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Transcatheter Aortic Valve Implantation in Dialysis Patients

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Key Words
Transcatheter aortic valve implantation · Dialysis · Surgical aortic valve replacement · Aortic stenosis

Abstract
Background/Aims: Transcatheter aortic valve implantation (TAVI) has emerged as a new therapeutic option for high-risk patients. However, dialysis patients were excluded from all previous studies. The aim of this study is to compare the outcomes of TAVI for dialysis patients with those for patients with chronic kidney disease (CKD) stages 3 and 4 and to compare TAVI with open surgery in dialysis patients. ***Methods:*** Part I: comparison of 10 patients on chronic hemodialysis with 116 patients with non-dialysis-dependent CKD undergoing TAVI. Part II: comparison of transcatheter (n = 15) with open surgical (n = 24) aortic valve replacement in dialysis patients. ***Results:*** Part I: dialysis patients were significantly younger (72.3 vs. 82.0 years; $p < 0.01$). Hospital stay was significantly longer in dialysis patients (21.8 vs. 12.1 days; p = 0.01). Overall 30-day mortality was 3.17%, with no deaths among dialysis patients. Six-month survival rates were similar (log-rank p = 0.935). Part II: patient age was comparable (66.5 vs. 69.5 years; p = 0.42). Patients in the surgical group tended to stay longer in hospital than TAVI patients (29.5 vs. 22.5 days; p = 0.35). ***Conclusion:*** TAVI is a safe procedure in patients on chronic hemodialysis. Until new data become available, we find no compelling reason to refuse these patients TAVI.

Background/Aims

Valvular heart disease is common in patients with end-stage renal disease (ESRD). In patients on chronic hemodialysis, aortic valve calcification is present in 25–55% and it occurs 10–20 years earlier than in the general population [1–9]. Pathophysiology and the rate of progression of cardiac valvular calcification in patients with ESRD appear to be different from those in the general population, with secondary hyperparathyroidism being one of the most important predisposing factors.

Symptomatic aortic stenosis carries a poor prognosis with 1- and 5-year survival of 60 and 32%, respectively [10], for nonsurgically managed patients. Aortic valve replacement is the only way to improve survival, but surgical aortic valve replacement (SAVR) has an estimated operative mortality of 4% in the general population [11]. One third of patients with severe valvular heart disease

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do not undergo surgery, however, because of advanced age or multiple comorbidities including chronic kidney disease (CKD) [12].

Since April 2002 transcatheter aortic valve implantation (TAVI) has emerged as a new therapeutic option for high-risk patients [13]. Meanwhile, several thousand such devices have been implanted worldwide and several studies on safety and outcomes of TAVI have been performed. TAVI, when compared with standard medical therapy, significantly reduces mortality in patients with severe aortic stenosis who are not suitable for surgery [14]. Up to 50% of patients undergoing TAVI in large studies had preexisting CKD [15]. However, patients with ESRD on chronic hemodialysis were excluded from all previous studies.

The aim of this study is to report the first preliminary experiences of patients on chronic hemodialysis undergoing TAVI. In the first part, outcomes of patients on chronic hemodialysis are compared with patients with CKD stages 3 and 4 undergoing TAVI at our center. In the second part, outcomes of open SAVR are compared with percutaneous aortic valve replacement in patients on chronic hemodialysis using a standardized questionnaire.

Patients and Methods

Part I

From November 2007 to May 2010, 200 patients with severe aortic stenosis not considered suitable for SAVR underwent TAVI at our institution. Patients were included in cases of symptomatic high-grade aortic stenosis defined by transthoracic echocardiography (aortic valve area <0.8 cm^2). In addition, at least one of the following inclusion criteria was mandatory: logistic European System for Cardiac Operative Risk Evaluation (logEuroSCORE) >15, age >80 years, patient refusing conventional surgery or life expectancy less than 5 years due to malignant disease. CKD was defined as a preprocedural eGFR <60 ml/min, equivalent to a CKD stage ≥3 according to K/DOQI. All patients provided signed informed consent for the procedure. Diagnostic heart catheterization was conducted prior to TAVI. In cases of hemodynamically relevant coronary artery disease, stent implantation was performed.

