

hospitalization. Despite these limitations, our study provides important insights into the incidence, risk factors, and outcomes of thrombotic events in hospitalized patients with viral pneumonia and may serve as a comparator once similar data emerge for SARS-CoV-2 pneumonia.

Disclosures

The authors have no conflicts of interest to disclose.

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1. Thompson WW, Shay DK, Weintraub E, Brammer L, Cox N, Anderson LJ, Fukuda K. Mortality associated with influenza and respiratory syncytial virus in the United States. *JAMA* 2003;289:179–186.
2. Smeeth L, Thomas SL, Hall AJ, Hubbard R, Farrington P, Vallance P. Risk of myocardial infarction and stroke after acute infection or vaccination. *N Engl J Med* 2004;351:2611–2618.
3. Bikdeli B, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, Driggin E, Nigoghossian C, Ageno W, Madjid M, Guo Y, Tang LV, Hu Y, Giri J, Cushman M, Quéré I, Dimakakos EP, Gibson CM, Lippi G, Favaloro EJ, Fareed J, Caprini JA, Tafur AJ, Burton JR, Francese DP, Wang EY, Falanga A, McLintock C, Hunt BJ, Spyropoulos AC, Barnes GD, Eikelboom JW, Weinberg I, Schulman S, Carrier M, Piazza G, Beckman JA, Steg PG, Stone GW, Rosenkranz S, Goldhaber SZ, Parikh SA, Monreal M, Krumholz HM, Konstantinides SV, Weitz JJ, Lip GYH. COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up: JACC State-of-the-Art Review. *J Am Coll Cardiol* 2020;75:2950–2973.
4. Tripathi B, Kumar V, Kalra A, Gupta T, Sawant AC, Sharma P, Arora S, Panhwar MS, Gopalan R, Deshmukh A, Pershad A, Gulati M, Bhatt DL. Influence of influenza infection on in-hospital acute myocardial infarction outcomes. *Am J Cardiol* 2020;130:7–14.

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Transcatheter Aortic Valve Implantation Outcomes in Chronic Kidney Disease Versus End-Stage Kidney Disease



Patients with end stage kidney disease on dialysis (ESKD-D) have a high risk of developing aortic stenosis (AS). The dystrophic calcification of the aortic annulus and leaflets occurs with worsening renal function, leading to an onset 10 to 20 years earlier than the general population, as well as faster progression.¹ Similarly, patients with less advanced chronic kidney disease (CKD) have been associated with increased postoperative mortality after cardiac procedures.² There is little data to answer the question of whether TAVI is safe in dialysis patients as they were excluded from the large trials and small trials offered mixed results.³ The aim of our study was to evaluate the impact of different stages of CKD on outcomes after TAVI.

We performed a retrospective cohort study using the National Readmissions Database (NRD), released by the Agency for Healthcare Research and Quality. The study population included patients with severe AS and CKD (IIIa, IIIb, IVa, and IVb) or ESKD-D who underwent TAVI between January 2012 and December 2017. We excluded patients with CKD stages I-II as they are considered clinically normal from a nephrology point of view and therefore may be underreported. We used ICD-9 and ICD-10 codes to identify eligible patients operated before and after October 2015, respectively.

We assessed the in-hospital outcomes including in-hospital mortality, stroke, permanent pacemaker implantation, blood transfusion, acute myocardial infarction (AMI), sepsis, length of hospital stay, and discharge with disability. “Discharge with disability” was defined as any disposition category not reported as routine discharge (including transfer to other care facilities, home health care, and discharge against medical advice). To assess 30-day readmission rates, we excluded patients who died during the index admission and patients who were discharged in December of each year to allow for at least 30 days of follow-up.

Our study included 42,147 CKD patients who underwent TAVI, including 36,070 patients who had CKD stage III, IV, or V not requiring dialysis, and 6,077 patients who had ESKD-D. The median age was 83 years in patients with CKD versus 75 years in patients with ESKD-D ($p < 0.001$). CKD patients were more likely to have congestive heart failure, atrial fibrillation, peripheral vascular disease, obesity, history of alcohol and drug abuse, but less likely to have coronary atherosclerosis, hypertension, diabetes mellitus, dyslipidemia, coagulopathy, smoking, and anemia (Table 1).

