In-Hospital Outcomes of Transcatheter Aortic Valve Implantation in Patients With End-Stage Renal Disease on Dialysis from a Large National Database.

Nirmanmoh Bhatia

Sahil Agrawal MD

Sushan Yang

Kapil Yadav

Manyoo Agarwal MD

See next page for additional authors

Published In/Presented At

Bhatia, N., Agrawal, S., Yang, S., Yadav, K., Agarwal, M., Garg, L., & ... Fredi, J. L. (2017). In-Hospital Outcomes of Transcatheter Aortic Valve Implantation in Patients With End-Stage Renal Disease on Dialysis from a Large National Database. *The American Journal Of Cardiology*, *120*(8), 1355-1358. doi:10.1016/j.amjcard.2017.07.022

In-Hospital Outcomes of Transcatheter Aortic Valve Implantation in Patients With End-Stage Renal Disease on Dialysis from a Large National Database

Nirmanmoh Bhatia, MD[a,*], Sahil Agrawal, MD[b], Sushan Yang, MD[c], Kapil Yadav, MD[d], Manyoo Agarwal, MD[e], Lohit Garg, MD[f], Nayan Agarwal, MD[g], Jamshid Shirani, MD[b], and Joseph L. Fredi, MD[a]

The outcomes of patients with end-stage renal disease on dialysis (chronic kidney disease stage 5 on dialysis [CKD 5D]) who undergo transcatheter aortic valve implantation (TAVI) are not well described due to the exclusion of this group in randomized trials. We analyzed the National Inpatient Sample database and compared clinical characteristics and in-hospital outcomes for patients with CKD 5D versus those without CKD 5D (nondialysis group) who underwent TAVI in 2011 to 2014 in the United States. The study population included 1,708 patients (4%) with CKD 5D and 40,481 patients (96%) without CKD 5D who underwent TAVI. Patients with CKD 5D were younger (75.3 ± 9.9 vs 81.4 ± 8.4 years, p <0.001), more likely to be men (62.8% vs 52%, p <0.001), and less likely to be Caucasian (73.6% vs 87.8%, p <0.001). Patients with CKD 5D were more likely to have congestive heart failure (16% vs 11.7%, p <0.001), diabetes with chronic complications (19% vs 5.4%, p <0.001), hypertension (86.5% vs 79.3%, p <0.001), and peripheral vascular disease (34.5% vs 29.4%, p <0.001), but were less likely to have atrial fibrillation (38.6% vs 44.8%, p <0.001) and chronic pulmonary disease (27.5% vs 33.6%, p <0.001). In-hospital mortality was significantly higher in the dialysis group (8.2% vs 4%; adjusted odds ratio 2.21, 95% confidence interval1.81 to 2.69, p <0.001) after adjusting for age, gender, co-morbidities, and hospital characteristics in a robust multivariate regression model. In conclusion, patients with CKD 5D who undergo TAVI have a higher in-hospital mortality than those without CKD 5D. **(Am J Cardiol 2017;120:1355–1358)**

Chronic kidney disease (CKD) is an independent predictor of procedural complications with percutaneous interventions, and these patients have a significantly higher risk of vascular and procedural complications as well as in-hospital deaths.[1] Whether these differences in outcomes persist with transcatheter aortic valve implantation (TAVI) is unclear. A recent small study found similar outcomes of TAVI in patients with end-stage renal disease (ESRD) compared with historical data of surgical valve replacement (SAVR) in this group.[2] Therefore, we sought to evaluate the in-hospital outcomes of patients with ESRD on dialysis (chronic kidney disease stage 5 on dialysis [CKD 5D]) who underwent TAVI compared with those without CKD 5D using the nationwide inpatient sample database.

