 2.34 [0.90–6.09]) but not significant after multivariable adjustment. Follow-up echocardiographic data, available in 63%, demonstrated no difference in structural heart valve deterioration over time among groups.

Conclusions: Patients with baseline renal insufficiency remain a challenging population with poor long-term outcomes despite procedural optimization with a transfemoral-first and an extremely low-contrast approach.

KEYWORDS

chronic kidney disease, contrast, mortality, stroke, transcatheter aortic valve replacement

1 | INTRODUCTION

Almost half of patients undergoing transcatheter aortic valve replacement (TAVR) in the United States have chronic kidney disease (CKD).¹ While smaller observational studies demonstrate no difference in 30-day mortality by baseline renal function,²⁻⁴ larger national data demonstrate an increased risk of in-hospital major bleeding complications, pacemaker requirement, and all-cause mortality, as well as increased risk of renal replacement therapy and all-cause mortality at 30 days and 1 year.⁵⁻⁸ Baseline CKD is associated with acute kidney injury postTAVR, which is independently associated with increased 30-day and one-year all-cause mortality.⁶ Alternatively, depending on the underlying mechanism of CKD, there may be an observed improvement in renal function after TAVR potentially due to increased renal perfusion, and this improvement in renal function may, in turn, attenuate the adverse effect of CKD on long-term mortality.⁹⁻¹¹ Long-term mortality data after TAVR in patients with CKD are limited. Moreover, most TAVR centers routinely employ a considerable amount of contrast,¹ which may contribute to acute kidney injury and adverse outcomes independent of the underlying disease. Given the increasing use of TAVR in intermediate and low-risk patients, the aim of this study is to assess long-term TAVR outcomes in CKD based on preprocedural GFR, specifically among patients with GFR < 30 ml/min, GFR 30–60 ml/min, and GFR >60 ml/min, in the context of an approach of aggressive contrast minimization.

2 | MATERIALS AND METHODS

2.1 | Study population

Retrospective chart review identified consecutive patients with aortic stenosis who underwent TAVR at a single tertiary academic medical center in New York City between September 2014 and January 2017. Patients with a history of hemodialysis were excluded from further analysis. This study received NYU School of Medicine Institutional Review Board approval with a waiver for the requirement of informed consent and is investigator-initiated with no outside funding.

2.2 | TAVR evaluation, procedure and contrast minimization approach

A multidisciplinary heart valve team evaluated each patient for either clinically-indicated TAVR or an institutional review board-approved study that included TAVR. Preprocedural aortic valve annular measurements were made with computed tomography using a low-contrast protocol (no more than 50 cc of contrast) and a high-speed acquisition dual source CT scanner.

Patients underwent TAVR with a self-expandable (first generation CoreValve or second generation CoreValve Evolut; Medtronic, Minneapolis, MN) or balloon expandable (second generation Sapien XT or third generation Sapien 3; Edwards Lifesciences, Irvine, California)

valve. Access site was selected based on computed tomography imaging. However, a “transfemoral-first” approach was taken in patients with hostile peripheral access using an endovascular approach to optimize access prior to TAVR.¹² TAVR was performed with adjunctive administration of intravenous unfractionated heparin for a goal activated clotting time of 200 to 250 s.

A systematic contrast minimization approach was employed whereby intra-arterial contrast iodixanol (GE Healthcare, Chicago, Illinois) with 1:1 dilution with normal saline was administered sparingly via a motorized contrast delivery system (ACIST CVi, ACIST Medical Systems Inc, MN) to guide device positioning and implantation. Importantly, peri-procedural complications such as paravalvular regurgitation were assessed by a structural imaging specialist via intra-procedural transthoracic echocardiography (TTE) rather than high contrast aortography.

Access closure was obtained using the preclose technique. Patients were monitored in the intensive care unit where they ambulated with assistance 2.5 to 3 hr after the procedure. Shortly after ambulation, patients were transferred to a telemetry unit and, if there were no new conduction disturbances requiring a permanent pacemaker placement, discharged home the following day.