The median length of stay following TAVI was 6 days in patients with ESKD-D compared to 4 days in CKD patients not requiring dialysis ($p < 0.001$). In-hospital mortality was higher in ESKD-D group compared to the CKD not requiring dialysis group (5.2% vs 3%, $p < 0.001$). Further, patients with ESKD-D were more likely to develop in-hospital AMI (6% vs 3.7%, $p < 0.001$), in-hospital sepsis (5% vs 1.7%, $p < 0.001$), require blood transfusion (21.6% vs 14.2%, $p < 0.001$), and need permanent pacemaker implantation (12.3% vs 11.2%, $p < 0.001$) following TAVI. The rates of in-hospital stroke and discharge with disability did not differ between both groups. Patients with ESKD-D were more likely to be readmitted within 30 days following discharge (25.5% vs 17.3%, $p < 0.001$) (Table 1).

The present study shows that ESKD-D patients who underwent TAVI were associated with a higher risk of in-hospital mortality, AMI, blood transfusion, sepsis, and 30-day readmission, as well as longer length of hospital stay, compared with CKD patients not requiring dialysis. However, the risk of in-hospital stroke and discharge with disability were similar between the two groups. These results are concordant with former studies in the literature.^{4,5} Despite the limitations of NRD data (including possible ICD-10 code misclassification, lack of data on procedural characteristics, and short follow-up), our results indicate that being on dialysis increases the risk of worse outcomes after TAVI. Future studies are encouraged to develop optimal risk stratification and outcome improvement strategies for patients undergoing TAVI with different CKD stages.

Table 1.

Baseline characteristics and outcomes of TAVI patients with chronic kidney disease (n = 42,147)

Variable	CKD not requiring dialysis (n = 36,070)	ESRD on dialysis (n = 6,077)	p Value
Age (years) median (IQR)	83 (77-87)	75 (68-82)	<0.001
Men	21,273 (59%)	3,769 (62%)	<0.001
Women	14,796 (41%)	2,308 (38%)	
<i>TAVI approach</i>			0.334
Endovascular	33,134 (91.9%)	5,605 (92.2%)	
Transapical	2,935 (8.1%)	472 (7.8%)	
<i>Admission type</i>			<0.001
Elective	26,556 (73.9%)	3,951 (65.1%)	
Nonelective	9,355 (26.1%)	2,116 (34.9%)	
<i>Hospital volume</i>			0.078
Low	7,445 (20.6%)	1,244 (20.5%)	
Middle	10,727 (29.7%)	1,712 (28.2%)	
High	17,897 (49.6%)	3,122 (51.4%)	
<i>Stage of chronic kidney disease</i>			
III	28,956 (68.7%)		
IV	6,704 (15.9%)		
V	410 (1%)		
<i>Comorbidities</i>			
Heart failure	29,415 (81.6%)	4,819 (79.3%)	<0.001
Coronary atherosclerosis	26,176 (72.6%)	4,165 (68.5%)	<0.001
Hypertension	33,396 (92.6%)	5,796 (95.4%)	<0.001
Liver disease	847 (2.3%)	250 (4.1%)	<0.001
Diabetes mellitus	15,221 (42.2%)	3,001 (49.4%)	<0.001
Anemia	9,144 (25.4%)	3,062 (50.4%)	<0.001
Dyslipidemia	24,707 (68.5%)	3,583 (59%)	<0.001
Coagulopathy	6,922 (19.2%)	1,300 (21.4%)	<0.001
Carotid artery disease	2,795 (7.7%)	302 (5%)	<0.001
Atrial fibrillation	16,276 (45.1%)	2,511 (41.3%)	<0.001
Peripheral vascular disorder	8,944 (24.8%)	1,411 (23.2%)	0.008
Obesity	6,168 (17.1%)	803 (13.2%)	<0.001
Smoker	12,249 (34%)	1,907 (31.4%)	<0.001
Alcohol abuse	200 (0.6%)	22 (0.4%)	0.06
Healed myocardial infarction	5,248 (14.5%)	869 (14.3%)	0.622
History of cerebrovascular disease	4,577 (12.7%)	750 (12.3%)	0.465
<i>In-hospital outcomes and 30-day readmission</i>			
LOS (days) median (IQR)	4 (2-9)	6 (3-13)	<0.001
Mortality	1,128 (3.1%)	318 (5.2%)	<0.001
Stroke	815 (2.3%)	136 (2.2%)	0.595
Blood transfusion	5,258 (14.6%)	1,314 (21.6%)	<0.001
Acute myocardial infarction	1,358 (3.8%)	367 (6%)	<0.001
Sepsis	642 (1.8%)	302 (5%)	<0.001
Permanent pacemaker implantation	4,036 (11.2%)	747 (12.3%)	0.012
Conversion to SAVR	66 (0.2%)	23 (0.4%)	0.004
Discharge with disability	18,744 (53.7%)	3,043 (52.8%)	0.242
30-Day readmission	5,547 (17.6%)	1,318 (25.5%)	<0.001

Data are presented as count (%) unless otherwise stated. p values <0.05 are statistically significant. TAVI = transcatheter aortic valve implantation; CKD = chronic kidney disease; LOS = length of hospital stay; ESKD-D = end-stage kidney disease requiring dialysis.

