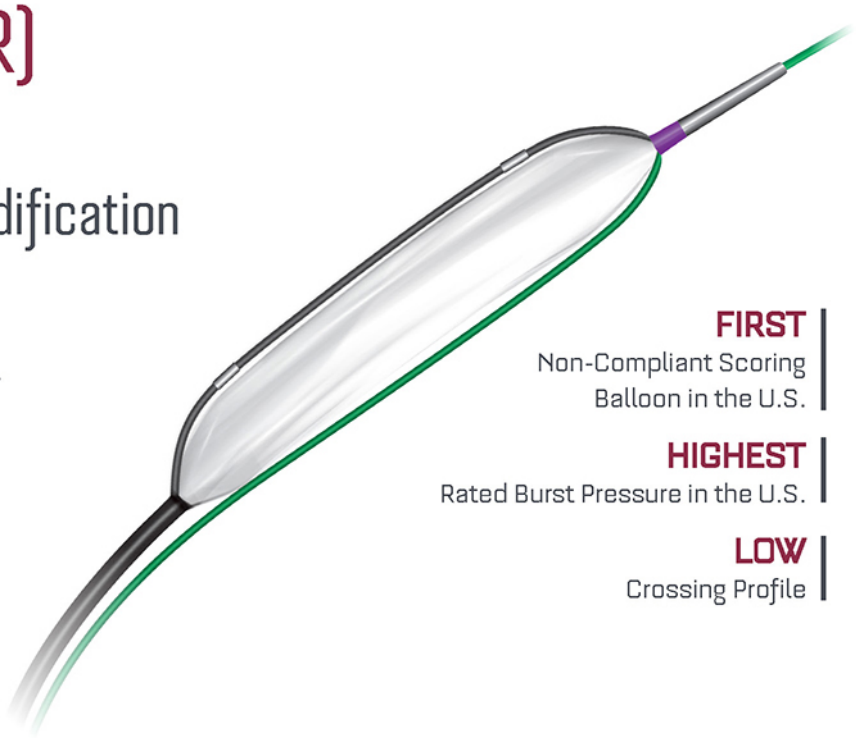
SCOREFLEX® NC SCORING PTCA CATHETER

scoreflex NC
Scoring PTCA Catheter

INDICATED FOR IN-STENT RESTENOSIS (ISR)

Focused Force Angioplasty for Non-Compliant Plaque Modification and Lesion Preparation



Scoreflex NC Scoring PTCA Catheter provides optimal safety and efficacy for ISR.

- Safely scores ISR lesions circumferentially and longitudinally.
- Non-compliant balloon provides minimal slip/watermelon seeding and dog-boning.

FIRST
Non-Compliant Scoring Balloon in the U.S.

HIGHEST
Rated Burst Pressure in the U.S.

LOW
Crossing Profile

In a clinical U.S. study with 12 centers and 200 patients, Scoreflex NC achieved **93.5%** device procedural success. **9.5%** of the cases were ISR.[1]

LEARN MORE

1. Kandzari D, et al. Cardiovasc Revasc Med. 2022;35:85-90

INDICATIONS: The Scoreflex NC Scoring PTCA Catheter is indicated for: Balloon dilatation of a de novo stenotic portion of a coronary artery and in-stent restenosis in coronary arteries in patients evidencing coronary ischemia for the purpose of improving myocardial perfusion.

CONTRAINDICATIONS: The use of the Scoreflex NC Scoring PTCA Catheter is contraindicated in the following patient types: Patients with an unprotected left main coronary artery; Patients with coronary artery spasm in the absence of a significant stenosis.

