Dialysis following Transcatheter Aortic Valve Implantation – risk factors and outcomes: An analysis from the UK TAVI Registry

Brief title: Dialysis requirement and outcomes after TAVI

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Structured Abstract

Background

Transcatheter aortic valve implantation (TAVI) is now established as an alternative treatment to surgical aortic valve replacement. Data examining the impact of dialysis on outcomes after TAVI are lacking.

Objectives

To determine the risk factors for post-TAVI dialysis and to determine the impact of pre-TAVI or post-TAVI dialysis on mortality.

Methods

The UK TAVI Registry was established to report outcomes on all TAVI procedures performed within the United Kingdom (2007-2014). Data was collected prospectively on 6464 patients with a median follow-up of 625 days.

Results

The proportion of patients on dialysis before TAVI has remained constant at 1.8%. After TAVI, the proportion of patients newly needing dialysis after TAVI has fallen from 6.1% (2007/8) to 2.3% (2013/4). The risk of new dialysis requirement after TAVI was independently associated with lower baseline renal function, year of procedure, impaired left ventricular function, diabetes, use of an Edwards valve, a non-transfemoral approach, need for open surgery and moderate to severe aortic regurgitation after the procedure. Requirement for new dialysis after TAVI was associated with higher mortality at 30 days (Hazard Ratio (HR) 6.44; 95% Confidence Intervals (CI) 4.87-8.53) and at four years (HR 3.54; 95%CI 2.99-4.19; $P<0.001$ for all) compared to patients without dialysis requirement.

Conclusions

The proportion of patients needing dialysis after TAVI has decreased over time. Post-TAVI dialysis is associated with increased mortality. Factors identified with dialysis requirement after TAVI require further investigation.

Key words: mortality, acute kidney injury, valve type

Condensed Abstract

Outcomes after TAVI in relation to dialysis requirements were examined in 6464 patients from the UK TAVI Registry. The proportion of patients on dialysis before TAVI has remained constant (1.8%), whereas the proportion newly needing dialysis has fallen from 6.1% (2007/8) to 2.3% (2013/4). The risk of new dialysis requirement was associated with lower eGFR, year, impaired LV function, diabetes, use of an Edwards valve, non-transfemoral approach, need for open surgery and moderate-to-severe aortic regurgitation post-procedure. Requirement for new dialysis after TAVI was associated with higher mortality at 30 days and at 4 years ($P<0.001$ for both).

Abbreviations

AKI – acute kidney injury

CI – confidence intervals

CKD – chronic kidney disease

CKD-EPI – Chronic Kidney Disease Epidemiology Collaboration

eGFR – estimated glomerular filtration rate

HR – hazard ratio

NICOR – National Institute of Cardiovascular Outcomes Research

OR – odds ratio

SAVR – surgical aortic valve replacement

TAVI – Trans-catheter aortic valve implantation

INTRODUCTION

Trans-catheter aortic valve implantation (TAVI) is now established as an effective treatment for patients with severe symptomatic aortic stenosis at high risk from a conventional cardiac surgical aortic valve replacement (SAVR). Factors such as advanced age, frailty, or high co-morbidity are used routinely to identify patients at high or, in selected cases, intermediate risk patients who might be better treated by TAVI rather than SAVR.(1) Worldwide, the use of TAVI is accelerating as registry and trial data indicate good medium term outcomes; over 100,000 procedures have now been performed.(2)

The prevalence of pre-procedural renal dysfunction in patients undergoing TAVI is high (50-60% with chronic kidney disease (CKD) stage 3 or worse)(3,4) and has been shown to be significantly associated with increased mortality(3,4) and acute kidney injury (AKI)(5) post-TAVI. However, although the reported new need for dialysis after TAVI has been examined in several studies,(6-22) most are single centre and report data on less than 300 patients with rates for post-procedure dialysis varying between 0% and 21%. A recent meta-analysis examining the impact of acute kidney injury (AKI) after TAVI analysed 13 studies and reported a rate of new dialysis of 5.8% (89 of 1528 patients).(5) A high (9-fold increase) mortality at 1 year associated with the need for dialysis after TAVI was reported in a single study of 270 subjects.(16) Data from the German TAVI-registry also suggested new dialysis requirement after TAVI was associated with higher mortality at 30-days but not at 1-year.(23) To the best of our knowledge no study has yet compared outcomes of patients requiring dialysis support after TAVI with those already on dialysis before the procedure.