Aortic annular dimension and ascending aortic diameter were assessed by CT scan. In all patients, TAVI was performed in the catheterization laboratory using local anesthesia and additional intravenous analgesia when necessary. Vascular access was obtained through the common femoral artery in all patients. A transcutaneous suture system was placed into the right or left common femoral artery. The CoreValve prosthesis (CoreValve Inc., Irvine, Calif., USA, since 2009: Medtronic, Meerbusch, Germany) was used in all patients. It consists of a trileaflet bioprosthetic pericardial tissue valve that is mounted and sutured in a self-expanding nitinol stent.

The logEuroSCORE was used as a risk calculator to estimate the probability of death. The primary endpoint was 30-day mortality, defined as death for any reason within 30 days after the intervention.

Part II

An anonymized, standardized questionnaire concerning aortic valve replacement was developed and sent to 55 hemodialysis centers in southern Germany (Bavaria). All patients who underwent aortic valve replacement during 2005 and 2010 and who were on chronic dialysis at the time of intervention were included. All modalities of replacement (open surgery, transfemoral, transapical, transaxillary) were included, resulting in a study population of 39 patients. The objectives of the questionnaire were gender, age at intervention, accompanying coronary intervention, length of hospital stay, mode and duration of dialysis and underlying renal disease. Patients were questioned on the presence of the following comorbidities: coronary heart disease, atrial fibrillation, arterial hypertension, chronic obstructive pulmonary disease, diabetes and peripheral artery disease. The study was approved by the institutional ethical review committee.

Statistical Analysis

Continuous variables are expressed as means with standard deviations of the mean (SD). Categorical variables are expressed as total counts and column percentages. Differences in variables were evaluated by using Student's t test (normal distributed data) for continuous variables and Fisher's exact test for categorical variables. Results were considered statistically significant if $p < 0.05$. Survival curves were generated using Kaplan-Meier methods and compared using a log-rank test. Statistical analyses were performed using SPSS, version 19.

Results

Part I

Baseline demographic and clinical characteristics of dialysis patients and patients with non-dialysis-dependent CKD undergoing TAVI at our center are reported in table 1.

Preprocedural eGFR was less than 60 ml/min in 126 patients, consisting of 116 patients with non-dialysis-dependent CKD with a mean eGFR of 43.1 ± 11.3 ml/min and 10 patients with ESRD on chronic hemodialysis. There were no significant differences in the following preexisting comorbidities: coronary heart disease, atrial fibrillation, arterial hypertension, chronic obstructive pulmonary disease, diabetes and peripheral artery disease. The logEuroSCORE as a risk calculator to estimate the probability of death was worse in the dialysis patients, but without statistical significance (32.6 ± 13.9 vs. 25.3 ± 13.6%; $p = 0.16$). Apart from kidney function, the only preprocedural significant difference was patient age at the time of intervention. Dialysis patients were signifi-

Table 1. Baseline demographics: part I

	Dialysis patients (n = 10)	Nondialysis patients (n = 116)	p value
Demographic data			
Age, years	72.3 ± 6.4	82.0 ± 5.6	<0.01
Male	80 (8/10)	40.5 (47/116)	0.21
Clinical data			
EuroSCORE, %	33 ± 14	25 ± 14	0.16
Hypertension	90 (9/10)	85 (98/116)	1
Diabetes mellitus	50 (5/10)	35 (41/116)	0.46
Coronary artery disease	78 (7/9)	54 (63/116)	0.30
Peripheral vascular disease	38 (3/8)	14 (16/116)	0.10
COPD	11 (1/9)	22 (25/116)	0.68
Atrial fibrillation	56 (5/9)	38 (44/116)	0.31

Baseline demographic and clinical characteristics of dialysis patients (n = 10) and patients with non-dialysis-dependent CKD (n = 116) undergoing TAVI. Single-center data from our department (n = 126). Continuous variables are expressed as means with SD of the mean. Categorical variables are expressed as percentages and total counts (total counts differ according to data collection).

