Impact of Dialysis on the Prognosis of Patients Undergoing Transcatheter Aortic Valve Implantation

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End-stage renal disease (ESRD) affects approximately 2% to 4% of patients with severe aortic stenosis. It is because these patients have been excluded from clinical trials, the impact of transcatheter aortic valve implantation (TAVI) in this patient group has not been thoroughly investigated. Between April 2008 and March 2015, 2,000 patients (dialysis group, n = 56 [2.8%]) were consecutively enrolled when diagnosed with severe aortic stenosis and eligible to undergo TAVI. Procedural and longer-term outcomes were analyzed and adjusted for differences in baseline characteristics. Patients on dialysis had a higher periprocedural mortality (10.7% vs 1.7%; adjusted odds ratio [adjOR] 5.65, 95% confidence interval [CI] 1.91 to 16.67; p = 0.002) and a lower Valve Academic Research Consortium (VARC)-II (VARC) defined device success (adjOR 0.34, 95% CI 0.15 to 0.79; p = 0.012). At 30 days, there was an increased rate of all-cause mortality (21.4 vs 4.8%; adjOR 4.90, 95% CI 1.96 to 12.26; p = 0.001), cardiovascular (adjOR 3.67, 95% CI 1.43 to 9.41; p = 0.007) and noncardiovascular mortality (adjOR 6.28, 95% CI 1.36 to 9.41; p = 0.019), myocardial infarction (adjOR 9.39, 95% CI 1.84 to 48.03; p = 0.007), bleeding (adjOR 2.48, 95% CI 1.06 to 5.83; p = 0.036) as well as the VARC-II defined early safety combined end point (adjOR 2.97, 95% CI 1.28 to 6.90; p = 0.012) associated with dialysis. Dialysis was associated with poor survival at one (57.1% vs 84.2%) and 3 years (26.8% vs 66.9%) with or without the consideration of the first 72 hours (p < 0.001; adjusted p < 0.001). Although, in the multivariable regression analysis, reduced ejection fraction, peripheral arterial disease, pulmonary hypertension (PH), frailty and dialysis were associated with 1-year mortality, only PH (> 60 mm Hg) remained significant in an analysis restricted to the dialysis patients (adjusted hazard ratio 2.68; 95% CI 1.18 to 5.88; p = 0.018). PH had a sensitivity of 45.8%, a specificity of 81.3%, and a positive predictive value of 64.7%. In conclusion, dialysis is an independent predictor of mortality in patients who underwent TAVI. Long-term mortality in dialysis patients appears to be largely determined by the kidney disease and/or dialysis itself whereas VARC-II defined complications are largely unaffected. An increased short-term mortality still calls for (pre-) procedural optimization. **(Am J Cardiol 2019;123:315−322)**

The prevalence of chronic kidney disease (CKD) in patients with aortic stenosis (AS) ranges from less than 10% to more than 50% depending on the definition of "CKD" and the population studied, whereas end-stage renal disease (ESRD) affects approximately 2% to 4% of patients who underwent treatment for AS.[1−5] The prevalence of AS is higher in patients with ESRD undergoing maintenance dialysis than in the general population due to the calcification of the aortic valve associated with secondary hyperparathyroidism.[6] Furthermore, aortic valve calcification occurs 10 to 20 years earlier and progresses more rapidly in patients with ESRD compared with the general population.[7] A number of analyses reported on the impact of CKD on clinical outcomes.[8−12] A meta-analysis by Gargiulo *et al* investigated the impact of moderate and severe preoperative CKD on clinical outcomes after TAVI and showed that they significantly worsened the TAVI prognosis by increasing the early and one-year all-cause mortality and significantly increased the risk of early stroke, acute kidney injury and the need for dialysis.[9] In the United States, Kobrin *et al* undertook an analysis of all Medicare fee-for-service patients and showed that, compared with nondialysis patients, transcatheter aortic valve implantation (TAVI) patients on dialysis had a significantly higher rate of mortality at 30 days and 1 year.[10] In clinical trials setting, the Placement of Aortic Transcatheter Valves trial was analyzed to confirm that preoperative severe renal dysfunction is a significant predictor for 1-year mortality.[11] All