Given the wide variation in the reported rates of dialysis after TAVI and the potentially very high mortality associated with this complication, there is a need for better information based upon larger data sets. Such data sets might also provide a better understanding of the risk factors associated with the need for post procedural dialysis allowing the design of preventative strategies. The objectives of this study were to firstly define the incidence of dialysis requirement after TAVI in the UK, secondly to determine pre-procedural and peri-procedural factors associated with the need for dialysis after TAVI and thirdly, to compare outcomes in patients requiring dialysis after TAVI with subjects already established on dialysis and those without any dialysis requirement.

METHODS

The database

The UK TAVI Registry has collected data on all TAVI procedures performed in the UK since 2007. The registry is managed by the National Institute for Cardiovascular Outcomes Research (NICOR) with clinical direction and strategy provided by the UK TAVI steering group (established in 2008). The UK TAVI dataset is collected using the web based interface from NICOR as previously described.(24) Case ascertainment is performed by comparing the centre's reported numbers of total procedures with the number of procedures uploaded to the NICOR. The national dataset between 2007 and 2014 was provided by NICOR to the investigators. Range checks to look for extreme values and assessments of internal consistency were applied during upload. All data including peri-procedural complications and complications up to hospital

discharge were self-reported according to the definitions within the national dataset.(1) Centres providing records with missing, extreme or inconsistent values were contacted and asked to check and modify records as appropriate. The pre-procedure estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula with serum creatinine recalibrated to be traceable to an isotope-derived mass spectroscopy method.(25) Patients not requiring dialysis support before the TAVI procedure were divided into five groups of GFR categories based on the widely used clinical classification(26): ≥ 60 (eGFR category>60); 45-59 (CKD stage 3a); 30-44 (CKD stage 3b); 15-29 (CKD stage 4); and <15 mL/min1.73 m^2 (CKD stage 5) Patients were also divided in to 3 groups depending on their dialysis requirements: patients who required dialysis before the TAVI procedure; those who newly required dialysis support after the TAVI procedure and those who did not require dialysis support either before or after the TAVI procedure.

Mortality tracking

A robust independent system for tracking mortality exists in England and Wales (two of the four countries in the United Kingdom covering 89% of the total UK population). The National Health Service Central Register performed case linkage to data held by the Office of National Statistics in May 2015 using each patient's unique National Health Service Number. Validated life status was available in 6464 of 7364 patients (88%) who underwent a TAVI procedure between 1st January 2007 and 31st December 2014 consistent with proportion of patients from England and Wales. This cohort was used for all the survival analyses. All patients provided written informed consent for the TAVI procedure. NICOR has support under section 251 of the NHS

Act 2006. Under NHS research governance arrangements, formal ethical approval was not required for this study.

Statistical Analysis

Statistical analysis was performed using SPSS V.23.0 statistical software (SPSS Inc, Chicago, Illinois, USA). Categorical data are presented as percentages and comparisons between groups were performed by the chi-squared test or the Fisher's exact test. Numerical data are presented as median (interquartile range) and comparisons performed using the Mann-Whitney-U test. All the variables used in the analysis had <5% of the values missing and were therefore treated as missing completely at random with case-wise deletion. Logistic regression analysis was used to assess the relationship between pre- and peri-operative factors and the need for dialysis post-procedure and in-patient mortality with the results expressed as an odds ratio (OR) with 95% confidence intervals (95% CI). Time-to-event data analysis for cumulative mortality at 30-days and 4-years were performed using the Cox Proportional hazards model and the results expressed as a Hazard Ratio (HR) with 95% CI. Multivariable models were adjusted for gender, age, left ventricular ejection fraction less than 30%, New York Heart Association functional status 3-4, peripheral vascular disease, known coronary artery disease, pre-existing atrial fibrillation, previous cardiac surgery, diabetes mellitus, chronic obstructive pulmonary disease, previous stroke, previous myocardial infarction, ascending aortic calcification, valve manufacturer (Medtronic, Edwards, other) non-transfemoral route, use of general anaesthetic, moderate-severe aortic regurgitation, myocardial infarction before discharge, stroke before discharge, cardiac tamponade, conversion to open surgery and major vascular complication. Kaplan-Meier survival curves were drawn to assess

differences between groups for the time to an event data and estimate mortality rates. Comparisons were made using the log-rank statistic. For all tests, a value of $P<0.05$ was considered significant.

RESULTS

Patient characteristics

Baseline demographic characteristics and risk factors of the study population divided by need for dialysis before or after TAVI are presented in Table 1. Of the 6464 patients included in the study, 117 (1.8%) were on dialysis before the TAVI procedure with the proportion of patients remaining constant over time (Figure 1; $P=0.704$). Over the whole study period, two hundred and two (3.1%) patients required dialysis for the first time after the TAVI procedure. The proportion of patients newly requiring dialysis post-TAVI has been declining over time with (Figure 1; $P<0.001$).