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The authors have no conflicts of interest to report. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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- Thourani VH, Forcillo J, Beohar N, Doshi D, Parvataneni R, Ayele GM, Kirtane AJ, Babaliaros V, Kodali S, Devireddy C, Szeto W, Herrmann HC, Makkar R, Ailawadi G, Lim S, Maniar HS, Zajarias A, Suri R, Tuzcu EM, Kapadia S, Svensson L, Condado J, Jensen HA, Mack MJ, Leon MB. Impact of preoperative chronic kidney disease in 2,531 high-risk and inoperable patients undergoing transcatheter aortic valve replacement in the PARTNER Trial. *Ann Thorac Surg* 2016;102:1172-1180.
- D'Errigo P, Moretti C, D'Ascenzo F, Rosato S, Biancarfi F, Barbanti M, Santini F, Ranucci M, Miceli A, Tamburino C, Onorati F, Santoro G, Grossi C, Fusco D, Seccareccia F, OBSERVANT Research Group. Transcatheter aortic valve implantation versus surgical aortic valve replacement for severe aortic stenosis in patients with chronic kidney disease stages 3b to 5. *Ann Thorac Surg* 2016;102:540-547.
- Rossignol P, Agarwal R, Canaual B, Charney A, Chatellier G, Craig JC, Cushman WC, Gansevoort RT, Fellström B, Garza D, Guzman N, Holtkamp FA, London GM, Massy ZA, Mebazaa A, Mol PGM, Pfeffer MA, Rosenberg Y, Ruilope LM, Seltzer J, Shah AM, Shah S, Singh B, Stefánsson BV, Stockbridge N, Stough WG, Thygesen K, Walsh M, Wanner C, Warnock DG, Wilcox CS, Wittes J, Pitt B, Thompson A, Zannad F. Cardiovascular outcome trials in patients with chronic kidney disease: challenges associated with selection of patients and endpoints. *Eur Heart J* 2019; 40:880-886.
- Gupta T, Goel K, Kolte D, Khera S, Villablanca PA, Aronow WS, Bortnick AE, Slovut DP, Taub CC, Kizer JR, Pyo RT, Abbott JD, Fonarow GC, Rihal CS, Garcia MJ, Bhatt DL. Association of chronic kidney disease with in-hospital outcomes of transcatheter aortic valve replacement. *J Am Coll Cardiol Intv* 2017;10:2050-2060.
- Dumontail N, van der Boon RMA, Tchetché D, Chieffo A, Van Mieghem NM, Marcheix B, Buchanan GL, Vahdat O, Serruys PW, Fajadet J, Colombo A, de Jaegere PP, Carrié D. 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.

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Trends and Outcomes of Transcatheter Valve Implantation in Patients With Prior Mediastinal Radiation



Transcatheter aortic valve implantation (TAVI) is a safe and effective alternative for patients with severe aortic stenosis (AS) irrespective of their surgical risk.^{1,2} Aortic stenosis is the most common radiation-induced valvular heart disease. Surgical aortic valve replacement is associated with higher operative mortality and morbidity among patients with prior mediastinal radiation.³ While a percutaneous approach appears appealing for patients with prior mediastinal radiation, these patients were excluded from pivotal randomized trials. We sought to evaluate outcomes of TAVI among patients with prior mediastinal radiation using a large national database.

We queried the Nationwide Readmissions Database (NRD) between 2013 and 2018, and identified hospitalizations for TAVI among patients with prior mediastinal radiation. We utilized the International Classification of Diseases Ninth or Tenth editions diagnostic codes for prior radiation (V15.3 and Z923) and diagnostic codes for history of breast cancer, lung cancer, Hodgkin's lymphoma, or other mediastinal tumors.⁴ We employed propensity score methodology to match hospitalizations for patients with previous mediastinal radiation to those without, at 1:1 ratio with a caliper width of 0.2. The propensity score was calculated using the following matching variables: Age, sex, chronic lung disease, chronic kidney disease (CKD), chronic dialysis, obesity, diabetes mellitus with complications, diabetes mellitus without complications, previous coronary artery bypass grafting, and prior myocardial infarction. A secondary analysis to evaluate in-hospital mortality was conducted using a multivariable regression analysis. The multivariable model

included the same matching variables. Analyses were conducted using complex sample analysis that adjusted for hospital type, bed-size, and stratification. The main study outcome was in-hospital mortality. Associations were considered significant if the p-value was <0.05 . Data from the NRD are publicly available and deidentified; hence, this study was exempt from institutional review board evaluation.