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these data are supported by the results of the Edwards SAPIEN Aortic Bioprosthesis European Outcome Registry, which showed that CKD is considered to be one of the strongest independent predictors of 1-year mortality following TAVI.[12] Although multicenter registries have advantages in their representativeness of clinical practice, their interpretation is hampered by site-specific approaches to TAVI including very experienced, but also quite unexperienced sites, resulting in a potential bias for the interpretation of data. As we are one of the largest centers for TAVI in Germany with a consecutive documentation of 2,000 patients receiving TAVI since April 2008, we aimed to explore differences in procedural and longer-term outcomes in dialysis patients compared with patients not undergoing dialysis under the assumption that single-center are less prone to disease unrelated bias.

Methods

The prospective TAVIK registry documented patients who underwent TAVI between April 2008 and March 2015 with the TAVIK team Karlsruhe, Germany.[13,14] Follow-up was conducted at outpatient visits or by telephone interview. The registry received approval from the responsible local ethics committee in Stuttgart and all patients provided written informed consent.

Two thousand patients were consecutively enrolled if they were diagnosed with severe AS and had been assigned to undergo TAVI by the Karlsruhe Heart Team, which included cardiologists and cardiac surgeons. The 2 principle criteria used to determine suitability for TAVI was a logistic EuroSCORE (ES) of ≥ 15 or age ≥ 75 years with a logistic ES of < 15. The presence of additional co-morbidities not considered in the ES, such as malignancy (but with a life expectancy greater than 1 year), liver cirrhosis, severe pulmonary disease with long-term provision of oxygen, frailty, and porcelain aorta were also evaluated. Patients who were unwilling to undergo surgical aortic valve replacement (SAVR) were also considered for TAVI. An unsuitable native aortic valve annulus was considered a contraindication for TAVI, as was a life expectancy less than 1 year or quality of life that was seriously affected by co-morbidities (such as dementia with disability, a previous major stroke, uncontrolled congestive heart failure, or cardiogenic shock).

Before the TAVI procedure, patients were evaluated using angiographic computed tomography (CT), transesophageal echocardiography and coronary angiography. The most appropriate transcatheter heart valve (THV) size was determined by measuring the diameter of the native annulus using CT combined with transesophageal echocardiography in the long-axis view at the level of leaflet insertion. The THVs implanted included the balloon-expandable SAPIEN, SAPIEN XT or SAPIEN 3 (Edwards Lifesciences); and the self-expanding CoreValve (Medtronic), ACURATE (Symetis), Portico Valve (St Jude Medical), and Jena Valve (Jena Valve Technology).

Patient characteristics were documented at baseline and details of the TAVI procedure recorded. These included access route, type of THV implanted and periprocedural complications. Device success was defined according to the Valve Academic Research Consortium (VARC)-II criteria[15] as no procedural mortality, correct positioning of a single valve, a mean valve gradient of < 20 mm Hg, and no moderate or severe aortic valve regurgitation. Early safety was also determined according to VARC-II parameters at 30 days. Patients were followed for up to 3 years post-TAVI.

Patients were divided into 2 cohorts: nondialysis group (n = 1,944) and the dialysis group (n = 56). Categorical variables were compared using the chi-square test of the Fisher's exact test, whereas continuous variables were compared using the student's *t* test, as appropriate. Data adjustments were made using the inverse probability of treatment weighting building a regression analysis model [16] using age, gender, ejection fraction (EF), coronary artery disease (CAD), previous coronary bypass graft, peripheral arterial disease, NYHA class IV and then using the calculated predicted probability as a weighting factor in the subsequent analysis. Cumulative mortality was assessed using Kaplan-Meier estimates. Mortality predictors were determined using univariate and multivariate Cox regression analyses. Data analysis was conducted using SPSS version 20 (IBM, Chicago, Illinois).

Results

Between April 2008 and March 2015, 2,000 consecutive patients with severe symptomatic AS underwent TAVI at our single centre in Karlsruhe, Germany. Of these patients, 56 patients (2.8%) were on dialysis before baseline.