2.3 | Variables of interest

Demographic variables were self-reported. Presence of hypertension and hyperlipidemia were defined by medical documented report or use of anti-hypertensive or lipid-lowering medications, respectively. Presence of diabetes mellitus was defined by medical documented report, use of glucose-lowering medications, or hemoglobin A1c >6.5%. Congestive heart failure was defined by medically documented report and a left ventricular ejection fraction of <55% on preTAVR echocardiogram. Carotid artery disease was defined as ≥50% stenosis on imaging or if prior percutaneous or surgical revascularization. Peripheral artery disease was defined as ankle-brachial index of <0.9 or if prior percutaneous or surgical revascularization. Chronic lung disease was defined by medical documented report or if pulmonary function test consistent with chronic obstructive pulmonary disease. History of CKD was defined as a glomerular filtration rate (GFR) of ≤60 mL/min. Echocardiographic data were obtained via transthoracic echocardiography and the reported aortic valve area was calculated via continuity equation. Data from the most recent preprocedural laboratory results (within 30 days of procedure), electrocardiogram, echocardiogram, and computed tomography were recorded. The number of days between the patient's admission and discharge, and between the patient's TAVR procedure and discharge, were recorded as the total length of stay and postprocedural length of stay, respectively.

2.4 | Outcomes

Outcomes were defined by the Valve Academic Research Consortium-2 (VARC-2) criteria where applicable.¹³ The primary outcome measure was all-cause mortality. Secondary outcomes included

intra-procedural complications, paravalvular regurgitation, patient-prosthesis mismatch, device success, and in-hospital complications of permanent pacemaker placement, cardiac tamponade, stroke, vascular complications, acute renal failure, bleeding, cardiac arrest, and in-hospital mortality. Device success was defined as absence of in-hospital mortality and correct positioning of a single prosthetic heart valve into the proper anatomical location (i.e., absence of device migration or need for a second prosthetic heart valve) and no severe patient-prosthesis mismatch and either mean aortic valve gradient <20 mmHg or peak velocity <3 m/s and no moderate or severe prosthetic valve regurgitation.¹³ In the subset of patients who had available follow-up data, structural heart valve deterioration was also evaluated. Structural heart valve deterioration was defined as valve-related dysfunction (mean aortic valve gradient ≥ 20 mmHg, effective area ≤ 0.9 cm² and/or dimensionless index <0.35 m/s and/or moderate or severe prosthetic valve regurgitation) or requirement of repeat aortic valve procedure.¹³

2.5 | Blinded computed tomography core lab analysis

The subset of patients with peri-TAVR stroke were analyzed retrospectively and blinded to baseline renal function for potential anatomical substrates by the NYU Langone Computed Tomography Core Lab (HJ). Parameters systematically analyzed were presence of possible/probable left atrial appendage thrombus, aortic arch atheroma and calcium (assessed semi-quantitatively), valve calcium severity (assessed quantitatively and semi-quantitatively), and valve morphology.

2.6 | Statistical analysis

Patients were stratified by preoperative GFR into three subgroups (≥ 60 ml/min, 30–60 ml/min, and <30 ml/min). Categorical variables are reported as frequencies and percentages and compared across renal groups using the chi-squared test. Continuous variables were reported as medians and interquartile ranges and compared across renal groups using Kruskal-Wallis test. The association between chronic renal insufficiency and survival time of patients was assessed using a Cox proportional-hazards model and adjusted for differences in baseline clinical and procedural characteristics based on univariate analysis and prespecified clinically significant confounding variables. The Kaplan-Meier method was used to construct time-to-event curves. Significance level was set at a two-sided alpha level of 0.05, and statistical analysis was completed using SPSS version 25.0 (IBM, Armonk, New York).

3 | RESULTS

3.1 | Baseline characteristics

Retrospective chart review identified 588 consecutive patients who underwent TAVR between September 2014 and January 2017, of which

13 (2.2%) were excluded for history of hemodialysis. Of the remaining 575 patients, 51.7% ($n = 297$) had a preprocedural GFR ≥ 60 ml/min, 42.1% ($n = 242$) had a preprocedural GFR 30–60 ml/min, and 6.3% ($n = 36$) had a preprocedural GFR <30 ml/min. Baseline clinical characteristics are shown in Table 1. Patients with lower GFR were older and had a higher prevalence of diabetes mellitus and congestive heart failure than patients with higher GFR. The median Society of Thoracic Surgeon (STS) predicted risk of mortality was in the intermediate-risk range in patients with a GFR ≥ 60 ml/min and those with a GFR 30–60 ml/min, while patients with a GFR <30 ml/min had a median Society of Thoracic Surgery predicted 30-day mortality risk in the high-risk range.