Factors associated with new requirement for dialysis after TAVI procedure

In a univariable analysis, the Logistic EuroSCORE (European System for Cardiac Operative Risk Evaluation) was associated with new requirement for dialysis after TAVI (OR 1.02 95% CI 1.01-1.03; $P<0.001$). The univariable and multivariable individual pre-procedural and peri-procedural factors associated with the new need for dialysis are shown in Table 2. In the multivariable analysis the pre-procedural factors were a lower eGFR (as a continuous variable), year of operation, a left ventricular ejection fraction less than 30% and a diagnosis of diabetes mellitus. Procedural factors associated with a new requirement for dialysis were a non-transfemoral approach, conversion to open surgery and use of an Edwards valve rather than a Medtronic valve. Having moderate to severe aortic regurgitation after the procedure

was also associated with an increased risk for new dialysis after TAVI. The year of procedure was inversely associated with the risk of requiring dialysis after TAVI in both univariable and multivariable analyses (Table 2). Excluding cases performed 2007-2008 made no appreciable difference to the result. In a model incorporating the year of procedure and the logistic EuroSCORE as a composite measure of patient co-morbidity only, the year of procedure remained inversely associated with the need for dialysis after TAVI (OR 0.85 95% CI 0.79-0.91; P<0.001).

Stages of CKD were grouped into moderate-advanced CKD, stages 3b-5 (OR 4.27 95% CI 2.93-6.22; P<0.001), and advanced CKD, stages 4-5 (OR 4.02 95% CI 2.97-5.43; P<0.001) and entered separately into the model replacing eGFR as a continuous variable. Both were independently associated with the need for dialysis post-TAVI and did not significantly alter the model.

The finding that use of the Edwards valve was associated with a higher risk of requiring dialysis after TAVI was unexpected. We, therefore, explored this relationship further. Patients receiving an Edwards valve were more co-morbid with an increased risk profile as evaluated by the logistic EuroSCORE (Supplementary Table 1). The proportion of patients with the variables found to be associated with the new need for dialysis after TAVI (Table 2) are presented in Supplementary Table 1. Proportionately many more patients receiving an Edwards valve had a non-transfemoral approach (34.2% v. 14.9%: P<0.001) and more required conversion to open surgery (1.3% v. 0.5%: P=0.004). However, proportionately fewer patients receiving an Edwards valve had moderate-to-severe aortic regurgitation after the procedure (4.8% v. 12.5%; P<0.001). Given that the non-transfemoral approach has

been consistently found to be associated with worse outcomes after TAVI and that the decision-making process for the choice of approach is difficult to quantify objectively, the logistic regression analyses were repeated excluding patients who underwent a non-femoral approach. The full univariable and multivariable associations in this model are shown in Supplementary Table 2. Use of an Edwards valve remained associated with an increased risk of requiring dialysis after the procedure (OR 1.85 95% CI 1.09-3.14; P=0.006).

Dialysis requirements and mortality

The median follow-up period was 625 (268-1208) days. Overall, 2486 (37%) patients died during the follow-up period. In total, 314 (4.9%) patients died during the hospital admission. Two hundred and twenty-three (3.7%) patients with no dialysis requirement, 9 (7.8%) patients on dialysis before the procedure and 82 (40.6%) patients requiring dialysis after TAVI died in hospital (P<0.001). The Kaplan-Meier cumulative survival curves are shown in Figure 2. The Kaplan-Meier mortality estimates in patients with no dialysis requirements were 0.06, 0.07, 0.08, 0.16 and 0.46 at 30-days, 60-days, 90-days, 1-year and 4-years respectively. These were significantly higher in patients requiring dialysis after the procedure at 0.35, 0.45, 0.50, 0.64 and 0.84 at the same time-points (log rank P<0.001). Mortality was also higher in patients requiring dialysis after TAVI compared with those already on dialysis before the procedure (log rank P<0.001).

The univariable and multivariable associations of dialysis requirement before or after TAVI with overall mortality at 30-days and at 4-years are presented in Table 3 and Supplementary Tables 3-4. Both dialysis requirements before and after TAVI were

independently associated with mortality at all time periods. For new dialysis requirement after TAVI, none of these associations were significantly affected by further adjustment for eGFR as a continuous variable, or by categorization of CKD stages to moderate-advanced CKD or advanced CKD. Valve make was not associated with mortality at any time period in the multivariable analyses (Supplementary Tables 3-4).