Patients in the dialysis group were significantly younger than patients in the nondialysis group (76.6 vs 81.9 years) and comprised significantly more male subjects (71.4% vs 44.9%) (Table 1). Patients in the dialysis group also had a more significant cardiac history than patients in the nondialysis group such as a lower EF (53.1% vs 56.9%), more CAD (83.9% vs 60.2%), more previous coronary artery bypass graft (33.9% vs 14.6%), a higher symptom status (NYHA IV 17.6 vs 7.0), and showed significantly more peripheral artery disease (PAD) compared with patients in the nondialysis group (35.7% vs 15.3%).

More patients in both the dialysis and nondialysis groups received TAVI through the transfemoral (TF) access route (53.6% and 65.1%, respectively) versus the transapical (TA) route (Table 1). Although more patients received a balloon expandable valve (85.7% and 76.5% of patients in the dialysis and nondialysis groups, respectively) than a self-expandable valve, difference was not statistically significant.

The 72-hour procedural mortality was approximately 6-fold higher in the dialysis group than the nondialysis group (10.7% vs 1.7%; adjusted odds ratio [adjOR] 5.65, 95% confidence interval [CI] 1.91 to 16.67; p = 0.002) (Table 2). Patients dying within the first 72 hours had a very high ES I (5 of 6 [83.3%] had an ES of more than 50%), whereas the rate was much lower in those that survived the procedure (6 of 50 [12.0%] had an ES of more than 50%; p = 0.013). Procedural complications were valve embolizations into the left ventricle (2 patients, leading to surgical conversion), resuscitation (1 patients because of low output), postinterventional bleedings (2 patients, leadings to rethoracotomy),

Table 1
Patient demographics, risk factors, and procedural characteristics

Variable	Dialysis		p Value
	No (n = 1,944)	Yes (n = 56)	
Age (years)	81.9 ± 5.4	76.6 ± 6.4	< 0.001
Men	44.9%	71.4%	< 0.001
Ejection fraction	56.9 ± 13.5	53.1 ± 13.3	0.034
Coronary artery disease	60.2%	83.9%	< 0.001
Previous myocardial infarction (< 90 d)	11.1%	17.9%	0.129
Previous percutaneous coronary intervention	19.9%	26.8%	0.234
Previous coronary artery bypass graft	14.6%	33.9%	< 0.001
Mitral valve disease (> IIo)	12.9%	16.1%	0.543
Previous valve surgery	3.3%	1.8%	1.0
Previous pacemaker	12.4%	9.1%	1.0
Unstable angina pectoris	0.3%	0%	1.0
New York Heart Association IV	7.0%	17.9%	0.006
Peripheral artery disease	15.3%	35.7%	< 0.001
Carotid stenosis	18.3%	23.2%	0.381
Major neurological deficits	10.0%	8.9%	1.0
Chronic obstructive pulmonary disease	11.5%	19.6%	0.087
Pulmonary hypertension (> 60 mm Hg)	20.4%	30.4%	0.092
Diabetes mellitus	26.9%	37.5%	0.093
Frailty	33.0%	44.6%	0.084
Porcelain aorta	6.4%	7.1%	0.779
Critical perioperative situation	1.4%	1.8%	0.551
Emergency case	1.4%	1.8%	0.551
Log EuroSCORE I (%)	20.7 ± 14.8%	32.8 ± 21.1%	< 0.001
Access route			0.007
Transfemoral	65.1%	53.6%	
Transapical	34.9%	46.4%	
Valve type			0.147
Balloon expandable valve (Sapien, Sapien XT and Sapien 3)	76.5%	85.7%	
Self-expandable valve (CoreValve, Symetis Accurate Neo, Portico and Jena Valve)	23.5%	14.3%	