Baseline echocardiographic data are shown in Table 2. Patients with lower GFR had a lower median aortic valve peak velocity and mean gradient, and a larger aortic valve area, compared to patients with higher GFR.

3.2 | Procedural characteristics

Transfemoral artery access (TFA) was used in 98.8% of cases, and a self-expanding valve was deployed in 72.5% of cases. Most (93.4%) cases were completed under monitored anesthesia care but a lower rate of monitored anesthesia care was used in patients with a lower GFR compared with higher GFR. Contrast dose was very low in all patients (median 23 ml [15–33]); patients with a GFR <30 ml/min received even less contrast (13 mL [8–20]) during the TAVR procedure compared to patients with GFR 30–60 ml/min (24 ml [14–33]) and GFR ≥ 60 ml/min (23 ml [15–33]). Patients with a lower GFR also had a longer postprocedure and total length of stay. (Table 3).

3.3 | Procedural outcomes

Overall, device success rate was high (91.0%) and complication rates were low with no difference by GFR subgroups (Table 4). However, rates of periprocedural stroke (0.7%, 2.1%, 11.1%; $p < .001$) and major vascular complication (0.3%, 0%, 2.8%; $p = .03$) were higher in patients with lower GFR. Although rate of acute renal failure (0%, 1.7%, 8.3%; $p < .001$) was higher in patients with lower GFR than those with higher GFR, the majority was of Stage 1 rather than Stage 2 or 3. Furthermore, in-hospital all-cause mortality was exceedingly low (0.3%, 0.4%, 0; $p = .93$) and did not differ among GFR subgroups (Table 4). Kaplan-Meier mortality estimates demonstrate an increase in one-year all-cause mortality with decreasing baseline renal function: GFR ≥ 60 mL/min 2.7%, GFR 30–60 ml/min 7%, and GFR <30 ml/min 8.3%, $p_{\log\text{-rank}} = 0.04$.

3.4 | Anatomical substrate for peri-procedural stroke

Of the 11 patients with peri-procedural stroke, a retrospective computed tomography Core Lab analysis blinded to baseline renal function was performed in eight patients to determine potential anatomical

TABLE 1 Baseline clinical characteristics

	GFR \geq 60 ml/min (n = 297)	GFR 30 to 60 ml/min (n = 242)	GFR <30 ml/min (n = 36)	p-value
Age, years	83 [76–87]	85 [81–89]	84 [78–89]	<.001
Male sex	170 (57.2%)	137 (56.6%)	18 (50.0%)	.71
Race				.53
White	253 (85.5%)	218 (90.5%)	32 (88.9%)	
Black	13 (4.4%)	7 (2.9%)	2 (5.6%)	
Asian	8 (2.7%)	2 (0.8%)	0	
Other	22 (7.4%)	14 (5.8%)	2 (5.6%)	
Hispanic ethnicity	19 (6.4%)	19 (7.9%)	2 (5.6%)	.76
Body mass index, kg/m ²	26.0 [22.9–29.6]	26.3 [23.8–30.0]	27.5 [22.7–31.0]	.69
History of tobacco use	145 (49.7%)	135 (56.5%)	14 (38.9%)	.08
Hypertension	239 (80.5%)	194 (80.2%)	31 (86.1%)	.69
Dyslipidemia	217 (73.1%)	190 (78.5%)	29 (80.6%)	.27
Diabetes mellitus	80 (26.9%)	80 (33.1%)	21 (58.3%)	.001
Prior myocardial infarction	28 (9.4%)	31 (12.8%)	4 (11.1%)	.46
Prior cardiac surgery	78 (26.3%)	70 (28.9%)	10 (27.8%)	.79
Congestive heart failure	217 (73.1%)	196 (81.0%)	31 (86.1%)	.04
Carotid artery disease	24 (8.1%)	32 (13.3%)	6 (16.7%)	.08
Peripheral artery disease	26 (8.8%)	25 (10.4%)	7 (19.4%)	.13
Chronic lung disease	65 (21.9%)	63 (26.0%)	8 (22.2%)	.52
Atrial arrhythmia	93 (31.3%)	85 (35.1%)	10 (27.8%)	.52
Prior stroke or transient ischemic attack	38 (12.8%)	31 (12.8%)	5 (13.9%)	.98
Society of Thoracic Surgeon predicted risk of mortality at 30 days, %	5.1 [3.6–6.8]	6.1 [4.6–8.5]	9.7 [6.9–12.9]	<.001