Methods

We analyzed data from the Nationwide Inpatient Sample (NIS) for years 2011 through 2014. The NIS contains data on inpatient hospital stays from all states participating in the Healthcare Cost and Utilization Project and provides data on roughly 8 million hospitalizations from about 1,000 hospitals each year.[3] The NIS is designed to approximate a 20% stratified sample of U.S. community hospitals, defined as "all non-federal, short-term, general, and other specialty hospitals, excluding hospital units of institutions," representing more than 95% of the U.S. population. Details of the NIS database have been described in previous publications.[4] Discharge weights provided by the NIS allow extrapolation to calculate expected national hospitalization rates.[3]

We used the International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) codes 35.05 and 35.06 to identify all patients 18 years of age or older who underwent TAVI from 2011 to 2014. Patients were stratified into groups of those on dialysis due to ESRD (CKD 5D), and the remainder constituted the control or the nondialysis group based on methods validated in previous studies from NIS.[4] We chose the principal diagnosis because it is considered the primary reason for hospital admission. Hospitalizations with missing data on patient age, gender, length of stay (LOS), or in-hospital death were excluded from analysis. We also

[a]Division of Cardiovascular Medicine, Vanderbilt University Medical Center, Nashville, Tennessee; [b]Division of Cardiovascular Medicine, St. Luke's University Health Network, Bethlehem, Pennsylvania; [c]Department of Internal Medicine, Vanderbilt University Medical Center, Nashville, Tennessee; [d]Division of Cardiovascular Medicine, Tulane University School of Medicine, New Orleans, Louisiana; [e]Department of Internal Medicine, University of Tennessee Health Science Center, Memphis, Tennessee; [f]Division of Cardiovascular Medicine, Lehigh Valley Health Network, Allentown, Pennsylvania; and [g]Division of Cardiovascular Medicine, University of Florida, Gainesville, Florida. Manuscript received May 10, 2017; revised manuscript received and accepted July 12, 2017.

See page 1358 for disclosure information.

*Corresponding author: Tel: 267-455-3196; fax: +1-615-936-2029.

E-mail addresses: dr.bhatia.n@gmail.com, n.bhatia@vanderbilt.edu (N. Bhatia).

0002-9149/
http://dx.doi.org/10.1016/j.amjcard.2017.07.022

excluded discharges in which patients were admitted and discharged alive on the same day. Lastly, we excluded discharges in which patients were hospitalized from other hospitals to avoid duplication of records. ICD-9-CM codes used to identify patient co-morbidities, in-hospital procedures, and outcomes are listed in Supplementary Table S1, which accompanies this article.

Baseline patient characteristics included demographics (age, gender, and race or ethnicity), the primary expected payer, the median household income for the patient's ZIP code, and other clinically relevant co-morbidities described in Table 1. We also studied hospital level variables, such as teaching status, bed size (small, medium, and large), hospital region (Northeast, Midwest, South, and West), and location (rural or urban).

The primary outcome of the study was all-cause in-hospital mortality. The secondary outcomes were LOS, occurrence of post-TAVI stroke, permanent pacemaker (PPM) implantation, vascular complications, iatrogenic cardiac complications, complications leading to open heart surgery, hemorrhage requiring transfusion, respiratory complications, and a composite of any postprocedure adverse event, which were identified using respective ICD-9-CM codes listed in Supplementary Table S1.

Weighted data were used for all statistical analyses. Categorical variables were expressed as frequency, and continuous variables were expressed as mean ± standard deviation. Pearson chi-square or Fischer's exact tests were used to compare categorical variables, and the Student *t* test was used to compare continuous variables. To determine the associations between CKD 5D status and outcomes of interest, a multivariable logistic regression model was constructed. Variables included in this model were age, gender, primary expected payer, median household income, co-morbidities, and hospital characteristics (region, bed size, location, and teaching status). Race and ethnicity data were missing in ~24% of the study population and were therefore not included in this model. Odds ratios and 95% confidence intervals were used to report the results of the logistic regression. All p values were 2-sided, with a significance threshold of <0.05. Statistical analyses were performed using IBM SPSS Statistics Version 23.0 (IBM Corporation, Armonk, New York).