DISCUSSION

Between 2007 and 2014 the incidence of AKI requiring new dialysis after TAVI in the UK was 3.1% but by 2013-2014 this had fallen to 2.1%. This decline was independent of patient co-morbidities and procedural characteristics recorded in the dataset. While most of the factors associated with the need for dialysis after TAVI were conventional risk factors for AKI, we found unexpectedly that use of an Edwards valve was independently associated with a greater need for new dialysis after the procedure. We have also shown that the new need for dialysis after a TAVI procedure is associated with higher mortality at 30-days, and 4-years after the procedure than that of patients on dialysis before TAVI and patients not requiring dialysis at all.

With 6464 patients at risk, this study is by far the largest reporting the incidence rate of the need for dialysis after TAVI. This contrasts with a recent meta-analysis of AKI after TAVI which, although reporting on 24 studies (5971 patients), found only 13 studies that gave the incidence of dialysis after TAVI with an at risk population of only 1058.(5) The need for dialysis in this study was 5.8%, which is much higher than the figure in our analysis. This may, in part relate to the year of treatment. Our large

population has allowed us to examine the incidence of the need for new dialysis over time. This has decreased significantly between 2007 and 2014. The decline appears to be independent of recorded pre-procedural individual risk factors and of the logistic EuroSCORE as a comorbidity score. Excluding cases undertaken in the first 2 years to allow for the unusually high risk of the early cases and a potential learning curve did not affect this finding. Although our study is not able to elucidate the reasons for this decline, possible explanations include changes in patient selection (with features not captured in the dataset), better procedural technique and better peri-procedural care optimising factors such as patient hydration, anaesthetics and sedation.

In this study we have identified a number of factors that are well recognised to be associated with a higher risk of post-procedural AKI leading to dialysis including pre-procedural kidney function and diabetes mellitus. With respect to procedural characteristics, in addition to a non-transfemoral approach we found that the use of an Edwards valve was associated with an increased risk of new dialysis requirement after TAVI. This association remained significant even when adjusted for co-morbidities. Furthermore, this association was still significant when procedures performed from the trans-femoral approach were considered in isolation (ie patients undergoing a non trans-femoral approach were excluded from the analysis). While the negative outcomes associated with use of a non-trans-femoral approach have been well described,(4,27,28) the association with the use of a particular valve or valve type has not. However, one retrospective, small study (118 patients) has also recently reported a higher rate of AKI associated with use of the Edwards valve compared with the Medtronic valve.(29) This association is difficult to explain given the excellent results reported by multiple investigators using this device.(27,30,31) It is notable that

although the Edwards valve was associated with an increased risk of dialysis requirement after TAVI it was not associated with increased mortality. While this study examines association and cannot show causation, possible mechanistic explanations require consideration. Possibilities include higher rates of micro-embolisation to the kidneys during the procedure, transient reduced perfusion due to the brief period of hypotension that occurs during rapid pacing and possible differences in radiographic contrast dose during valve positioning. While the Edwards valve is loaded onto the deployment balloon in the descending aorta, this process does not onvolve significant contact with the aortic wall and seems unlikely to cause micro-embolization to renal arteries. The period of hypotension during rapid ventricular pacing is usually less than one minute but it is possible that this insult might precipitate AKI in patients, with already compromised hemodynamics. Nevertheless, a previous study found no association between AKI and the number of pacing episodes.(18) Unfortunately, the TAVI registry does not collect data on contrast utilization. Finally, the influence of unmeasured risk factors such as frailty and co-morbid burden of disease that might be associated with use of an Edwards valve cannot be excluded. The wide experience and good results reported with the valve may have led operators to choose this valve in cases at higher risk for AKI. Low numbers of other balloon expandable valves used in the UK during this time mean that it is not possible to determine whether this association is present for other balloon expandable valves.

The proportion of patients requiring dialysis for AKI after TAVI has decreased to a rate about equal to that after SAVR.(5) Interestingly, a recent report of 133 patients (58% TAVI, 42% SAVR) has reported a greater risk of AKI in patients treated with

TAVI, compared to patients undergoing SAVR.(32) This may be a result of patient selection as well as differences in the procedural renal insults.