Abbreviation: GFR, glomerular filtration rate.

Note: Continuous variables are shown as median [interquartile range] and compared across baseline renal function groups using Kruskal-Wallis test. Categorical variables are shown as frequency (proportion) and compared across baseline renal function groups using chi-square test.

TABLE 2 Baseline echocardiographic data

	GFR \geq 60 ml/min (n = 297)	GFR 30 to 60 ml/min (n = 242)	GFR <30 ml/min (n = 36)	p-value
Aortic valve peak velocity, m/s	4.1 [3.7–4.5]	4.1 [3.6–4.5]	3.8 [3.4–4.1]	.004
Mean gradient, mmHg	39 [31–46]	38 [30–47]	36 [25–41]	.09
Aortic valve area, cm ²	0.73 [0.60–0.85]	0.70 [0.57–0.80]	0.80 [0.70–0.90]	.001
Normal left ventricular ejection fraction, %	236 (79.5%)	178 (73.9%)	22 (61.1%)	.03
Left ventricular ejection fraction, %	65 [55–70]	62 [50–68]	60 [40–65]	.04
Left ventricular end-diastolic dimension, cm	4.4 [3.8–4.8]	4.5 [3.9–5.1]	4.6 [4.1–5.1]	.11
Interventricular septum thickness, cm	1.3 [1.2–1.5]	1.3 [1.2–1.4]	1.3 [1.2–1.5]	.57
Posterior/inferolateral wall thickness, cm	1.2 [1.1–1.3]	1.2 [1.1–1.3]	1.2 [1.1–1.3]	.45
Aortic regurgitation (moderate or severe), %	41 (14.0%)	31 (13.0%)	7 (19.4%)	.58
Mitral regurgitation (moderate or severe), %	52 (17.6%)	55 (22.9%)	9 (25.0%)	.25
Mitral stenosis (severe), %	5 (1.7%)	4 (1.7%)	0	.74
Tricuspid regurgitation (severe), %	7 (2.4%)	7 (2.9%)	0	.57

Abbreviation: GFR, glomerular filtration rate.

Note: Continuous variables are shown as median [interquartile range] and compared across baseline renal function groups using Kruskal-Wallis test. Categorical variables are shown as frequency (proportion) and compared across baseline renal function groups using chi-square test.

TABLE 3 Procedural data

	GFR ≥60 ml/ min (n = 297)	GFR 30 to 60 ml/ min (n = 242)	GFR <30 ml/ min (n = 36)	p- value
Procedure status, %				.34
Elective	282 (94.9%)	228 (94.2%)	32 (88.9%)	
Urgent	15 (5.1%)	14 (5.8%)	4 (11.1%)	
Access, %				.45
Transfemoral	296 (99.7%)	236 (97.5%)	36 (100%)	
Transapical	1 (0.3%)	4 (1.7%)	0	
Subclavian	0	1 (0.4%)	0	
Transaortic	0	1 (0.4%)	0	
Anesthesia, %				.01
Monitored anesthesia care	284 (96.3%)	220 (90.9%)	31 (86.1%)	
General anesthesia	11 (3.7%)	22 (9.1%)	5 (13.9%)	
Device, %				.06
First generation self-expanding valve	63 (21.2%)	56 (23.1%)	5 (13.9%)	
Second generation self-expanding valve	154 (51.9%)	118 (48.8%)	21 (58.3%)	
First generation balloon-expandable valve	5 (1.7%)	16 (6.6%)	3 (8.3%)	
Second generation balloon-expandable valve	75 (25.3%)	52 (21.5%)	7 (19.4%)	
Predilation, %	109 (36.9%)	78 (32.5%)	8 (22.2%)	.17
Postdilation, %	107 (36.3%)	74 (30.8%)	15 (41.7%)	.27
Contrast use, ml	23 [15–33]	24 [14–33]	13 [8–20]	<.001

Abbreviation: GFR, glomerular filtration rate.