Results

In January 2011 to December 2014, a total of 8,463 patients corresponding to a national estimate of 42,189 underwent TAVI. Of these, 1,708 (4%) had CKD 5D (dialysis group) and the remainder 40,481 (96%) patients constituted the control group (nondialysis group). Patients in the dialysis group were younger, more likely to be male, and less likely to be Caucasian (Table 1). Hospital characteristics, including bed size, teaching status, region, and urban location, were similar between the 2 groups (Table 1). Patients in the dialysis group had a higher prevalence of congestive heart failure, diabetes with chronic complications, hypertension, and peripheral vascular disease but had a lower prevalence of atrial fibrillation and chronic pulmonary disease (Table 1).

Patients in the dialysis group had a 2.21 times higher incidence of in-hospital death than those not on dialysis after adjusting for age, gender, co-morbidities, and hospital characteristics in a robust multivariate regression model (Table 2).

Table 1
Baseline demographics, hospital characteristics and co-morbidities of patients who underwent transcatheter aortic valve implantation in the United States from 2011–14

Variable	Dialysis		p value
	No (N = 40,481)	Yes (N = 1,708)	
Age (Mean± SD)	81.4 ± 8.4	75.3 ± 9.9	**<0.001**
Male	21,042 (52%)	1073 (62.8%)	**<0.001**
Female	19,439 (48%)	635 (37.2%)	**<0.001**
White*	33,060 (87.8%)	1168 (73.6%)	**<0.001**
Black	1287 (3.4%)	240 (15.1%)	**<0.001**
Hispanic	1396 (3.7%)	75 (4.7%)	**<0.05**
Asian or Pacific Islander	400 (1.0%)	30 (1.9%)	**<0.01**
Native American	70 (0.2%)	10 (0.6%)	**<0.01**
Other	1452 (3.9%)	65 (4.1%)	0.648
Non-Elective Hospitalization	9,451 (23.4%)	664 (38.9%)	**<0.001**
Primary expected payer			0.460
Medicare	36,453 (90.2%)	1,513 (89.1%)	
Medicaid	404 (1%)	45 (2.7%)	
Private insurance	2,860 (7.1%)	100 (5.9%)	
Self-pay	175 (0.4%)	15 (0.9%)	
No charge	15 (0.01%)	0 (0%)	
Other	519 (1.3%)	25 (1.5%)	
Median household income (percentile)			**<0.001**
0 to 25th	8177 (20.6%)	440 (25.8%)	
26th to 50th	9,871 (24.8%)	429 (25.1%)	
51st to 75th	10,221 (25.7%)	439 (25.7%)	
76th to 100th	11,490 (28.9%)	400 (23.4%)	
Bed size†			0.184
Small	1,925 (4.8%)	70 (4.1%)	
Medium	6,462 (16%)	325 (19%)	
Large	32,095 (79.3%)	1,313 (76.9%)	
Urban Location	40,186 (99.3%)	1698 (99.4%)	0.58
Teaching Hospital	36,039 (89.0%)	1,533 (89.8%)	0.304
Region			0.849
Northeast	10,432 (25.8%)	435 (25.5%)	
Midwest	8,975 (22.2%)	339 (19.8%)	
South	13,763 (34%)	684 (40.0%)	
West	7,311 (18.1%)	250 (14.6%)	
Transfemoral TAVI	32,412 (80.1%)	1,353 (79.2%)	0.388
Atrial Fibrillation‡	18,155 (44.8%)	660 (38.6%)	**<0.001**
Coronary Artery Disease‡	2971 (7.3%)	105 (6.1%)	0.07
Heart Failure‡	4,720 (11.7%)	274 (16%)	**<0.001**
Chronic Pulmonary Disease‡	13,601 (33.6%)	470 (27.5%)	**<0.001**
Uncomplicated Diabetes ‡	11,559 (28.6%)	494 (28.9%)	0.744
Diabetes with Chronic Complications‡	2,171 (5.4%)	535 (19%)	**<0.001**
Hypertension‡	32,094 (79.3%)	1,478 (86.5%)	**<0.001**
Obesity‡	5,699 (14.1%)	220 (12.9%)	0.167
Peripheral Vascular Disease‡	11,898 (29.4%)	589 (34.5%)	**<0.001**

TAVI = Trans-catheter aortic valve implantation.