In this study, we have shown that a new requirement for dialysis after TAVI was associated with a greater than six-fold increased risk of mortality at 30 days compared to non dialysis requiring controls while patients established on dialysis before TAVI had a greater than two-fold increased risk. This difference suggests that the dialysis procedure itself accounts for only part of the excess mortality associated with the new use of dialysis. However, there is almost certainly an inherent selection bias in patients accepted for TAVI already requiring dialysis treatment. This assertion is supported by the observation that this group of patients had the lowest median age. The risks associated with AKI are long term as evident from the increased risk of mortality present at 4-years. Whether interventions designed to prevent the need for dialysis after TAVI will improve outcomes requires further investigation.(33)

Study strengths and weaknesses

The strengths are the inclusion of all consecutive patients treated in the UK. This is a large number of patients with a wide range of risk profiles. Indeed our study is 6 times the size of a meta-analysis quantifying the risk of dialysis after a TAVI procedure. The UK TAVI Registry has captured every TAVI performed at all active units within the UK from the inception of the procedure in this country, and thus includes the entire "learning curve" and early experience of adopting centers without bias by center selection. The data collection shares the weaknesses of other national registry programs. There is a balance between the size of the dataset and the ability and/or willingness to collect it accurately. Thus potentially informative data, involving the

need for prior balloon aortic valvuloplasty, contrast volume, recent contrast use for CT, angiography or angiography, bleeding and recovery of renal function after dialysis may not have been included. Other than mortality tracking, the accuracy and completeness of the data are self-reported and other than range checks and checks for internal validity, there are no external validation processes in place. Also, apart from mortality, later clinical and quality-of-life follow-up is limited. We investigated estimated rather than measured GFR in this study, and whilst this was (and will likely remain) a practical necessity we acknowledge the imperfection of the estimated measure. As use of conscious sedation rather than general anaesthetic for TAVI occurred in large numbers only after 2014 we are unable to comment on the impact of this evolving approach.

Conclusions

Although the risk of requiring dialysis after TAVI appears to be decreasing, the very high mortality associated with this complication means that it warrants further investigation of potentially preventable risk factors.

Clinical Perspectives

The reported rates of dialysis post TAVI differ widely and there is little information on outcomes after this complication. The incidence of dialysis requirement post-TAVI has been decreasing over time but is associated with a very high mortality. Further studies are needed to assess interventions and procedural/technique changes designed to lower the risk of significant acute kidney injury resulting in the need for dialysis post-TAVI.

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Figure Titles and Legends

Figure 1. Percentage of patients on dialysis before TAVI and with new requirement for dialysis after TAVI (2007-2014).

The proportion of patients on dialysis undergoing TAVI has remained constant over the study time period whereas the proportion of patients requiring dialysis for the first time after the procedure has declined.

Figure 2. Kaplan-Meier Curves for all-cause cumulative survival.

Study patients are divided according to the need for dialysis either before or after TAVI (global log-rank test $P<0.001$). Patients requiring dialysis after TAVI had a higher mortality than both patients already on dialysis (pair-wise log-rank test $P<0.001$) and those with no dialysis requirement (pair-wise log-rank test $P<0.001$).

Table 1: Clinical and procedural characteristics of the study population according to dialysis requirements before or after TAVI.

	No dialysis	Dialysis before	Dialysis after	*P value	†P value
Number of TAVI procedures (%)	6145 (95.1)	117 (1.8)	202 (3.1)		
Male (%)	3258 (53.2)	75 (64.7)	117 (57.9)	0.197	0.284
Age (years)	83 (77-87)	77 (71-82)	83 (77-87)	0.961	<0.001
Logistic EuroSCORE	17.8 (11.6-27.1)	29.0 (15.2-41.7)	21.0 (14.5-35.8)	<0.001	0.056
GFR (ml/min/1.73m²)	45.1 (33.7-60.8)	N/A	31.5 (22.1-40.4)	<0.001	N/A
GFR categories/CKD stages (%)					
eGFR >60 ml/min/1.73m²	1545 (25.1)	N/A	13 (6.4)	<0.001	N/A
CKD stage 3	3451 (56.2)	N/A	91 (45.0)		
CKD stage 4	991 (16.1)	N/A	80 (39.6)		
CKD stage 5	88 (1.4)	117 (100)	13 (6.4)		
Missing eGFR	70 (1.1)	N/A	5 (2.5)		
LVEF<30% (%)	545 (8.9)	17 (14.5)	30 (14.9)	0.006	1.000
NYHA 3-4 (%)	4968 (81.2)	96 (82.8)	172 (85.1)	0.338	0.632
PVD (%)	1420 (23.2)	32 (27.6)	78 (38.6)	<0.001	0.051
Any CAD (%)	2580 (42.7)	49 (43.4)	105 (52.2)	0.007	0.158
Pre-existing AF (%)	1547 (25.4)	30 (25.9)	56 (27.7)	0.460	0.793
Previous cardiac surgery (%)	1931 (31.6)	37 (31.6)	59 (29.2)	0.490	0.704