Note: Continuous variables are shown as median [interquartile range] and compared across baseline renal function groups using Kruskal-Wallis test. Categorical variables are shown as frequency (proportion) and compared across baseline renal function groups using chi-square test.

substrates for stroke. The analysis was not performed in three patients who developed stroke: one patient with baseline GFR ≥60 ml/min with a valve-in-valve TAVR, one patient with GFR 30–60 ml/min with insufficient scan quality, one patient with GFR <30 ml/min with no preTAVR scan available.

No potential anatomical substrate was identified in the one patient with GFR ≥60 ml/min who developed a stroke. Of the four patients with GFR 30–60 ml/min who developed a stroke, three were identified to have a potential anatomical substrate (one had severe aortic arch atheroma, one had possible left atrial appendage thrombus, and one had severe aortic arch calcium and probably left atrial appendage thrombus). Of the three patients with GFR <30 ml/min who developed a stroke, all three were identified to have potential anatomical substrate (all three had severe aortic atheroma and one also had possible left atrial appendage thrombus and severe aortic arch calcium). Overall, patients with baseline CKD were more likely to have a potential anatomical substrate identified and patients with the worst renal function were more likely to have severe aortic atheroma as a potential anatomical substrate.

3.5 | Long-Term outcomes

Patients were followed-up for a median of 811 days [125–1,151]. Kaplan-Meier mortality estimates demonstrate an increase in long-

term mortality with decreasing baseline renal function: GFR ≥60 ml/min 20.5% [95% confidence interval 10.7%–29.2%], GFR 30–60 ml/min 35.9% [16.4%–50.8%], and GFR <30 ml/min 36.7% [6.0%–57.3%], $p_{\log\text{-rank}} = 0.04$ (Figure 1). When compared to GFR ≥60 ml/min, risk of all-cause mortality was higher in patients with GFR 30–60 ml/min (HR 1.61 [1.00–2.59]) and GFR <30 ml/min (HR 2.41 [1.06–5.48]). However, after adjustment for age, presence of diabetes mellitus, presence of congestive heart failure, type of anesthesia used, and contrast use, the risk of all-cause mortality did not differ in patients with GFR 30–60 ml/min (aHR 1.61 [0.91–2.83]) or GFR <30 ml/min (aHR 2.34 [0.90, 6.09]) when compared with GFR ≥60 ml/min (Table 5).

Follow-up data to evaluate for structural heart valve deterioration was available in 63% (n = 363) of the patients (GFR ≥60 ml/min n = 190, 64%; GFR 30–60 ml/min n = 154, 64%; GFR <30 ml/min n = 19, 53%) and was observed in 16% (n = 58) of the patients (GFR ≥60 ml/min n = 27, 14.2%; GFR 30–60 ml/min n = 25, 16.2%; GFR <30 ml/min n = 6, 31.6%; $p = .14$) at a median follow-up of 840 days [interquartile range 361–1,190]. The risk of structural heart valve deterioration over time in patients postTAVR by baseline renal function was as follows: GFR ≥60 ml/min Reference; GFR 30–60 ml/min HR 1.16 [0.67–2.00]; GFR <30 ml/min HR 2.45 [0.98–6.11]. For every one unit change in GFR, the risk of structural heart valve deterioration also did not differ over time (beta 0.99 [0.97–1.01]).