* Data for Race was available in 39,253 patients (37,665 not on dialysis and 1,588 on dialysis).

† Number of beds categories is specific to hospital location and teaching status, available at *http://www.hcup-us.ahrq.gov/db/vars/hosp_bedsize/nisnote.jsp*.

‡ As pre-defined in the database or extracted from the database using International Classification of Diseases, Ninth Edition, Clinical Modification Diagnosis or Clinical Classification Software codes (Supplementary Table S1).

Table 2
Outcomes of patients who underwent transcatheter aortic valve implantation in the United States from 2011-14

Outcomes	Dialysis		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
	No (N = 40,481)	Yes (N = 1,708)		
All-cause in-hospital mortality	1628 (4%)	140 (8.2%)	2.13 (1.78–2.55), p < 0.001	**2.21 (1.81–2.69), p < 0.001**
Post-TAVI stroke	578 (1.4%)	10 (0.6%)	0.41 (0.22–0.76), p < 0.01	**0.40 (0.20–0.81), p < 0.05**
Permanent pacemaker implantation	4074 (10.1%)	215 (12.6%)	1.29 (1.11–1.49), p < 0.01	**1.37(1.17–1.59), p < 0.001**
Vascular complications	2781 (6.9%)	145 (8.5%)	1.26 (1.06–1.50), p < 0.05	**1.36 (1.13–1.63), p < 0.01**
Iatrogenic cardiac complications	3786 (9.4%)	170 (10%)	1.07 (0.91–1.26), p = 0.41	**1.24 (1.04–1.47), p < 0.05**
Open heart surgery	675 (1.7%)	45 (2.6%)	1.60 (1.18–2.17), p < 0.01	1.02 (0.74–1.42), p = 0.9
Any respiratory complication	5445 (13.5%)	265 (15.5%)	1.18 (1.03–1.35), p < 0.05	0.95 (0.82–1.1), p = 0.5
Hemorrhage requiring transfusion	4657 (11.5%)	299 (17.5%)	1.63 (1.43–1.86), p < 0.001	**2.16 (1.87–2.48), p < 0.001**
Any post-TAVI adverse event	16,573 (40.9%)	879 (51.5%)	1.53 (1.39–1.69), p < 0.001	**1.61 (1.45–1.79), p < 0.001**
Length of stay in days (mean ± SD)	7.88 ± 7.01	12.46. ± 11.53	**p < 0.001**	

CI = Confidence interval; OR = Odds ratio; TAVI = Trans-catheter aortic valve implantation.

Post-TAVI stroke was significantly lower in the dialysis group, but PPM implantation, vascular complications, iatrogenic cardiac complications, hemorrhage requiring surgery, and any post-TAVI adverse event were significantly higher in the dialysis group after adjusting for confounders (Table 2).

Discussion

In this large, multicenter, real-world data, we were able to demonstrate that patients with ESRD on dialysis (CKD 5D) who undergo TAVI have a higher in-hospital mortality and a higher risk of post-TAVI adverse events, including PPM placement, vascular complications, iatrogenic cardiac complications, and hemorrhage requiring transfusions than those not on dialysis. These data suggest that the decision to perform TAVI in patients with CKD 5D should be individualized, carefully assessing the risk and benefit with meticulous pre- and intraprocedural planning and postprocedural care to avoid adverse events in this high-risk subgroup. The in-hospital mortality of the dialysis group at 8.2% is high; however, given that over 50% of untreated patients with severe AS die at 5 years[5] and operative mortality for SAVR in patients with ESRD with severe AS approaches 20%,[2] TAVI may still be the best therapeutic option for severe AS in patients with CKD 5D.