Diabetes mellitus (%)	1378 (22.5)	34 (29.1)	70 (34.7)	<0.001	0.324
COPD (%)	1779 (29.1)	38 (32.5)	68 (33.8)	0.156	0.902
Previous stroke (%)	1038 (17.0)	28 (23.9)	43 (21.3)	0.128	0.580
Previous MI (%)	1317 (21.5)	28 (23.9)	57 (28.2)	0.030	0.433
AAC (%)	1066 (17.4)	28 (23.9)	38 (18.8)	0.199	0.001
Procedural Characterisitics					
Valve Manufacturer					
Edwards (%)	3421 (56.0)	64 (54.7)	149 (73.8)	<0.001	0.001
Medtronic (%)	2477 (40.5)	48 (41.0)	51 (25.2)		
Other (%)	216 (3.5)	5 (4.3)	2 (1.0)		
Non-transfemoral approach (%)	1524 (24.8)	31 (26.5)	99 (49.0)	<0.001	<0.001
General anaesthetic (%)	5260 (85.9)	100 (85.5)	189 (93.6)	0.001	0.027
AR (moderate/severe) (%)	450 (7.5)	9 (7.8)	34 (17.0)	<0.001	0.026
MI before discharge (%)	30 (0.5)	0 (0)	1 (0.5)	0.968	1.000
Stroke before discharge (%)	137 (2.2)	2 (1.7)	12 (5.9)	0.006	0.101
Tamponade (%)	97 (1.6)	2 (1.7)	7 (3.5)	0.049	0.495
Conversion to open surgery (%)	53 (0.9)	0 (0)	10 (5.0)	<0.001	0.016
Major vascular complication (%)	366 (6.0)	4 (3.4)	18 (8.9)	0.098	0.070

*Comparison between group requiring dialysis after and group with no dialysis requirement.

†Comparison between group requiring dialysis before TAVI and group with new dialysis requirement after TAVI

Continuous values are summarized by median (interquartile range) or mean ± standard deviation. Categorical values are summarized by count (percentage).

Abbreviations; AAC= ascending aortic calcification,; AR=aortic regurgitation; CAD=coronary artery disease; COPD=chronic obstructive pulmonary disease;; CKD=chronic kidney disease; GFR=glomerular filtration fraction; LVEF=left ventricular ejection fraction; MI=myocardial infarction; N/A= non-applicable; NYHA=New York Heart Association; PVD=peripheral vascular disease; TAVI=transcatheter aortic valve implantation

Table 2. Significant logistic regression multivariable associations of need for dialysis after procedure (patients on dialysis before procedure excluded from analysis).

	Odds Ratio (95% CI)	P-value
Pre-procedural characteristics		
eGFR (ml/min/1.73m²)	0.95 (0.94-0.96)	<0.001
Left ventricular ejection fraction < 30%	1.53 (1.01-2.33)	0.048
Diabetes mellitus	1.63 (1.19-2.23)	0.002
Year of procedure	0.89 (0.82-0.96)	0.004
Procedural and post-procedural features		
Valve manufacturer		
Medtronic	1	
Edwards	1.92 (1.35-2.72)	<0.001
Other	0.71 (0.17-2.97)	0.637
Non-transfemoral approach	2.46 (1.81-3.34)	<0.001
AR post-procedure (moderate/severe)	3.012 (1.99-4.57)	<0.001
Conversion to open surgery	9.59 (4.39-20.96)	<0.001

Abbreviations: AR=aortic regurgitation; CKD=chronic kidney disease; COPD=chronic obstructive pulmonary disease; eGFR=estimated glomerular filtration fraction; NYHA=New York Heart Association.

Multivariable models adjusted for gender, age, left ventricular ejection fraction less than 30%, New York Heart Association functional status 3-4, peripheral vascular disease, known coronary artery disease, pre-existing atrial fibrillation, previous cardiac surgery, diabetes mellitus, chronic obstructive pulmonary disease, previous stroke, previous myocardial infarction, ascending aortic calcification, valve manufacturer, non-transfemoral route, use of general anaesthetic, moderate-severe aortic regurgitation after procedure, myocardial infarction before discharge, stroke before discharge, cardiac tamponade, conversion to open surgery and major vascular complication.

Table 3. Cox-regression univariable and multivariable associations with 30-day, and 4-year mortality.