WARNINGS: When using this type of device, the following warnings should be observed: This device is intended for single use only. Do not resterilize and/or reuse, as this can potentially result in compromised device performance and increased risk of cross-contamination. This balloon is not intended for the expansion or delivery of a stent. PTCA in patients who are not acceptable candidates for coronary artery bypass graft surgery require careful consideration, including possible hemodynamic support during PTCA, as treatment of this patient population carries special risk. To reduce the potential for vessel damage, the inflated diameter of the balloon should approximate the diameter of the vessel just proximal and distal to the stenosis.When the catheter is exposed to the vascular system, it should be manipulated while under high-quality fluoroscopic observation. Do not advance or retract the catheter unless the balloon is fully deflated under vacuum. If resistance is met during manipulation, determine the cause of the resistance before proceeding. Applying excessive force to the catheter can result in tip or catheter breakage, catheter kink, or balloon separation. Do not twist the catheter shaft in excess of 180 degrees when the tip is constrained.Balloon pressure should not exceed the rated burst pressure (RBP) indicated on the package. The rated burst pressure is based on the results of in vitro testing. At least 99.9 percent of the balloons, (with a 95 percent confidence) will not burst at or below their rated burst pressure. Use of a pressure monitoring device is recommended to prevent over pressurization. To reduce the potential for air embolus into the vessel, use only the recommended balloon inflation medium. Never use air or any gaseous medium to inflate the balloon. Do not re-straighten a kinked hypotube; straightening a kinked metal shaft may result in breakage of the shaft. PTCA should only be performed at hospitals where emergency coronary artery bypass graft surgery can be quickly performed in the event of a potentially injurious or life-threatening complication.

PRECAUTIONS: Use the catheter prior to the "Use By" date specified on the package. Prior to angioplasty, the catheter should be examined to verify functionality and ensure that its size and shape are suitable for the specific procedure for which it is to be used. The catheter system should be used only by physicians trained in percutaneous transluminal coronary angioplasty. During the procedure, appropriate anticoagulant and coronary vasodilator therapy must be provided to the patient as needed. After the procedure, anticoagulant therapy should be continued for a period of time as determined by the physician. Never advance the Scoreflex NC Scoring PTCA Catheter without the guidewire extending from the tip. Do not use oil-based contrast medium, organic solvents, or alcohols; there is a possibility of catheter leak, damage, or lubrication loss. The balloon deflation time has been established as 15 seconds based on in vitro bench testing results. Do not reinsert the PTCA catheter into the coil dispenser after procedural use. Discard all disposable devices used during this procedure per local requirements for medical device waste disposal.

CAUTION: Federal law (USA) restricts this device to the sale by or on the order of a physician.

See the instructions for use before performing Scoreflex NC Scoring PTCA Catheter procedures for detailed information regarding the procedure, indications, contraindications, warnings, precautions, and potential adverse events.

Distributed by:

CSI | CARDIOVASCULAR SYSTEMS, INC.
1225 Old Hwy 8 NW
St. Paul, MN 55112
T: 651.259.1600
877.274.0901
F: 612.677.3355
www.csi360.com

Manufactured by:

OrbusNeich®
Pioneers in life-changing technologies
1 Jinkui Road,
Futian Free Trade Zone,
Shenzhen, 518038, China
T: +86.755.8358.0181
F: +86.755.8358.0169
www.OrbusNeich.com

Received: 24 July 2020 | Revised: 13 October 2020 | Accepted: 26 October 2020

DOI: 10.1002/ccd.29378

VALVULAR AND STRUCTURAL HEART DISEASES

Original Studies

WILEY

EDITORIAL COMMENT: Expert Article Analysis for:
Transcatheter aortic valve replacement and chronic kidney disease: Close friends or sworn enemies?

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

Justyna Rzucidlo MD[1] | Vita Jaspan MD[1] | Darien Paone MD[2] | Hasan Jilaihawi MD[1] | Yuhe Xia MS[3] | Anna Kapitman BA[2] | Makoto Nakashima MD, PhD[1] | Yuxin He MD[1] | Homam Ibrahim MD[1] | Illya Pushkar MPH[2] | Peter J. Neuburger MD[4] | Muhamed Saric MD[1] | Daniel Bamira MD[1] | Sonja Paschke MD[2] | Chloe Kalish BA[2] | Cezar Staniloae MD[1] | Binita Shah MD[1,5] | Mathew Williams MD[2]

[1]Department of Medicine, Division of Cardiology, NYU Langone Health, New York, New York

[2]Department of Cardiothoracic Surgery, NYU Langone Health, New York, New York

[3]Department of Biostatistics, NYU Langone Health, New York, New York

[4]Department of Anesthesiology, Perioperative Care & Pain Medicine, NYU Langone Health, New York, New York

[5]Department of Medicine, Division of Cardiology, VA New York Harbor Healthcare System: Manhattan Campus, New York, New York

Correspondence
Binita Shah MD, NYU Grossman School of Medicine, 423 East 23rd Street, 12023-W, New York, NY 10010.
Email: binita.shah@nyumc.org

Funding information
Edwards; Boston Scientific; Edwards Lifesciences

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.