Patients with CKD 5D who underwent TAVI were younger. This finding is consistent with previous data suggesting that patients with ESRD not only develop AS earlier but have a faster progression to severe AS, attributed to the underlying metabolic abnormalities (calcium and phosphate metabolism).[6] The dialysis group had a significantly higher prevalence of co-morbidities such as hypertension, diabetes with complications, peripheral vascular disease, and congestive heart failure compared with patients without ESRD. This finding is expected as many co-morbidities are independent risk factors for developing CKD and ESRD.[7]

We observed a higher rate of post-TAVI PPM implantation in the dialysis group. This finding may be attributed to a higher prevalence of conduction system abnormalities in patients with ESRD,[8] which can predict post-TAVI PPM implantation.[9] Some studies have also shown that a higher calcium score (more frequent and severe in patients with ESRD) may predict post-TAVI PPM implantation[10]; however, this remains controversial.[11] Given the nature of the database, we could not obtain details on preexisting conduction system abnormalities, calcium scores, or types of prosthesis (self-expanding vs balloon expandable). Patients with ESRD are known to have a higher incidence of bleeding abnormalities, likely due to abnormal platelet function.[12] This can predispose this subgroup to a high incidence of bleeding and vascular complications after invasive procedures such as percutaneous coronary interventions.[13] Therefore, our results reporting a higher rate of vascular complications in this group are expected.

The higher LOS observed in the dialysis group (Table 2) could be due to the higher incidence of post-TAVI complications such as vascular complications, PPM implantations, iatrogenic cardiac complications, and hemorrhage requiring transfusion. Previous studies have observed that patients who undergo PPM implantations after valve surgeries have a higher hospital LOS. Similarly, vascular complications after other percutaneous procedures such as PCI also prolong LOS.[14] As such, ESRD itself is a predictor of longer LOS.[15]

Our findings of a higher rate of stroke may be reflective of the very small number of events in the study population. The all-cause in-hospital mortality after TAVI was more than double (8.2% vs 4%) in patients with CKD 5D versus other patients. This may appear high, however, given the much higher mortality (over 50% at years) in untreated patients with severe aortic stenosis (AS) and the much higher operative mortality (20%) in this subgroup, suggesting that TAVI may not be withheld in patients with CKD 5D.[2,5] Other smaller studies have compared SAVR with TAVI in patients with ESRD and found similar results.[2] Taken together, these results support the use of TAVI in patients with CKD 5D.

Despite using a large, real-world, multicenter database, our study has several limitations. The accuracy of certain variables may not be consistent across all hospitals due to differences in hospital coding practices. Because NIS is a discharge level database, it is unable to distinguish among multiple hospitalizations of the same patient. However, because we only included patients who underwent TAVI as a primary procedure, it is unlikely that rehospitalizations of the same patients are captured. Also, data outcomes during repeat hospitalizations are not available with the use of this database. NIS precludes

assessment of patient presentation, details of TAVI procedure such as the type of valve used, preexisting conduction system abnormalities, and society of thoracic surgeons (STS) risk scores, which may impact outcomes. Lastly, despite utilizing a robust multivariable regression model, some residual unmeasured confounders impacting outcomes may remain. However, these are the largest real-world data examining a nationally representative patient sample over 4 years and are likely to overcome most of these limitations, and our findings are very likely reflective of true real-world in-hospital outcomes of patients with CKD 5D who undergo TAVI.

In conclusion, using a large, real-world, multicenter database, we demonstrated that patients with CKD 5D who undergo TAVI have a higher in-hospital mortality and adverse events than those without CKD 5D. These data suggest that the decision to perform TAVI in patients with CKD 5D should be individualized. Given the much higher mortality of untreated AS as well as SAVR in this population, TAVI may be the most feasible therapy in this scenario.

Disclosures

The authors have no conflicts of interest to disclose.

Supplementary Data

Supplementary data associated with this article can be found, in the online version, http://dx.doi.org/10.1016/j.amjcard.2017.07.022.