TABLE 4 Procedural outcomes

	GFR \geq 60 ml/min (n = 297)	GFR 30 to 60 ml/min (n = 242)	GFR <30 ml/min (n = 36)	p-value
Intra-procedural complications, %				
Conversion to alternative access	0	0	0	–
Femoral artery rupture	1 (0.3%)	0	0	.63
Annulus rupture	0	0	0	–
Device migration	2 (0.7%)	1 (0.4%)	0	.83
Ectopic valve deployment	0	0	0	–
Valve-in-valve	6 (2.0%)	2 (0.8%)	0	.38
Coronary artery obstruction	0	0	0	–
Cardiac tamponade	1 (0.3%)	1 (0.4%)	0	.93
Heart block	19 (6.4%)	17 (7.0%)	1 (2.8%)	.63
Paravalvular regurgitation				
None	64 (21.6%)	65 (26.9%)	4 (11.1%)	.15
Trace	108 (36.5%)	95 (39.3%)	14 (38.9%)	
Mild	109 (36.8%)	71 (29.3%)	14 (38.9%)	
Moderate	15 (5.1%)	11 (4.5%)	4 (11.1%)	
Severe	0	0	0	
Patient-prosthesis mismatch				
Moderate	15 (5.2%)	27 (11.4%)	3 (8.8%)	.11
Severe	5 (1.7%)	4 (1.7%)	0	
Device success, %	268 (90.2%)	223 (92.1%)	32 (88.9%)	.67
In-hospital complications, %				
Permanent pacemaker placement	34 (11.5%)	38 (15.8%)	5 (13.9%)	.35
Cardiac tamponade	1 (0.3%)	1 (0.4%)	0	.93
Stroke	2 (0.7%)	5 (2.1%)	4 (11.1%)	<.001
Vascular complication	4 (1.3%)	2 (0.8%)	1 (2.8%)	.58
Major vascular complication	1 (0.3%)	0	1 (2.8%)	.03
Acute renal failure	0	5 (2.1%)	3 (8.3%)	<.001
Stage 1	0	3 (1.2%)	3 (8.3%)	
Stage 2 or 3	0	2 (0.8%)	0	
Bleeding	31 (10.5%)	35 (14.5%)	3 (8.3%)	.29
Life-threatening or disabling	2 (0.7%)	1 (0.4%)	1 (2.8%)	.40
Major	2 (0.7%)	2 (0.8%)	0	
Minor	27 (9.1%)	32 (13.2%)	2 (5.6%)	
Cardiac arrest	1 (0.3%)	2 (0.8%)	0	.66
Postprocedure length of stay, days	1 [1–2]	2 [1–3]	2 [1–4]	.01
Total length of stay, days	2 [1–3]	2 [2–4]	3 [2–8]	<.001
In-hospital all-cause mortality, %	1 (0.3%)	1 (0.4%)	0	.93

Abbreviation: GFR, glomerular filtration rate.

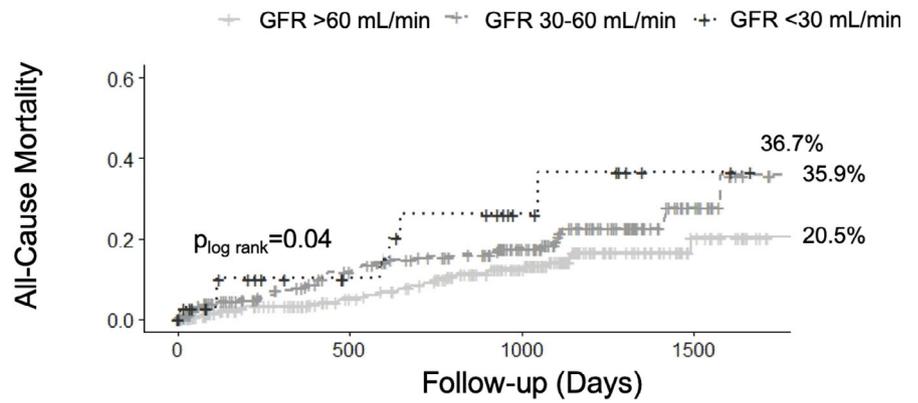
Note: Continuous variables are shown as median [interquartile range] and compared across baseline renal function groups using Kruskal-Wallis test. Categorical variables are shown as frequency (proportion) and compared across baseline renal function groups using chi-square test.