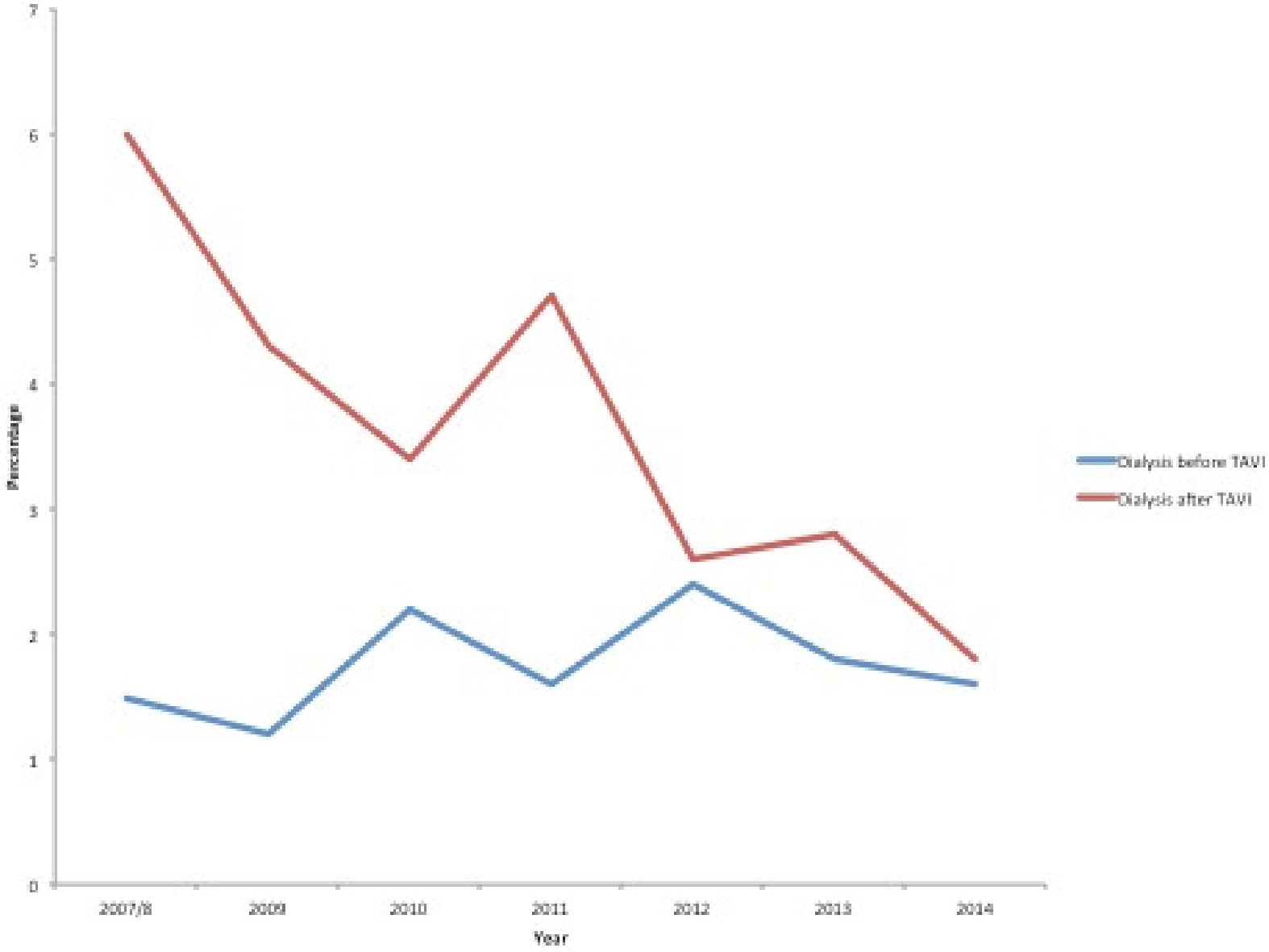
Need for dialysis before or after TAVI	Univariable Analysis		Multivariable Analysis	
	Hazard Ratio (95% CI)	P-value	Hazard Ratio (95% CI)	P-value
At 30 Days				
No	1		1	
Before	1.78 (0.91-3.45)	0.090	2.29 (1.17-4.46)	0.015
After	9.29 (7.15-12.08)	<0.001	6.44 (4.87-8.53)	<0.001
After*	9.27 (7.13-12.05)	<0.001	6.63 (5.00-8.77)	<0.001
At 4 Years				
No	1		1	
Before	2.16 (1.68-2.77)	<0.001	2.46 (1.90-3.18)	<0.001
After	4.46 (3.79-5.24)	<0.001	3.54 (2.99-4.19)	<0.001
After*	4.45 (3.78-5.24)	<0.001	3.25 (2.73-3.87)	<0.001