Table 2
Composite end points

Variable	Dialysis		Unadjusted OR (95% CI)	Unadjusted p value	Adjusted OR‡ (95% CI)	Adjusted p value‡
	No (n = 1,944)	Yes (n = 56)				
Device success*	89.9%	75.0%	0.34 (0.18−0.63)	< 0.001	0.34 (0.15−0.79)	0.012
Procedural mortality (72-h)	1.7%	10.7%	6.74 (2.71−16.78)	0.001	5.65 (1.91−16.67)	0.002
Aortic valve mean gradient ≥ 20 mm Hg	3.0%	1.8%	0.58 (0.08−4.27)	1.0	0.51 (0.07−3.83)	0.513
Incorrect positioning	0.6%	1.8%	3.20 (0.41−25.18)	0.289	1.96 (0.24−15.76)	0.528
Second valve	3.0%	10.7%	3.83 (1.58−9.30)	0.008	4.7 (1.46−15.14)	0.010
Moderate/severe regurgitation	1.3%	0%	-	1.0	-	-
Early (30-day) safety†	13.2%	33.9%	3.39 (1.92−5.98)	< 0.001	2.97 (1.28−6.90)	0.012
All-cause mortality	4.8%	21.4%	5.37 (2.74−10.50)	< 0.001	4.90 (1.96−2.26)	0.001
All Stroke	5.2%	5.4%	1.02 (0.31−3.33)	1.0	0.41 (0.1−1.68)	0.219
Life-threatening	4.2%	10.7%	2.76 (1.15−6.62)	0.032	1.16 (0.35−3.76)	0.811
Major vascular complications	3.1%	7.1%	2.38 (0.83−6.78)	0.106	3.81 (0.85−7.02)	0.080
Coronary artery obstruction requiring intervention	0.5%	1.8%	3.52 (0.44−27.95)	0.269	1.41 (0.18−11.50)	0.744
Valve-related dysfunction requiring repeat procedure	0%	0%	-	-	-	-

* Defined as absence of procedural mortality AND correct positioning into proper anatomical location AND single prosthetic heart valve AND aortic valve gradient < 20 mm Hg AND no moderate/severe prosthetic valve regurgitation.

† Includes all-cause mortality, all strokes, life-threatening bleeding, coronary artery obstruction requiring intervention, major vascular complication, valve-related dysfunction requiring repeat procedure (balloon aortic valvuloplasty [BAV], TAVI or SAVR) but not AKI stage 2 or 3 (including renal replacement therapy).

‡ Adjustment on significant different basic parameters (age, gender, ejection fraction, coronary artery disease, previous coronary artery bypass graft, peripheral arterial disease, New York Heart Association IV) and transapical/transfemoral.

coronary occlusion (1 patients, left coronary artery receiving PCI) and second valve because of aortic insufficiency (1 patient).

The early (30-day) safety, defined as all-cause mortality, all strokes, life-threatening bleeding, and/or valve-related dysfunction requiring a repeat procedure (balloon aortic valvuloplasty, TAVI of SAVR), was significantly better in the nondialysis group versus the dialysis group (13.2% vs 33.9%; adjOR 2.97, 95% CI 1.28 to 6.90).

Successful implantation of the valve−defined as the absence of procedural mortality, correct positioning into the proper anatomical location, single prosthetic heart valve, aortic valve gradient <20 mm Hg and no moderate or severe prosthetic valve regurgitation−was significantly lower in patients in the dialysis group (75.0%) versus patients in the nondialysis group (89.9%; adjOR 0.34, 95% CI 0.15 to 0.79).

At 30-days, total mortality (adjOR 4.90, 95% CI 1.96 to 12.26), cardiovascular mortality (adjOR 3.67, 95% CI 1.43 to 9.41), noncardiovascular mortality (adjOR 6.28, 95% CI 1.36 to 9.41), myocardial infarction (adjOR 9.39, 95% CI 1.84 to 48.03) as well as the VARC-II defined early safety (adjOR 2.97, 95% CI 1.28 to 6.90) was associated with dialysis (Table 3). Bleeding complications were also more frequently observed in dialysis patients (37.5% vs 18.6%; adjOR 2.84, 95% CI 1.06 to 5.83), and because there were nominal differences in life-threatening bleeding and major bleeding, only minor bleeding complications were borderline significant (adjOR 2.84, 95% CI 0.95 to 8.49).

There were no significant differences between patients in the dialysis group and nondialysis groups for stroke (5.4% vs 5.2%), disabling stroke (1.8% vs 2.3%), nondisabling stroke (3.6% vs 3.0%), vascular complications (8.9% vs 9.2%), major vascular complications (7.1% vs 3.1%), minor vascular complications (1.8% vs 6.1%), new permanent pacemaker implantation (21.7% vs 15.0%) and moderate or severe paravalvular leaks (0% vs 1.4%), respectively.