Table 2. Baseline demographics: part II

	SAVR (n = 24)	TAVI (n = 15)	p value
Demographic data			
Age, years	66.5 ± 11.1	69.5 ± 11.1	0.42
Male	79 (19/24)	73 (11/15)	0.71
Clinical data			
Hypertension	88 (21/24)	87 (13/15)	1
Diabetes mellitus	26 (6/23)	40 (5/15)	0.48
Coronary artery disease	68 (15/22)	86 (12/14)	0.43
Peripheral vascular disease	30 (7/23)	33 (4/12)	1
COPD	13 (3/23)	14 (2/14)	1
Atrial fibrillation	35 (8/23)	46 (6/13)	0.72

Baseline demographic and clinical characteristics of dialysis patients after TAVI (n = 15) and SAVR (n = 24). Data retrieved from an anonymized, standardized questionnaire sent to 55 hemodialysis centers (n = 39). Continuous variables are expressed as means with SD of the mean. Categorical variables are expressed as percentages and total counts (total counts differ according to data collection).

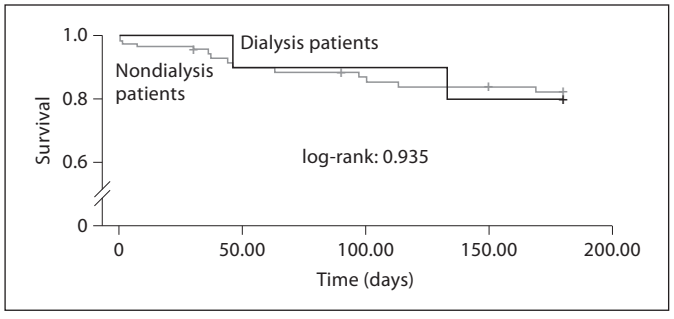

Fig. 1. Kaplan-Meier survival curves of dialysis patients and patients with non-dialysis-dependent CKD undergoing TAVI. Survival rates are similar in both groups (log-rank p = 0.935) with no deaths within 30 days after intervention and a survival rate of 80% after 6 months in the dialysis group.

cantly younger than patients not in need of dialysis (72.3 ± 6.4 vs. 82.0 ± 5.6 years; p < 0.01).

There were no significant differences between dialysis patients and patients in the CKD group with respect to stroke, bleeding or vascular access problems: stroke 0% (0/10) versus 0.8% (1/126; p = 0.77), major bleeding 0% (0/10) versus 8.7% (11/126; p = 0.31), puncture site hematoma requiring operation 10% (1/10) versus 1.6% (2/126; p = 0.43) and development of a false aneurysm at the puncture site 20% (2/10) versus 8.7% (11/126; p = 0.30).

The mean length of hospital stay was 12.9 ± 8.75 days. Patients on chronic hemodialysis stayed significantly longer in hospital than patients in the CKD group (21.8 ± 11.9 vs. 12.1 ± 8.0 days; p = 0.01).

For calculation of overall mortality, all 126 patients were considered. Overall 30-day mortality was 3.17% (4/126). 30-day mortality in the CKD group was 3.45% (4/116). There were no deaths within 30 days among patients who were on chronic hemodialysis. Survival rates 6 months after intervention were similar in both groups (log-rank p = 0.935), with a survival of 80% in the dialysis group. Kaplan-Meier survival curves of the two groups are shown in figure 1.

Part II

Questionnaires were sent back by 26 of the 55 hemodialysis centers with complete data collection of 39 dialysis patients. Baseline demographic and clinical characteristics of the 39 dialysis patients after TAVI and SAVR are reported in table 2.

61.5% of patients (24/39) underwent open surgery and transcutaneous aortic valve replacement was per-

formed in 38.5% (15/39): 60% (9/15) transfemoral, 20% (3/15) transapical and 20% (3/15) transaxillary. In patients with SAVR, 83.3% (20/24) received bioprosthetic valves and 16.6% (4/24) mechanical prosthetic valves. There were no significant differences in the following preexisting comorbidities: coronary heart disease, atrial fibrillation, arterial hypertension, chronic obstructive pulmonary disease, diabetes and peripheral vascular disease. The preprocedural patient age in the SAVR and TAVI groups was similar (66.5 ± 11.1 vs. 69.5 ± 11.1 years; p = 0.42).