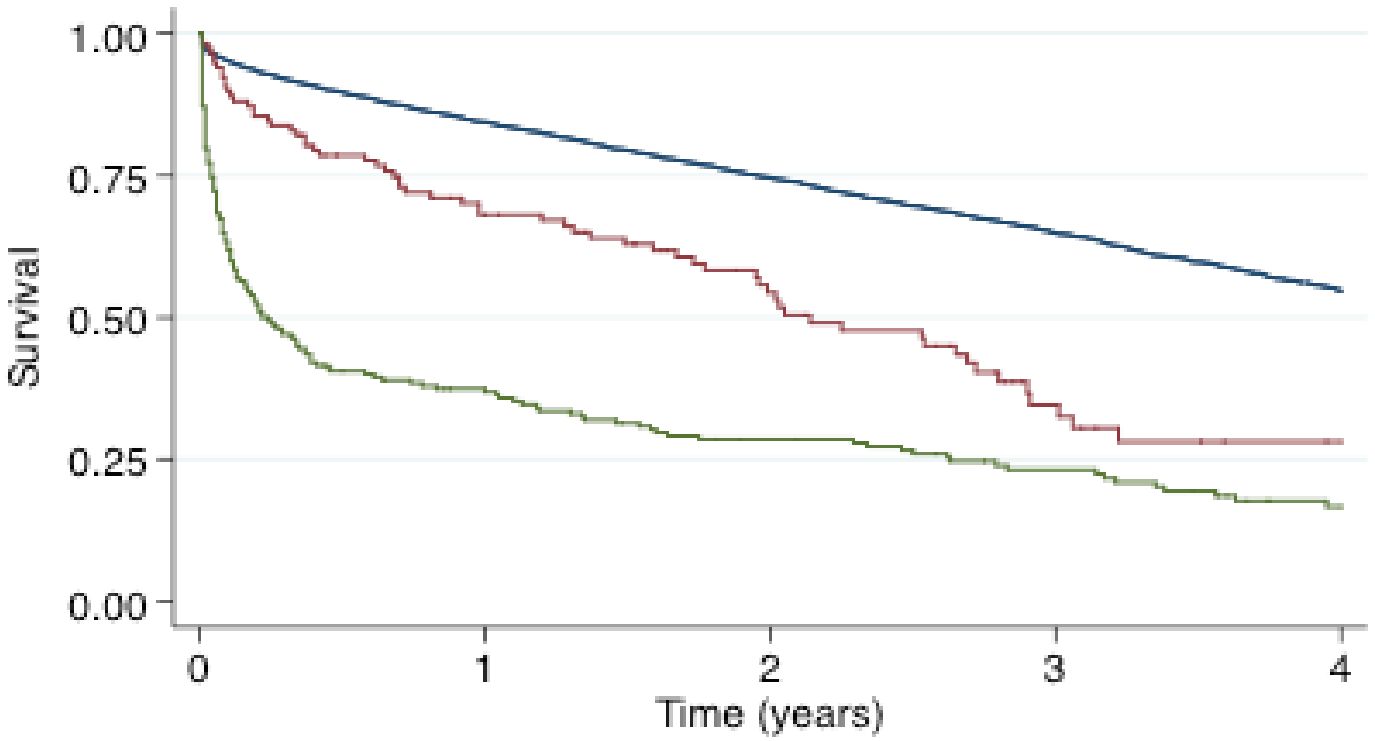
Multivariable models adjusted for gender, age, left ventricular ejection fraction less than 30%, New York Heart Association functional status 3-4, peripheral vascular disease, known coronary artery disease, pre-existing atrial fibrillation, previous cardiac surgery, diabetes mellitus, chronic obstructive pulmonary disease, previous stroke, previous myocardial infarction, ascending aortic calcification, valve manufacturer, non-transfemoral route, use of general anaesthetic, moderate-severe aortic regurgitation

after procedure, myocardial infarction before discharge, stroke before discharge, cardiac tamponade, conversion to open surgery and major vascular complication.

*also adjusted for eGFR as a continuous variable with patients previously on dialysis excluded from the analysis.

Abbreviations: CI=confidence intervals, TAVI=trans-catheter aortic valve implantation


7
6
5
4
3
2
1
0
Percentage
2007/8
2009
2010
2011
2012
2013
2014
Year
Dialysis before TAVI
Dialysis after TAVI



Number at risk

No dialysis	6145	4210	2750	1889	1009
Dialysis before	117	69	41	17	9
Dialysis after	202	68	46	31	16