The long-term survival of patients in the dialysis groups was lower than that of patients in the nondialysis group (78.6% vs 95.2% 30-day survival, 57.1% vs 84.2% 1-year survival, 51.8% vs 76.3% 2-year survival, and 26.8% vs 66.9% 3-year survival, respectively (unadjusted and adjusted $p<0.001$; Figure 1). A landmark analysis shows that the significantly higher death rate in patients on dialysis was independent from the significant difference in periprocedural (72-hour) mortality (adjusted $p<0.001$ over 3 years) (Figure 2).

The univariate and multivariate regression analysis for all study subjects (n = 2,000) shows that beyond classical factors such as EF, PAD, pulmonary hypertension, and overall frailty, dialysis is an independent predictors of 1-year mortality (hazard ratio [HR] 2.5,95% CI 1.63 to 3.84) (Table 4). Focussing on patients in the dialysis group, the multivariate regression analysis shows that pulmonary hypertension (>60 mm Hg) is associated with an increased 1-year mortality (HR 2.63, 95% CI 1.18 to 5.88, $p=0.018$). Pulmonary hypertension had a sensitivity of 45.8%, a specificity of 81.3%, a positive predictive value of 64.7%, and a negative predictive value of 66.7% ($p=0.041$).

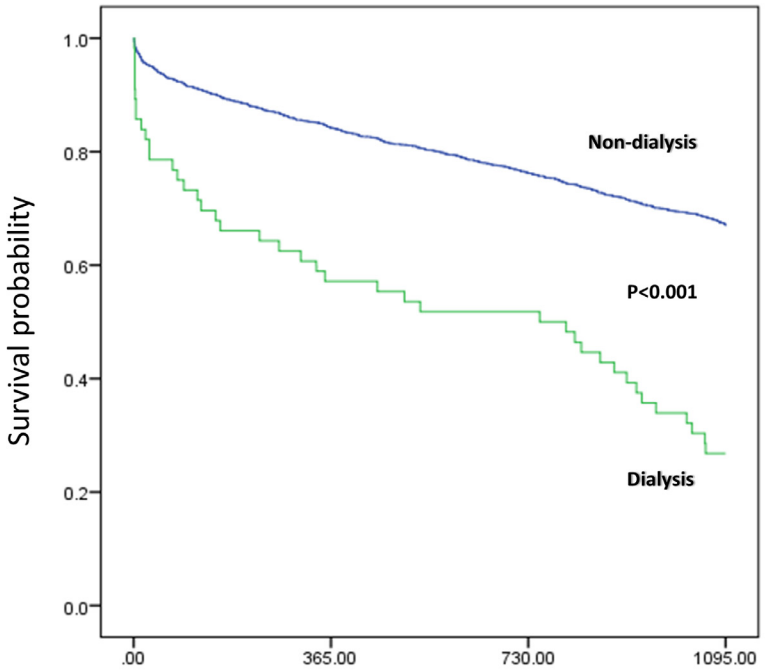
Discussion

ESRD in patients with severe AS affects approximately 2% to 4% of patients. As patients with ESRD undergoing dialysis have been excluded from clinical trials on the outcomes of transcatheter aortic valve replacement we sought to explore differences in procedural and longer-term risks in patients with or without dialysis at baseline. We found that dialysis was associated with a very poor longer-term