The mean length of hospital stay was 26.4 ± 21.7 days. Patients undergoing SAVR stayed longer in hospital than patients undergoing TAVI, but this trend was not significant (29.5 ± 25.8 vs. 22.5 ± 13.1 days; p = 0.35).

There are no solid survival data from the SAVR group, as questionnaires were mainly retrieved from living patients still performing hemodialysis in the corresponding centers.

Discussion

The prevalence of aortic valve calcification is higher in patients with CKD than in the general population and dialysis has been proposed to be an independent risk factor for aortic valve calcification [1–9]. Different studies on SAVR in dialysis patients have been performed [16–18], showing an increased surgical risk in these patients. The largest study of 5,858 dialysis patients undergoing surgical valve replacement found an in-hospital mortality rate of 20.7% [18]. Apart from a high general morbidity, possible reasons might be the need for general anesthesia and problems in perioperative fluid management and dialysis. Since the number of patients with CKD is increasing and life expectancy is extending, the incidence of dialysis patients requiring aortic valve replacement is expected to increase in the future.

TAVI, as a new interventional procedure, might be a suitable alternative for these high-risk patients. A first randomized trial by Smith et al. [19] demonstrated that TAVI and SAVR are associated with a similar survival at 1 year in high-risk patients with severe aortic stenosis. Unfortunately, this study excluded patients with severe renal insufficiency and there are no data at all on TAVI in dialysis patients.

In this study, we report the first experiences of a series of patients on chronic hemodialysis undergoing TAVI at our center (n = 10). Moreover, we analyzed TAVI in comparison to SAVR in dialysis patients (n = 39) using an anonymized, standardized questionnaire, sent to 55 dialysis centers in southern Germany (Bavaria).

Results from our questionnaire showed a similar preprocedural patient age of dialysis patients in the TAVI and in the SAVR group (69.5 vs. 66.5 years; p = 0.42), but on the other hand, dialysis patients were significantly younger than patients not in need of dialysis undergoing TAVI at our center (72.3 vs. 82.0 years; $p < 0.01$). One potential reason might be the faster progression rate of cardiac valvular calcification in patients with ESRD compared to the normal population [1–9]. The higher EuroSCORE reflects the poor preinterventional clinical status of these patients, making them not suitable for open surgery.

The length of hospital stay after TAVI is significantly longer in patients on chronic hemodialysis compared to nondialysis patients (21.8 vs. 12.1 days; p = 0.031). Once more, this illustrates the poor clinical status of this patient group, complicating postinterventional convalescence. However, according to our questionnaire, dialysis patients still tend to leave hospital earlier after TAVI than after SAVR (22.5 days vs. 29.5 days; p = 0.35). This is certainly a consequence of the less-invasive procedure and is in agreement with the data of Smith et al. [19], who also reported a shorter index hospitalization in the TAVI group. Accelerating discharge from hospital may not only reduce cost but, more importantly, may be of great benefit for the improved rehabilitation of these severely ill patients.

Comparing patients on chronic hemodialysis with nondialysis patients undergoing TAVI, we found no difference in the 30-day or 6-month mortality rates, respectively. Overall 30-day mortality was 3.17%, with no deaths within 30 days among dialysis patients who underwent TAVI at our center. These preliminary data derived from a first small cohort suggest that dialysis patients undergoing TAVI do not have an increased risk for in-hospital mortality compared to other patients. Survival rates for dialysis patients 6 months after intervention were similar to those patients not in need of dialysis (log rank p = 0.935).

Our first experiences show that TAVI can be performed safely in dialysis patients, whereas open surgery is still associated with a substantial rate of in-hospital mortality up to 20.7% [18]. In addition, one has to assume that patients who undergo TAVI do not qualify for SAVR due to higher age and more severe comorbidities, thus making an even worse outcome very likely for such patients. Due to the small population size, however, it is difficult to compare our results with historical outcomes after surgical aortic valve repair.

In summary, TAVI seems to be a safe procedure in dialysis patients. Nevertheless, much larger studies are needed to evaluate the long-term outcome of TAVI in these patients and to compare this new interventional technique with the traditional open-valve surgery in this growing patient population. Until new data become available, we find no compelling reason to refuse TAVI to patients on chronic hemodialysis. TAVI can be safely applied in dialysis as well as in nondialysis patients, who are not suitable for open surgery. A possible superiority of TAVI for patients on dialysis compared to open surgery should be the subject of future studies.