1. Kim SM, Tripathy DR, Park SW, Park B, Son JW, Lee JW, Youn YJ, Ahn SG, Ahn MS, Kim JY, Yoo BS, Lee SH, Yoon J. Impact of chronic kidney disease on clinical outcomes in diabetic patients undergoing percutaneous coronary intervention in the era of newer-generation drug-eluting stents. *Korean Circ J* 2017;47:222–230.
2. Szerlip M, Kim RJ, Adeniyi T, Thourani V, Babaliaros V, Bavaria J, Herrmann HC, Anwaruddin S, Makkar R, Chakravarty T, Rovin J, Creighton D, Miller DC, Baio K, Walsh E, Katinic J, Letterer R, Trautman L, Herbert M, Farkas R, Rudolph J, Brown D, Holper EM, Mack M. The outcomes of transcatheter aortic valve replacement in a cohort of patients with end-stage renal disease. *Catheter Cardiovasc Interv* 2016;87:1314–1321.
3. Healthcare Cost and Utilization Project (HCUP). Overview of the National (Nationwide) Inpatient Sample (NIS). Agency for Healthcare Research and Quality, Rockville, MD. Available at: http://www.hcup-us.ahrq.gov/nisoverview.jsp. Accessed on April 1, 2017.
4. Bhatia N, Agrawal S, Garg A, Mohananey D, Sharma A, Agarwal M, Garg L, Agrawal N, Singh A, Nanda S, Shirani J. Trends and outcomes of infective endocarditis in patients on dialysis. *Clin Cardiol* 2017;doi:10.1002/clc.22688.
5. Ross J Jr, Braunwald E. Aortic stenosis. *Circulation* 1968;38:61–67.
6. Urena P, Malergue MC, Goldfarb B, Prieur P, Guedon-Rapoud C, Petrover M. Evolutive aortic stenosis in hemodialysis patients: analysis of risk factors. *Nephrologie* 1999;20:217–225.
7. Kazancioglu R. Risk factors for chronic kidney disease: an update. *Kidney Int Suppl (2011)* 2013;3:368–371.
8. Kambur TR, Das M, Agarwal R. The natural history of symptomatic cardiac conduction-system disease in end-stage renal disease. *Nephrol Dial Transplant* 2016;31:1973–1975.
9. Nazif TM, Dizon JM, Hahn RT, Xu K, Babaliaros V, Douglas PS, El-Chami MF, Herrmann HC, Mack M, Makkar RR, Miller DC, Pichard A, Tuzcu EM, Szeto WY, Webb JG, Moses JW, Smith CR, Williams MR, Leon MB, Kodali SK, Office PP. Predictors and clinical outcomes of permanent pacemaker implantation after transcatheter aortic valve replacement: the PARTNER (Placement of AoRtic TraNscathetER Valves) trial and registry. *JACC Cardiovasc Interv* 2015;8:60–69.
10. Latsios G, Gerckens U, Buellesfeld L, Mueller R, John D, Yuecel S, Syring J, Sauren B, Grube E. "Device landing zone" calcification, assessed by MSCT, as a predictive factor for pacemaker implantation after TAVI. *Catheter Cardiovasc Interv* 2010;76:431–439.
11. Al-Azzam F, Greason KL, Krittanawong C, Williamson EE, McLeod CJ, King KS, Mathew V. The influence of native aortic valve calcium and transcatheter valve oversize on the need for pacemaker implantation after transcatheter aortic valve insertion. *J Thorac Cardiovasc Surg* 2017;153:1056–1062, e1051.
12. Kaw D, Malhotra D. Platelet dysfunction and end-stage renal disease. *Semin Dial* 2006;19:317–322.
13. Attallah N, Yassine L, Fisher K, Yee J. Risk of bleeding and restenosis among chronic kidney disease patients undergoing percutaneous coronary intervention. *Clin Nephrol* 2005;64:412–418.
14. Isik T, Ayhan E, Uluganyan M, Gunaydin ZY, Uyarel H. Predictors of prolonged in-hospital stay after primary percutaneous coronary intervention for ST-elevation myocardial infarction. *Angiology* 2016;67:756–761.
15. Apel M, Maia VP, Zeidan M, Schinkoethe C, Wolf G, Reinhart K, Sakr Y. End-stage renal disease and outcome in a surgical intensive care unit. *Crit Care* 2013;17:R298.