Table 3
Valve Academic Research Consortium (VARC) II complications: 30 days

Variable	Dialysis		Unadjusted OR (95% CI)	Unadjusted p value	Adjusted OR* (95% CI)	Adjusted p value*
	No (n = 1,944)	Yes (n = 56)				
Total mortality	4.8%	21.4%	5.37 (2.74−10.50)	<0.001	4.90 (1.96−12.26)	0.001
Cardiovascular death	3.3%	17.9%	6.28 (3.04−13.00)	<0.001	3.67 (1.43−9.41)	0.007
Noncardiovascular death	1.5%	3.6%	2.45 (0.57−10.51)	0.215	6.28 (1.36−29.09)	0.019
Myocardial infarction	1.1%	5.4%	4.95 (1.44−17.03)	0.031	9.39 (1.84−48.03)	0.007
Stroke	5.2%	5.4%	1.02 (0.31−3.33)	1.0	0.41 (0.1−1.68)	0.219
Disabling	2.3%	1.8%	0.79 (0.11−5.80)	1.0	0.18 (0.02−1.38)	0.100
Nondisabling	3.0%	3.6%	1.20 (0.29−5.06)	0.684	0.60 (0.11−3.16)	0.542
Bleeding	18.6%	37.5%	2.62 (1.51−4.56)	0.001	2.48 (1.06−5.83)	0.036
Life-threatening	4.2%	10.7%	2.76 (1.15−6.62)	0.032	1.16 (0.35−3.76)	0.811
Major	5.1%	7.1%	1.42 (0.50−4.0)	0.532	1.81 (0.49−6.67)	0.374
Minor	9.3%	19.6%	2.38 (1.21−4.68)	0.018	2.84 (0.95−8.49)	0.061
Vascular complications	9.2%	8.9%	0.97 (0.38−2.45)	1.0	1.95 (0.57−6.68)	0.287
Major	3.1%	7.1%	2.38 (0.83−6.78)	0.106	3.81 (0.57−6.68)	0.080
Minor	6.1%	1.8%	0.28 (0.04−2.05)	0.254	0.91 (0.12−6.76)	0.924
New permanent pacemaker implantation	15.0%	21.7%	1.58 (0.77−3.22)	0.211	2.42 (0.92−6.41)	0.075
Moderate/severe regurgitation	1.4%	0%	−	1.0	−	−

* Adjustment on significant different basic parameters (age, gender, ejection fraction, coronary artery disease, previous coronary artery bypass graft, peripheral arterial disease, New York heart Association IV) and transapical/transfemoral access.



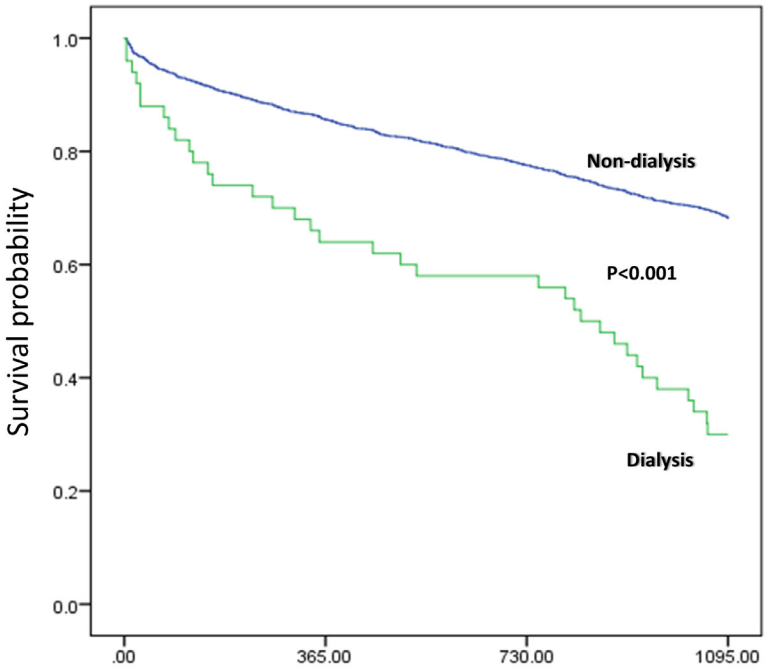
Pts at risk	2000	1680	1511	1320
No-dialysis	1944	1638	1483	1305
Dialysis	56	32	29	15
Survival (%)				
No-dialysis	95.2	84.2	76.3	66.9
Dialysis	78.6	57.1	51.8	26.8

Figure 1. Survival post TAVI.

(3-year) survival (26.5%) at comparable VARC-II defined complications. A landmark analysis of the data suggests that this is related to short-term procedural mortality as well as to the outcomes of patients being alive after 72 hours. We only found pulmonary hypertension to be associated with an adverse effect on survival after 1 year in a multivariable analysis, but it had a low specificity and sensitivity.