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Disclosure Statement

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References

1 Baglin A, Hanslik T, Vaillant JN, Boulard JC, Moulonguet-Doleris L, Prinseau J: Severe valvular heart disease in patients on chronic dialysis. A five-year multicenter French survey. Ann Med Interne (Paris) 1997;148:521–526.

2 Braun J, Oldendorf M, Moshage W, Heidler R, Zeitler E, Luft FC: Electron beam computed tomography in the evaluation of cardiac calcification in chronic dialysis patients. Am J Kidney Dis 1996;27:394–401.

3 Bryg RJ, Gordon PR, Migdal SD: Doppler-detected tricuspid, mitral or aortic regurgitation in end-stage renal disease. Am J Cardiol 1989;63:750–752.

4 London GM, Pannier B, Marchais SJ, Guerin AP: Calcification of the aortic valve in the dialyzed patient. J Am Soc Nephrol 2000;11:778–783.

5 Maher ER, Pazianas M, Curtis JR: Calcific aortic stenosis: a complication of chronic uraemia. Nephron 1987;47:119–122.

6 Stinebaugh J, Lavie CJ, Milani RV, Cassidy MM, Figueroa JE: Doppler echocardiographic assessment of valvular heart disease in patients requiring hemodialysis for end-stage renal disease. South Med J 1995;88:65–71.

7 Straumann E, Meyer B, Misteli M, Blumberg A, Jenzer HR: Aortic and mitral valve disease in patients with end stage renal failure on long-term haemodialysis. Br Heart J 1992;67:236–239.

8 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.

9 Varma R, Aronow WS, McClung JA, Garrick R, Vistainer PF, Weiss MB, Belkin RN: Prevalence of valve calcium and association of valve calcium with coronary artery disease, atherosclerotic vascular disease, and all-cause mortality in 137 patients undergoing hemodialysis for chronic renal failure. Am J Cardiol 2005;95:742–743.

10 Varadarajan P, Kapoor N, Bansal RC, Pai RG: Clinical profile and natural history of 453 nonsurgically managed patients with severe aortic stenosis. Ann Thorac Surg 2006;82:2111–2115.

11 Edwards FH, Peterson ED, Coombs LP, DeLong ER, Jamieson WR, Shroyer ALW, Grover FL: Prediction of operative mortality after valve replacement surgery. J Am Coll Cardiol 2001;37:885–892.

12 Iung B, Baron G, Butchart EG, et al: A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease. Eur Heart J 2003;24:1231–1243.

13 Cribier A, Eltchaninoff H, Bash A, Borenstein N, Tron C, Bauer F, Derumeaux G, Anselme F, Laborde F, Leon MB: Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. Circulation 2002;106:3006–3008.

14 Leon MB, Smith CR, Mack M, et al: Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010;363:1597–1607.

15 Rodes-Cabau J, Webb JG, Cheung A, et al: Transcatheter aortic valve implantation for the treatment of severe symptomatic aortic stenosis in patients at very high or prohibitive surgical risk: acute and late outcomes of the multicenter Canadian experience. J Am Coll Cardiol 2010;55:1080–1090.

16 Lucke JC, Samy RN, Atkins BZ, Silvestry SC, Douglas JM Jr, Schwab SJ, Wolfe WG, Glower DD: Results of valve replacement with mechanical and biological prostheses in chronic renal dialysis patients. Ann Thorac Surg 1997;64:129–132, discussion 132–133.

17 Tanaka K, Tajima K, Takami Y, Okada N, Terazawa S, Usui A, Ueda Y: Early and late outcomes of aortic valve replacement in dialysis patients. Ann Thorac Surg 2010;89:65–70.

18 Herzog CA, Ma JZ, Collins AJ: Long-term survival of dialysis patients in the United States with prosthetic heart valves: should ACC/AHA practice guidelines on valve selection be modified? Circulation 2002;105:1336–1341.

19 Smith CR, Leon MB, Mack MJ, et al: Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 2011;364:2187–2198.