Our analysis yielded 224,264 hospitalizations for TAVI. Among those, 3,242 (1.5%) had prior mediastinal radiation, with a rising trend over time (141 in 2013 vs 887 in 2018, $P_{\text{trend}}=0.01$). Admissions with prior mediastinal radiation were younger (76.35 ± 10.20 vs 80.22 ± 8.45 years, $p < 0.001$), and likely women (79.4% vs 45.7%, $p < 0.001$). Admissions with prior mediastinal radiation were more likely to have chronic lung disease and prior tobacco abuse, but less likely to have heart failure, CKD, hypertension, diabetes, and prior CABG. After propensity matching, the standardized mean differences for all matching variables were $<10\%$.

In-hospital mortality was lower among those with prior mediastinal radiation versus none in the unmatched cohort (0.8% vs 2.1%; odds ratio [OR] 0.37; 95% confidence interval [CI] 0.20 to 0.68, $p = 0.01$), propensity-matched cohort (0.8% vs 2.2%; OR 0.35; 95% CI 0.17 to 0.73, $p = 0.01$), and on multivariable analysis (OR 0.37; 95% CI 0.20 to 0.69, $p = 0.01$). After propensity-matching, those with prior mediastinal radiation had lower rates of cardiogenic shock (0.9% vs 1.8%, $p = 0.03$), acute kidney injury (6.4% vs

11.2%, $p < 0.001$), major bleeding (11.0% vs 13.7%, $p = 0.03$), blood transfusion (7.9% vs 11.2%, $p = 0.01$), prolonged mechanical ventilation (0.6% vs 1.4%, $p = 0.02$), and discharge to nursing facility (11.0% vs 15.0%, $p = 0.01$). There were no significant differences between both groups in the rates of cardiac arrest (1.5% vs 1.7%, $p = 0.68$), hemodialysis requirement (0.4% vs 0.5%, $p = 0.57$), acute ischemic stroke (1.2% vs 2.1%, $p = 0.05$), acute hemorrhagic stroke (0% vs 0.2%, $p = 0.05$), cardiac tamponade/hemopericardium (0.5% vs 1.1%, $p = 0.06$), vascular complications (0.3% vs 0.6%, $p = 0.22$), respiratory complications (1.4% vs 2.0%, $p = 0.27$), ventricular arrhythmias (2.9% vs 2.8%, $p = 0.89$), complete heart block (10.8% vs 9.1%, $p = 0.09$), and pacemaker implantation (8.9% vs 8.8%, $p = 0.93$). Admissions with prior mediastinal radiation were associated with shorter median (interquartile range) length of hospital stay (3[3] vs 3[4], $p < 0.001$).

The present study is the first to-date to compare outcomes of TAVI among those with previous mediastinal radiation versus none. Our analysis showed that TAVI is increasingly utilized among select patients with prior mediastinal radiation.

We also demonstrated that TAVI among those with previous mediastinal radiation was associated with favorable in-hospital mortality, morbidity and shorter length of hospital stay compared with those without prior mediastinal radiation. With advancement in cancer therapies and improved survival of cancer patients, the prevalence of aortic stenosis among survivors with

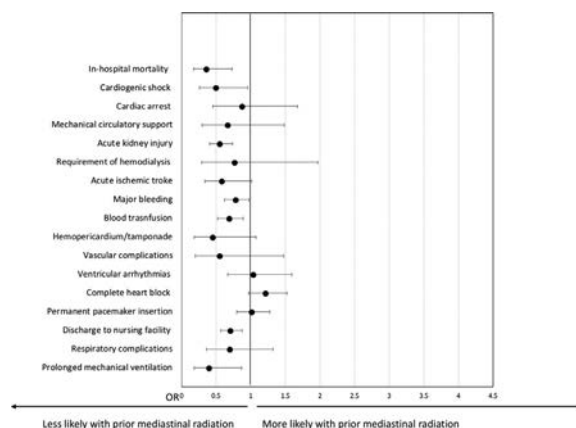


Figure 1. Forrest plot for in-hospital outcomes after matching those with prior mediastinal radiation versus without.