Dialysis was associated with a very poor longer-term (3-year) survival (26.5%). This is substantially lower than in an Italian report of 27,642 patients of all ages being on dialysis and followed for 5 years (44.4% survival)[17] and in a report considering only elderly patients aged over 70 years where the survival rate was 25.5% after 4 years.[18] It is also lower than in long-term TAVI trials in patients with or without ESRD such as Placement of Aortic Transcatheter Valves I where the survival rate after was 32.2% at 5 years.[19] It implies that it may not be the dialysis alone and the concurrent morbidity but also the AS-related hazards driving the long-term prognosis in our population of dialysis patients. Nonetheless TAVI performance is worthwhile in dialysis patients as data from the CURRENT AS registry suggests that early AVR (TAVI or SAVR) was associated with a reduced mortality at 5 years (60.6 vs 75.5%; adjHR 0.62; 95% CI 0.43 to 0.90; p = 0.01).[20]

To separate the TAVI related from the disease-related hazard, we performed a landmark analysis after 72 hours, which suggested that dialysis patients have a significantly worse short-term, periprocedural mortality (10.7%) compared with patients without dialysis (mortality risk 1.7%; adjOR 5.65, 95% CI 1.91 to 16.67) whereas the longer-term hazards remained unaffected. It is higher than in a recent report on patients with CKD5D and/or kidney transplant patients (n = 30; 5%),[21] but substantially lower (20.7%) than in a report of dialysis patients who underwent SAVR between 1978 and 1998.[22] This is noteworthy as it may still leave room for a reduction of procedure-related hazards. In an attempt to explore reasons for this unexpected risk increase, we found that those patients dying within the first 72 hours had a very high ES I, whereas the rate was much lower in those that survived the procedure. We observed valve embolizations, resuscitation, postinterventional bleeding, coronary occlusion, second valve because of aortic insufficiency with only postinterventional potentially related to dialysis and/or dialysis-related medication. Further potential but so far unproven levers are a careful access selection (TF > TA), valve selection, short-procedural time without lengthy repositioning and balloon dilation and the avoidance of paravalvular leakage and close hemodynamic monitoring to avoid instability.



Pts at risk	1960	1668	1511	1319
No-dialysis	1910	1636	1482	1304
Dialysis	50	32	29	15
Survival (%)				
No-dialysis	96.9	85.7	77.5	68.1
Dialysis	88.0	64.0	58.0	30.0

Figure 2. Landmark analysis: Survival without periprocedural mortality (72 hours).

The multivariate regression analysis in patients receiving dialysis indicates that there are no variables or combinations thereof making patients ineligible for TAVI (survival probability <1 year). This implies that dialysis is not a contraindication for TAVI per se but rather a risk factor for a poor longer-term outcome. PH (>60 mm Hg) was the only variable being associated with a reduced mortality. PH is characterized by either (1) precapillary pulmonary hypertension based on a high pressure in the pulmonary artery and increased resistance of the capillary bed or (2) postcapillary pulmonary hypertension based on a high pressure in the pulmonary artery, normal capillary resistance and poor

Table 4
Regression analysis: 1-year mortality overall (n = 2,000)

	Univariate		Multivariate	
	HR (95%CI)	P-value	HR (95%CI)	p Value
Age	1.01 (0.99−1.03)	0.442		
Male gender	0.88 (0.70−1.12)	0.337		
Ejection fraction	1.02 (1.02−1.03)	<0.001	1.02 (1.01−1.02)	<0.001
Coronary artery disease	1.26 (0.98−1.60)	0.076		
Previous myocardial infarction	1.53 (1.09−2.14)	0.018	0.84 (0.62−1.14)	0.271
Previous percutaneous coronary intervention (<90 day)	1.19 (0.89−1.57)	0.262		
Previous coronary artery bypass graft	1.40 (1.03−1.89)	0.037	0.86 (0.64−1.14)	0.287
Mitral valve disease (≥II)	1.67 (1.22−2.28)	0.002	0.77 (0.58−1.02)	0.063
Previous valve surgery	1.12 (0.59−2.12)	0.736		
Peripheral artery disease	1.64 (1.22−2.19)	<0.001	1.31 (1.01−1.72)	0.043
Carotid stenosis	1.19 (0.83−1.50)	0.488		
Major neurological deficits	1.45 (1.02−2.07)	0.046	0.89 (0.64−1.24)	0.487
Chronic obstructive pulmonary disease	1.27 (0.90−1.79)	0.194		
Pulmonary hypertension (>60 mm Hg)	1.51 (1.15−1.97)	0.004	1.33 (1.05−1.72)	0.020
Diabetes	1.31 (1.03−1.67)	0.031	0.92 (0.73−1.15)	0.456
Frailty	2.15 (1.70−2.73)	<0.001	1.84 (1.47−2.27)	<0.001
Dialysis	3.91 (2.27−6.73)	<0.001	2.5 (1.63−3.84)	<0.001