4 | DISCUSSION

To our knowledge, this is the first study to evaluate long-term outcomes after TAVR performed in the United States by baseline renal function and demonstrates several key findings in the real-world setting where a transfemoral-first and extremely low-contrast approach

is used. First, relatively few patients with a GFR <30 ml/min undergo TAVR. Second, there was no difference in all-cause in-hospital mortality with increasing baseline renal dysfunction, and although one-year mortality rates increased with decreasing renal function, the rates were numerically lower than reported national data. Third, by about 4 years postTAVR, all-cause mortality is estimated to occur in more

FIGURE 1 Kaplan–Meier estimates of long-term all-cause mortality in patients not on dialysis undergoing transcatheter aortic valve replacement by preprocedural renal function



Number at risk	
GFR >60 mL/min	297 181 118 20
GFR 30-60 mL/min	242 149 101 19
GFR ≤30 mL/min	36 18 8 2

TABLE 5 Association between preprocedural renal function and long-term all-cause mortality in patients undergoing transcatheter aortic valve replacement

	Unadjusted model		Adjusted model	
	Hazard ratio [95% confidence interval]	p-value	Hazard ratio [95% confidence interval]	p-value
GFR ≥60 ml/min	Reference		Reference	
GFR 30 to 60 ml/min	1.61 [1.00, 2.59]	.049	1.61 [0.91, 2.83]	.10
GFR <30 ml/min	2.41 [1.06, 5.48]	.037	2.34 [0.90, 6.09]	.08

Abbreviation: GFR, glomerular filtration rate.

Note: The model was adjusted for age, diabetes mellitus, heart failure, anesthesia type, and contrast volume.

than one third of patients with preprocedural CKD compared to one fifth of patients without preprocedural CKD. Lastly, patients with CKD carry a higher risk of peri-procedural vascular complications and stroke.

4.1 | Prevalence of severe renal dysfunction in patients undergoing TAVR

In the current study, 6.3% of patients undergoing TAVR had a preprocedural GFR <30 ml/min (CKD stage 4 or 5) but were not on hemodialysis. This is consistent with national data of 44,778 patients from the STS/American College of Cardiology Transcatheter Valve Therapy (STS/ACC TVT) registry which demonstrated 5.8% of patients not on hemodialysis who undergo TAVR have CKD stage 4 or 5.¹ Though this center's heart valve team does not defer TAVR based on chronic CKD alone, the reasons for the low rate of patients with GFR <30 ml/min at this center and nationally cannot be elucidated with the current data. The majority of patients with CKD who undergo TAVR have CKD stage 3, which represented 42% in the current study and 43% in the STS/ACC TVT registry.¹ A report from the United Kingdom,

however, demonstrated a higher 17.5% rate of CKD stage 4 or 5 not on HD in patients undergoing TAVR, while another large multinational cohort of TAVR centers in Europe, Israel, and Japan demonstrated a 35% rate of CKD stage 4 or 5 not on HD in patients undergoing TAVR.^{14,15}

4.2 | In-hospital and long-term mortality in patients with severe renal dysfunction undergoing TAVR

Importantly, we observed no increase in in-hospital mortality with worsening baseline renal dysfunction. However, an analysis of the National Inpatient Sample⁶ found an elevated risk of in-hospital mortality with CKD, which we did not observe in the present analysis. Furthermore, the unadjusted estimated mortality rates of all-cause mortality at 1 year after TAVR in the current study (3% in the no CKD patients, 7% in the CKD stage 3 patients, and 8% in the CKD stage 4 and 5 patients) were numerically lower than the 1-year mortality rates reported in the STS/ACC TVT registry (18% in the no CKD patients, 22% in the CKD stage 3 patients, and 31% in the CKD stage