Binita Shah and Mathew Williams are co-senior authors

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 cm^2 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

TABLE 1 Baseline clinical characteristics

	GFR ≥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 ≥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.

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 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).

TABLE 4 Procedural outcomes

	GFR ≥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				.11
Moderate	15 (5.2%)	27 (11.4%)	3 (8.8%)	
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.

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]).

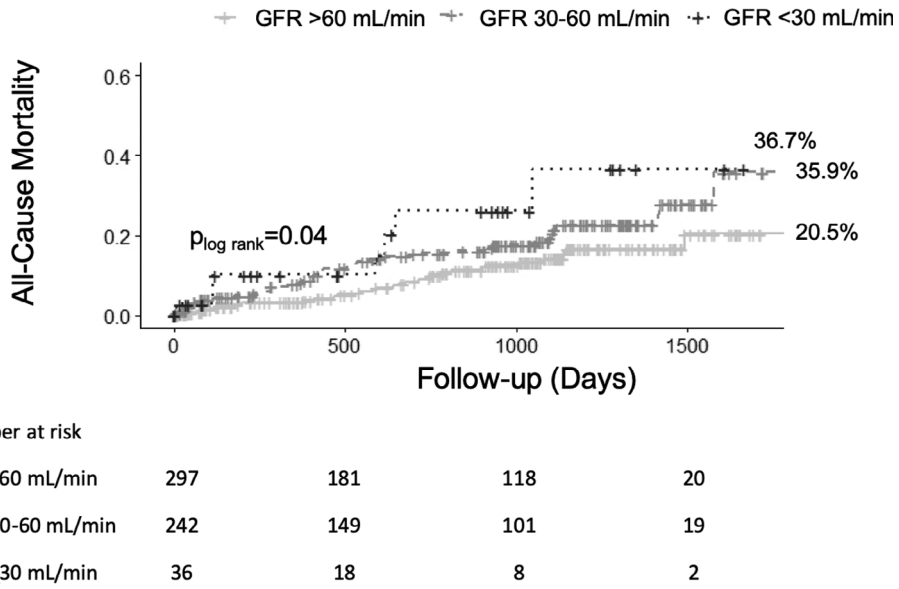


FIGURE 1 Kaplan–Meier estimates of long-term all-cause mortality in patients not on dialysis undergoing transcatheter aortic valve replacement by preprocedural renal function

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.

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 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 Sample[6] 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 ≥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.

ACKNOWLEDGEMENTS

Dr Shah is supported in part by the Biomedical Laboratory Research & Development Service of the VA Office of Research and Development (iK2CX001074) and NIH/NHLBI (R01HL146206).

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.