left ventricular function and/or mitral valve disease.[23] Although we have good reasons to believe that postcapillary hypertension was the principal reason for PH in our patient population, no diagnostic work-up was performed to provide evidence to support this. Indeed, Agarwal reported that, in patients who underwent dialysis, the left atrial diameter was an independent predictor of all-cause mortality (HR 2.17; 95% CI 1.31 to 3.61) and volume control deemed an attractive target to improve PH.[24] As such PH appears to be no specific predictor of outcomes in TAVI patients, but of patients who underwent dialysis per se. In our analyses, PH had a low sensitivity and specificity, essentially confirming this notion.

Managing patients with PH undergoing surgical procedures is very challenging and is associated with high morbidity and mortality due to right ventricular failure, arrhythmias, and ischemia leading to hemodynamic instability.[25] Data shows that patients with a reduction of pulmonary artery systolic pressure after TAVI had a more favorable prognosis than patients with persistent severe PH,[26] but there is no formal evidence to suggest strategies how to prepare patients for TAVI aiming at improving the long-term outcome. Nonspecific therapeutic options after TAVI may include endothelin inhibitors, phosphodiesterase inhibitor sildenafil, and vasodilatory prostaglandins.[27]

Our study was conducted in 2,000 consecutive patients who underwent TAVI, but only 56 patients (2.8% of study subjects) were receiving dialysis. As a result of the small number of subjects in the dialysis group, the power of some of the analyses to result in significant results may be reduced. Patients in the dialysis group had a worse cardiac history and noncardiac co-morbidities than patients in the nondialysis group and this may have impacted on the survival statistics for this group. To compensate for this, we presented adjusted p values for the different basic parameters including age, gender, EF, CAD, previous coronary artery bypass graft, PAD, and NYHA IV), as well as route of access for the TAVI procedure (TF vs TA).

The clinical implications of this research and based on our own clinical experience are as follows: The decision to perform TAVI in a particular dialysis patient will be guided by general high-risk criteria as outlined for TAVI patients in general. The criteria include ES risk, frailty and life expectancy. If patients are bed-ridden or suffer from severe dementia and do not have the necessary social support after the procedure TAVI is less likely in our institution. From a procedural perspective, patients on dialysis frequently show heavy calcification which has an impact on valve selection and requires a careful preprocedural CT work-up. Furthermore patients may benefit from TF TAVI with a short-procedural time without pre- or postdilation and without repositioning.

In conclusion, dialysis is an independent predictor of procedural and long-term mortality in patients who underwent TAVI. VARC-II defined complications are largely comparable to patients who did not underwent dialysis. Although long-term mortality appears to be largely determined by the kidney disease and/or dialysis itself, short-term mortality still calls for (pre-) procedural optimization.

Disclosures

Gerhard Schymik and Holger Schröfel are proctors for Edwards Lifesciences, Medtronic and abbott. Peter Bramlage is a consultant for Edwards Lifesciences. Alexander Würth declares to be a proctor for Boston Scientific. No conflict of interest was declared by the other authors.

Author Contributions

All authors except Peter Bramlage established, and conducted the registry. Gerhard Schymik, Panagiotis Tzamalis and Peter Bramlage designed the statistical approach, analysis and interpretation. Peter Bramlage drafted the first version of the manuscript, which all other authors revised for important intellectual content. All authors approved the final version of the manuscript to be submitted.

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