4 and 5 patients).¹ Of the 575 patients in the current study, 73 patients died prior to reaching 4-year follow-up and 69 patients were available for analysis. All-cause mortality rates after about 4 years in the current study were numerically closer to nationally reported 1-year data (21% in the no CKD patients and 36% in the CKD stage 3 patients, and 37% in the CKD stage 4 and 5 patients). The mortality rates seen in this study did not differ between patients with GFR 30–60 ml/min and GFR \geq 60 ml/min. However, a trend towards increased mortality was observed in the GFR < 30 ml/min group and the lack of significance may be due to the low sample size of the GFR <30 ml/min group ($n = 36$). Overall, the baseline characteristics between the current study and STS/ACC TVT data are similar, with the exception of a three-fold higher reported rate of peripheral artery disease and a concomitant lower rate of transfemoral access (70% in the STS/TVT registry) when compared with the current study.¹ Patients with renal disease have diffuse vascular disease, which may affect the approach to access during TAVR. However, our group utilizes a “transfemoral first” approach with the use of percutaneous balloon angioplasty to “pretreat” occlusive disease of the iliofemoral arteries prior to TAVR wherever feasible.¹² Furthermore, the use of contrast was markedly lower in the current study (median 23 ml overall; 13 ml in GFR < 30) compared to national reports (median 105 ml overall; 72–80 ml in stage 4 and 5 CKD),¹ and is partly due to our use of 50% diluted contrast. It is possible that the strategy of transfemoral-first and extremely low-contrast use may have accounted for the observed improved outcomes particularly in the CKD population.

4.3 | Peri-procedural risk of stroke in the CKD population

The current study also found significantly higher rates of in-hospital stroke postTAVR in patients with lower preprocedural renal function, with the highest risk of stroke seen in the GFR < 30 group. Overall, this is consistent with prior data demonstrating higher risks of peri-procedural complications in patients with CKD.^{1,13,16,17,18} The increased rate of stroke is likely explained by multifactorial mechanisms, including the increased prevalence of atherosclerosis and platelet dysfunction observed in advanced CKD patients. Shishikura et al reported more severe atherosclerosis with poor baseline renal function in patients undergoing TAVR and found this to be correlated with peri-procedural acute kidney injury.¹⁹ In a retrospective analysis of potential anatomical substrates of stroke blinded to renal dysfunction, we found CKD patients to be more likely to have a potential anatomical substrate identified; moreover, severe aortic atheroma emerged as a prevalent anatomical substrate in the CKD population. Given the small numbers, however, this finding remains hypothesis-generating.

Stroke remains an unpredictable and rare, albeit serious, complication after TAVR. Although there are strong proponents of cerebral embolic protection,²⁰ its systematic adoption has thus far been variable in the setting of extremely low rates of stroke in contemporary studies.²¹ Many centers, including our own, have not adopted its

routine use since the identification of an at-risk subset has remained elusive. In this study we identify a significantly elevated risk of stroke in patients with worse baseline renal function and found a signal for a corresponding higher frequency of severe aortic arch atheroma. The use of cerebral embolic protection in this subgroup of patients specifically warrants evaluation via a clinical trial.

4.4 | Study limitations

This study has several limitations, including those inherent to a retrospective study design. Second, this was a single-center study and therefore the results may not be generalizable to the entire TAVR population. Third, the sample size of the CKD stage 4 and 5 group was small and therefore limits our ability to make conclusions from the adjusted analysis regarding long term complications stratified by GFR group. Fourth, data on re-hospitalizations, acute kidney recovery, and quality of life were not evaluated, and data on structural valve deterioration was only limited to the 63% of the cohort with available follow-up data and was limited to follow up of less than 5 years.

4.5 | Conclusions

Patients with baseline renal insufficiency remain a challenging population with poor long-term outcomes despite procedural optimization with a transfemoral-first approach and an extremely low-contrast approach. Given the prevalence of severe aortic arch atheroma in patients with low baseline GFR and peri-procedural stroke, cerebral embolic protection may be of consideration in this population.

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AUTHORS CONTRIBUTION

Binita Shah serves on the advisory board for Philips Volcano and Radux Devices and as a consultant for Terumo Medical. Hasan Jilaihawi serves as a consultant to Edwards Lifesciences, Medtronic, and Boston Scientific; and has received grant/research support from Edwards Lifesciences, Medtronic, HLT, and Abbott Vascular. Muhamed Saric, Cezar Staniloae, Peter J. Neuburger, and Mathew Williams are on the Speakers' bureau for Medtronic. Muhamed Saric is also on an advisory board for Siemens and the Speakers' bureau for Phillips, and Mathew Williams also receives research funding from Edwards Lifesciences and Medtronic. Homam Ibrahim serves as a proctor for Medtronic. The other authors report no other relationships with industry. There are no conflicts of interest present with this manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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