ORCID

Binita Shah https://orcid.org/0000-0001-8872-8001

REFERENCES

1. Hansen JW, Foy A, Yadav P, et al. Death and dialysis after transcatheter aortic valve replacement. An Analysis of the STS/ACC TVT Registry JACC Cardiovasc Interv. 2017;10:2064-2075.
2. Bagur R, Webb JG, Nietlispach F, et al. Acute kidney injury following transcatheter aortic valve implantation: predictive factors, prognostic value, and comparison with surgical aortic valve replacement. Eur Heart J. 2010;31:865-874.
3. Muhammed Zeeshan K, Martyn RT, Abhishek J, et al. The effects of VARC-defined acute kidney injury after transcatheter aortic valve implantation (TAVI) using the Edwards bioprosthesis. EuroIntervention. 2012;8:563-570.
4. Cheungpasitporn W, Thongprayoon C, Kashani K. Transcatheter aortic valve replacement: a Kidney's perspective. J Renal Inj Prev. 2016; 5:1-7.
5. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. New England J Med. 2010;363:1597-1607.
6. Gupta T, Goel K, Kolte D, et al. Association of Chronic Kidney Disease with in-Hospital Outcomes of Transcatheter aortic valve replacement. J Am Coll Cardiol Intv. 2017;10:2050-2060.
7. Aregger F, Wenaweser P, Hellige GJ, et al. Risk of acute kidney injury in patients with severe aortic valve stenosis undergoing transcatheter valve replacement. Nephrology Dialysis Transplantation. 2009;24: 2175-2179.
8. KONG WY, YONG G, IRISH A. Incidence, risk factors and prognosis of acute kidney injury after transcatheter aortic valve implantation. Nephrol Ther. 2012;17:445-451.
9. Wessely M, Rau S, Lange P, et al. Chronic kidney disease is not associated with a higher risk for mortality or acute kidney injury in transcatheter aortic valve implantation. Nephrology Dialysis Transplantation. 2012;27:3502-3508.
10. Nguyen TC, Babaliaros VC, Razavi SA, et al. Impact of varying degrees of renal dysfunction on transcatheter and surgical aortic valve replacement. J Thorac Cardiovasc Surg. 2013;146:1399-1407.
11. Voigtländer L, Schewel J, Martin J, et al. Impact of kidney function on mortality after transcatheter valve implantation in patients with severe aortic valvular stenosis. Int J Cardiol. 2015;178:275-281.
12. Staniloae CS, Jilaihawi H, Amoroso NS, et al. Systematic Transfemoral Transarterial Transcatheter aortic valve replacement in hostile vascular access. Struct Heart. 2019;3:34-40.
13. Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the valve academic research Consortium-2 consensus document*. J Thorac Cardiovasc Surg. 2013;145:6-23.
14. Ferro CJ, Chue CD, de Belder MA, et al. Impact of renal function on survival after transcatheter aortic valve implantation (TAVI): an analysis of the UKTAVI registry. Heart. 2015;101:546-552.
15. Codner P, Levi A, Gargiulo G, et al. Impact of renal dysfunction on results of Transcatheter aortic valve replacement outcomes in a large multicenter cohort. Am J Cardiol. 2016;118:1888-1896.
16. Szerlip M, Zajarias A, Vemalapalli S, et al. Transcatheter aortic valve replacement in patients with end-stage renal disease. J Am Coll Cardiol. 2019;73:2806-2815.
17. Dumonteil N, van der Boon RMA, Tchetche D, et al. Impact of preoperative chronic kidney disease on short- and long-term outcomes after transcatheter aortic valve implantation: a pooled-RotterdAm-Milano-Toulouse in collaboration plus (PRAGMATIC-plus) initiative substudy. Am Heart J. 2013;165:752-760.
18. Allende R, Webb JG, Munoz-Garcia AJ, et al. Advanced chronic kidney disease in patients undergoing transcatheter aortic valve implantation: insights on clinical outcomes and prognostic markers from a large cohort of patients. Eur Heart J. 2014;35:2685-2696.
19. Shishikura D, Kataoka Y, Pisaniello Anthony D, et al. The extent of aortic atherosclerosis predicts the occurrence, severity, and recovery of acute kidney injury after Transcatheter aortic valve replacement. Circ Cardiovasc Interv. 2018;11:e006367.
20. Seeger J, Gonska B, Otto M, Rottbauer W, Wöhrle J. Cerebral embolic protection during Transcatheter aortic valve replacement significantly reduces death and stroke compared with unprotected procedures. J Am Coll Cardiol Intv. 2017;10:2297-2303.
21. Herrmann HC, Thourani VH, Kodali SK, et al. One-year clinical outcomes with SAPIEN 3 Transcatheter aortic valve replacement in high-risk and inoperable patients with severe aortic stenosis. Circulation. 2016;134:130-140.

How to cite this article: Rzucidlo J, Jaspan V, Paone D, et al. Long-term outcomes after transcatheter aortic valve replacement with minimal contrast in chronic kidney disease. *Catheter Cardiovasc Interv*. 2021;98:319–327. https://doi.org/10.1002/ccd.29378